British Society for Developmental Biology
2018 Spring Meeting

Celebrating 70 years of the BSDB

15-18 April 2018 University of Warwick

Organisers: Alistair McGregor Berenika Plusa Josh Brickman Sally Lowell

BSDB www.bsdb-meetings.co.uk

The Company of Biologists

The BSDB thank our post-doc and PhD student members for their nominations for developmental biologists to appear on this image

BSDB Spring Meeting – At A Glance Programme 2018

Sunday 15 April, 2018

12.00	Registration
12.00	Careers Session
15.00	Plenary Lecture: E Wieschaus
15.30	Plenary Lecture: M Leptin
16.00	Refreshments
16.45	Beddington Medal Talk: E Favuzzi
17.15	Plenary Lecture: M Bronner
17.45	Dinner
19.00	The History and Future of Developmental Biology T Horder N Hopwood Panel Discussion
21.00	Roundtable discussions and drinks reception
22.00	Late bar

Monday 16 April, 2018

07.30	Registration	
07.30	Breakfast	
09.00	Plenary Lecture: M Freeman	
Session 1 09.35	Tissue and Organ Development	Developmental Gene Regulatory Networks
09.35	H Semb	J Briscoe
10.05	A Sawala	V Papaioannou
10.20	R Prajapati	
10.35	F Watt	I Amit
11.05	Refreshment break	
11.40	P Tam	E Furlong
12.10	J Januschke	R Williams
12.25	K Kaestner	M Levine
12.55	AJ Copp	T Knudsen
13.10	Lunch	
Session 2 14.30	Mechanisms of Global Gene Regulation	Cell Biology and Development
14.30	R Krumlauf	J Raff
15.00	C Telfer	E Pillai
15.15	A Ferguson-Smith	J Vincent
15.45	P Gilardi-Hebenstreit	H Lovegrove
16.00	Refreshment break	
16.30	P Tomancak	M Saitou
17.00	E Heard	K Anderson
17.30	P Hajkova	S Wilson
18.15	Plenary Lecture: J Rossant	
18.45	Dinner	
20.00	Waddington Medal Talk	
21.00	Student and postdoc social event	

Tuesday 17 April, 2018

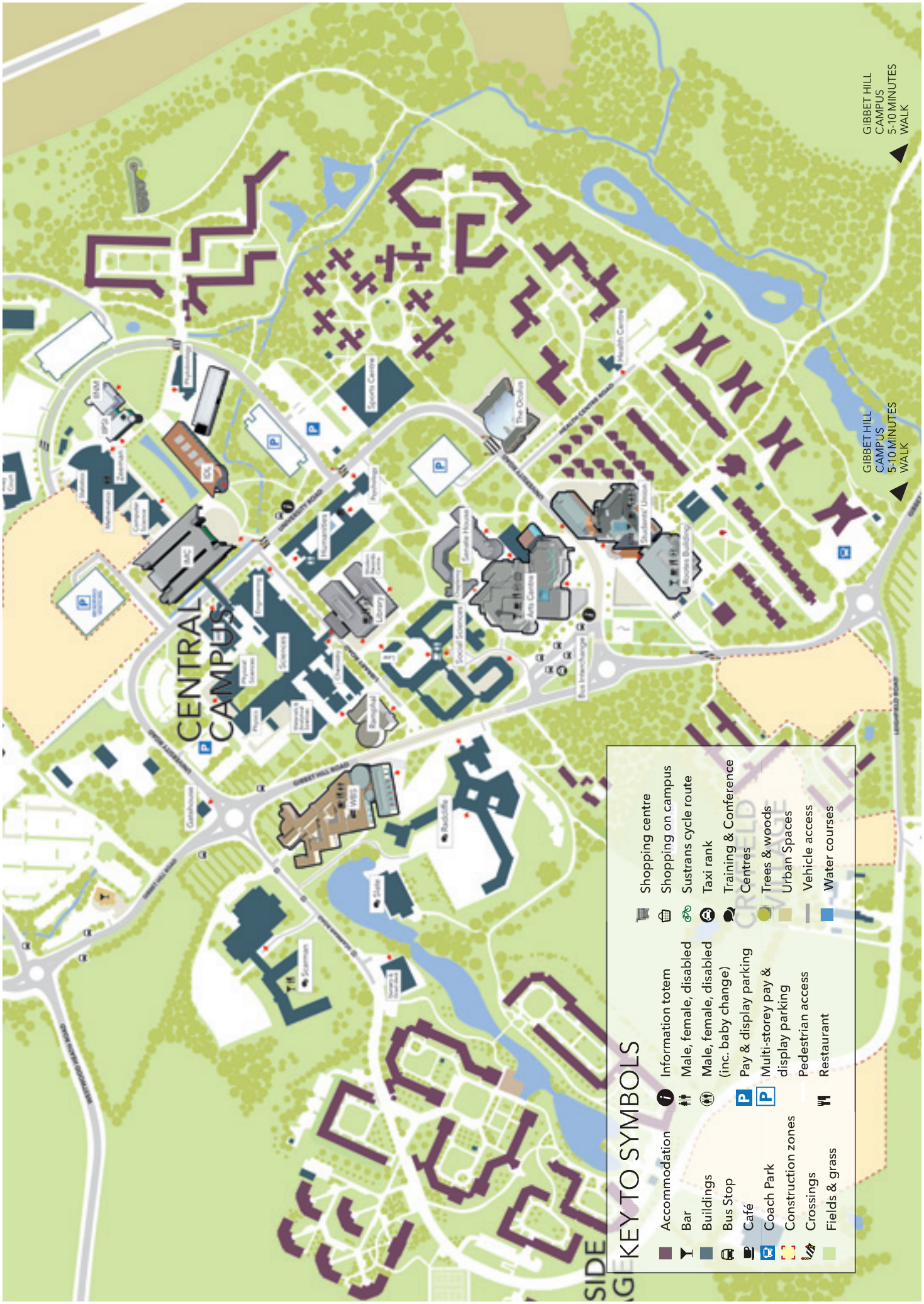
07.30	Registration	
07.30	Breakfast	
09.00	Plenary Lecture: S Carroll	
Session 3 09.35	Stem Cells and Regeneration	Evo Devo
09.35	M Götz	P Lemaire
10.05	J Solana	J Hagen
10.20	G Keller	C Extavour
10.50	G Findlay	G Thomsen
11.05	Refreshment break	
11.40	A Smith	K Sears
12.10	E Tanaka	M Tsiantis
12.40	P Tesar	P Holland
13.10	Lunch	
Session 4 14.30	Cell Fate Decisions	Positional Information
14.30	N Papalopulu	L Niswander
15.00	S Menchero	A Huang
15.15	O Pourquie	H Hamada
15.45	C Thompson	S Morgani
16.00	Refreshment break	
16.30	J Sharpe	K Storey
17.00	J Kimble	Y Bellaiche
17.30	N Geldner	J Traas
18.00	AGM	
18.30	Dinner	
20.00	Conference dinner and anniversary party	

Wednesday 18 April, 2018

08.00	Registration
07.30	Breakfast
09.30	Plenary Lecture: O Leyser
10.00	Plenary Lecture: C Eaves
10.30	Refreshment break
11.00	Plenary Lecture: E Robertson
11.30	Cheryl Tickle Medal Talk C Ruhrberg
12.00	Plenary Lecture: J Gurdon
12.30	Closing remarks
12.30	Take away lunch

see meeting reports at the end of this file

CAMPUS MAP


CENTRAL CAMPUS
GIBBET HILL CAMPUS 5-10 MINUTES WALK
GIBBET HILL CAMPUS 5-10 MINUTES WALK
KEY TO SYMBOLS
Accommodation
Bar
Buildings
Bus Stop
Café
Coach Park
Construction zones
Crossings
Fields & grass
Information totem
Male, female, disabled
Male, female, disabled (inc. baby change)
Pay & display parking
Multi-storey pay & display parking
Pedestrian access
Restaurant
Shopping centre
Shopping on campus
Sustrans cycle route
Taxi rank
Training & Conference Centres
Trees & woods
Urban Spaces
Vehicle access
Water courses

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ORGANISERS

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Conference Registration
The Registration Desk is located in the Student Union Building on Sunday 15 April and in the Oculus Building Monday 16 – Wednesday 18 April.

The Registration Desk will be open at the following times:

Sunday 15 April	12.00 – 18.00 Student Union Building
Monday 16 April	07.30 – 20.00 The Oculus Building
Tuesday 17 April	07.30 – 18.00 The Oculus Building
Wednesday 18 April	08.00 – 12.00 The Oculus Building

On registering, you will receive a name badge, conference programme and abstract book.

Please note that non-residential delegates will not be allowed access to evening meals, with the exception of the conference dinner if a ticket has been purchased.

The Reception team, located in the Atrium of the Student Union Building, is available to answer your queries from 07.00 to 23.00. Here you can also ask about the following:

- General information
- Information on connecting to wifi around the campus
- Lost property
- Request additional bedroom supplies such as pillows, blankets, clock radio or a bath mat
- Arrange for secure luggage storage

Checking in/out
Rooms will be available from 15.00 to 22.45 for check in at the Student Union Building. Please vacate your bedroom by 09.30 on your day of departure. All luggage and belongings are to be removed at that time. On arrival, please inform Reception of any difficulties you may have in the unlikely event of an evacuation (e.g. hearing or walking difficulties).

Attendees will be provided with a key card, which gives access both to your room and the entry door to the residence. On the day of departure, key cards can be left at the Conference Reception (in the Students Union building), Rootes Restaurant (in the Rootes building) or in one of the boxes situated in the entrance halls of each residence.

You can contact Reception by internal phone from your hall of residence using extension *28910, or by direct line on 024 7652 8910 (NOTE: all internal numbers are free, but whenever using pay phones always prefix the internal number with a star*).

Internet Access
If you would like to access the wifi network then please follow the instructions below:

1. Connect your device to the '**Warwick Guest**' wireless network.
2. Upon your first attempt to access online content with the web browser, you will be redirected to the Warwick Guest Wireless web page (most Apple devices will automatically perform this step).
3. If you already have a valid Warwick Guest account, please login with those credentials, otherwise please continue to create yourself a Warwick Guest account N.B. This is NOT the same account used on the 'conferences' wireless network.
4. Click the link within the sentence 'Click here to create an account' and select 'Attending a conference'.
5. Please provide your details, including a valid mobile phone number, to which your generated guest login will be sent.
6. Follow the web links to return to the Warwick Guest Wireless webpage and login.
7. If you do not have a mobile phone, choose the option 'Click here to register if you do not have a mobile phone' at the bottom of the page to have your login details sent to your email address.

If you have any questions, please ask at Conference Reception or any of the Information Points around campus (e.g. Rootes Building and Warwick Arts Centre).

Guests should be able to connect up to three wireless devices to the internet. Wifi is available in all accommodation.

Sports Facilities
Delegates have use of some of the comprehensive sports facilities including swimming and fitness suite free of charge. Other facilities are available for a nominal charge and need to be booked in advance. Details and opening times are available at Reception or by visiting the website below. Delegates need to present their bedroom key cards at the reception to gain access. See www.warwick for more information.

Shops / Banks / Cash Machines
The campus has a range of facilities available to all delegates. There are a number of retail shops on campus; a grocery store, post office, pharmacy, bookshop and hairdressers. For more information, including opening times please visit the following website: http://www.warwickretail.com.

Warwick Arts Centre cinema offers discounted cinema rates. These can be purchased from the box office and proof of delegate status is required (not applicable for Met Opera Live or NT Live screenings).

There are branches of Barclays and Santander; both have cash machines in the Students Union Atrium (directly next to Rootes building). There is also a cash machine outside Rootes Grocery Store.

Meals and Refreshments
Breakfast (07.30 – 09.00) will be served in the Rootes Restaurant, Rootes Building for anyone booked on a residential package. Tea/coffee breaks and lunches will be served in the exhibition space in the The Oculus Building. Dinners will be served in the Rootes Restaurant with the exception of the conference dinner on Tuesday evening that will be served in the Panorama Suite, Rootes Building.

The lively Rootes Restaurant offers excellent buffet style food every day – with a cooked or continental breakfast, a hot and cold buffet selection at lunch and a two course evening meal. The bar is located on the first floor of the Rootes Social Building and is the ideal place to network and relax at the end of the day. It serves draught beers, a good selection of bottled beers, wines, spirits, soft drinks and a variety of teas and coffees.

Social Events

Sunday 15 April – Dinner 17:45 – 19:00 – Rootes Building

Sunday 15 April – Roundtable Discussions and Drinks Reception 21.00 – 22.00 – Panorama Suite, Rootes Building
All attendees are encouraged to contribute to these informal discussions. Drinks will be provided.

Monday 16 April – Dinner 18:45 – 20:00 – Rootes Building

Waddington Medal Talk 20:00 – 21:00

Self service dinner will be served at 18:45 in the Rootes Restaurant for all residential delegates before the Waddington Medal Talk.

Monday 16 April – Student and postdoc social event – 21:00 – OC1.01
An opportunity to meet with colleagues and enjoy complimentary drinks utilising your free drinks voucher, which can be found in the back of your delegate badge. Please hand this in at the bar in exchange for your drink. Please note that a cash bar will only be available in the Arts Centre as well as the bar in Rootes Building.

Tuesday 17 April – Conference Dinner from 20:00 – Panorama Suite, Rootes Building
On Tuesday there is a conference dinner which is a semi-formal evening. It is a great time to come together towards the end of the conference and enjoy a delicious three-course meal with a disco afterwards. This will be held in the Panorama Suite.

Tuesday 17 April – Dinner 18:30 – 20:00 – Rootes Building
There will be a self service dinner available for all delegates who have booked a residential package and are not attending the conference dinner.

Health and Safety
Accidents, security breaches and other incidents occurring on University premises during your stay must be reported immediately to the Warwick Conferences Reception, where a form should be completed. If you fall ill during your stay Warwick Conferences Reception can arrange medical assistance if required. A first-aider is on duty at the University of Warwick at all times.

To view all health and safety policies within the venue please click on the link below:
http://www2.warwick.ac.uk/services/safety/health_and_safety/policy.

Fire
In the event of fire alarm activation the evacuation assembly points are located clear of the main exit of each building. Please ensure all passageways and emergency exits are unobstructed.

Emergency
In the event of an emergency or accident please dial extension *22222 on any internal phone or 024 7652 2222 externally to be in direct contact with the 24 hour Security Staff.

Security
The University security staff are on duty 24 hours a day should you require their assistance. Please take necessary security precautions; lock your door at night, keep valuables secure and out of sight and do not walk alone at night on campus. Do not leave rooms unlocked or property unattended at any time.

Smoking Policy
All buildings onsite are non-smoking, including all bedrooms.

First Aid
First Aid facilities are available from the First Aid Team on campus. Please contact a member of Warwick Conferences Staff immediately for assistance with first aid.

Attendees are requested to use common sense precautions at all times and to ensure that conference delegate badges are worn at all times. Should any suspicious or unidentified articles be discovered, it must be reported to the Conference Organisers desk IMMEDIATELY.

BSDB Spring Meeting – Programme 2018

Sunday 15 April 2018

12.00 – 18.00	**Registration** – Students Union Building
12.00 – 14.30	**Careers Session** (sign-up required) – Panorama Suite, Rootes Building
15.00 – 15.30	**Plenary Lecture** - OC1.05 **Chair: Josh Brickman** **PL01 Eric Wieschaus – Princeton University, HHMI, New Jersey, USA** Mechanical Tension and Epithelial Mesenchymal Transitions in Drosophila
15.30 – 16.00	**Plenary Lecture** – OC1.05 **Chair: Josh Brickman** **PL02 Maria Leptin – EMBO, Heidelberg, Germany** Morphogenesis: from whole organism integration to biophysical principles
16.00 – 16.45	**Refreshments and Poster Viewing** – Foyer, Oculus Building
16.45 – 17.15	**Beddington Medal Talk** – OC1.05 **Chair: Simon Bullock** **PL03 Emilia Favuzzi - Harvard Medical School, Cambridge, USA** Cell-specific programs regulate inhibitory synapse specificity
17.15 – 17.45	**Plenary Lecture** – OC1.05 **Chair: Michelle Ware** **PL04 Marianne Bronner – California Institute of Technology, California, USA** Gene regulatory and signaling events in neural crest development
17.45 – 19.00	**Dinner** – Rootes Restaurant, Rootes Building
19.00 – 20.30	**The History and Future of Developmental Biology** – OC1.05 **Chair: Claudio Stern** **H01 Tim Horder – University of Oxford, Oxford, UK** The value of history: history as a resource for the future **H02 Nick Hopwood – University of Cambridge, Cambridge, UK** Inclusion and exclusion in the history of developmental biology
	H03 Panel Discussion on the Future of Developmental Biology Jonathan Slack
21.00 – 22.00	**Roundtable discussions and drinks reception** – Panorama Suite, Rootes Building
22.00 – 00.00	**Late bar**

Monday 16 April 2018

07.30 – 20.00	**Registration** – Foyer, Oculus Building	
07.30 - 09.00	**Breakfast** – Rootes Restaurant, Rootes Building	
09.00 – 09.30	**Plenary Lecture** – OC1.05 **Chair: Rita Sousa-Nunes** **PL05 Matthew Freeman – University of Oxford, Oxford, UK** Confessions of an ex-developmental biologist	
Session 1 09.35 – 13.10	**Tissue and Organ Development** – OC1.05 **Chair: Richard Gardner**	**Developmental Gene Regulatory Networks** – OC0.03 **Chair: Abigail Tucker**
09.35 – 10.05	**S01 Henrik Semb – University of Copenhagen, Copenhagen, Denmark** How morphogenesis directs cell fate	**S05 James Briscoe – The Francis Crick Institute, London, UK** The Gene Regulatory Logic for Reading the Sonic Hedgehog Gradient In The Vertebrate Neural Tube
10.05 – 10.20	**O1 Annick Sawala – The Francis Crick Institute, London, UK** Signalling and metabolic mechanisms for selective organ growth during starvation	**S06 Virginia Papaioannou – Columbia University Medical Center, New York, USA** Multiple Roles of the T-box gene, Tbx6
10.20 – 10.35	**O2 Ravindra Prajapati – King's College London, London, UK** A role for PRDM1 in cell fate decisions in the ectoderm	
10.35 – 11.05	**S02 Fiona Watt – King's College London, London, UK** Regulation of homeostasis in mammalian epidermis	**S07 Ido Amit – Weizmann Institute of Science, Israel** The power of ONE: Immunology in the age of single cell genomics
11.05 – 11.40	**Refreshment break and exhibition/poster viewing time** – Foyer, Oculus Building	
11.40 – 12.10	**S03 Patrick Tam – Children's Medical Research Institute, Westmead, Australia** Mouse gastrulation: The interplay of transcription and signalling activity for germ layer formation	**S08 Eileen Furlong – EMBL, Heidelberg, Germany** Functional insights into genome topology and enhancer function during embryonic development
12.10 – 12.25	**O3 Jens Januschke – University of Dundee, Dundee, UK** A chemical genetics approach to study atypical protein kinase C (aPKC) function in Drosophila	**O5 Ruth Williams – University of Oxford, Oxford, UK** Genome-wide analysis of gene expression and chromatin architecture in vivo reveals intricate gene regulatory networks underlying cranial neural crest development
12.25 – 12.55	**S04 Klaus Kaestner – University of Pennsylvania, Philadelphia, USA** Subepithelial Foxl1-positive telocytes are the source of Wnts that support intestinal crypts	**S09 Mike Levine – Princeton University, Princeton, USA** Visualization of Transvection in Living Drosophila Embryos
12.55 – 13.10	**O4 AJ Copp – University College London, London, UK** Biomechanics of neural tube formation in mammals	**O6 Teresa Knudsen – University of Copenhagen, Copenhagen, Denmark** Linking self-renewal and differentiation
13.10 – 14.30	**Lunch and exhibition/poster viewing time** – Foyer, Oculus Building	

Monday 16 April 2018 *continued*

Session 2 **14.30 – 18.00**	**Mechanisms of Global Gene Regulation** – OC1.05 **Chair: Jim Smith**	**Cell Biology and Development** – OC0.03 **Chair: Daniel St Johnston**
14.30 – 15.00	**S10 Robb Krumlauf – Stowers Institute for Medical Research, Missouri, USA** Hox genes and the hindbrain: A story in segments	**S15 Jordan Raff – University of Oxford, Oxford, UK** Centrioles as a model to study organelle size control
15.00 – 15.15	**O7 Caroline Telfer – University of Oxford, Oxford, UK** Dissecting the upstream regulation of the GATA genes during heart development	**O9 Eva Pillai – University of Cambridge, Cambridge, UK** Mechanical regulation of chemical signalling in the developing Xenopus brain
15.15 – 15.45	**S11 Anne Ferguson-Smith – University of Cambridge, Cambridge, UK** Variable silencing of the repeat genome – implications for non-genetic inheritance	**S16 Jean-Paul Vincent – The Francis Crick Institute, London, UK** Just-right Wnt signalling for coordinated control of growth and patterning
15.45 – 16.00	**O8 Pascale Gilardi-Hebenstreit – IBENS, Paris, France** Function, cooperation and evolution of multiple enhancers governing the expression of a vertebrate developmental gene	**O10 Holly Lovegrove – The University of Manchester, Manchester, UK** Asymmetric cell division during angiogenesis
16.00 – 16.30	**Refreshment break and poster/exhibition viewing time** – Foyer, Oculus Building	
16.30 – 17.00	**S12 Pavel Tomancak – MPI-CBG, Dresden, Germany** The Physics of Blastoderm Flow during Early Gastrulation of Tribolium castaneum	**S17 Mitinori Saitou – Kyoto University, Kyoto, Japan** Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans
17.00 – 17.30	**S13 Edith Heard – Institut Curie, Paris, France** Developmental dynamics of X-chromosome structure	**S18 Kathryn Anderson – Sloan Kettering Institute, New York, USA** The Dynamics of The Epithelial-To-Mesenchymal Transition During Mouse Gastrulation
17.30 – 18.00	**S14 Petra Hajkova – Imperial College London, London, UK** Reprogramming in the mouse germ line	**S19 Steve Wilson – University College London, London, UK** Breaking symmetry in the developing brain
18.15 – 18.45	**Plenary Lecture** – OC1.05 **Chair: Berenika Plusa** **PL06 Janet Rossant – Hospital for Sick Children, Toronto, Canada** Making the mouse blastocyst	
18.45 – 20.00	**Dinner** – Rootes Restaurant, Rootes Building	
20.00 – 21.00	**Waddington Medal Talk** – OC1.05 **Chair: Ottoline Leyser** **PL07 Speaker TBA**	
21.00 onwards	**Student and postdoc social event** – OC1.01	

Tuesday 17 April 2018

07.30 – 18.00	**Registration** – Foyer, Oculus Building	
07.30 - 09.00	**Breakfast** – Rootes Restaurant, Rootes Building	
09.00 – 09.30	**Plenary Lecture** – OC1.05 **Chair: Alistair McGregor** **PL08 Sean Carroll – HHHMI / University of Wisconsin, Chevy Chase, USA** Rattlesnake Tales	
Session 3 **09.35 – 13.10**	**Stem Cells and Regeneration** – OC1.05 **Chair: Alexandra Ashcroft**	**Evo Devo** – OC0.03 **Chair: Michael Akam**
09.35 – 10.05	**S20 Magdalena Götz – LMU München, Planegg-Martinsried, Germany** Novel regulators of neurogenesis – from centrosomes to nucleoli	**S25 Patrick Lemaire – CNRS, University of Montpellier, Montpeillier, France** How invariant is ascidian development (and why?)
10.05 – 10.20	**O11 Jordi Solana – Oxford Brookes University, Oxford, UK** Using single-cell technologies and planarians to study stem cells, their differentiation and their evolution	**O13 Joanna Hagen – Oxford Brookes University, Oxford, UK** What's under the kilt? tartan is a likely causative gene for rapid male genitalia divergence between Drosophila species
10.20 – 10.50	**S21 Gordon Keller – University of Toronto, Ontario, Canada** Modeling human cardiovascular development with pluripotent stem cells	**S26 Cassandra Extavour – Harvard University, Cambridge, USA** Network analysis of signaling pathways reveals new mechanisms regulating the development and evolution of reproductive output in Drosophila
10.50 – 11.05	**O12 Greg Findlay – University of Dundee, Dundee, UK** Phosphoproteomics Identifies a Bimodal EPHA2 Receptor Switch that Promotes Embryonic Stem Cell Differentiation	**O14 Gerry Thomsen – Stony Brook University, Stony Brook, USA** Wnt signaling regulates head regeneration in the starlet sea anemone Nematostella vectensis
11.05 – 11.40	**Refreshment break and poster/exhibition viewing time** – Foyer, Oculus Building	
11.40 – 12.10	**S22 Austin Smith – University of Cambridge, Cambridge, UK** Pluripotency: plasticity and order	**S27 Karen Sears – UCLA, Los Angeles, USA** Developmental origin and evolution of bats
12.10 – 12.40	**S23 Elly Tanaka – Research Institute of Molecular Pathology, Vienna, Austria** Triggering Limb Regeneration	**S28 Miltos Tsiantis – Max Panck Institute, Cologne, Germany** The genetic basis for diversification of leaf form: from understanding to reconstructing
12.40 – 13.10	**S24 Paul Tesar – Case Western Reserve University, Ohio, USA** Pluripotent stem cell technologies for studying myelin development and regenerative therapies	**S29 Peter Holland – University of Oxford, Oxford, UK** What is evolutionary conversation? Lessons from ParaHox genes of unusual animals
13.10 – 14.30	**Lunch and poster/exhibition viewing time** – Foyer, Oculus Building	
Session 4 **14.30 – 18.00**	**Cell Fate Decisions** - OC1.05 **Chair: Kim Dale**	**Positional Information** - OC0.03 **Chair: Phil Ingham**
14.30 – 15.00	**S30 Nancy Papalopulu – Faculty of Biology, Medicine and Health, Manchester, UK** Quantitative and dynamic analysis of neurogenesis with single cell resolution at the tissue level	**S35 Lee Niswander – University of Colorado Boulder, Colorado, USA** Visualizing neural tube closure and uncovering the causes of neural tube defects

Tuesday 17 April 2018 *continued*

15.00 – 15.15	**O15 Sergio Menchero – CNIC, Madrid, Spain** Triggering of cell differentiation in the mouse preimplantation embryo is driven by Notch at compaction	**O17 Anqi Huang – National University of Singapore, Singapore** Embryonic geometry underlies phenotypic variation in decanalized conditions
15.15 – 15.45	**S31 Olivier Pourquie – Harvard Medical School, Boston, USA** Deconstructing the Segmentation Clock oscillator in vitro	**S36 Hiroshi Hamada – Centre for Developmental Biology, Kobe, Japan** Role of motile and immotile cilia in left-right symmetry breaking
15.45 – 16.00	**O16 Christopher Thompson – University of Manchester, Manchester, UK** Robust cell type proportioning by a noisy oscillator	**O18 Sophie Morgani, Memorial Sloan Kettering Cancer Center, New York, USA** Micropattern differentiation of mouse pluripotent stem cells recapitulates embryo regionalized cell fate patterning
16.00 – 16.30	**Refreshment break and poster/exhibition viewing time** – Foyer, Oculus Building	
16.30 – 17.00	**S32 James Sharpe – EMBL, Barcelona, Spain** Limbs, Turing Patterns and the 50th anniversary of the French Flag Problem	**S37 Kate Storey – University of Dundee, Dundee, UK** FGF/Erk promotion of polycomb-mediated repression regulates neural differentiation onset
17.00 – 17.30	**S33 Judith Kimble – University of Wisconsin-Madison, Madison, USA** Molecular and network understanding of a sperm/oocyte cell fate decision	**S38 Yohanns Bellaiche – Institut Curie, Paris, France** Mitosis and epithelial morphogenesis
17.30 – 18.00	**S34 Niko Geldner – University of Lausanne, Lausanne, Switzerland** The root endodermis - an independent way of building a polarised epithelium	**S39 Jan Traas – Laboratory of Plant Reproduction and Development, Lyon, France** Flower development : from morphodynamics to morphomechanics
18.00 – 19.00	**AGM** – OC1.05	
18.30 – 20.00	**Dinner** – Rootes Restaurant, Rootes Building (for residential guests who are not attending the conference dinner only)	
20.00 onwards	**Conference dinner and anniversary party** – Panorama Suite, Rootes	

Wednesday 18 April 2018

08.00 – 12.00	**Registration** – Foyer, Oculus Building
07.30 - 09.00	**Breakfast** – Rootes Restaurant, Rootes Building
09.30 – 10.00	**Plenary Lecture** – OC1.05 **Chair: Megan Davey** **PL09 Ottoline Leyser – University of Cambridge, Cambridge, UK** Dual mode strigolactone signaling and the bud activation switch
10.00 – 10.30	**Plenary Lecture** – OC1.05 **Chair: Megan Davey** **PL10 Connie Eaves – BC Cancer Agency, Vancouver, Canada** Single-cell analyses suggest new complexities in the changing landscape of primitive human blood-forming cells
10.30 – 11.00	**Refreshment break** – Foyer, Oculus Building
11.00 – 11.30	**Plenary Lecture** – OC1.05 **Chair: Sally Lowell** **PL11 Elizabeth Robertson – University of Oxford, Oxford, UK** Specification of the definitive endoderm and midline progenitors in the early post-implantation mouse embryo
11.30 – 12.00	**Cheryl Tickle Medal Talk** – OC1.05 **Chair: Cheryl Tickle** **PL12 Christina Ruhrberg – UCL Institute of Ophthalmology, London, UK** Cheryll Tickle Medal Lecture: Using the mouse embryo hindbrain as a model to understand neuronal and vascular development.
12.00 – 12.30	**Plenary Lecture** – OC1.05 **Chair: Sally Lowell** **PL13 John Gurdon – University of Cambridge, Cambridge, UK** The stability and reversal of gene expression in development
12.30 – 12.40	**Closing remarks** – OC1.05
12.30 onwards	**Take away lunch and delegates depart** – Foyer, Oculus Building

SPONSORS AND EXHIBITORS

The BSDB would like to thank the following organisations for their generous support of the Spring Conference 2018.

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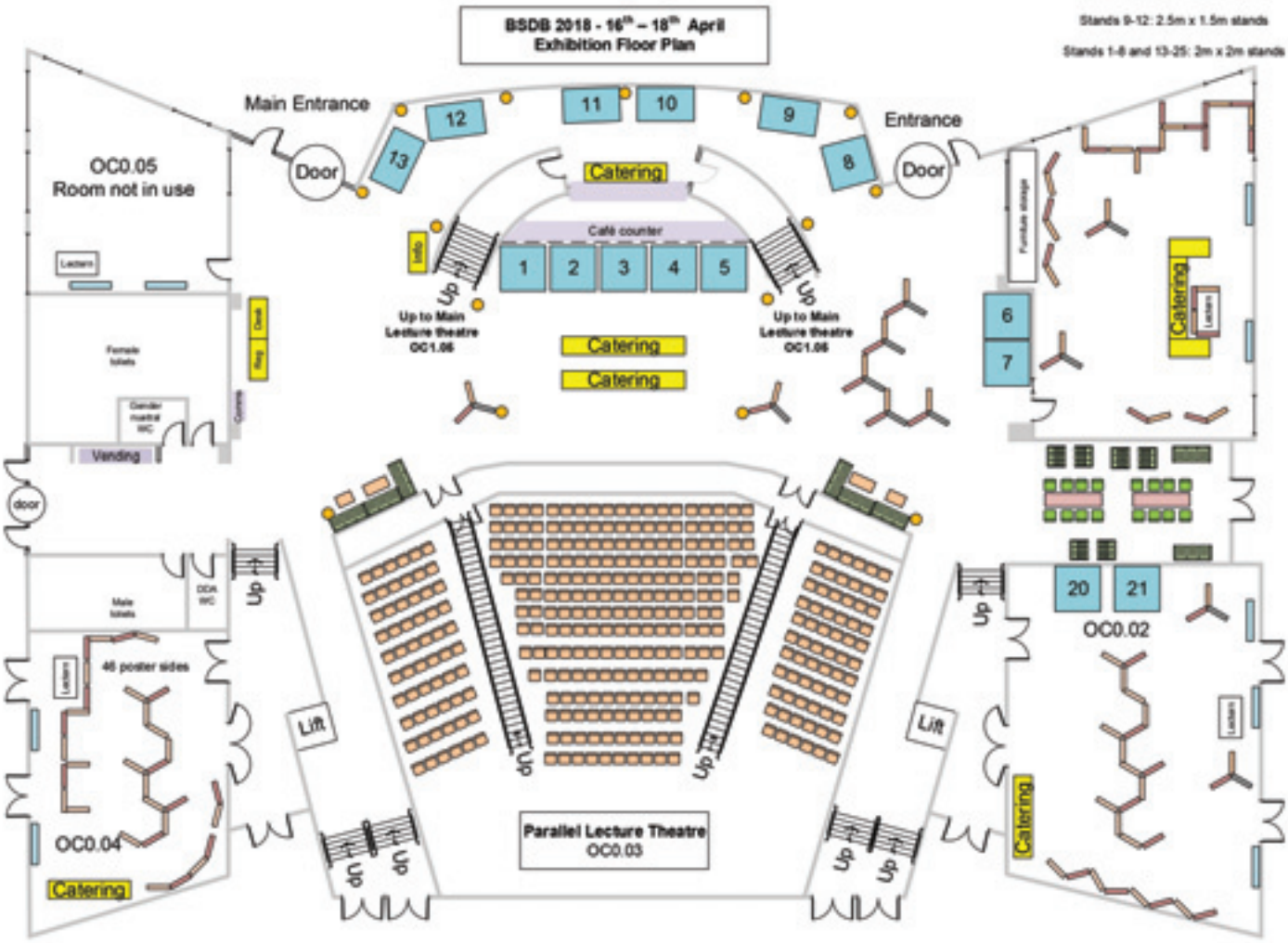

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2BScientific Ltd

Stand 8
Alvéole

Stand 9
DMDD

Stand 10
Intavis

Stand 11
Abcam

Stand 12
Indigo Scientific

Stand 13
Stratech Scientific Ltd

Stand 20
International Mouse Phenotyping Consortium

Stand 21
PeproTech

EXHIBITOR INFORMATION

Stands 1 & 2

The Company of Biologists
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The Company of Biologists is a not for profit publishing organisation dedicated to supporting and inspiring the biological community. The Company publishes five specialist peer-reviewed journals: Development, Journal of Cell Science, Journal of Experimental Biology, Disease Models & Mechanisms and Biology Open. It offers further support to the biological community by facilitating scientific meetings and communities, providing travel grants for researchers and supporting research societies.

Stand 3

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Stand 3

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Bitplane is the creator of Imaris, the world's leading scientific Image analysis software for 3D/4D images from light-sheet, confocal, spinning-disk, multi-photon and wide-field fluorescent microscopes. Imaris is the tool of choice for leading scientists for their applications involving large data (>1TB) visualization, animation, cell lineage, surface rendering, filament tracing of neuronal dendrites/vessels, tracking of particles, and cell division/inter-intracellular analyses. Imaris enables researchers at the cutting edge of discoveries to further expand the built-in functions of Imaris by interfacing with programming languages (MATLAB, Python, Java) and plug-ins from Fiji and ImageJ.

Stand 4

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Stand 5

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Stand 6

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Stand 7

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Stand 8

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Created from work carried out by three research experts, Alvéole's goal is to make the control of living cells the future of cell biology. A company specialized in devices for controlling the cellular microenvironment, Alvéole presents its first device PRIMO: a contactless and maskless custom micropatterning device for cell control. PRIMO enables researchers to control the chemistry and topography of cell microenvironment on all standard cell culture substrates and study their impacts on cell development.

Stand 9

DMDD (Deciphering the Mechanisms of Developmental Disorders)
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Website: www.dmdd.org.uk

DMDD (dmdd.org.uk) provides a free database of image and phenotype data for embryonic lethal knockout mouse lines. Using high-resolution episcopic microscopy (HREM) and tissue histology we identify structural abnormalities in embryos and placentas for each line. We also provide embryo gene expression profiles. Search the data to identify and explore genes and phenotypes relevant to your research. For updates follow us @dmdduk.

Stand 10

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The INTAVIS AG is specialized on the development of systems for the automation of complex protocols in life sciences. The InsituPro VSi represents 20 years of experience in automating in situ hybridization and immunostainings on a wide range of organisms and tissues. It can process whole mounts, vibratome sections, thin sections on slides or cells on coverslips. The BioLane HTI-16V is the economical alternative for various techniques such as immunodetection, ISH and western blot staining.

Stand 11

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As an innovator in reagents and tools, Abcam's purpose is to serve life science researchers globally to achieve their mission, faster. Providing the research and clinical communities with tools and scientific support, the Company offers highly validated biological binders and assays to address important targets in critical biological pathways.

Stand 12

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Optical HREM is a technique for imaging embryos or small samples (1 to 25mm) in 3D at high resolution. Initially used to show the sample morphology in great detail, optical HREM is also now being used for multi channel fluorescence imaging.

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Stand 13

Stratech Scientific Ltd
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Stand 20

International Mouse Phenotyping Consortium
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The International Mouse Phenotyping Consortium (IMPC) is an international programme to find the function of every protein-coding gene in the mouse genome. Our objectives include to test each mutant mouse line, discover and ascribe biological function to each gene, maintain and expand collaborative networks, and lastly to provide a centralised data centre and portal. Please explore our free, online database!

Stand 21

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OVERVIEW OF SHORT TALKS AND SPEAKER ABSTRACTS

These meetings have a longstanding reputation for being informal and an opportunity to present unpublished work. As such, we request that the permission of the speaker or poster presenter is obtained before any public communication of the work.

Sunday 15 April, 2018
Plenary Lecture
OC1.05

PL01 15:00 – 15:30
Mechanical Tension and Epithelial Mesenchymal Transitions in Drosophila
M Weng, **EF Wieschaus**

Plenary Lecture

PL02 15:30 – 16:00
Morphogenesis: from whole organism integration to biophysical principles
M Leptin

Beddington medal talk

PL03 16:45 – 17:15
Cell-specific programs regulate inhibitory synapse specificity
E Favuzzi

Plenary Lecture

PL04 17:15 – 17:45
Gene regulatory and signaling events in neural crest development
M Bronner

19:00 – 21:00
The History and Future of Developmental Biology

H01
The value of history: history as a resource for the future
T Horder

H02
Inclusion and exclusion in the history of developmental biology
N Hopwood

H03
The Future of Developmental Biology
Panel-led open discussion chaired by Claudio Stern

H04
Roundtable Discussions
Discussion on the Future of Developmental Biology with PI hosts

Monday 16 April, 2018
Plenary Lecture
OC1.05

PL05 09:00 – 09:30
Confessions of an ex-developmental biologist
M Freeman

Monday 16 April, 2018
Tissue and Organ Development
09:35 – 13:10
OC1.05

S01 09:35 – 10:05
How morphogenesis directs cell fate
H Semb

O1 10:05 – 10:20
Poster Number: P224
Signalling and metabolic mechanisms for selective organ growth during starvation
A Sawala, AP Gould

O2 10:20 – 10:35
Poster Number: P225
A role for *PRDM1* in cell fate decisions in the ectoderm
RS Prajapati, M Hinze, A Streit

S02 10:35 – 11:05
Regulation of homeostasis in mammalian epidermis
F Watt

S03 11:40 – 12:10
Mouse gastrulation: The interplay of transcription and signalling activity for germ layer formation
PPL Tam

O3 12:10 – 12:25
Poster Number: P1
A chemical genetics approach to study atypical protein kinase C (aPKC) function in Drosophila
J Januschke, M Hannaford, N Loyer, F Tonelli

S04 12:25 – 12:55
Subepithelial Foxl1-positive telocytes are the source of Wnts that support intestinal crypts
KH Kaestner

O4 12:55 – 13:10
Poster Number: P226
Biomechanics of neural tube formation in mammals
GL Galea, ND Greene, **AJ Copp**

Monday 16 April, 2018
Developmental Gene Regulatory Networks
09:35 – 13:10
OC0.03

S05 09:35 – 10:05
The gene regulatory logic for reading the sonic hedgehog gradient in the vertebrate neural tube
J Briscoe

S06 10:05 – 10:35
Multiple Roles of the T-box gene, *Tbx6*
VE Papaioannou

S07 10:35 – 11:05
I Amit

S08 11:40 – 12:10
Functional insights into genome topology and enhancer function during embryonic development
E Furlong

O5 12:10 – 12:25
Poster Number: P129
Genome-wide analysis of gene expression and chromatin architecture *in vivo* reveals intricate gene regulatory networks underlying cranial neural crest development
RM Williams, D Gavriouchkina, I Candido-Ferreira, E Repapi, U Senanayake, J Telenius, J Hughes, T Sauka-Spengler

S09 12:25 – 12:55
Visualization of Transvection in Living Drosophila Embryos
B Lim, T Fukaya, T Heist, **M Levine**

O6 12:55 – 13:10
Poster Number: P130
Linking self-renewal and differentiation:
T Knudsen, W Hamilton, A Nielsen, A Trusina, J Brickman

Monday 16 April, 2018
Mechanisms of Global Gene Regulation
14:30 – 18:00
OC1.05

S10 14:30 – 15:00
Hox genes and the hindbrain: A story in segments
HJ Parker, B DeKumar, LM Wiedemann, **R Krumlauf**

O7 15:00 – 15:15
Poster Number: P111
Dissecting the upstream regulation of the GATA genes during heart development
C Telfer, F Simões, T Sauka-Spengler, P Riley, R Patient

S11 15:15 – 15:45
Variable silencing of the repeat genome – implications for non-genetic inheritance
A Kazachenka, T Bertozzi, MK Sjoberg, N Walker, DJ Adams, **AC Ferguson-Smith**

S12 16:30 – 17:00
The Physics of Blastoderm Flow during Early Gastrulation of Tribolium castaneum
S Munster, A Jain, A Mietke, SW Grill, **P Tomancak**

S13 17:00 – 17:30
Developmental dynamics of X-chromosome structure
E Heard

S14 17:30 – 18:00
Reprogramming in the mouse germ line
PWS Hill, HG Leitch, CE Requena, Z Sun, R Amouroux, M Roman-Trufero, M Borkowska, J Terragni, R Vaisvila, S Linnett, H Bagci, G Dharmalingham, V Haberle, B Lenhard, Y Zheng, S Pradham, **P Hajkova**

O8 15:45 – 16:00
Poster Number: P112
Function, cooperation and evolution of multiple enhancers governing the expression of a vertebrate developmental gene
P Torbey, E Thierion, S Collombet, J.P. Concordet, C Desmarquet Trin-Dinh, P Charnay, **P Gilardi-Hebenstreit**

Monday 16 April, 2018
Cell Biology and Development
14:30 – 18:00
OC0.03

S15 14:30 – 15:00
Centrioles as a model to study organelle size control
MG Aydogan, A Wainman, S Saurya, TL Steinacker, A Caballe, ZA Novak, J Baumbach, N Muschalik, **JW Raff**

O9 15:00 – 15:15
Poster Number: P2
Mechanical regulation of chemical signalling in the developing *Xenopus* brain
EK Pillai, K Franze

S16 15:15 – 15:45
Just-right Wnt signalling for coordinated control of growth and patterning
I McGough, E Ordan, H Nojima, C Alexandre, **JP Vincent**

O10 15:45 – 16:00
Poster Number: P3
Asymmetric cell division during angiogenesis
HE Lovegrove, G Costa, SP Herbert

S17 16:30 – 17:00
Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans
MS Saitou

S18 17:00 – 17:30
The Dynamics of The Epithelial-To-Mesenchymal Transition During Mouse Gastrulation
KV Anderson, A Francou, R Hernández-Martínez, T Omelchenko

S19 17:30 – 18:00
Breaking symmetry in the developing brain
SW Wilson

Monday 16 April, 2018
Plenary Lecture
OC1.05

PL06 18:15 – 18:45
Making the mouse blastocyst
J Rossant

PL07 20:00 – 21:00
Waddington medal talk

Tuesday 17 April, 2018
Plenary Lecture
OC1.05

PL08 09:00 – 09:30
Rattlesnake Tales
SB Carroll

Tuesday 17 April, 2018
Stem Cells and Regeneration
09:35 – 13:10
OC1.05

S20 09:35 – 10:05
Novel regulators of neurogenesis – from centrosomes to nucleoli
M Götz

O11 10:05 – 10:20
Poster Number: P189
Using single-cell technologies and planarians to study stem cells, their differentiation and their evolution
J Solana

S21 10:20 – 10:50
Modeling human cardiovascular development with pluripotent stem cells
G Keller

O12 10:50 – 11:05
Poster Number: P190
Phosphoproteomics Identifies a Bimodal EPHA2 Receptor Switch that Promotes Embryonic Stem Cell Differentiation
R Fernandez-Alonso, M Budzyk, A Helbig, J Hukelmann, A Lamond, E Petsalaki, **GM Findlay**

S22 11:40 – 12:10
Pluripotency: plasticity and order
A Smith

S23 12:10 – 12:40
Triggering Limb Regeneration
EM Tanaka

S24 12:40 – 13:10
Pluripotent stem cell technologies for studying myelin development and regenerative therapies
PJ Tesar

Tuesday 17 April, 2018
Evo Devo
09:35 – 13:10
OC0.03

S25 09:35 – 10:05
How invariant is ascidian development (and why?)
L Guignard, UM Fiuza, B Leggio, E Faure, J Laussu, L Hufnagel, G Malandain, C Godin,
P Lemaire

O13 10:05 – 10:20
Poster Number: P149
What's under the kilt? *tartan* is a likely causative gene for rapid male genitalia divergence between *Drosophila* species
JFD Hagen, C Mendes, K M Tanaka, A Blogg, A P McGregor, MDS Nunes

S26 10:20 – 10:50
Network analysis of signaling pathways reveals new mechanisms regulating the development and evolution of reproductive output in Drosophila
T Kumar, L Blondel, **CG Extavour**

O14 10:50 – 11:05
Poster Number: P150
Wnt signaling regulates head regeneration in the starlet sea anemone *Nematostella vectensis*
Y Iwasaki, M Lee, **GH Thomsen**

S27 11:40 – 12:10
Developmental origin and evolution of bats
KE Sears

S28 12:10 – 12:40
The genetic basis for diversification of leaf form: from understanding to reconstructing
M Tsiantis

S29 12:40 – 13:10
What is evolutionary conversation? Lessons from ParaHox genes of unusual animals
PWH Holland, Y Dai, AD Hargreaves, G Li, F Xu

Tuesday 17 April, 2018
Cell Fate Decisions
14:30 – 18:00
OC1.05

S30 14:30 – 15:00
Quantitative and dynamic analysis of neurogenesis with single cell resolution at the tissue level
N Papalopulu, C Manning, X Soto, V Biga

O15 15:00 – 15:15
Poster Number: P89
Triggering of cell differentiation in the mouse preimplantation embryo is driven by Notch at compaction
S Menchero, A Lopez-Izquierdo, MJ Andreu, J Sainz de Aja, I Rollan, M Kang, R Benedito, T Rayon, AK Hadjantonakis, M Manzanares

S31 15:15 – 15:45
Deconstructing the Segmentation Clock oscillator in vitro
O Pourquie

O16 15:45 – 16:00
Poster Number: P90
Robust cell type proportioning by a noisy oscillator
N Gruenheit, EJ Johnson, K Parkinson, K Nagayama, J Llewellyn, B Stewart, T Keller, W van Zon, SL Cotter, **CRL Thompson**

S32 16:30 – 17:00
Limbs, Turing Patterns and the 50th anniversary of the French Flag Problem
J Sharpe

S33 17:00 – 17:30
Molecular and network understanding of a sperm/oocyte cell fate decision
J Kimble

S34 17:30 – 18:00
The root endodermis – an independent way of building a polarised epithelium
N Geldner

Tuesday 17 April, 2018
Positional Information
14:30 – 18:00
OC0.03

S35 14:30 – 15:00
Visualizing neural tube closure and uncovering the causes of neural tube defects
LA Niswander

O17 15:00 – 15:15
Poster Number: P177
Embryonic geometry underlies phenotypic variation in decanalized conditions
A Huang, TE Saunders

S36 15:15 – 15:45
Role of motile and immotile cilia in left-right symmetry breaking
H Hamada

O18 15:45 – 16:00
Micropattern differentiation of mouse pluripotent stem cells recapitulates embryo regionalized cell fate patterning
SM Morgani, JJ Metzger, J Nichols, ED Siggia, AK Hadjantonakis

S37 16:30 – 17:00
FGF/Erk promotion of polycomb-mediated repression regulates neural differentiation onset
KG Storey, C I Semprich

S38 17:00 – 17:30
Mitosis and epithelial morphogenesis
Y Bellaiche

S39 17:30 – 18:00
Flower development : from morphodynamics to morphomechanics
J Traas

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL09 09:30 – 10:00
Dual mode strigolactone signaling and the bud activation switch
O Leyser

Plenary Lecture

PL10 10:00 – 10:30
Single-cell analyses suggest new complexities in the changing landscape of primitive human blood-forming cells
CJ Eaves, DJHF Knapp, CA Hammond, A Lorzadeh, F Wang, M MacAldaz, T Hui, MTJ von Leonhout, N Aghaeepour, PH Miller

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Plenary Lecture

PL11 11:00 – 11:30
Specification of the definitive endoderm and midline progenitors in the early post-implantation mouse embryo
E Robertson

Cheryll Tickle Medal

PL12 11:30 – 12:00
Cheryll Tickle Medal Lecture: Using the mouse embryo hindbrain as a model to understand neuronal and vascular devleopment
C Ruhrberg

Plenary Lecture

PL13 12:00 – 12:30
The stability and reversal of gene expression in development
JB Gurdon

OVERVIEW OF ABSTRACTS SELECTED FOR POSTERS

Cell biology and development

Poster Number: P1
A chemical genetics approach to study atypical protein kinase C (aPKC) function in Drosophila
J Januschke, M Hannaford, N Loyer, F Tonelli

Poster Number: P2
Mechanical regulation of chemical signalling in the developing *Xenopus* brain
EK Pillai, K Franze

Poster Number: P3
Asymmetric cell division during angiogenesis
HE Lovegrove, G Costa, SP Herbert

Poster Number: P4
Investigating Mitotic Nuclear Dynamics of Pseudo-Stratified Epithelia in Drosophila melanogaster
NJ Kirkland, Y Mao, E Paluch

Poster Number: P5
PIERCE1 mediates left-right patterning through ciliary motility
H Farley, J Keynton, J Thompson, D Asante, H Hilton, C Esapa, P Lackie, J Lucas, D Norris

Poster Number: P6
Towards deciphering the molecular mechanism regulating Wnt cytoneme formation
S Scholpp, B Mattes, L Brunt

Poster Number: P7
Investigating the co-ordinated transcriptional networks regulating myogenesis
C McQueen, R J White, M E Pownall

Poster Number: P8
Apical and basal matrix remodelling control epithelial morphogenesis
MC Diaz de la Loza, RP Ray, PS Ganguly, S Alt, JR Davis, A Hoppe, N Tapon, G Salbreux, BJ Thompson

Poster Number: P9
Airborne particulate matter from Jeddah induces severe cardiovascular defects in chick embryo
MM Abu-Elmagd, AM Abuzenadah, MH Al-Qahtani

Poster Number: P10
Frizzled-10 mediates Wnt1 induced neurogenesis in the developing spinal cord
A F Alrefaei, A Munsterberg, G Wheeler

Poster Number: P11
Inter-dependent apical microtubule and actin dynamics orchestrate centrosome retention and neuronal delamination
I Kasioulis, RM Das, KG Storey

Poster Number: P12
Organizers in Development: Is Hensen's node a stem cell niche?
T Solovieva, CD Stern

Poster Number: P13
Cdc42 regulation during epithelial cell polarity establishment
KR Massey, MT Pressé, F Pichaud

Poster Number: P14
Spatio-temporal regulation of cerebellar granule cell neurogenesis
V Rook, C Brennan, A Stollewerk, R Wingate, T Butts

Poster Number: P15
Physical mechanisms of epiblast and primitive endoderm segregation in the mouse embryo
AY Yanagida, SA Achouri, CR Revell, GS Stirparo, DC Cassani, EP Paluch, KC Chalut, JN Nichols

Poster Number: P16
Modulation of Rok membrane dissociation rate by Crb/aPKC triggers Rok planar polarisation during morphogenesis
CM Sidor, TJ Stevens, J Boulanger, MJ Bailey, KE Prehoda, TJ Harris, K Roeper

Poster Number: P17
Integrin signaling in epiblast morphogenesis and cell survival
MA Mole, ABS Weberling, M Zernicka-Goetz

Poster Number: P18
The ECM protein Agrin localizes to the developing epicardium and is essential for coronary vessel formation
X Sun, E Bassat, E Tzahor, PR Riley

Poster Number: P19
Regulation of Yorkie by Mask in *Drosophila*
N Borreguero-Muñoz, GC Fletcher, CM Sidor, A Elbediwy, BJ Thompson

Poster Number: P20
Sema3A acts as a repellent for the medial longitudinal fascicle in the embryonic chicken brain
AS Caulfield, KL Riley, FR Schubert

Poster Number: P21
Role of *Pbx1* heterogeneity in mesoderm specification
V Castilglioni, L Mariani, X Guo, E Ferretti

Poster Number: P22
Oct4 regulates the embryonic axis and coordinates exit from pluripotency and germ layer specification in the mouse embryo
C Mulas, G Chia, KA Jones, GG Stirparo, J Nichols

Poster Number: P23
Making the first cell fate decision in the early mouse embryo: polarity matters in space and time
M Zhu, M Zernicka-Goetz

Poster Number: P24
The role of the primary cilium during neuron repolarisation in the developing CNS
GC Toro-Tapia, RM Das

Poster Number: P25
Cellular mechanisms of sensory organ segregation in the embryonic inner ear
ZC Chen, N Daudet

Poster Number: P26
XMAP215, Eb1 and tau jointly regulate microtubule polymerisation and organisation in axons
I Hahn, A Voelzmann, J Fuelle, J Parkin, N Sánchez-Soriano, **A Prokop**

Poster Number: P27
The role of Polycomb-group complex PRC2 in human pancreatic cell differentiation
C Fabian, F Soares, K Jhaveri, P Rugg-Gunn

Poster Number: P28
Radially-polarised cell behaviours drive tube budding from an epithelium
YE Sanchez-Corrales, GB Blanchard, K Röper

Poster Number: P29
The role of mRNA capping in ESCs and early embryo development
J Silva, O Suska, V Cowling

Poster Number: P30
Netrins guide axons of the tract of the posterior commissure by repulsion during early embryonic brain development
M Ware, A Caulfield, FR Schubert

Poster Number: P31
Mud is required for axon guidance at the midline of the Drosophila central nervous system
S Gajendra, S Alsbury, S Cate, T H Chung, K Mitchell, **G Tear**

Poster Number: P32
The mouse hematopoietic stem cell lineage fails to develop beyond the pro-HSC stage in the absence of blood flow
E Azzoni, V Frontera, J Harman, SEJ Jacobsen, MFTR De Bruijn

Poster Number: P33
Does differentiation of the first cell lineages in *in vitro* cultured preimplantation rabbit embryo depend on developmental dynamics?
A Stachowiak, J Chołoniewski, A Duszewska, P Gręda, A Piliszek, JA Modliński

Poster Number: P34
Lineage segregation, X chromosome dynamics and regulation of pluripotency during pig embryogenesis revealed by single cell RNA-seq.
P Ramos-Ibeas, F Sang, S Withey, W Tang, Q Zhu, D Klisch, M Loose, A Surani, **R Alberio**

Poster Number: P35
Chicken primordial germ cells require CXCR4 and c-Kit signalling for directed vascular migration and colonisation of the chick embryonic gonads
A Idoko-Akoh, L Taylor, HM Sang, MJ McGrew

Poster Number: P36
Polo kinase is recruited to the mitotic pericentriolar material by Spd-2 to drive centrosome maturation in flies
I Alvarez Rodrigo, L Gartenmann, Z Novak, JW Raff

Poster Number: P37
Klf family genes expression in preimplantation rabbit embryos
K Filimonow, D Winiarczyk, A Piliszek

Poster Number: P38
Identification and characterisation of molecular networks driving mesoderm differentiation
L Mariani, X Guo, Q Wang, K Schachter, E Ferretti

Poster Number: P39
The mirtron miR-1010 regulates the nAcRß2 to ensure synaptic homeostasis in *Drosophila*
C Amourda, TE Saunders

Poster Number: P40
Using fluorescence lifetime imaging of NAD(P)H and live confocal imaging of mitochondrial membrane potential to elucidate the developmental origins of cell metabolism in inner ear sensory epithelia
TS Blacker, JE Gale, **ZF Mann**

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Development of the cardiac lymphatic system in the adult zebrafish and its role in homeostasis and repair
MRM Harrison, X Feng, S Schulte-Merker, C Lien

Poster Number: P194
Inflammatory cytokine IL-1β inhibits tendon formation by equine adult and fetal tenocytes, but ESC-derived tenocytes are protected
A McClellan, R Evans, S Kan, F Atkinson, C Holland, D Guest

Poster Number: P195
Generation of a reporter cell line to identify determinants of cortical interneuron fate
MCS Cruz Santos, ML Li

Poster Number: P196
Mapping the cellular dynamics of liver regeneration using targeted photoactivatable cell ablation
CSL Bailey, EA Ober

Poster Number: P197
Probing the skeletal stem cell niche through functional investigation of Prx1 expressing cells
S Pretorius, S Roberts, M Logan

Poster Number: P198
Alternative splicing control over naïve and primed pluripotency throughout mammalian embryo development
V Rodriguez-Vaello, C Wyatt, B Pernaute, J Nichols, M Irimia

Poster Number: P199
Regulation of the proliferation of neural stem cells in the adult hippocampus by Shh signalling
MA Ortiz, N Urban, S Vaga, F Guillemot

Poster Number: P200
Mechanisms of Selective Advantage in Cultures of Human Pluripotent Stem Cells
CJ Price, I Barbaric

Poster Number: P201
Defining pluripotency in 3D: from embryonic stem cell identity to morphogenesis
MN Shahbazi, A Scialdone, N Skorupska, A Weberling, G Recher, M Zhu, A Jedrusik, LG Devito, L Noli, IC Macaulay, C Buecker, Y Khalaf, D Ilic, T Voet, JC Marioni, M Zernicka-Goetz

Poster Number: P202
Reprogramming pancreatic ductal organoids into insulin-producing β-cells
R Azzarelli, S Rulands, S Nestorowa, B Gottgens, M Huch, BD Simons, A Philpott

Poster Number: P203
Tissue Mechanics Partition the Stem Zones Fuelling Axial Elongation
T R Wood, A Kyrsting, J Stegmaier, I Kucinski, C F Kaminski, R Mikut, **O Voiculescu**

Poster Number: P204
Identification of SIRT1 activation-mediated pancreatic β-cell regeneration and function as a therapeutic potential for diabetes
SY Wu, PS Leung

Poster Number: P205
Capturing formative pluripotency
M Kinoshita, A Smith

Poster Number: P206
How Do Stem Cells Find Thier Niche?
SJ Habib, S Junyent, C Garcin, I Bordeu Weldt, TJ Trieu, J Szczerkowski, G Preissner

Poster Number: P207
Antioxidant role of lipid droplets in the neural stem cell niche of *Drosophila*
E Islimye, AP Bailey, AP Gould

Poster Number: P208
Determining the Metabolic Underpinnings of Totipotency
RA Bone, AR Riviero, SM Morgani, JM Brickman

Poster Number: P209
Oct4 Coordinately Regulates Cell Cycle Determinants to Promote Embryonic Stem Cell Fitness
M Lowndes, H Peradziryi, WB Hamilton, E Morganti, ML Nielsen, JM Brickman

Poster Number: P210
A single-cell screening approach to brain tumour initiation
LR Diaz, J Gil-Ranedo, K Jaworek, J Marques, E Costa, T Bossing, CS Barros

Poster Number: P211
Monitoring the origin and progression of neural stem cell (NSC) derived tumours using a Drosophila model
E Zacharioudaki, J Falo-Sanjuan, SJ Bray

Poster Number: P212
Whole organ liver architecture and homeostasis in adult zebrafish
EM Ambrosio, EA Ober

Poster Number: P213
Investigating the role of a novel Nanog interacting partner in mESCs self-renewal
M Vojtek, NP Mullin, I Chambers

Poster Number: P214
A robust and dynamic macrophage transcriptional response after injury is dependent upon the local environment during zebrafish heart regeneration
FC Simoes, A Kenyon, D Gavriouchkina, M Weinberger, E Masmanian, T Sauka-Spengler, P Riley

Poster Number: P215
Isolation of skeletal stem cells and progenitors from embryonic limb cartilage
LV Verbeeck, PT Tylzanowski, LG Geris, FL Luyten

Poster Number: P216
Deciphering integrin adhesion and signalling in *Drosophila* intestinal stem cells
JG Bohere, G Kolahgar

Poster Number: P217
Epigenetic and genetic effects of gender on reprogramming and Pluripotency
V Pasque

Poster Number: P218
Initiation and interpretation of transcription factor dynamics during embryonic neurogenesis
J Kursawe, C Manning, V Biga, N Papalopulu

Poster Number: P219
WNT signalling maintains ductal progenitor cells in adult salivary glands
AA Ahmed, IM Miletich

Poster Number: P220
The effect of hyperglycaemia on expression of let-7 microRNAs during macrophage differentiation and polarisation in tissue regeneration
I Salman, MR Ronshaugen, KA Mace

Poster Number: P221
Implementation of the three body axes and axial extension ex vivo in Gastruloids
DA Turner, N Moris, L Beccari, M Girgin, P Baillie-Johnson, A-C Cossy, MP Lutolf, D Duboule, A Martinez Arias

Poster Number: P222
Regulated mRNA stability of the proto-oncogene, *myc*, by the RNA binding protein Imp determines neural stem cell size in the developing *Drosophila* brain
TJ Samuels, I Davis

Poster Number: P223
Developmental transition from naïve pluripotency to lineage specification
M Rostovskaya, AG Smith

Poster Number: P270
Modelling MAPK pathway overactivation in the mouse brain
JE Cooper, YF Li, JC Pickles, S Haston, D Hargrave, TS Jacques, JP Martinez-Barbera

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The role of cellular senescence and its associated secretome in paediatric Adamantinomatous Craniopharyngioma (ACP)
S Manshaei, S Haston, JM Gonzalez-Melijem, J Gil, JP Martinez-Barbera

Tissue and Organ Development

Poster Number: P224
Signalling and metabolic mechanisms for selective organ growth during starvation
A Sawala, AP Gould

Poster Number: P225
A role for *PRDM1* in cell fate decisions in the ectoderm
RS Prajapati, M Hinze, A Streit

Poster Number: P226
Biomechanics of neural tube formation in mammals
GL Galea, ND Greene, **AJ Copp**

Poster Number: P227
The role of Sox9 in the initial stages of salivary gland development and regeneration
L Chatzeli, M Gaete, AS Tucker

Poster Number: P228
Investigating the role of macrophages in the development of the cardiac lymphatic vasculature
JM Vieira, TJ Cahill, X Sun, CVD Campo, S Norman, AM Lord, SE Jacobsen, PR Riley

Poster Number: P229
Foxp1 controls neural stem cell maintenance and demarcates the early phase of cortical neurogenesis
CA Pearson, D Moore, H Tucker, Hu H, A Miquelajauregui Graf, BG Novitch

Poster Number: P230
Working towards cell therapies for diabetes: identifying conditions to better induce and expand pancreatic endocrine progenitors in vitro
CA Plumb, GM Morrison, SM Pollard

Poster Number: P231
Regulation of neural tube growth by the morphogens Shh and BMP
K Kuzmicz, A Kicheva

Poster Number: P232
Epithelial cell rearrangement dynamics during mouse neural tube development
L Bocanegra, A Kicheva

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Poster Number: P234
ABSTRACT WITHDRAWN

Poster Number: P235
Bridging structure and function in multicellular organ design using network science
GW Bassel, MDB Jackson, H Xu, S Duran-Nebreda, P Stamm

Poster Number: P236
The role of Stem Cells in Tooth Root Development
R Lav, A.S. Tucker

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Apnoia, a new Crumbs regulator for proper breathing in flies
K Skouloudaki, DK Papadopoulos, E Knust

Poster Number: P238
The Development of Olfactory Ensheathing Cells from the Neural Crest
SN Perera, R Williams, D Buehler, T Sauka-Spengler, M Southard-Smith, CVH Baker

Poster Number: P239
Selective Filopodia Adhesion Ensures Robust Cell Matching in the *Drosophila* Heart
S Zhang, C Amourda, D Garfield, **TE Saunders**

Poster Number: P240
Maternal transmission of an *Igf2r* domain 11: IGF2 binding mutant (*Igf2r*I^{1565A}) results in partial lethality, overgrowth and intestinal adenoma progression
J Hughes, M Surakhy, S Can, M Ducker, F Szele, C Bühnemann, E Carter, M Crump, S Frago, **AB Hassan**

Poster Number: P241
Mechanical strain regulates the Hippo pathway in *Drosophila*
GC Fletcher, MC Diaz-de-la-Loza, N Borreguero-Munoz, M Holder, M Aguilar-Aragon, BJ Thompson

Poster Number: P242
Tympanic membrane development: a tale of two parts
M Mozaffari, AS Tucker

Poster Number: P243
Exploring the role of *Flk-1/Kdr* in mesodermal derivatives of the post-gastrulation mouse embryo
A Binagui-Casas, D Simpson, A Salzano, T Chandra, V Wilson, A Medvinsky

Poster Number: P244
Concentration, DNA-binding kinetics and variability of Zelda underlie the timing of Zygotic Genome Activation in Drosophila
DK Papadopoulos, A Klosin, K Skouloudaki, B Vellutini, A Hyman, P Tomancak

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3D Analysis of Mouse Embryo by X-ray Computed Tomography
T Zikmund, M Tesarova, M Buchtova, M Novotna, M Kavkova, M Kaucka, G Comai, E Heude, S Hankeova, E Andersson, S Tajbakhsh, I Adameyko, J Kaiser

Poster Number: P246
Notch signalling regulates the emergence of thymic epithelial lineage required for T-cell tolerance induction
D Liu, Al Kousa, KE O'Neill, F Guillemot, SR Tomlinson, U Koch, F Radtke, CC Blackburn

Poster Number: P247
Activity-dependent regulation of interneuron survival sculpts cortical networks
FK Wong, K Bercsenyi, V Sreenivasan, A Portalés, M Fernández, O Marín

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Epithelial apical vertices are important for morphogenesis
TF Finegan, **NH Hervieux**, AF Fletcher, GB Blanchard, BS Sanson

Poster Number: P249
Building and breaking epithelial integrity in the neural tube: an optogenetic approach
CE Buckley

Poster Number: P250
Crosstalk between *Lgr5* positive epithelial cells and mesenchymal FGF10 is essential for CVP development
S Zhang, HS Choi, JM Lee, HS Jung

Poster Number: P251
Nicotinamide adenine dinucleotide phosphate (NADPH) oxidases 1 (NOX1) and NOX4 expression during mouse lung and liver development
KMB Weerasekara Mudiyanselage, HY Kim, HS Jung

Poster Number: P252
Neuromesodermal Progenitors are Conserved Source of Spinal Cord with Divergent Growth Dynamics
A Attardi, T Fulton, M Florescu, G Shah, L Muresan, J Huisken, A van Oudenaarden, **B Steventon**

Poster Number: P253
Understanding lethality throughout development: the Sanger high throughput recessive lethality screen
E Siragher, C Mazzeo, C Tudor, M Dabrowska, R McLaren, E Tuck, C Lelliott, T Mohun, D Adams, **A Galli**

Poster Number: P254
High heterotypic interfacial tension is the motor for cell sorting at embryonic boundaries
F Fagotto, L Canty, E Zarour, L Kashkooli, P Francois

Poster Number: P255
Understanding congenital disease through investigations of human embryonic and fetal development
D Gerrelli, B Crespo Lopez, N Moreno, S Lisgo, SJ Lindsay, AJ Copp

Poster Number: P256
Analysis of abnormal embryo morphology using 3D imaging techniques
J Cleak, SJ Johnson, Z Szoke-Kovacs, N Horner, MLC Husbandry Team, S Wells, H Westerberg, L Teboul

Poster Number: P257
Hepatic progenitor cell heterogeneity and their potential during liver differentiation
IA Unterweger, EA Ober

Poster Number: P258
Development of morphology annotation in the embryonic phenotyping pipeline used by the International Mouse Phenotyping Consortium
SJ Johnson, N Horner, J Cleak, Z Szoke-Kovacs, MLC Husbandry Team, S Wells, H Westerberg, L Teboul

Poster Number: P259
Novel insights into the regulation of dermal white adipose tissue: Defining dermal progenitor cell fate using a three-dimensional spheroid model
AC Gilmore, JD Glover, DJ Headon, CAB Jahoda

Poster Number: P260
Quantitative modelling and analysis of epithelial morphogenesis
J Kursawe, RE Baker, **AG Fletcher**

Poster Number: P261
Hair follicle dermal condensation forms via Fgf20 primed cell cycle exit, cell motility, and aggregation
LC Biggs, **OJM Mäkelä**, SM Myllymäki, R Das Roy, K Närhi, J Pispa, T Mustonen, ML Mikkola

Poster Number: P262
Notch signalling: its implication in phenotypical heterogeneity of Holoprosencephaly
H Hamdi-Rozé, M Ware, A Rizzo, H Guyodo, V David, **V Dupé**

Poster Number: P263
Modelling Kallmann Syndrome in the zebrafish: crucial roles for *Fgf* signalling and *anosmin* in olfactory development and GnRH neuron migration and evidence for a common signaling pathway
I Mason, S Cadman, L Iyengar, G Philp, P Bouloux

Poster Number: P264
Adprhl1 action in the developing vertebrate heart:- Comparison of *Adprhl1* knockout in the frog and mouse
SJ Smith, N Towers, TJ Mohun

Poster Number: P265
Conditional deletion of Wt1 in pleuroperitoneal folds leads to congenital diaphragmatic hernias
L Cleal, N Hastie, **YY Chau**

Poster Number: P266
Gestational exposure to dioxin as an environmental risk factor for neurodevelopmental disease
TE Gileadi, Z Hore, AK Lundebye, C Hogstrand, B Stockinger, C Fernandes, MA Basson

Poster Number: P267
Axial emergence through self-organization in Gastruloids, controlled aggregates of embryonic stem cells
V Trivedi, A Martinez-Arias

Poster Number: P268
Spatially restricted regulation of cell competition by the cytokine Spätzle
L Alpar, C Bergantinos, L A Johnston

Sunday 15 April, 2018
Plenary Lecture
OC1.05

PL01 15:00 – 15:30
Mechanical Tension and Epithelial Mesenchymal Transitions in Drosophila
M Weng, **EF Wieschaus**

HHMI Molecular Biology, Princeton University, Princeton University, USA

Although the Snail transcriptional factor was initially identified due to its role in mesodermal determination in Drosophila, subsequent studies have shown it to be the major regulator of epithelial-mesenchymal transitions (=EMT) in both vertebrates and invertebrates. In Drosophila mesoderm, we find that Snail expression is necessary and sufficient to down-regulate levels of maternally supplied E-Cadherin in junctions without affecting other E-Cadherin pools in the cell, and that that this junction specific loss is associated with down-regulation of the polarity protein Par3/Bazooka (Baz). The decrease in E-Cad and Baz levels begins during mid-cellularization but at the onset of gastrulation, however, loss of E-Cad and disassembly of mesodermal junctions is transiently blocked. This block is associated with an increase in myosin driven tension on junctions during the cell shape changes that internalize the mesoderm. Once the mesoderm has been fully internalized, this tension is released and the epithelial mesenchymal transition occurs.

Sunday 15 April, 2018
Plenary Lecture
OC1.05

PL02 15:30 – 16:00
Morphogenesis: from whole organism integration to biophysical principles
M Leptin

EMBO, Heidelberg, Germany

Now that the highly successful reductionist approaches applied by developmental biologist over the last decades have nearly solved many of the genetic cascades from cell fate determination to the players in the cell that mediate the physical changes of morphogenesis, it is time for a more integrated understanding of development. Using gastrulation in Drosophila, we have on the one hand returned to a more encompassing view to determine how cell populations across the entire embryo cooperate during morphogenesis. Physical manipulations and force measurements are beginning to give us insights into the logic of the mechanical forces and interactions in the embryo. At the same time, we drive reductionism even further and to understand the behavior of molecules and the forces they exert to affect cell shape. We have developed simulations and a theoretical model to study the role of the cytoskeleton and understand the rules by which it directs morphogenesis.

Sunday 15 April
Beddington medal talk
OC1.05

PL03 16:45 – 17:15
Cell-specific programs regulate inhibitory synapse specificity
E Favuzzi

Harvard Medical School, Cambridge, USA

Understanding how neuronal connections are established and organized in functional networks during development is critical to understand brain function. In the mammalian cortex, GABAergic interneurons are characterized by a remarkable diversity of types and connectivity patterns. As such, they are uniquely suited to orchestrate functionally relevant circuit-specific roles and critically shape cortical function. Yet, how inhibitory circuit specificity is achieved during development is largely unknown. We revealed the transcriptional dynamics of different cortical interneurons during brain wiring and identified subtype-enriched synaptic molecules. Moreover, we showed that the connectivity of different interneurons relies on the cell-specific expression of such synaptic genes. Altogether, our results demonstrate that highly selective molecular programs emerging during development in cortical interneurons support their early wiring and underlie inhibitory circuit specificity.

Sunday 15 April, 2018
Plenary Lecture
OC1.05

PL04 17:15 – 17:45
Gene regulatory and signaling events in neural crest development
M Bronner

California Institute of Technology, Pasadena, USA

The neural crest is a population of multipotent, migratory stem/progenitor cells in vertebrate embryos. These cells migrate from the neural tube along defined pathways, populate numerous sites and differentiate into diverse cells types including melanocytes, sensory and autonomic neurons, and the craniofacial skeleton. However, neural crest populations differ along the neural axis; e.g. only cranial neural crest cells give rise to cartilage and bone of the face, and only cardiac/vagal neural crest cells contribute to the heart and enteric nervous system. We have performed transcriptome analysis of these different neural crest populations to identify gene regulatory networks (GRNs) that confer axial level specific identify to these different neural crest cell populations. By characterizing the function of transcriptional and signaling components, we aim to understand the steps that define the neural crest from the time of induction at the neural plate border to their differentiation into diverse cell types.

Sunday 15 April, 2018
The History and Future of Developmental Biology
19.00 - 21.00
OC1.05

H01
The value of history: history as a resource for the future
T Horder

University of Oxford, Oxford, UK

In any science priorities evolve. A dominant trend in developmental biology has been the selection of a few model organisms and a concentration of interest on specific organ systems; the modes of investigation have evolved as new techniques became available. The result is ever-increasing specialization, technically and conceptually. Genetics, molecular biology, phylogenesis and evolution theory have become increasingly specialized provinces. No one person can adequately cover them all. Embryogenesis is inherently an integrated process and a very complex one: are our present dispersed and specialialised perspectives adequate or have gaps in our understanding widened?

Perspectives on embryogenesis in earlier stages of the historical development of the subject were, by comparison, broader. A comprehensive variety of species were documented in great detail. Earlier modes of analysis not addressable by modern techniques have become neglected. Access to these rich and vast resources requires historical awareness. Through examples I will show how earlier perspectives can reorientate current priorities and, by reminding us about developmental phenomena still in need to explanation, potentially lead to a more coordinated and integrated understanding.

H02
Inclusion and exclusion in the history of developmental biology
N Hopwood

University of Cambridge, Cambridge, UK

Scientific disciplines are made, not found. They embody commitments to particular questions and approaches, audiences and scopes; they exclude as well as include. The talk will present ‘developmental biology’, the field made after World War II, as in these respects a typical discipline (not an all-encompassing term for research on development). To clarify the preconditions for developmental biology, and to provide some comparisons, I shall also review various research programmes that were launched in the late nineteenth century. Of these, developmental biologists tend to know much about experimental embryology, but less about attempts to revive comparative evolutionary studies or the establishment of human embryology as a specialized field. Contrasting developmental biology with these and other kinds of embryo research will offer resources, and perhaps even strategies, for thinking about renewal today, when not unusually a period of soul-searching has followed decades of great success.

H03
Panel Discussion on the future of Developmental Biology – chaired by Claudio Stern

We strongly encourage everyone to attend this session. There will be the opportunity to contribute to this important discussion about the future of our field.

Panelists include: Jonathan Slack, James Briscoe and Patrick Lemaire

Roundtable Discussions
PhD students and postdocs are encouraged to meet and discuss the future of developmental biology with PI hosts including Janet Rossant, Ben Steventon, Jordan Raff, Patrick Lemaire, Alistair McGregor, James Briscoe, Megan Davey, Ottoline Leyser, Peter Holland, Marianne Bronner, Elia Benito-Gutierrez, Karen Sears, Sean Carroll, Olivier Pourquie, Abigail Tucker and Elly Tanaka.

Monday 16 April, 2018
Plenary Lecture
OC1.05

PL05 09:00 – 09:30
Confessions of an ex-developmental biologist
M Freeman

Dunn School of Pathology, University of Oxford, Oxford, UK

Much of developmental biology is about cells making choices. Most of those choices are determined by signals between cells. Somewhere along the way of my work as a Drosophila developmental geneticist, I realised I was becoming more interested in the machinery of signalling – wanting to understand the language of development in molecular detail. As geneticists and biochemists, we tend to represent signalling pathways as diagrams where arrows connect molecular components. Yet signalling doesn't occur in abstract space but within and between cells, so the cell biology of they systems needs to be considered. For these reasons our work is increasingly focused on the cell biology of proteins of the rhomboid-like superfamily, mainly in mammals. Overall, our work emphasises the need to understand intercellular communication in the context of the cells that send and receive the signals.

Monday 16 April, 2018
Tissue and Organ Development
09:35 – 13:10
OC1.05

S01 09:35 – 10:05
How morphogenesis directs cell fate
H Semb

NNF center for Stem Cell Biology, University of Copenhagen, Copenhagen, Denmark

Changes in tissue architecture contribute to transient and sustained niches that govern the behavior of stem and progenitor cells. While data on the extrinsic regulation of the decision to self-renew or differentiate is emerging, less is known about the environmental cues that direct multipotent progenitors into their various lineages. The pancreas originates from two epithelial foregut evaginations that gradually transform into a complex tubular epithelial network. Within each branch the trunk domain consists of bipotent progenitors (biPPs) that give rise to both duct and endocrine lineages, whereas the tips give rise to acinar cells. While Notch signaling is required for biPP maintenance, sustained and reduced Notch activity leads to birth of the duct and endocrine lineages, respectively. Identification of the extracellular cues and the underlying cellular and molecular mechanisms behind the choice of biPPs to differentiate into either the duct or endocrine lineage will be discussed.

O1 10:05 – 10:20
Poster Number: P224
Signalling and metabolic mechanisms for selective organ growth during starvation
A Sawala, AP Gould

Physiology & Metabolism Lab, The Francis Crick Institute, London, UK

The growth of developing animals is tightly coordinated with nutrient availability. Some organs, however, are able to grow during starvation because their growth is spared at the expense of other tissues. Here we investigate the control of growth sparing in the wing imaginal disc of *Drosophila*. We find that, surprisingly, the insulin receptor is required for wing growth during starvation and this receptor is activated by Ilp6 secreted from fasted adipose tissue. This indicates that starvation switches off the insulin-like peptides that promote the growth of all organs but switches on Ilp6, which selectively stimulates the growth of spared tissues. Furthermore, we show that wing disc sparing relies upon glycogenolysis, lipolysis, autophagy and, most critically, the transcription factor Foxo in non-spared adipose tissue. We propose a dual role for Foxo in nutrient mobilization and Ilp6 production to ensure a balance between nutrient supply and growth factors during starvation.

O2 10:20 – 10:35
Poster Number: P225
A role for PRDM1 in cell fate decisions in the ectoderm
RS Prajapati, M Hinze, A Streit

Craniofacial Development and Stem Cell Biology, Dental Institute, King's College London, London, UK

The pre-neural ectoderm gives rise to the neural plate, the neural crest, and the pre-placodal ectoderm, which ultimately form the central and peripheral nervous system. Here we show that the transcription factor *Prdm1* is expressed in the pre-neural ectoderm, but is lost as neural, neural crest and placode-specific genes are initiated. Loss-of-function reveals that Prdm1 is required for all three fates, but normally inhibits pluripotency genes. In contrast, misexpression of Sox2 (neural), Foxd3 (crest), or Six1 (placodal) causes *Prdm1* reduction suggesting that these factors interact in a negative feedback loop. We also show that Prdm1 binds to the promoters of neural, neural crest and placodal genes and mediates the removal of repressive histone marks by recruiting histone demethylases. Our model suggests that Prdm1 facilitates fate decisions in the early nervous system by controlling histone modifications at the promoter regions of key fate determinants.

S02 10:35 – 11.:05
Regulation of homeostasis in mammalian epidermis
FM Watt

CSCRM, King's College London, London, UK

Mammalian epidermis is renewed throughout adult life via a stem cell compartment. In recent years several distinct stem cell populations have been identified in adult mouse epidermis and Wnt/beta-catenin signalling has emerged as a key pathway that regulates stem cell self-renewal and lineage selection. Nevertheless, new data suggest a complexity in the pathways controlling epidermal homeostasis that has not been appreciated previously. It is now evident that the differentiation trajectory followed by cells that leave the stem cell compartment is not obligatorily unidirectional: during wound healing differentiated cells can undergo dedifferentiation to become stem cells. Furthermore, although the transcriptional response of keratinocytes that receive a Wnt signal is well characterised, keratinocytes in close proximity to the Wnt-receiving cell are also co-opted to undergo a change in cell fate. In my presentation I will integrate new and published observations into a working model of epidermal homeostasis.

S03 11:40 – 12:10
Mouse gastrulation: The interplay of transcription and signalling activity for germ layer formation
PPL Tam[1,2]

[1]Embryology Unit, Children's Medical Research Institute, Westmead, Australia; [2]School of Medical Sciences, Sydney Medical School, University of Sydney, Sydney, Australia

Gastrulation is a critical milestone of embryogenesis at which the multipotent embryonic cells are allocated to the progenitors of tissue lineages in the germ layers. Through the inductive modulation of the functional output of genome activity, the concerted execution of developmental program empowers tissue morphogenesis and the building of body parts. Analysis of the developmental-spatial transcriptome of the post-implantation mouse embryo revealed the transition from cellular pluripotency to lineage specification during gastrulation and identified the developmental correlate of the epiblast cells fates with region/lineage-specific transcriptional profile and signalling activity. In the gastrulating embryo, spatially delimited agonistic and antagonistic signalling activity in the germ layers underpins the pattering of embryonic tissue. The elucidation of the molecular network activity, enabled by population and single-cell analytics, has provided insights into the choreography of developmental process that underpins lineage allocation, tissue differentiation and morphogenesis.

O3 12:10 – 12:25
Poster Number: P1
A chemical genetics approach to study atypical protein kinase C (aPKC) function in Drosophila
J Januschke[1], M Hannaford[1], N Loyer[1], F Tonelli[2]

[1]Cell & Developmental Biology, University of Dundee, Dundee, UK; [2]MRC PPU, University of Dundee, Dundee, UK

The Par protein complex is a major regulator of cell polarity across species. The Par proteins and aPKC in particular are required for asymmetric stem cell division in the developing fly brain. However, these cells divide rapidly posing the problem to differentiate between immediate and further downstream consequences of loss of gene functions using standard genetics. Targeted inactivation of kinases, like aPKC, can be achieved by chemical genetics: the kinase is engineered to become sensitive to an ATP competitive inhibitor. Using genome editing we engineered an inhibitor sensitive aPKC mutant ($aPKC^{AS4}$) in *Drosophila*. In the absence of the inhibitor, that does not have an effect on wild-type cells, $apkc^{AS4}$ homozygous mutant flies are indistinguishable from wild type, but addition of the inhibitor reproduces known phenotypes of loss of aPKC. I will present our findings obtained using quantitative live cell imaging and targeted inhibition of aPKC on neural stem cells and epithelia.

S04 12:25 – 12:55
Subepithelial Foxl1-positive telocytes are the source of Wnts that support intestinal crypts
KH Kaestner

Genetics, University of Pennsylvania, Philadelphia, USA

Stem cell niches provide essential signals and growth factors to sustain proliferation and self-renewal of stem cells in regenerative organs such as the intestine. Here, we identify subepithelial telocytes as an obligatory source of Wnt proteins, without which intestinal stem cells cannot be maintained. Telocytes are large but rare mesenchymal cells that are marked by Foxl1 and expression and form a subepithelial plexus that extends from the stomach to the colon. While supporting the entire epithelium, Foxl1$^+$ telocytes compartmentalize the production of Wnt ligands and inhibitors to enable localized pathway activation. Conditional gene ablation of Porcupine (Porcn), which is required for functional maturation of all Wnt proteins, in Foxl1$^+$ telocytes causes cessation of Wnt signaling to intestinal crypts, loss of stem cell proliferation, and death of mutant mice within four days of tamoxifen treatment. Thus, Foxl1$^+$ telocytes are the critical source of niche signals to intestinal stem cells.

O4 12:55 – 13:10
Poster Number: P226
Biomechanics of neural tube formation in mammals
GL Galea, ND Greene, **AJ Copp**

Institute of Child Health, University College London, London, UK

Mammalian neurulation requires the generation and transmission of mechanical force to enable neural tube closure. Using laser-ablation of living mouse embryos, and mosaic reporter-gene expression, we created strain-maps around the active spinal closure site. The entire caudal region is biomechanically coupled, via rostro-caudal F-actin cables that extend along the neural fold tips from the ‘zippering point’. These cables transmit force for closure that is generated by medio-lateral F-actin/myosin profiles within the flat neuroepithelium. Late in closure, the F-actin cables come to encircle the closing region (neuropore) and a new closure point arises at the caudal-most extremity of the neuropore. Laser ablation shows that the new closure point diminishes stress experienced by the main zippering point, providing ‘stress accommodation’ that facilitates final closure. Genetic (e.g. Vangl2, Zic2 mutations) and non-genetic (e.g. valproic acid) influences that cause spina bifida disrupt specific elements of this biomechanical network.

Monday 16 April, 2018
Developmental Gene Regulatory Networks
09:35 – 13:10
OC0.03

S05 09:35 – 10:05
The gene regulatory logic for reading the sonic hedgehog gradient in the vertebrate neural tube
J Briscoe

The Francis Crick Institute, London, UK

Neuronal subtype specification in the vertebrate neural tube is one of the best-studied examples of embryonic pattern formation. Distinct neuronal subtypes are generated in a precise spatial order from progenitor cells according to their location along the anterior-posterior and dorsal-ventral axes. Underpinning this organization is a complex network of extrinsic and intrinsic factors. Secreted proteins, including Sonic Hedgehog (Shh) and BMP family members act in a graded fashion to organize the pattern of neurogenesis. This is a dynamic process in which increasing concentrations and durations of exposure to the signals generate neurons with distinct. Underpinning this process is a transcription network controlled by the patterning signals that plays an essential role in determining the graded response of cells. The accurate patterning of the neural tube and the specification of neuronal subtypes at appropriate positions within the neural tube relies on the continuous processing and constant refinement of the cellular response to graded signaling inputs.

S06 10:05 – 10:35
Multiple Roles of the T-box gene, *Tbx6*
VE Papaioannou

Genetics and Development, Columbia University Medical Center, New York, USA

T-box transcription factors play many roles in embryonic development and are associated with developmental birth defects in humans. *Tbx6* is a T-box gene with a relatively simple expression pattern but with multiple roles in development including the determination of cell fate during gastrulation, differentiation of the somites and left-right body axis determination. In humans, mutations in *TBX6* have been implicated in dominant spondylocostal dysostosis. The talk will cover studies on this gene and the mechanisms of its action in producing these various phenotypes including new data on its role in left-right axis determination.

S07 10:35 – 11:05
The power of ONE: Immunology in the age of single cell genomics
I Amit

Weizmann Institute of Science, Israel

The immune system is a complex, dynamic and plastic network composed of various interacting cell types that are constantly sensing and responding to environmental cues. From very early on, the immunology field has invested great efforts and ingenuity to characterize the various immune cell types and elucidate their functions. However, accumulating evidence indicates that current technologies and classification schemes are limited in their ability to account for the functional heterogeneity of immune processes. Single cell genomics hold the potential to revolutionize the way we characterize complex immune cell assemblies and study their spatial organization, dynamics, clonal distribution, pathways, and crosstalk. This emerging field can greatly affect basic and translational research of the immune system. I will discuss how recent single cell genomic studies are changing our perspective of various immune related pathologies from cancer to neurodegeneration. Finally, I will consider recent and forthcoming technological and analytical advances in single cell genomics and their potential impact on the future of immunology research and immunotherapy.

S08 11:40 – 12:10
Functional insights into genome topology and enhancer function during embryonic development
E Furlong

EMBL, Heidelberg, Germany

Complex patterns of temporal and spatial gene expression are regulated by enhancers; *cis*-regulatory elements that recruit multiple transcription factors, leading to a very defined output of expression. Enhancers can be located in close proximity to, or at great distances from, their target gene. Our previous work indicates that embryonic enhancers are often in close proximity to their target promoters hours before the gene is expressed during embryogenesis, suggesting that pre-formed chromatin topologies may prime the system for rapid activation (when the enhancers presumably come in even closer proximity), at least within the rapidly developing *Drosophila* embryo.

To better understand the relationship between chromatin organization and transcriptional regulation, we are using genomics (Hi-C, Capture C), genetic deletions, and high-resolution imaging to determine when, and how, enhancer-promoter proximity is established during embryogenesis. Going back to earlier and earlier stages in embryogenesis, we have measured the distances of enhancer-promoter interactions in individual nuclei using quantitative FISH at multiple loci. In addition to examining the function of different trans factors, we are using CRISPR deletion, as well as more global rearrangements, to dissect the functional relationship between genome organisation and gene expression in *cis*. We have also uncovered new functions for enhancers themselves, indicating that these elements can have multiple roles in the regulation of developmental programs.

O5 12:10 – 12:25
Poster Number: P129
Genome-wide analysis of gene expression and chromatin architecture *in vivo* reveals intricate gene regulatory networks underlying cranial neural crest development

RM Williams[1], D Gavriouchkina[1], I Candido-Ferreira[1], E Repapi[2], U Senanayake[1], J Telenius[2], J Hughes[2], T Sauka-Spengler[1]

[1]Weatherall Institute of Molecular Medicine, Radcliffe Department of Medicin, University of Oxford, Oxford, UK; [2]Weatherall Institute of Molecular Medicine,Computational Biology Research G, University of Oxford, Oxford, UK

The neural crest (NC) is a multipotent embryonic population that gives rise to a wide range of derivatives in the vertebrate embryo. The process of NC formation is orchestrated by an intricate network of gene regulatory interactions, previously proposed as the NC gene regulatory network (NC-GRN). Here we decipher NC-GRN circuits genome-wide using chromatin and cis-regulatory profiling of the cranial NC cells. By conducting a comprehensive survey of their chromatin and transcriptional landscapes, we uncover accessibility dynamics and chromosome conformation thus identifying a full complement of active NC enhancers. Analysis of enhancer organisation genome-wide, together with a survey of their mediator complex occupancy and H327Ac modifications reveals a 'super-enhancer'-like signature of clustered elements controlling key NC regulators. The identified single-cell transcriptional signatures of cranial NC cells in combination with global enhancer profiling allows us to propose, for the first time, a high-resolution representation of the cranial NC GRN.

S09 12:25 – 12:55
Visualization of Transvection in Living Drosophila Embryos

B Lim[1], T Fukaya[2], T Heist[3], **M Levine**[3]
[1]Chemical Engineering, University of Pennsylvania, Philadelphia, USA; [2]Institute of Molcular and Cellular Biosciences, University of Tokyo, Tokyo, Japan; [3]Lewis-Sigler Institute and Department of Molecular Biology, Princeton University, Princeton, USA

Transcriptional enhancers switch genes on and off in response to a variety of intrinsic and external signals. We use the early Drosophila embryo as a model for visualizing gene activity in development. Traditional fixed tissue methods provided insights into the spatial control of gene expression. Recent live imaging methods reveal the occurrence of transcriptional bursts. A typical burst persists for a few minutes and produces tens of transcripts. Strong enhancers produce more freqent bursts than weak enhancers, but the size and duration of individual bursts remain constant. In order to visualize long-range enhancer-promoter interactions we established a transvection assay, whereby a shared enhancer on one allele regulates the expression of a linked reporter gene in trans on the other homolog. These studies are consistent with a hub and condensate model, whereby chromosomal loop domains serve as traps for the accumulation and coordinate release of multiple Pol II complexes.

O6 12:55 – 13:10
Poster Number: P130
Linking self-renewal and differentiation

T Knudsen[1], W Hamilton[1], A Nielsen[2], A Trusina[2], J Brickman[1]

[1]Center for Stem Cell Biology, University of Copenhagen, Copenhagen, Denmark; [2]Niels Bohs Institute, University of Copenhagen, Copenhagen, Denmark

Embryonic stem cells (ESCs) are supported by a network of transcription factors (TFs) known as the pluripotency network. While the population of ESCs that expresses these factors is closest to embryonic epiblast, expression *in vivo* indicates additional roles in lineage specification. Is there a role of specific pluripotency factors in lineages specification and how does this relate to their support of ESC self-renewal? Here we explore these questions with respect to the pluripotency TF Esrrb. Based on analysis of Esrrb's behavior in Nanog mutants, we suggest that it has two roles; to stimulate self-renewal while preserving competency for primitive endoderm differentiation. Thus, in the presence of Nanog, Esrrb inhibits differentiation and supports pluripotency, but in its absence, promotes differentiation. Moreover, Nanog and Esrrb ratio was found to be regulated by Fgf/ERK signaling, suggesting a model in which signaling modulates the relative stoichiometry of these two TFs to mediate lineage choice.

Monday 16 April, 2018
Mechanisms of Global Gene Regulation
14:30 – 18:00
OC1.05

S10 14:30 – 15:00
Hox genes and the hindbrain: A story in segments
HJ Parker, B DeKumar, LM Wiedemann, **R Krumlauf**

Krumlauf Group, Syowers Institute for Medical Research, Kansas City, MO, USA

The vertebrate hindbrain is a highly conserved co-ordination center of the CNS where regional diversity is achieved through a process of segmentation. The Hox family of transcription factors are coupled to this process and provide a molecular framework for specifying the unique identities of hindbrain segments. Analyses have provided significant insight into the gene regulatory networks and signaling cascades underlying the functional roles of the Hox family in patterning the hindbrain. This framework has enabled us to determine the degree to which the Hox hindbrain regulatory network is conserved during evolution. Analyses in mouse tissues and ES cell models have identified Hox target genes and uncovered direct regulatory cross-talk between the pluripotential and Hox-dependent networks. Retinoid signaling controls the maintenance of hemapopoetic stems cells through long-range regulation of multiple HoxB genes. These studies provide insight into molecular mechanisms and pathways that modulate the balance between states of stemness and differentiation.

O7 15:00 – 15:15
Poster Number: P111
Dissecting the upstream regulation of the GATA genes during heart development
C Telfer[1,2], F Simões[1,2], T Sauka-Spengler[1], P Riley[2], R Patient[1]

[1]Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, UK; [2]Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK

The cardiac GATA transcription factors (TFs) play vital roles in cardiogenesis. While their function as cardiac effectors has been well studied, precise molecular mechanisms driving their activity have yet to be parsed. Using ATAC-seq we identified putative enhancers, accessible during development and regeneration, around the *gata4*, *5* and *6* loci in cardiomyocytes. We tested the activity of these *cis*-regulatory elements using a novel, highly efficient reporter system in zebrafish.

Analysis of the enhancer-driven reporter activity showed high specificity: Gata5-enh5 drives activity in a subset of cells that co-localize with second heart field progenitors, while Gata5-enh12 drives activity restricted to the ventricle.

We zoomed into these enhancer sequences, identifying TF binding site motifs, and tested the requirement of overrepresented regulators by mutating their binding sites. These direct interactions are being tested by ChIP-PCR. Capture-C is currently being performed to reveal topologically associating domains, ultimately revealing the functional interaction between these enhancers and their regulated genes.

S11 15:15 — 15:45
Variable silencing of the repeat genome – implications for non-genetic inheritance
A Kazachenka[1], T Bertozzi[1], MK Sjoberg[2], N Walker[1], DJ Adams[2], **AC Ferguson-Smith**[1]

[1]Department of Genetics, University of Cambridge, Cambridge, UK; [2]Experimental Cancer Genetics, Wellcome Trust Sanger Institute, Cambridge, UK

Genetic models of epigenetic inheritance can provide useful insights into mechanisms, stability and heritability of modified states. Endogenous retroviruses (ERVs) are a class of LTR retrotransposons representing around one quarter of the repetitive elements in the murine genome. Most are epigenetically silenced. However, in two classic mouse models, Agouti viable yellow (A^{vy}) and Axin fused (Axin(Fu)), a member of the IAP class of ERV has inserted in the vicinity of the *agouti* and *axin* genes respectively, and been variably DNA methylated between individuals; this is associated with transcriptional variability of the associated genes, and non-genetically conferred phenotypic variation which can be transmitted across generations. Such alleles are known as metastable epialleles. Here we present a genome-wide systematic screen for novel metastable epialleles with or without an impact on transcription using mouse strain-specific datasets that we generated as part of the BLUEPRINT reference epigenome project (EUFP7 BLUEPRINT grant HEALTH-F5-2011-282510). The properties, impact and heritability of these alleles has been explored and provided useful insights into the impact of the epigenetic control of repetitive elements on the mammalian genome, and transgenerational epigenetic inheritance.

O8 15:45 – 16:00
Poster Number: P112
Function, cooperation and evolution of multiple enhancers governing the expression of a vertebrate developmental gene
P Torbey[1], E Thierion[1], S Collombet[1], J.P. Concordet2, C Desmarquet Trin-Dinh[1], P Charnay[1], **P Gilardi-Hebenstreit**[1]

[1]IBENS, INSERM U1024, CNRS UMR 8197, Paris, France; [2]Museum national d'histoire naturelle, CNRS UMR 7196, INSERM U1154, Paris, France

Developmental genes harbour multiple transcriptional enhancers that act concomitantly to achieve precise spatiotemporal expression. To provide insights into the mechanisms involved in the regulation of a vertebrate gene, we investigated the case of *Krox20* gene required for the specification of rhombomeres 3 and 5. We have functionally characterized, by in vivo deletions, 6 elements, spread on a large distance, that cooperate during the initiation and the maintenance of *Krox20* expression. By investigations of chromatin organisation, we show that besides its classical enhancer function, one initiating element is permanently required in cis to potentiate the autoregulatory activity of an enhancer by increasing its accessibility. Additionally, despite having the same profile of expression, the *cis*-regulation of *Krox20* differs between zebrafish and mice. This study reveals both a strong enhancer redundancy for the expression of a developmental gene, and an unexpected plasticity in the function and number of enhancers throughout vertebrate evolution.

S12 16:30 – 17:00
The Physics of Blastoderm Flow during Early Gastrulation of Tribolium castaneum
S Munster[1,2,3], A Jain[1], A Mietke[2], SW Grill[2,3], **P Tomancak**1

[1]MPI-CBG, Dresden, Germany; [2]MPI-PKS, Dresden, Germany; [3]TU Dresden, Dresden, Germany

The early embryo of the red flour beetle, Tribolium castaneum, initially consists of a single-layered blastoderm covering the yolk uniformly that differentiates into an embryonic rudiment as well as extraembryonic amnion and serosa. The germband anlage forms inside the egg during gastrulation when the embryonic rudiment condenses and folds along the ventral midline; this process is accompanied by large scale flow and expansion of the extraembryonic serosa which ultimately covers the entire surface of the egg, thus engulfing the growing embryo. The mechanical properties of these tissues and the forces governing these processes in Tribolium, as well as in other species, are poorly understood. Here, we present our findings on the dynamics of myosin in the early blastoderm of Tribolium using multiview lightsheet live imaging of transiently labeled wild type embryos. We quantitatively measure the global distribution of myosin throughout the flow phase and present a physical description that couples the contractile forces generated by myosin to the mechanical properties of the blastoderm. In particular, we describe the overall tissue as a thin, actively contractile, viscous bulk medium that exhibits friction with the vitelline membrane. This description accurately captures the large-scale deformation the tissue undergoes during the initial stages of gastrulation. Our findings lay a foundation for the physical description of gastrulation in Tribolium and will allow, in combination with the well-studied Drosophila paradigm, for the first time the comparative analysis of blastoderm tissue morphogenesis.

S13 17:00 – 17:30
Developmental dynamics of X-chromosome structure
E Heard

Institut Curie, Paris, France

X-chromosome inactivation during early female development is an essential epigenetic process that is required to achieve appropriate dosage for X-linked gene products. We are interested in understanding how the differential treatment of the two X chromosomes in the same nucleus is set up during development and how this differential expression is then maintained, or reversed in certain circumstances such as the inner cell mass of the mouse embryo or in the germ line. The establishment of X inactivation involves the non-coding Xist RNA that triggers chromosome-wide chromatin re-organisation and gene silencing. Recent insights have been made into the nature of these chromosome-wide changes, including the global loss of topologically associated domains (TADs)[1,2]. However, little is known about the underlying mechanisms and the precise relationship between 3D chromosome structure and altered gene expression states on the X chromosome. Results of our recent studies, using a combination of chromosome-conformation capture technologies and high-resolution microscopy in differentiating embryonic stem cells and *in vivo* mouse embryos, will be presented where we have investigated (i) the degree to which 3D chromatin organization into topologically associated domains (TADs) is involved in monoallelic *Xist* regulation during development and (ii) the relationship between 3D structure and regional escape from X inactivation on the inactive X chromosome.

1. Nora, E.P. *et al* (2012). Spatial partitioning of the regulatory landscape of the X-inactivation centre. *Nature* 485, 381–385.
2. Giorgetti, L. *et al*l (2014) Predictive polymer modeling reveals coupled fluctuations in chromosome conformation and transcription. *Cell*, 157: 950–963.

S14 17:30 – 18:00

Reprogramming in the mouse germ line

PWS Hill[1,2], HG Leitch[1,2], CE Requena[1,2], Z Sun[3], R Amouroux[1,2], M Roman-Trufero[1,2], M Borkowska[1,2], J Terragni[3], R Vaisvila[3], S Linnett[1,2], H Bagci[1,2], G Dharmalingham[1,2], V Haberle[1,2], B Lenhard[1,2], Y Zheng[3], S Pradhan[3], **P Hajkova**[1,2]

[1]MRC London Institute of Medical Sciences, London, UK; [2]Imperial College London, London, UK; [3]New England Biolabs, Massachusetts, USA

Gametes are highly specialized cells that can give rise to the next generation through their ability to generate a totipotent zygote. In mice, germ cells are first specified in the developing embryo (around embryonic day (E) 6.25) as primordial germ cells (PGCs). Following subsequent migration into the developing gonad, PGCs undergo a wave of extensive epigenetic reprogramming around E10.5–E11.52–11, including genome-wide loss of 5-methylcytosine. The underlying molecular mechanisms of this process have remained unclear, leading to our inability to recapitulate this step of germline development in vitro. Using an integrative approach, our recent work shows that this complex reprogramming process involves coordinated interactions among promoter sequence characteristics, DNA (de)methylation, the polycomb (PRC1) complex and both DNA demethylation-dependent and -independent functions of TET1 to enable the activation of a critical set of germline reprogramming-responsive genes involved in gamete generation and meiosis. Our results also reveal an unexpected role for TET1 in safeguarding but not driving DNA demethylation in gonadal PGCs. Collectively, our work uncovers a fundamental biological role for gonadal germline reprogramming and identifies the epigenetic principles of the PGC-to-gonocyte transition that will help to guide attempts to recapitulate complete gametogenesis in vitro.

Monday 16 April, 2018
Cell Biology and Development
14:30 – 18:00
OC0.03

S15 14:30 – 15:00
Centrioles as a model to study organelle size control
MG Aydogan[1], A Wainman[1], S Saurya[1], TL Steinacker[1], A Caballe[1], ZA Novak[1], J Baumbach[2], N Muschalik[2], **JW Raff**[1]

[1]Sir William Dunn School of Pathology, University of Oxford, Oxford, UK; [2]MRC Laboratory of Molecular Biology, University of Cambridge, Cambridge, UK

How organelles grow to the right size is a fundamental problem in cell biology. Centrioles are an excellent model for studying organelle size control as their regular structure means that the question of 3D-size can be simplified to a question of 1D-length. Here, we quantify the kinetics of centriole growth in living *Drosophila* embryos. We show that the conserved centriole protein Plk4 determines the rate and period of centriole growth, and establishes an inverse relationship between them: the more active the Plk4, the faster the centrioles grow, but the faster Plk4 is inactivated and centriole growth ceases. Thus, Plk4 functions as a homeostatic-clock to ensure that centrioles grow to the correct size. Clock mechanisms are a common feature of biological systems (such as the circadian clock and the vertebrate segmentation clock), and our findings suggest that they can be used to set organelle size.

O9 15:00 – 15:15
Poster Number: P2
Mechanical regulation of chemical signalling in the developing *Xenopus* brain
EK Pillai, K Franze

Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK

Studies of nervous system development have focused on the role of chemical signalling in guiding neuronal axons; however, neurons also respond to mechanical signals in their environment. We found that neurons grow along stiffness gradients in the developing *Xenopus* brain. Mechanosensitive ion channels (MSCs) are key players in transducing these mechanical cues into intracellular signals. Pharmacological blocking of MSCs and knockdown of the MSC Piezo1 caused severe pathfinding errors in the developing *Xenopus* optic tract. In addition to affecting axon growth, downregulation of Piezo1 dramatically altered the expression of semaphorin3A, a chemical guidance cue known to be critical in axon pathfinding. Our results thus indicate that the expression of chemical guidance cues may be modulated by tissue mechanics during development. As mechanical changes occur throughout development, during ageing and post-injury, this study could allow us to better understand how chemical signalling may be influenced by tissue mechanics during these processes.

S16 15:15 – 15:45
Just-right Wnt signalling for coordinated control of growth and patterning
I McGough, E Ordan, H Nojima, C Alexandre, **JP Vincent**

Cell Interactions Laboratory, The Francis Crick Institute, London, UK

During development, growth and patterning are coordinated by a handful of signalling pathways. For example, signalling by Wingless, the main Drosophila Wnt controls growth and patterning in the wing precursors of Drosophila. We have shown that Wingless does not need to be released from secreting cells for near normal development. Yet, Wingless signalling controls growth throughout the wing precursor, a tissue that reaches 35000 cells at pupariation. I will discuss how a short-range protein could have a seemingly long-range action. Although Wingless release is not essential, we found that it does contribute to full activation of signalling in wild type wing precursors. Moreover, as Wingless is handed over from secreting cells to its cognate receptors in receiving cells, its lipid moiety must transit through the (aqueous) extracellular space. I will discuss our experimental approaches to address this handover problem.

O10 15:45 – 16:00
Poster Number: P3
Asymmetric cell division during angiogenesis
HE Lovegrove, G Costa, SP Herbert

Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Our work is aimed at understanding how cells can successfully divide whilst limiting the impact of mitosis on their primary function, such as cell migration or tissue morphogenesis. In particular, we are addressing this question by exploring how mitosis takes place during the complex and dynamic process of angiogenesis.

Our work has uncovered a novel mode of asymmetric cell division, which produces daughter cells of differing size and shape during angiogenesis *in vitro* and *in vivo*. This allows daughter cells to quickly re-establish the important cellular hierarchies required for efficient collective migration and blood vessel morphogenesis. Recent work is also uncovering that asymmetry in the actin cytoskeleton may limit the extent of mitotic cell rounding in these cells, leading to a retention of interphase cell shape. Incomplete mitotic rounding may endow daughter cells with a memory of their pre-mitotic motile state, ensuring that the primary cellular function is rapidly re-established following division.

S17 16:30 – 17:00

Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans

MS Saitou[1,2,3,4]

[1]Department of Anatomy and Cell Biology, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [2]ERATO, JST, Kyoto, Japan; [3]iCeMS, Kyoto University, Kyoto, Japan; [4]CiRA, Kyoto University, Kyoto, Japan

The germ cell lineage ensures the creation of new individuals, perpetuating/diversifying the genetic and epigenetic information across the generations. We have been investigating the mechanism for germ cell development, and have shown that mouse embryonic stem cells (mESCs)/induced pluripotent stem cells (miPSCs) are induced into primordial germ cell-like cells (mPGCLCs) with a robust capacity both for spermatogenesis and oogenesis. We have also shown that human iPSCs (hiPSCs) with a primed pluripotency robustly generates human PGCLCs (hPGCLCs) with a property of human early PGCs. Moreover, by investigating the development of cynomolgus monkeys, we have defined a developmental coordinate of the spectrum of pluripotency among mice, monkeys, and humans, and have made an unexpected finding that the germ cell lineage in primates is specified in the amnion. I would here discuss our efforts towards understanding the mechanism of and reconstituting in vitro of germ cell development in mice, monkeys, and humans.

S18 17:00 – 17:30

The Dynamics of The Epithelial-To-Mesenchymal Transition During Mouse Gastrulation

KV Anderson, A Francou, R Hernández-Martínez, T Omelchenko

Developmental Biology, Sloan Kettering Institute, New York, USA

Epithelial-mesenchymal transitions (EMTs) are dynamic processes in which cells in stable epithelia acquire the ability to migrate and organize new tissues. Normal EMTs are required for organization of the body axis and for organ development, and abnormal EMTs drive fibrosis and tumor progression. Despite their importance, the dynamics and regulation of the cellular events of mammalian EMTs *in vivo* are poorly understood. We study genes that regulate specific cell biological processes that are required for this EMT. These include genes that regulate the stochastic ingression of individual cells from the epiblast epithelium, such as *Crumbs2* and *Lulu* (*Epb41l5*), genes that regulate changes adhesion, such as *p120-catenin*, and genes that regulate the directed collective migration of the newly formed mesenchymal cells, such as *b-Pix* (*Arhgef7*) and *Strip1*, which encodes a component of the Striatin Interacting Phosphatases and Kinases (STRIPAK) protein complex.

S19 17:30 – 18:00
Breaking symmetry in the developing brain
SW Wilson

Cell and Developmental Biology, UCL, London, UK

It is likely that the nervous systems of all bilaterally symmetric animals are left-right asymmetric with respect to processing of information and control of behavior. However, we know very little about how asymmetries arise in development, how they are encoded in circuits and what their importance is for nervous system function. We use developmental, genetic, imaging and behavioural approaches to study habenular asymmetry in zebrafish to address these issues. One focus is to determine the mechanisms that lead to neurons on the left and the right acquiring different character and I will discussf several mutants in which neurons on left and right are symmetric. These mutants are also a useful resource to study functional differences between circuitry on left and right and how asymmetry impacts behavior.

Group members and our many collaborators will be acknowledged in the presentation. Our research is supported by the Wellcome Trust and MRC.

Monday 16 April, 2018
Plenary Lecture
OC1.05

PL06 18:15 – 18:45
Making the mouse blastocyst
J Rossant[1,2,3]

[1]Program in Developmental and Stem Cell Biology, University of Toronto, Toronto, Canada; [2]Hospital for Sick Children, University of Toronto, Toronto, Canada; [3]Department of Molecular Genetics, University of Toronto, Toronto, Canada

The mammalian blastocyst contains about 100 cells and only three distinct cell types. One cell type, the epiblast, gives rise to all cell types of the body and to pluripotent embryonic stem cells, while the other two cell types give rise to placental and other support cells. The key transcription factors and signaling pathways specifying cell fate in the blastocyst and its derived stem cells have been identified. By undertaking a careful experimental assessment of the dynamic processes of lineage commitment and combining it with in vivo imaging and single cell gene expression analysis, we hope to understand how the mammalian preimplantation embryo can self-organize in time and space to generate the mature blastocyst. Development of human and mouse blastocysts show similarities and differences that can inform our understanding of the different pluripotent states of human and mouse stem cells.

Tuesday 17 April, 2018
Plenary Lecture
OC1.05

PL08 09:00 – 09:30
Rattlesnake Tales
SB Carroll

Molecular Biology, University of Wisconsin, Madison, WI, USA

The origin of novelty is one of the central questions of evolution. My laboratory has been focused on the genetic and developmental mechanisms underlying the evolution of animal form, and more recently, on biochemical novelties such as the evolution of snake venom. While the general mechanisms involved are distinct, the one common lesson these two pursuits have provided is, in biology, to expect the unexpected.

Tuesday 17 April, 2018
Stem Cells and Regeneration
09:35 – 13:10
OC1.05

S20 09:35 – 10:05
Novel regulators of neurogenesis – from centrosomes to nucleoli
M Götz

Neurogenesis in development and adulthood share many regulators, but also exhibit profound differences. Here I will discuss novel regulators of neurogenesis that are common in developmental and adult neurogenesis, but perform different functions. I briefly will start with the epigenetic regulator protein Uhrf1 and compare its role during development (Ramesh *et al.*, 2016) with surprisingly different functions in adult neurogenesis. I will then proceed to talk about a novel centrosomal protein which we identified in our screen separating radial glial cells that self-renew from those that generate basal progenitors (Pinto *et al.*, 2008, 2009). This novel centrosomal protein is higher in those subtypes of radial glial cells that generate basal progenitors and plays key roles in regulating the entry to and exit from the basal progenitor compartment. If time permits I will discuss our new unpublished data on the molecular function of Trnp1 which is higher expressed in self-renewing radial glial cells. Taken together, these new players highlight subtype-specificity in processes that were previously considered to be rather commonly regulated.

O11 10:05 – 10:20
Poster Number: P189
Using single-cell technologies and planarians to study stem cells, their differentiation and their evolution
J Solana

Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, UK

Single cell transcriptomics methods will revolutionize the way we study stem cells and developmental processes such as regeneration. We applied single cell transcriptomics to the planarian *Schmidtea mediterranea*, which contains pluripotent stem cells that continuously differentiate to all adult cell types. By obtaining thousands of single cell profiles we provide the near-complete cell type atlas of the whole adult stage. We characterize all major lineages of planarian differentiated cells, including previously uncharacterized types. Using a combination of single cell sequencing and RNAi for the first time we identify progenitors for most of these lineages. By applying lineage reconstruction algorithms we elucidate their differentiation tree into all their differentiation products. Our study shows the advantages of using single cell sequencing to analyse stem cells and developmental processes and pave the way for the identification of stem cells and the reconstruction of complete lineage trees in other organisms.

S21 10:20 – 10:50
Modeling human cardiovascular development with pluripotent stem cells
G Keller

University of Toronto, Ontario, Canada

Human pluripotent stem cells (hPSCs) represent a novel cell source for modeling human cardiovascular development and disease in vitro and for developing new therapies to replace or regenerate heart tissue damaged by age or disease. To study and treat diseases that affect specific regions of the heart, it is essential to be able to generate different cardiomyocyte subtypes from hPSCs. Most protocols established to date support the development of mixed cardiovascular cell populations that contain ventricular, atrial and sinoatrial cardiomyocytes. In this study, we used a developmental biology-based approach to identify the key signaling pathways that promote the efficient differentiation of ventricular and atrial cardiomyocytes, with the goal of generating populations highly enriched in each of these cardiac subtypes. We found that retinoic acid (RA) signaling at the mesoderm stage of development is essential for specifying the human atrial lineage. Additionally, we show that atrial and ventricular cardiomyocytes develop from distinct mesodermal subpopulations that can be identified by the expression of retinaldehyde dehydrogenase 2 (RALDH2), an enzyme involved in RA synthesis and glycophorin A (CD235a) respectively. The RALDH2$^+$ atrial mesoderm, but not the CD235a$^+$ ventricular mesoderm responds to retinol (RA precursor) to generate atrial cardiomyocytes demonstrating that this lineage is specified through an autocrine signaling loop during human heart development. Further molecular and functional analyses have shown that the generation of optimal atrial and ventricular cardiomyocyte populations depends on appropriate mesoderm specification. Taken together, these findings provide strong evidence that the human atrial and ventricular lineages segregate early at the mesoderm stage of development. With these developmental insights, we are now able to generate populations highly enriched in specific cardiomyocyte subtypes appropriate for cell-based therapy and disease modeling applications.

O12 10:50 – 11:05
Poster Number: P190
Phosphoproteomics Identifies a Bimodal EPHA2 Receptor Switch that Promotes Embryonic Stem Cell Differentiation
R Fernandez-Alonso[1], M Budzyk[1], A Helbig[2], J Hukelmann[3], A Lamond[3], E Petsalaki[4], **GM Findlay**[1]

[1]MRC-PPU, School of Life Sciences, University of Dundee, Dundee, UK; [2]Institute for Experimental Medicine, Christian Albrechts University, Kiel, Germany; [3]GRE, School of Life Sciences, University of Dundee, Dundee, UK; [4]European Bioinformatics Institute, EMBL, Cambridge, UK

Embryonic Stem Cell (ESC) differentiation is associated with dynamic remodelling of cellular signalling networks, although it remains a major challenge to pinpoint key molecular events driving this process. Here, we use phosphoproteomic profiling to identify an FGF4 mediated phosphorylation switch centred upon the Ephrin receptor EPHA2 in differentiating ESCs. Quantitative proteomics reveals EPHA2 as the major trans-membrane kinase in ESCs, which functions to support pluripotency gene expression and restrain lineage commitment by antagonising ERK1/2 signalling. Upon ESC differentiation, FGF4 utilises cooperative strategies to disable EPHA2. FGF4-dependent RSK activation inhibits EPHA2 via Ser/Thr phosphorylation, whilst FGF4-ERK1/2 signalling disrupts a core pluripotency circuit required for *Epha2* transcription. In vivo, EPHA2 expression is established upon assembly of the pluripotency gene regulatory network in the embryonic epiblast. Our data thereby uncover a role for EPHA2 in pluripotency maintenance, and identify a bimodal mechanism by which FGF4 signalling inhibits EPHA2 to reinforce transition from pluripotency towards differentiation.

S22 11:40 – 12:10
Pluripotency: plasticity and order
A Smith

Stem Cell Institute, University of Cambridge, Cambridge, UK

The regulative capability of single cells to engender all primary embryonic lineages is termed pluripotency. Despite differences in timing, morphogenesis, and deployment of individual transcription factors, the fundamental programme of pluripotency may be broadly conserved in mammalian embryos. In vitro observations of fluctuating gene expression and phenotypic heterogeneity have fostered a conception of pluripotency as intrinsically metastable and precarious. However, in the embryo and in defined culture environments the properties of pluripotent cells change in an orderly manner. Two sequential pluripotent states, termed naïve and primed, are generally recognised. However, pluripotency follows a developmental trajectory of phased progression rather than bistability. Specifically, a process of capacitation is required to endow naïve cells with competence for lineage specification. Capacitation entails remodelling of transcriptional, epigenomic, signalling and metabolic networks, collectively conferring responsiveness to lineage specification cues. Illuminating these formative events will reveal core attributes of pluripotency that are predicted to be generic.

S23 12:10 – 12:40
Triggering Limb Regeneration
EM Tanaka

Research Institute of Molecular Pathology, IMP, Vienna, Austria

Regrowth of a severed limb in the axolotl is a spectacular example of regeneration – the remaining portion of the limb is able to activate stem cells so that the replace the appropriate part of the limb, and rebuild the complex architecture of the different, interacting cells types. This process occurs in three morphologically and molecularly definable stages, wound-healing, blastemal formation, and patterning. I will talk about our work that has identified wound signals that initiate regeneration, and how the connective tissue cells orchestrate the building of the blastema and the patterning of the regenerate. A stable positional code is maintained in the adult limb that is central for controlling the amputation specificity and controlling that the correct parts of the limb are produced.

S24 12:40 – 13:10

Pluripotent stem cell technologies for studying myelin development and regenerative therapies

PJ Tesar

Genetics & Genome Sciences, Case Western Reserve University, Cleveland, Ohio, USA

Oligodendrocyte progenitor cells (OPCs) are endogenous stem cells in the central nervous system that serve as the predominant source of myelinating oligodendrocytes. Oligodendrocyte loss or dysfunction can lead to significant motor and cognitive disability in patients due to myelination deficits. We have developed technologies that enable the rapid and robust generation of OPCs from pluripotent stem cells and via direct cell reprogramming technologies. These in vitro generated OPCs serve as a powerful platform to understand oligodendrocyte development and to discover therapeutic compounds for enhancing myelination. I will discuss our recent efforts to use high-throughput phenotypic screening of pluripotent stem cell-derived OPCs to uncover new aspects of oligodendrocyte biology.

Tuesday 17 April, 2018
Evo Devo
09:35 – 13:10
OC0.03

S25 09:35 – 10:05
How invariant is ascidian development (and why?)

L Guignard[1,2,3], UM Fiuza[1,4], B Leggio[1,2,5], E Faure[1,2,5,6], J Laussu[1], L Hufnagel[4], G Malandain[7], C Godin[2,5], **P Lemaire**[1,5]

[1]CRBM, Université de Montpellier, Montpellier, France; [2]Inria team Virtual Plants, Université de Montpellier, Montpellier, France; [3]Janelia Research Campus, Howard Hughes Medical Institute, Asburn, USA; [4]Cell Biology and Biophysics Unit, EMBL, Heidelberg, Germany; [5]Institut de biologie Computationnelle, Université de Montpellier, Montpellier, France; [6]IRIT, Universités de Toulouse I et III, Toulouse, France; [7]Inria Team Morpheme, Université Côte d'Azur, Sophia Antipolis, France

Canalization of developmental processes ensures the reproducibility and robustness of embryogenesis within each species. In its extreme form, found in ascidians, early embryonic cell lineages are invariant between embryos within and between species, despite rapid genomic divergence.

To resolve this paradox, we used live light-sheet imaging and digitalization to quantify individual cell behaviours in embryos and explore the forces that canalize their development. This quantitative approach revealed that individual cell geometries and cell contacts are strongly constrained up to the end of neurulation.

Using computational simulations to explore the origin of constraints, we found that in the mesendoderm, the precise area of contacts between signalling and responding cells, rather than ligand concentration as observed in vertebrate embryos, provides the quantitative information for the outcome of cell inductions controlling cell fate specification. This mode of induction thus constrains cell geometries, while relaxing constraints on the level of expression of signalling ligands and receptors.

O13 10:05 – 10:20
Poster Number: P149
What's under the kilt? *tartan* is a likely causative gene for rapid male genitalia divergence between *Drosophila* species

JFD Hagen, C Mendes, KM Tanaka, A Blogg, AP McGregor, MDS Nunes

Biological and Medical Sciences, Oxford Brookes University, Oxford, UK

Although *Drosophila simulans* and *Drosophila mauritiana* diverged only 240 thousand years ago, there are already striking differences in the morphology of the male genitalia. The claspers, which are important for correct positioning of the male during copulation, are twice as large in *D. mauritiana* than in *D. simulans*. In order to unravel how this rapid trait evolution is facilitated in the genome, we performed Quantitative Trait Loci and introgression mapping. This revealed a 177kb candidate region on the left arm of the third chromosome underlying 16.6% of clasper size divergence between the species. An RNAi screen in *D.melanogaster*, differential gene expression analysis and *in situ* hybridisation has identified *tartan*, a LRR transmembrane protein, as the likely causative gene. To prove *tartan* is the divergent gene, we are currently using CRISPR/Cas9 to generate reciprocal hemizygotes. If correct, this would indicate novel roles for LRR proteins in regulating organ size development, morphological evolution and potentially reproductive isolation between closely related species.

S26 10:20 – 10:50

Network analysis of signaling pathways reveals new mechanisms regulating the development and evolution of reproductive output in Drosophila

T Kumar[1], L Blondel[2], **CG Extavour**[1,2]

[1]Organismic and Evolutionary Biology, Harvard University, Cambridge, USA; [2]Molecular and Cellular Biology, Harvard University, Cambridge, USA

A major challenge in development is determining which gene regulatory network (GRNs) function in a given developmental process, and how GRNs change over evolutionary time to generate morphological variations impacting fitness, and thus subject to natural selection. We use the Drosophila ovary as a system to address these challenges. The ovary comprises egg-producing structures called ovarioles. Ovariole number correlates positively with egg-laying, such that ovariole number likely impacts fitness. We previously identified Hippo signaling as a major regulator of ovariole number. Here we present the results of a screen for new Hippo-dependent and -independent modulators of reproductive capacity. Network analysis of screen phenotypes yielded two major novel outcomes. First, we predict involvement of previously untested genes in ovariole number regulation. Second, we identify genetic modules that are likely “on/off” switches for reproductive capacity, and modules that provide “fine tuning” dials through which evolution generates ovariole number variation across species.

O14 10:50 – 11:05

Poster Number: P150

Wnt signaling regulates head regeneration in the starlet sea anemone *Nematostella vectensis*

Y Iwasaki, M Lee, **GH Thomsen**

Biochemistry & Cell Biology, Stony Brook University, Stony Brook, USA

We are using the anthozoan cnidarian *Nematostella vectensis* to investigate regenerative mechanisms and the evolution of regeneration. The aboral fragment (physa) of an adult Nematostella polyp regenerates an entire body, and we find that all *wnts* in the genome are expressed sequentially in the amputated physa as new head and body structures reform. In contrast, *wnt* genes are not activated at the complementary aboral-facing cut site on the polyp “amputee”, thus indicating that the wnt response is polarized to the prospective site of head formation. MAPK signaling induced by wounding is required to initiate *wnt* expression during head regeneration, and blocking Wnt signaling inhibits head regeneration and associated blastema-like cell proliferation. Our findings demonstrate that polarized Wnt signaling is essential for regeneration of head and body structures in the amputated physa. Moreover, Hydrozoan and Anthozoan cnidarians appear to share a conserved, Wnt-dependent mechanism for oral regeneration.

S27 11:40 – 12:10
Developmental origin and evolution of bats
KE Sears

Ecology and Evolutionary Biology, UCLA, Los Angeles, USA

Comprising 20% of mammals, bats (Order Chiroptera) are the only mammals capable of powered flight. Bats achieves powered flight through specializations in their forelimbs, including novel wing membranes. Once in the air, bats experienced a massive adaptive radiation into diverse ecological niches. As a result, today's bats have highly diverse diets and, in association, highly diverse phenotypes in systems such as the teeth and eyes. My lab is investigating the developmental mechanisms through which bats arose and then diversified. In regard to bat origins, our studies suggest that the novel aspects of the bat wing membrane arose not through a redeployment of a limb-like outgrowth program, but rather through novel expression of other genes. In regard the subsequent radiation, we have found that development of both the teeth and eye systems is highly plastic in bats, and this likely provided the raw material necessary for adaptive radiation by natural selection.

S28 12:10 – 12:40
The genetic basis for diversification of leaf form: from understanding to reconstructing
M Tsiantis

Department of Comparative Development and Genetics, Max Planck Institute for Plant Breeding Research, Cologne, Germany

A key challenge in biology is to understand how diversity in organismal form is generated. While key regulators that shape the body plans of model organisms have been identified, less is known about how the balance of conservation versus divergence of relevant developmental pathways influences cell growth to generate morphological diversity. To help address this issue, we developed the *Arabidopsis thaliana* relative *Cardamine hirsuta* into a versatile system for studying morphological evolution. We use a combination of genetics, advanced imaging and computational modelling to understand the mechanisms through which leaf morphology evolved in these species, resulting in simple leaves in *A. thaliana* and complex leaves with leaflets in *C. hirsuta*. Here, I will present our findings on identifying such mechanisms and in conceptualizing how they regulate the number, position and timing of leaflet production. I will also discuss progress on understanding the physiological relevance of these different leaf shapes.

S29 12:40 – 13:10

What is evolutionary conversation? Lessons from ParaHox genes of unusual animals

PWH Holland[1], Y Dai[1], AD Hargreaves[1], G Li[2], F Xu[1,3]

[1]Department of Zoology, University of Oxford, Oxford, UK; [2]School of Life Sciences, Xiamen University, Xiamen, China; [3]Institute of Oceanology, Chinese Academy of Sciences, Qingdao, China

Many genes encoding transcription factors (e.g. Hox genes, ParaHox genes and others) have similar expression patterns in the embryos and adults of widely divergent animal taxa. This discovery of evolutionary conservation, made collectively by dozens of labs worldwide, constitutes one of the most important advances in twentieth century biology. The similar gene expression patterns suggest that a fundamental set of genes was deployed in patterning the embryo very early in animal evolution and then has been retained ever since. But questions remain. First, do conserved transcription factors regulate the same target genes in different species? Second, do similar expression patterns imply equivalent biological functions? Third, under what conditions can otherwise conserved genes escape from ancestral roles? I will explore these question using our recent studies on ParaHox genes in marine invertebrates and desert-living rodents.

S30 14:30 – 15:00
Quantitative and dynamic analysis of neurogenesis with single cell resolution at the tissue level

N Papalopulu, C Manning, X Soto, V Biga

Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

In recent years, our understanding of how neural pronenitors make cell state transitions has been transformed by discovery of ultradian oscillations of Hes transcription factors in neural progenitors. Most studies have been done in cultured dissociated cells and it is not clear what are the single cell dynamics at tissue level.

Here, we take a quantitative and dynamic approach to analyse single-cell heterogeneity in Hes expression at the tissue level, using mouse and zebrafish protein reporter knock-ins for Hes5 and Her6 respectively. We find that complex dynamics, with both short and long term trends, can be grouped together and related back to the position, division properties of the cell and path to differentiation. Mutagenesis of the knock-in Her6 reporter in zebrafish shows that changing Her6 dynamics locks cells in a normally transitory progenitor state. These findings allow insight into the single cell heterogeneity, dynamics and organisation of neural tissue in vivo.

O15 15:00 – 15:15
Poster Number: P89
Triggering of cell differentiation in the mouse preimplantation embryo is driven by Notch at compaction

S Menchero[1], A Lopez-Izquierdo[1], MJ Andreu[1], J Sainz de Aja[1], I Rollan[1], M Kang[2], R Benedito[1], T Rayon[1,3], AK Hadjantonakis[2], M Manzanares[1]

[1]Cell & Developmental Biology, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; [2]Developmental Biology, Sloan-Kettering Institute, New York, USA; [3]The Francis Crick Institute, London, UK

The onset of cell differentiation in the mammalian embryo entails the loss of totipotency to favor the appearance of the first lineages. The regulation of *Cdx2*, key element in the trophectoderm, has been attributed to the differential activity of the Hippo pathway in polarized and unpolarized blastomeres. We have shown that Notch cooperates with Hippo in this regulation. Further analysis of Notch activity during preimplantation stages indicates that it is active at 4-cell stage. Notch affects the initial expression of *Cdx2* in the morula, which is reinforced by Hippo. Using an inducible mosaic model, we found that differences in Notch levels in the early embryo determines cell fate at blastocyst stage. Moreover, single embryo transcriptome profiling in *Rbpj* null morulae indicates that Notch regulates repressors that block naïve pluripotency markers. These findings suggest that Notch is boosting the trigger of initial differentiation that is then reinforced by other morphogenetic programs.

S31 15:15 – 15:45
Deconstructing the Segmentation Clock oscillator in vitro
O Pourquie

Department of Genetics, Harvard Medical School and Department of Pathology, Brigham and Woman's Hospital, Massachusetts, USA

The periodic segmentation of the vertebrate body axis into somites, and later vertebrae, relies on a genetic oscillator (the Segmentation Clock) driving the rhythmic activity of signaling pathways in the presomitic mesoderm (PSM). While the clock is often presented as a population of phase-entrained oscillators, whether its oscillations are an intrinsic property of individual cells or represent a population-level phenomenon is not known. Using tail bud explants from mouse embryos, we show that oscillations are a collective property of PSM cells which can be actively triggered *in vitro* by a dynamical quorum sensing signal. We demonstrate that inhibiting Yap signaling is sufficient to predictably switch isolated PSM cells from a quiescent to an oscillatory state *in vitro*, a behavior reminiscent of excitability in other systems. We have also engineered a human iPS line carrying a fluorescent reporter driven by the regulatory sequences of the HES7 cyclic gene. This line can be efficiently induced to differentiate to a PSM fate in vitro by activating Wnt and inhibiting BMP signaling. Human PSM-like cells exhibit regular oscillations with a 5 hour periodicity. Together, this work argues that the mammalian segmentation clock behaves as an excitable system, introducing a novel paradigm to study such dynamics in vertebrate morphogenesis. Furthermore, we identify and characterize the human Segmentation Clock, introducing a robust in vitro system to dissect the molecular clockwork underlying this oscillator.

O16 15:45 – 16:00
Poster Number: P90
Robust cell type proportioning by a noisy oscillator
N Gruenheit[1,2], EJ Johnson[2], K Parkinson[2], K Nagayama[2], J Llewellyn[2,3], B Stewart[1,2], T Keller[2], W van Zon[2], SL Cotter[2,3], **CRL Thompson**[1,2]

[1]Department of Genetics, Evolution and Environment, University College London, London, UK; [2]Division of Developmental Biology and Medicine, University of Manchester, Manchester, UK; [3]School of Mathematics, Faculty of Science and Engineering, University of Manchester, Manchester, UK

Cell-cell heterogeneity has puzzled developmental biologists because it might prevent cell populations from behaving in a coordinated fashion. On the other hand, cell-cell heterogeneity could increase the spectrum of differentiation possibilities of cells in a uniform environment. However, remarkably little is known about the origin of heterogeneity, or if it can be controlled to generate reproducible cell type proportioning *in vivo*. Our studies, using experimentation and modeling in *Dictyostelium*, have allowed us to address these questions. Firstly, we find cell cycle position is quantitatively linked to responsiveness to differentiation inducing signals. Secondly, variation in cell cycle length ensures cells are randomly distributed throughout the cell cycle. Finally, perturbation of optimal cell cycle heterogeneity is buffered by compensatory changes in global signal responsiveness. These studies represent a major mechanistic advance because they reveal heterogeneity in cell cycle position can be optimised and harnessed to generate robust cell-type proportioning during embryonic development.

S32 16:30 – 17:00
Poster Number: P90
Limbs, Turing Patterns and the 50th anniversary of the French Flag Problem
J Sharpe

EMBL, Barcelona, Spain

The most famous metaphor for tissue patterning, introduced by Lewis Wolpert in 1968, has it's 50th anniversary this year. It was published in the same year as a classic developmental observation: the ZPA-induced mirror-image duplication of chick wing digits by Saunders and Gasseling (1968). These two papers went hand-in-hand to dominate much of our thinking about limb patterning (and developmental biology in general) over the subsequent decades, while older ideas about self-organisation, such as Turing patterns, faded into the background.

My group has been developing data-driven computer models of limb development which deal with both patterning and tissue growth. By integrating theory and data, these models have helped us reveal the role and possible mechanisms of self-organisation in digit patterning. But they also go further, proposing how the two key alternative types of patterning – self-organisation and positional information – can work together to achieve more interesting and robust patterns. Within this context I will discuss here the original contributions of the French Flag Problem and Turing Patterning.

Wolpert, L. (1968) The French Flag Problem: A Contribution to the Discussion on Pattern Development and Regulation. *In The Origin of Life: Toward a Theoretical Biology*. pp. 125-133
Saunders, J.W. and Gasseling, M.T. (1968). Ectodermal and mesenchymal interactions in the origin of limb symmetry. *In Epithelial Mesenchymal Interactions*. pp. 78- 97.

S33 17:00 – 17:30
Molecular and network understanding of a sperm/oocyte cell fate decision
J Kimble[1,2]

[1]HHMI, USA; [2]Biochemistry, University of Wisconsin, Madison, USA

Germ cells reside in male or female gonads that signal gamete differentiation as male or female, respectively. Yet germ cell-intrinsic factors utlmately determine gamete choice. These intrinsic factors are best understood in *C. elegans*, where a genetic regulatory network ends with FOG-1 and FOG-3, to specify the sperm fate. We now provide evidence that FOG-1 and FOG-3 bind and repress RNAs of the oogenic program and hence act biochemically as terminal regulators of the sperm/oocyte decision. The regulatory network acting upstream of FOG-1 and FOG-3 includes transcription factors and ERK/MAP kinase, but the FOG post-transcriptional regulators are responsible for specification of gamete fate. In adult animals, FOG-1 and FOG-3 and their upstream regulatory network must be maintained in sperm- or oocyte-promoting mode to prevent an adult switch in sexual fate. Intriguingly, mutants in upstream regulators can create an intermediate network state that renders the sperm/oocyte decision vulnerable to chemical reprogramming.

S34 17:30 – 18:00
The root endodermis – an independent way of building a polarised epithelium
N Geldner

DBMV, University of Lausanne, Lausanne, Switzerland

At the inception of complex multi-cellularity has been the development of polarised cell layers that restrict extracellular diffusion. In plants, an endodermis surrounds the central vasculature of the root as a protective sheath. It restricts extracellular diffusion by ring-shaped Casparian strips, hydrophobic impregnations of the primary plant cell wall. Analogous to animal tight and adherens junctions and bearing superficial resemblance, Casparian strips have evolved independently and have an entirely different molecular composition. I will report on our current understanding of the molecular players and mechanisms that lead to the precisely aligned network of ring-like cell wall modifications, able to efficiently seal the extracellular space and protect the inner transporting tissues from the soil environment, while still allowing uptake of mineral nutrient and water to occur.

Tuesday 17 April, 2018
Positional Information
14:30 – 18:00
OC0.03

S35 14:30 – 15:00
Visualizing neural tube closure and uncovering the causes of neural tube defects
LA Niswander

Molecular, Cellular and Developmental Biology, University of Colorado, Boulder, USA

The Niswander lab focuses on the common and severe birth defect in which the neural tube, the precursor of the brain and spinal cord, fails to close. We approach the study of neural tube defects from the viewpoint of genetics, epigenetics, and environmental factors. We use the mouse embryo as a model of human development to ask what are the genes that regulate NT closure and how do these novel genes function. Time-lapse imaging is expanding our understanding of the normal cell behaviors that drive NT closure. This imaging platform then allows us to determine the link between novel molecular regulators and cell behaviors and how these molecular/cellular changes affect the highly coordinated process of neural tube closure. Through collaborative efforts we are also exploring the genetic causes of NTD in humans. We use cell-based assays to better understand the impact of genetic variants observed in the human NTD cohorts.

O17 15:00 – 15:15
Poster Number: P177
Embryonic geometry underlies phenotypic variation in decanalized conditions
A Huang[1], TE Saunders[1,2,3]

[1]Mechanobiology Institute, National University of Singapore, Singapore, Singapore; [2]Department of Biological Sciences, National University of Singapore, Singapore, Singapore; [3]IMCB, A Star, Singapore, Singapore

In the process of development, many mutations cause increased variability in phenotypic outcomes, a phenomenon termed decanalization. While many of such variations can be attributed to genetic and environmental perturbations, phenotypic discordance remains even in isogenic model organisms raised in homogeneous environments. To understand the mechanisms underlying phenotypic variation, we used Drosophila embryonic patterning as model and identified embryonic geometry as one factor predetermining patterning outcomes in decanalized conditions. By simultaneously manipulating the morphogen Bicoid and embryonic geometry, we found that while in wild-type embryos, the patterns formed always scale in proportion to embryonic size, the segmentation gene boundaries shift away from the scaled positions according to the total embryonic length under manipulated conditions. Further analysis of the gene regulatory network acting downstream of the morphogen shows that, patterning defects are introduced at the vulnerable points of the gene network in the face of limited absolute physical space.

S36 15:15 – 15:45
Role of motile and immotile cilia in left-right symmetry breaking
H Hamada

Center for Developmental Biology, Riken, Kobe, Japan

There has been rapid progress in understanding how left-right (L-R) asymmetry develops during embryogenesis. L-R symmetry breaking in the mouse and other vertebrates, which takes place after the two other body axes are fixed, involves unidirectional fluid flow in the node or an equivalent region. Cilia, both motile and immotile, play centrals role in L-R symmetry breaking. Thus, motile cilia generate the uni-directional flow while immotile cilia sense the flow. In the mouse embryo, rotational movement of cilia in the node can generate leftward flow because rotational axis of cilia is posteriorly tilted. Despite recent progress, there remain several important questions. In my talk, I would like to address some of them such as 1) how the flow is sensed by immotile cilia (possible role of ciliary Ca^+ in flow sensing), 2) readouts of flow-induced signal, and 3) evolutionary conservation of the symmetry-breaking mechanism among vertebrates.

O18 15:45 – 16:00
Micropattern differentiation of mouse pluripotent stem cells recapitulates embryo regionalized cell fate patterning
SM Morgani[1,2], JJ Metzger[3], J Nichols[2], ED Siggia[3], AK Hadjantonakis[1]

[1]Developmental Biology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, USA; [2]Wellcome Trust-Medical Research Council Centre for Stem Cell Research, University of Cambridge, Cambridge, UK; [3]Center for Studies in Physics and Biology, The Rockefeller University, New York, USA

During gastrulation epiblast cells exit pluripotency as they specify and spatially arrange the three germ layers of the embryo. Similarly, human pluripotent stem cells (PSCs) undergo spatially organized fate specification on micropatterned surfaces. Since in vivo validation is not possible for human, we developed a mouse PSC micropattern system and, with comparisons to mouse embryos, reveal the specification of distinct regional identities. BMP/WNT/ACTIVIN/FGF directed mouse PSCs to undergo an epithelial-to-mesenchymal transition and pattern posterior mesoderm fates. WNT/ACTIVIN/FGF pattern anterior identities, including definitive endoderm. Chemical or genetic disruption of pathways and genes critical for gastrulation results in comparable phenotypes within the in vitro micropattern differentiation indicating that this system recapitulates aspects of in vivo development. The mouse micropattern system offers a robust scalable method to generate cell types present in vivo, resolve how signals promote identities and generate patterns, and compare mechanisms operating in vivo and in vitro and across species.

S37 16:30 – 17:00
FGF/Erk promotion of polycomb-mediated repression regulates neural differentiation onset
KG Storey, CI Semprich

Cell & Developmental Biology, University of Dundee, Dundee, UK

FGF/Erk signalling maintains an undifferentiated progenitor cell state in many developing tissues. In the elongating body axis, such signalling is active in the tailbud and maintains, along with Wnt, axial progenitors that give rise to neural and mesodermal cells. Previous work has shown that loss of FGF signalling promotes onset of neural differentiation as epiblast cells leave the tailbud; and specifically elicits chromatin decompaction around neural differentiation gene loci. Here we show that inhibition of Erk activity mediates rapid decompaction around the neural differentiation gene *Pax6* in mouse embryos and in human spinal cord precursors in vitro, where this correlates with a stepwise dissociation of the polycomb-repressive-complex (PRC). Using ATAC-Seq we demonstrate that Erk inactivation increases chromatin accessibility across hundreds of neural differentiation genes. As the PRC represses gene transcription but also recruits RNAPolII, our findings here suggest that FGF/Erk signalling poises cells for differentiation by promoting this repressive complex.

S38 17:00 – 17:30
Mitosis and epithelial morphogenesis
Y Bellaiche

Department of Genetics and Developmental Biology, Institut Curie Cnrs Inserm, Paris, France

Recent advances in imaging, cell biology, signal transduction and biophysics have framed the study of tissue morphogenesis in terms of collective cell dynamics and the interplay between biochemical and mechanical processes. Recent findings have confirmed that proliferative epithelial tissues reshape via morphogenetic processes such as cell shape change and cell rearrangements. Yet cell division remodels adherent junctions and modulates both tissue mechanics and tissue dynamics. Therefore its role and interplay with the other morphogenetic processes need to be understood to decipher the mechanisms of tissue morphogenesis. During my talk I will describe some of our latest works that aim to understand the mechanisms of mitotic spindle orientation, propagation of cell polarization through division and how cell division impacts on the global shape and organization of epithelial tissue.

S39 17:30 – 18:00
Flower development: from morphodynamics to morphomechanics
J Traas

Plant Reproduction and Development, ENS-Lyon, Lyon, France

In higher plants the shoot apical meristem (SAM) continuously generates leaves, flowers, and branches. In the past decades, many components of the gene regulatory networks in the SAM have been identified. However, little is known about the spatiotemporal coordination between gene expression patterns and growth at the cellular and tissue level. This lack of understanding is mainly due to the lack of comprehensive quantification of organ wide cell properties (geometry, topology, biophysics, …) over time with regards to the underlying molecular networks. We address this problem in early flower development of *Arabidopsis thaliana* using high resolution confocal time lapse imaging, combined with genetic and biophysical approaches. Hereby we are focusing on the cell wall, which plays a central role in the control of growth rates and growth directions.

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL09 09:30 – 10:00
Dual mode strigolactone signaling and the bud activation switch
O Leyser

Sainsbury Laboratory, University of Cambridge, Cambridge, UK

The degree of shoot branching is an excellent example of plant developmental plasticity. Branches develop from axillary buds established in the axil of each leaf. The buds can remain dormant, or activate to produce a branch, and this switch is regulated by diverse endogenous and exogenous factors, allowing plants to tune their development according to the prevailing environmental conditions. A growing body of evidence suggests that a central regulator of this process is the shoot auxin transport network. The self-organising properties of this network mediate competition between buds, with reinforcement, balancing growth across the shoot system. In addition, local expression of the *BRC1* gene in the bud affects its ability to activate. This dual-mode system is likely to provide robustness to the bud activation switch. Interestingly, in Arabidopsis, the branch regulating hormone, strigolactone, appears to regulate both the auxin transport network and *BRC1* expression.

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL10 10:00 – 10:30
Single-cell analyses suggest new complexities in the changing landscape of primitive human blood-forming cells
CJ Eaves[1,2,3], DJHF Knapp[1,2], CA Hammond[1,2], A Lorzadeh[4,6], F Wang[1,3], M MacAldaz[1,5], T Hui[4,6], MTJ von Leonhout[6], N Aghaeepour[7], PH Miller[1]

[1]Terry Fox Laboratory, BC Cancer Agency, Vancouver, Canada; [2]Department of Medicine, University of British Columbia, Vancouver, Canada; [3]Department of Medical Genetics, University of British Columbia, Vancouver, Canada; [4]Department of Microbiology and Immunology, University of British Columbia, Vancouver, Canada; [5]Interdisciplinary Oncology Program, University of British Columbia, Vancouver, Canada; [6]Michael Smith Laboratories, University of British Columbia, Vancouver, Canada; [7]Baxter Laboratory for Stem Cell Biology, Dept of Microbiology & Immunology, Stanford University, Palo Alto, USA

The hematopoietic system has served as a paradigm for elucidating events that enable multiple types of mature cells to be generated lifelong. We have recently characterized a new subset of human hematopoietic cells that appear selectively endowed with this competence, based on their serial transplantability in immunodeficient mice. Single-cell functional and molecular analyses of these cells indicate weakly linked, but developmentally altered, variability in their pace of cell cycle entry, lineage outputs, global methylome, transcriptional and signalling profiles. These findings suggest that human cells with poised hematopoietic potential are endowed with a unique spectrum of features that separately regulate their subsequent survival, proliferation, and eventual lineage program restriction and activation in a semi-preserved fashion. These act in concert with external cues and developmentally determined programmatic alterations. This gives the compartment as a whole an apparently flatter landscape of initial “state” changes than historically envisaged, superimposed on a developmentally determined framework.

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL10 11:00 – 11:30
Specification of the definitive endoderm and midline progenitors in the early post-implantation mouse embryo
E Robertson

Dunn School of Pathology, University of Oxford, Oxford, UK

During the earliest stages of post-implantation development the epiblast undergoes a transition described as lineage priming which allows cells to acquire competence for cell fate allocation during the process of gastrulation. Our previous experiments argue that a continuum of graded signaling by the TGFbeta growth factor Nodal are required to establish initial axis polarity of the embryo, and later coordinate the spatiotemporal specification of discrete cell progenitors. We will discuss recent experiments aimed at addressing how Nodal signalling contributes initially to lineage priming and then at later stages is responsible for the activation of a key downstream effector pathways. In particular our work shows that Nodal-dependent activation of the T-box transcription factor Eomesodermin governs discrete context dependent transcriptional programmes that sequentially pattern the embryonic axis and specify definitive endoderm and midline progenitors during mouse gastrulation.

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL12 11:30 – 12:00
Cheryll Tickle Medal Lecture: Using the mouse embryo hindbrain as a model to understand neuronal and vascular devleopment
C Ruhrberg

UCL Institute of Ophthalmology, University College London, London, UK

Since the days of my postdoctoral training, I have come to appreciate the versatility of the mouse embryo hindbrain as a model system to elucidate novel molecular and cellular mechanisms of neuronal and vascular development. Accordingly, I will present my team's past and current work on shared neurovascular signalling pathways that guide migrating hindbrain motor neurons or hindbrain-derived neural crest cells to their targets, and I will demonstrate that hindbrain-derived neural crest cells orchestrate vascular remodelling in the embryo to allow the adult heart to function properly. I will continue my presentation by discussing how my team has investigated hindbrain development to learn more about the role of neural progenitors and microglia in promoting brain vascularisation as well as the reciprocal role of brain vasculature in regulating neural progenitor behaviour. Finally, I will conclude by showing unpublished data demonstrating that a subset of vascular cells shares a developmental lineage with microglia.

Wednesday 18 April, 2018
Plenary Lecture
OC1.05

PL13 12:00 – 12:30
The stability and reversal of gene expression in development
JB Gurdon

Gurdon Institute, University of Cambridge, Cambridge, UK

Hardly ever do embryonic cells that have embarked on a cell differentiation pathway reverse or change that commitment, which is very stable. Somatic cell nuclear transfers to eggs (in second meiotic metaphase) can reverse this process, but with low efficiency. Overexpressed transcription factors can also change cell fate, as can iPS, but at a low efficiency. However, the mechanisms by which transcription factors can change cell fate is still unclear.

We have been exploring transcription factor action by use of nuclear transfer to amphibian oocytes in first meiotic prophase with no DNA synthesis or cell division. Some pluripotency genes in transplanted nuclei undergo a very large transcriptional activation from quiescence within a few hours. We are investigating to what extent this effect depends on the binding of transcription factors. Our aim is to understand to what extent the stability and reversal of gene expression is dependent on transcription factor activity.

POSTER ABSTRACTS

Cell biology and development

Poster Number: P1
A chemical genetics approach to study atypical protein kinase C (aPKC) function in Drosophila
J Januschke[1], M Hannaford[1], N Loyer[1], F Tonelli[2]

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The Par protein complex is a major regulator of cell polarity across species. The Par proteins and aPKC in particular are required for asymmetric stem cell division in the developing fly brain. However, these cells divide rapidly posing the problem to differentiate between immediate and further downstream consequences of loss of gene functions using standard genetics. Targeted inactivation of kinases, like aPKC, can be achieved by chemical genetics: the kinase is engineered to become sensitive to an ATP competitive inhibitor. Using genome editing we engineered an inhibitor sensitive aPKC mutant ($aPKC^{AS4}$) in *Drosophila*. In the absence of the inhibitor, that does not have an effect on wild-type cells, $apkc^{AS4}$ homozygous mutant flies are indistinguishable from wild type, but addition of the inhibitor reproduces known phenotypes of loss of aPKC. I will present our findings obtained using quantitative live cell imaging and targeted inhibition of aPKC on neural stem cells and epithelia.

Poster Number: P2
Mechanical regulation of chemical signalling in the developing *Xenopus* brain
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Studies of nervous system development have focused on the role of chemical signalling in guiding neuronal axons; however, neurons also respond to mechanical signals in their environment. We found that neurons grow along stiffness gradients in the developing *Xenopus* brain. Mechanosensitive ion channels (MSCs) are key players in transducing these mechanical cues into intracellular signals. Pharmacological blocking of MSCs and knockdown of the MSC Piezo1 caused severe pathfinding errors in the developing *Xenopus* optic tract. In addition to affecting axon growth, downregulation of Piezo1 dramatically altered the expression of semaphorin3A, a chemical guidance cue known to be critical in axon pathfinding. Our results thus indicate that the expression of chemical guidance cues may be modulated by tissue mechanics during development. As mechanical changes occur throughout development, during ageing and post-injury, this study could allow us to better understand how chemical signalling may be influenced by tissue mechanics during these processes.

Poster Number: P3
Asymmetric cell division during angiogenesis
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Our work is aimed at understanding how cells can successfully divide whilst limiting the impact of mitosis on their primary function, such as cell migration or tissue morphogenesis. In particular, we are addressing this question by exploring how mitosis takes place during the complex and dynamic process of angiogenesis.

Our work has uncovered a novel mode of asymmetric cell division, which produces daughter cells of differing size and shape during angiogenesis *in vitro* and *in vivo*. This allows daughter cells to quickly re-establish the important cellular hierarchies required for efficient collective migration and blood vessel morphogenesis. Recent work is also uncovering that asymmetry in the actin cytoskeleton may limit the extent of mitotic cell rounding in these cells, leading to a retention of interphase cell shape. Incomplete mitotic rounding may endow daughter cells with a memory of their pre-mitotic motile state, ensuring that the primary cellular function is rapidly re-established following division.

Poster Number: P4
Investigating Mitotic Nuclear Dynamics of Pseudo-Stratified Epithelia in Drosophila melanogaster
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Pseudo-stratified Epithelia (PSE) is commonly found in developing tissues. The compact structure provides the cell density to undergo morphogenesis. For proper cell division, nuclei translocate to the apical surface prior to mitosis via a process called inter-kinetic nuclear migration (IKNM).

We are studying IKNM within the Drosophila wing disc, which possesses intermediate-height PSE. Through studies in other systems, it is known that short epithelia depend on actomyosin, whilst tall epithelia utilise microtubule transport. In the wing disc, we have identified a novel role for lateral adhesions and actomyosin regulators in mediating proper IKNM. Analysing live nuclear movements has revealed distinct dynamics of apical and basal translocation. We observe differential daughter nuclei behaviour for reintegrating into the nuclear layers that we hypothesise is required for pseudostratification. Furthermore, mutants of actomyosin regulators show mis-regulation of nuclear behaviours and indicate that IKNM in our system, may be analogous to cells migrating in confinement.

Poster Number: P5
PIERCE1 mediates left-right patterning through ciliary motility
H Farley[1], J Keynton[1], J Thompson[2], D Asante[1], H Hilton[1], C Esapa[1], P Lackie[2], J Lucas[2], D Norris[1]

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Motile cilia in the embryonic node drive a leftwards fluid flow that serves to establish normal left-right asymmetry. *Pierce1* mutants exhibit randomised situs and heart defects which are indicative of faulty left-right patterning. Live imaging of node cilia demonstrates reduced ciliary beat frequency and altered beat pattern; particle image velocimetry has confirmed that while motile, these cilia no longer drive leftwards nodal flow. Motile cilia lining the adult trachea function to clear mucus from the lungs. Analysis of *Pierce1* tracheal cilia reveals abnormal beating, making *PIERCE1* a candidate primary ciliary dyskinesia (PCD) gene. This is supported by transmission electron microscopy work showing inner and outer dynein arm deficiencies in the tracheal cilia of homozygous animals. Current work focuses on further characterisation of ciliary motility defects in this mouse line, as well as functional characterisation of the *PIERCE1* protein in cell culture.

Poster Number: P6
Towards deciphering the molecular mechanism regulating Wnt cytoneme formation
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Wnt proteins regulate many processes in development and tissue homeostasis. It has been postulated that Wnt/beta-catenin signalling form concentration gradients across responsive tissues and act as morphogens. However, little is known about the transport mechanism for these lipid-modified signalling proteins in vertebrates.

We show that Wnt8a is transported on short, actin-based filopodia to contact responding cells and activate signalling during neural plate formation in zebrafish[1]. Recent results demonstrate that the receptor kinase Ror2 activates the beta-catenin independent pathway to regulate the formation of these Wnt-positive cytonemes in zebrafish, in the intestinal crypt and in gastric cancer cells[2, unpub.)]. Enhanced formation of cytonemes increases the effective signalling range and, consistently, reduction in cytonemes leads to a restricted distribution of the ligand and a limited signalling range.

We conclude that a cytoneme-based transport system for Wnt is important for Wnt/beta-catenin signaling in vertebrates.

1. Stanganello et al., 2015;
2. Brinkmann et al., 2016

Poster Number: P7
Investigating the co-ordinated transcriptional networks regulating myogenesis
C McQueen, RJ White, ME Pownall

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Recent advances in analysis of small RNAs have enabled the exciting opportunity to study the regulation of RNA polymerase III transcription at genome-wide scale. This work has revealed that transcriptional output by RNA Polymerase III, like Polymerase II, is differentially regulated between tissues and during development. This indicates that developmental transcriptional networks are potentially more complex than previously thought, involving cross-talk between multiple polymerases. Polr3G, a subunit unique to RNA Polymerase III, is associated with maintaining pluripotency and proliferation in hESCs and exists in 2 distinct forms in mammals and in Xenopus. I will present the expression profiles of Polr3G and its paralog Polr3gL during Xenopus development, the specific expression of Polr3G in the skeletal muscle lineage and investigation into its regulation. The results of custom tRNA microarrays demonstrating differential regulation of tRNAs in the muscle lineage in response to changes in expression of Polr3G and Polr3gL will be presented.

Poster Number: P8
Apical and basal matrix remodelling control epithelial morphogenesis
MC Diaz de la Loza[1], RP Ray[5], PS Ganguly[2], S Alt[2,6], JR Davis[3], A Hoppe[4], N Tapon[3], G Salbreux[2], BJ Thompson[1]

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The generation of form in living organisms is one of the most fascinating unsolved problems in biology. Here we examine the columnar-to-cuboidal cell shape change that reduces apical-basal cell height and expands cell width to drive elongation of the wings and legs of *Drosophila*. This morphogenetic event requires remodelling of both the apical and basal extracellular matrix that encapsulates the limb, releasing the constraining force that previously maintained columnar cell shape. Matrix remodelling is induced by specific proteases in wings and legs, and does not occur in limbs that fail to elongate, such as the haltere. Limb elongation is made anisotropic by planar polarised Myosin-II, which drives convergent-extension along the proximal-distal axis. Subsequently, Myosin-II relocalises to lateral membranes to accelerate columnar-to-cuboidal transition and isotropic tissue expansion. Thus, remodelling of both the apical and basal extracellular matrix induces dynamic three-dimensional changes in actomyosin contractility to drive epithelial morphogenesis.

Poster Number: P9
Airborne particulate matter from Jeddah induces severe cardiovascular defects in chick embryo
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Air pollution in Saudi Arabia is among the highest in the world. This pollution has been mainly attributed to heavy road smoke and strong sandstorms. Many studies have reported serious impacts of the airborne particulate matter (PM) collected from different cities in Saudi Arabia on health including cancer, respiratory disease, atherosclerosis, skin irritation, inflammation, and metabolic syndrome. However, the side effects of the PM on embryonic development have not been yet properly investigated. We treated early chick embryos with various PMs collected from Jeddah at different time-course. After only a few hours of treatment, severe disruption of the cardiovascular system including impaired vascular development, internal haemorrhage, and heart enlargement was detected. This resulted in a severe lethality of all treated embryos. Such defects indicate a high congenital malformation induction potential to the Saudi newborn. PM effects on signalling transduction pathway(s) which could mediate these cardiovascular phenotypes are currently being elucidated.

Poster Number: P10
Frizzled-10 mediates Wnt1 induced neurogenesis in the developing spinal cord
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Wnt/FZD signalling activity is required for many steps of spinal cord development, including cell proliferation and specification. Wnt ligands bind to Frizzled receptors and Lrp5/6 co- receptors and initiate canonical, β-catenin-dependent, Wnt signalling. Here, we show FZD10 is expressed in the dorsal neural tube and overlaps with expression of Wnt1, markers of dorsal progenitors and of interneurons. In vivo gain- and loss-of-function approaches in chick neural tube show a role of FZD10 in spinal cord development. The knock-down of FZD10 in developing neural tube, using shRNA, led to a decrease in cell proliferation and in the expression domains of neural markers Pax6, Pax7, Lhx1/5 and Tuj-1. Furthermore, FZD10 expression is regulated by Wnt1, as we demonstrate that Targeted mis-expression of Wnt1 up-regulated FZD10 expression in the dorsal spinal cord. We propose that FZD10 is required for spinal cord development and for mediating Wnt1 signaling during neurogenesis.

Poster Number: P11
Inter-dependent apical microtubule and actin dynamics orchestrate centrosome retention and neuronal delamination
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Detachment of new-born neurons from the neuroepithelium is required for correct neuronal architecture and functional circuitry. This delamination process involves adherens-junction disassembly and actomyosin-mediated abscission, during which the centrosome is retained while apical/ciliary membrane are shed. The cell biological mechanisms mediating delamination are, however, poorly understood. Using live-tissue and super-resolution imaging, here we uncover a centrosome-nucleated microtubule wheel, which aligns with the actin-cable and adherens-junctions within the apical end-foot of chick and mouse neuroepithelial cells. These microtubules maintain adherens-junctions while actin maintains microtubules, adherens junctions and end-foot dimensions. During neuronal delamination, actomyosin constriction generates a focal actin-microtubule tunnel through which the centrosome translocates prior to abscission. This movement requires interdependent actin and microtubule activity; furthermore, centrosome compromise indicates that this organelle nucleates microtubules required for delamination. These findings identify new cytoskeletal structures and interactions that orchestrate neuronal delamination and may inform mechanisms underlying normal and pathological epithelial cell detachment.

Poster Number: P12
Organizers in Development: Is Hensen's node a stem cell niche?
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'Organizers' are regions in an embryo that play a fundamental role in development by inducing and patterning surrounding tissues. Hensen's node is an organizer that induces and patterns neural tissue and contributes cells to axial and paraxial mesoderm. Previous work using single-cell lineage analysis suggested that the node contains resident stem cells, but it is not clear whether it represents a stem cell niche that would induce and maintain stem cells. Through a series of heterotopic grafts in the chick we show that the node can specify resident cell behaviour in cells that do not normally enter the node. *In situ* hybridisation reveals that these resident cells express Hensen's node markers. When these cells are re-grafted into the node of a second host, they appear to self-renew. These data suggest that the node can induce and maintain stem cells and is therefore a stem cell niche.

Poster Number: P13
Cdc42 regulation during epithelial cell polarity establishment
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Apical-basal cell polarity is essential for the integrity and function of epithelial tissues but how it is regulated is not fully understood. The conserved PAR complex (cdc42-PAR6-aPKC-PAR3) regulates epithelial polarity, in particular the formation of the cell-cell contacts called the *zonula adherens* (*za*). PAR complex assembly at the apical pole of the cell requires the activation of Cdc42. This raises the possibility that localizing GEFs and GAPs, which control the active state of cdc42, may act as a mechanism of polarity during epithelial morphogenesis. To test this hypothesis we conducted a reverse genetic screen for RhoGEFs and RhoGAPs in the *Drosophila* pupal retina. I will present the results of this screen and on-going work on two novel GEFs which we find regulate PAR complex assembly, apical-junctional separation and ZA specification in the fly pupal photoreceptor.

Poster Number: P14
Spatio-temporal regulation of cerebellar granule cell neurogenesis
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Cerebellar granule cell progenitors (GNPs) are one of the most prominent neuronal progenitor populations in the developing brain. They are born during development from the rhombic lip of the 4th ventricle and migrate tangentially to form a transient proliferative layer covering the surface of the cerebellar anlage; the external granule layer (EGL). Developmental Notch and BMP pathways have been implicated in GNP neurogenesis, however results show BMP signalling may be more transient and spatially regulated than previous data suggests, and also implies the underlying Purkinje cells have a more complex role in GNP development. To target the EGL and study cell behaviour following genetic manipulation, we have optimised the inducible genetic manipulation of the chicken cerebellum. Using immunofluorescence and reporter constructs, we have characterised activity of both pathways in the EGL, which, in conjunction with the inducible system, is enabling investigation into spatio-temporal genetic mechanisms regulating GNP development *in vivo*.

Poster Number: P15
Physical mechanisms of epiblast and primitive endoderm segregation in the mouse embryo
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A blastocyst is composed of trophectoderm, epiblast (EPI), and primitive endoderm (PrE). EPI- and PrE-specific transcription factors are expressed in the inner cell mass (ICM) in a random "salt and pepper" pattern at E3.75. These two lineage progenitors segregate into the appropriate cell layers and differentiate toward mature EPI and PrE by E4.5. However, how each ICM cell segregates into two lineages is still unclear. Physical forces are thought to regulate embryo development. However, its involvement in the early embryo, specifically in EPI and PrE segregation is not yet understood. To assess the individual cell physical properties and whole actin cytoskeleton network regulating them, we performed scRNAseq, measured the single cell surface tension, extracted interfacial tension and quantified the cell membrane dynamics. Understanding the mechanical properties of EPI and PrE will provide an important avenue for approaching the cell specification and morphogenesis in the embryo.

Poster Number: P16
Modulation of Rok membrane dissociation rate by Crb/aPKC triggers Rok planar polarisation during morphogenesis
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The MyosinII activator Rok is involved in a variety of morphogenetic processes during embryonic development. We have shown previously in the Drosophila embryonic salivary gland placode that Rok is planar polarised at the tissue boundary through a negative regulation by the apical polarity proteins Crumbs (Crb) and aPKC. Intriguingly, despite Crb, aPKC and Rok being expressed in the whole tissue, this effect is specific to the boundary of the tissue. Using FRAP in embryos expressing endogenously tagged Rok, we find that Rok membrane dissociation rate is lower at the boundary of the tissue, where Crb and aPKC membrane levels are lower. Moreover, aPKC can phosphorylate the Rok membrane association region in vitro, suggesting Rok phosphorylation by aPKC might be responsible for the difference in Rok membrane dissociation rate. Finally, computer simulations show that such differences in Rok membrane dissociation rate are sufficient to explain Rok planar polarisation at the tissue boundary.

Poster Number: P17
Integrin signaling in epiblast morphogenesis and cell survival
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Integrins are transmembrane receptors which mediate interactions of epithelial cells with the underlying basement membrane. They act by regulating several aspects of epithelia morphogenesis from cytoskeleton architecture to cell survival and cell cycle progression. We found that the integrins play an essential role for the epiblast morphogenesis at the stage of implantation. In particular they regulate the precise spatio-temporal localization and assembly of the contractile cytoskeleton to ensure initiation of the apical pole as the future site of lumenogenesis. In contrast to previous studies, integrin signaling appears to be dispensable for the initial establishment of apico-basal polarity in mouse embryonic stem cells. In addition to morphogenesis, integrin signaling appears to also provide essential survival signals for epiblast cells to progress through implantation upon exiting from naïve pluripotency.Thus, in this study, we unveiled a sophisticated signaling pathway driven by integrin signaling which ensures epiblast polarization, morphogenesis and survival upon embryo implantation.

Poster Number: P18
The ECM protein Agrin localizes to the developing epicardium and is essential for coronary vessel formation
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The extracellular matrix (ECM) is a highly dynamic protein network interacting with cells attaching to it during organ development. Agrin, a proteoglycan protein, was recently reported to promote heart regeneration after myocardial infarction. However, its role during heart development has not been studied. Agrin was found to localize specifically within the embryonic epicardium from E14.5. The distribution of Agrin was non-homogenous and overlapped with several other ECM components including Itga4 but not laminin. These selective co-localizations suggest potential cooperative signals on discrete sub-populations of epicardial cells. Close observation revealed an inverse relationship between Agrin expression and epithelial-to-mesenchyme transition (EMT) markers β-catenin and ZO-1. Loss of Agrin in global knock-out mice resulted in coronary vessel defects, whereby the forming vascular plexus failed to branch and extend towards the apex of the heart. Studies are ongoing to determine the precise role of Agrin within the developing epicardium and during coronary angiogenesis.

Poster Number: P19
Regulation of Yorkie by Mask in *Drosophila*
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The transcriptional coactivator Yorkie (Yki) in flies and its homologue Yes-associated protein (YAP) in mammals is one of the main regulators of growth in epithelial tissues. Active Yki/YAP translocates from the cytoplasm into the nucleus where it induces the expression of genes that drive cell proliferation, growth and survival. As a consequence, YAP overexpression promotes tumour formation in humans. The conserved Multiple ankyrin repeats single KH domain (Mask) protein has been previously identified as a regulator of Yki activity and tissue growth in *Drosophila*. We have found evidences about the mechanism of Yki regulation by Mask, since silencing of *mask* changes the ratio of nuclear to cytoplasmic levels of Yki in *Drosophila* follicular epithelium surrounding the egg chambers. This indicates a role of Mask in the translocation of Yki to the nucleus. These results provide new insights into Yki physiological regulation.

Poster Number: P20
Sema3A acts as a repellent for the medial longitudinal fascicle in the embryonic chicken brain
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The medial longitudinal fascicle (MLF) is a major tract in the conserved early axon scaffold. It originates in the caudal diencephalon, from which it projects caudally in a tight bundle along the ventral midline. Our aim was to characterise the guidance cues that determine the strictly caudal projection of the MLF. The MLF neurones express the Sema3 receptors Neuropilin1 and PlexinA4, and Sema3A is expressed just rostral to the MLF. Ectopic expression of Sema3A within the path of the MLF interfered with the outgrowth of the MLF. In vitro assays confirmed that Sema3A acts as chemorepellent for MLF axons. Correspondingly, after blocking Sema3A signalling in vivo genetically or pharmacologically, MLF axons lost their strict caudal projection pattern. Our results demonstrate that Sema3A repulsion, mediated by Neuropilin1 and Plexin A4, is a key guidance cue for the MLF axons.

Poster Number: P21
Role of *Pbx1* heterogeneity in mesoderm specification
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Blood, bone and muscle cells arise during gastrulation from specific pools of mesodermal progenitors (MPs), but the mechanisms generating this variety are still elusive. Understanding how MPs originate is critical to implement efficient protocols applicable to tissue repair and regenerative medicine. We found that Pbx1 transcription factor plays a critical role in the formation of posterior MPs. Pbx1 exhibits heterogeneous levels of expression in mouse epiblast stem cells (mEpiSCs). Therefore, we hypothesized that different levels of Pbx1 could be critical to generate specific MPs. To address this question, we established *Pbx1-Venus* mEpiSCs, using BAC recombination to assemble two different reporter constructs. We cloned *Venus* into either exon1 or exon2 of a *Pbx1*-containing BAC and found that the exon2-*Venus* lines mirrored the expression levels of endogenous *Pbx1*. Currently, we are using these lines to FACS-sort high and low Pbx1-expressing cells to test their capacity to differentiate into specific MPs.

Poster Number: P22
Oct4 regulates the embryonic axis and coordinates exit from pluripotency and germ layer specification in the mouse embryo

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How different germ layers are specified from the uncommitted, pluripotent epiblast of the mouse post-implantation embryo, remains unclear. Multiple signalling pathways act in spatially restricted domains to co-ordinately instruct specific fates. Evidence also points towards a role for the transcription factor Oct4 in this process, although its function has not been thoroughly studied in this context due to its pleiotropic roles in development. Here we employ conditional deletion of *Oct4* to assess its role in fate specification. We find that expression domains of lineage markers were disrupted: definitive endoderm expanded, anterior/posterior region boundaries became blurred and an ectopic posterior-like domain appeared anteriorly. While the primitive streak initially forms in the presumptive proximal-posterior region, epithelial-to-mesenchymal transition is impeded by dramatic increase of E-cadherin. This leads to failure to generate germ layers. We are therefore using *in vitro* models to study the mechanism by which Oct4 regulates embryonic patterning, coordinating multiple fates.

Poster Number: P23
Making the first cell fate decision in the early mouse embryo: polarity matters in space and time

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The formation of apical domain initiates the first lineage segregation event in the early mouse embryo. After symmetric and asymmetric cell divisions, the polarised cells become Trophectoderm and the apolar cells contribute to Inner cell mass. How apical domain is assembled, as well as the factors determining the division patterns are still unclear. Here, we found that the increased Par complex stability, together with actomyosin asymmetry triggered by Protein Kinase C (PKC)-Rho GTPase pathway, drives apical domain formation. Moreover, we found that the timing of cell polarisation appears heterogeneous, and this is associated with first a/symmetric division patterns and then the final lineage allocation. Such heterogeneous polarity timing lies downstream of epigenetic regulations. To conclude, our results provide a detailed scheme of *de novo* cell polarity establishment, and illustrate a model of how epigenetic factors modulate the cell fates through tuning the timing of key developmental events such as cell polarity.

Poster Number: P24
The role of the primary cilium during neuron repolarisation in the developing CNS

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Proper establishment of neuronal polarity is crucial during spinal cord development. Differnetiating neurons undergo apical abscission, which mediates loss of apical cell polarity and dis-assembly of the primary cilium, leading to delamination from the neuroepithelium. As the primary cilium plays an important role in transducing diverse signalling pathways, this suggests that newborn neurons undergo a resetting of their signaling state. We show that the delaminating neuron retains a pro-cilium like structure, which acts as the site for primary cilium reassembly. Strikingly, intraflagellar trafficking is re-established during delamination, suggesting that the re-assembled primary cilium is actively transducing signals, which we show, is essential for normal axonal growth. This suggests that differentiating neurons undergo a re-setting of their signaling state through re-assembly of the primary cilium, leading to correct axon placement.

Poster Number: P25
Cellular mechanisms of sensory organ segregation in the embryonic inner ear
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The inner ear contains multiple sensory organs separated by non-sensory epithelial domains. The mechanisms of development of these organs remain unclear. Here, we studied the expression of the prosensory marker Sox2 during the formation of two sensory organs, the anterior and the lateral cristae, in developing chick otocysts. We found that the cristae arise at the edge of a larger Sox2-expressing pan-sensory domain. Over time, the distance between the cristae and the pan-sensory domain increase, suggesting a segregation process. This is accompanied by striking changes in cell morphology at the interface of segregating sensory organs: cells enlarge, become elongated and progressively align along the lateral border of the cristae. Multicellular rosettes and phosphorylated myosin regulatory light chain staining are present throughout the sensory and non-sensory domains of the otocyst, suggesting that acto-myosin contractility is involved in cristae segregation. We are now using pharmacological and genetic approaches to test this hypothesis.

Poster Number: P26
XMAP215, Eb1 and tau jointly regulate microtubule polymerisation and organisation in axons
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Axons are the cable-like processes of neurons which electrically wire our bodies and need to survive for decades. Axon physiology and morphogenesis depend on parallel bundles of microtubules (MTs). To understand the regulatory networks underlying MT bundle formation and maintenance, we use *Drosophila* genetics in primary neurons and *in vivo*. Analyses of >50 actin- and/or MT-binding regulators have led to novel understanding of the machinery that regulates MT de-/polymerisation in axons (Voelzmann, 2016, *BrainResBulletin* 126, 226ff). We find that Eb1, Tau and XMAP215 are key constituents of the polymerisation machinery, which has further important functions in MT bundle organisation through a spectraplakin-mediated guidance mechanism. Lowering tubulin supply affects formation of this machinery in an 'all-or-nothing' mode affecting MT abundance but not organisation. Therefore, fly genetics provides a powerful strategy to decipher complex cytoskeletal machinery and deduce important new concepts. Supported by BBSRC and Leverhulme Trust

Poster Number: P27
The role of Polycomb-group complex PRC2 in human pancreatic cell differentiation
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The ability to direct cell differentiation through epigenetic manipulation is an underexplored area in stem cell and developmental biology, with a shortage of mechanistic studies of epigenetic pathways in human tissue formation. The Polycomb Repressive Complex, PRC2, which catalyses the repressive H3K27me3 mark, is required for numerous cell fate decisions and is an attractive target for modulation. During pancreatic differentiation, the distribution of H3K27me3 changes and PRC2 inhibition modifies the pancreatic cell populations formed.

In this project, we will use ChIP-Seq to monitor H3K27me3 as a readout of PRC2 activity, during human pluripotent stem cell to pancreatic beta-cell differentiation. We will investigate PRC2 loss of function using chemical inhibitors and CRISPR knockouts. We will also attempt to produce an auxin-inducible degron system for PRC2, which would allow precise temporal control of PRC2. These experiments will allow us to investigate the functional role of epigenetic mechanisms during long-term, human tissue development.

Poster Number: P28
Radially-polarised cell behaviours drive tube budding from an epithelium
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The budding of tubular organs from flat epithelial sheets is a vital morphogenetic process. Cell behaviours that drive such processes are only starting to be unraveled. Using live-imaging and morphometric methods we show that in addition to apical constriction, radially oriented directional intercalation plays a major contribution to the early stages of invagination of the salivary gland tube in the *Drosophila* embryo. Extending analyses in 3D, we find that near the pit of invagination, isotropic apical constriction leads to strong cell wedging, and further from the pit cells interleave circumferentially, suggesting apically driven behaviours. Supporting this, junctional myosin is enriched in, and neighbour exchanges biased towards the circumferential orientation. In a mutant failing pit specification, neither are biased due to an inactive pit. Thus, tube budding depends on a radially-polarised pattern of apical myosin leading to radially oriented 3D cell behaviours, with a close mechanical interplay between invagination and intercalation.

Poster Number: P29
The role of mRNA capping in ESCs and early embryo development
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The mRNA cap consists of a series of co-transcriptional modifications on the nascent transcripts that confer protection from degradation and mediate RNA processing and translation. The mature cap and first and second transcribed nucleotides are methylated by RNMT-RAM, CMTR1 and CMTR2, respectively. Recently, our lab showed that RNMT and RAM are differentially regulated across mouse primary tissues and, in particular, during the process of neural differentiation. Indeed, it was shown that the expression of pluripotency-associated genes is dependent on high levels of RAM in ESCs. We further characterised the expression of the capping enzymes in the early stages of mouse embryo development and are investigating the mechanisms by which mRNA capping determines the differentiation process. Our data indicates a role for CMTR1 in controlling the first stages of exit from pluripotency as its absence impairs the process of proliferation in differentiation conditions.

Poster Number: P30
Netrins guide axons of the tract of the posterior commissure by repulsion during early embryonic brain development
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The tract of the posterior commissure (TPC) is part of the early scaffold of axon tracts in the developing anterior brain. The TPC axons follow a narrow path in the caudal pretectum, suggesting tight control by axon guidance signals. Immunohistochemistry and *in situ* hybridisation was used to analyse the relationship between netrin 1, netrin 2, Unc5 receptors and the early tracts during development of the chick brain. Interestingly, netrin1 and netrin2 are expressed ventral, rostral and caudal to the TPC, leaving a netrin-free channel along the midbrain-forebrain boundary. Consistent with Netrins acting as repellents, misexpression of netrin1 and netrin2 by *in ovo* electroporation caused misguidance of the TPC axons and failure of TPC formation. The MLF was not affected, suggesting that even if neurons are intermingled, they use different ques for guiding their axons to the correct target.

Poster Number: P31

Mud is required for axon guidance at the midline of the Drosophila central nervous system

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The study of axon guidance at the midline of the central nervous system in the Drosophila embryo has allowed the identification and study of factors directing axonal growth. The initial simple model of a balance of the Netrin attractant and Slit repellent guiding axons at the midline has recently been superseded by the discovery of additional midline guidance molecules which are revealed in the absence of Netrin signalling. We have identified mushroom body defect (mud) as a further factor required to guide commissural axons. Genetic interaction studies show that mud acts downstream of some, but not all, of the pathways known to be required for midline guidance. This has also uncovered a potential new role for wnt5, Lis1 and frizzled in Netrin-independent axon guidance which may be mediated by mud. Structure function studies have revealed an essential role for the N-terminal calponin-homology domain suggesting mud may regulate the underlying cytoskeleton.

Poster Number: P32

The mouse hematopoietic stem cell lineage fails to develop beyond the pro-HSC stage in the absence of blood flow

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Hematopoietic stem cells (HSCs) emerge through a continuum of precursor stages, pro- and pre-HSCs. Studies in zebrafish implicated blood flow in this process. However, this is less clear in the mouse as embryos without blood flow die before functional HSCs emerge. Here we assessed the effect of flow on HSC precursor cells. In *Ncx1-/-* embryos that lack flow, hemogenic endothelium and pro-HSCs emerge at a normal frequency, although in reduced numbers. *Ncx1-/-* pro-HSCs were severely impaired in their function and failed to mature into functional HSCs *ex vivo*. Gene expression analysis identified an aberrant signature in pro-HSCs and hemogenic endothelium isolated from *Ncx1-/-* embryos, with upregulation of endothelial genes and downregulation of hematopoietic genes, in line with a block in hematopoietic development. Ongoing experiments assess the involvement of candidate developmental signaling pathways to elucidate the mechanism by which blood flow affects the development of pro-HSCs along the HSC lineage.

Poster Number: P33

Does differentiation of the first cell lineages in in vitro cultured preimplantation rabbit embryo depend on developmental dynamics?

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Preimplantation embryo development is the time of rapid morphological changes and first cell lineages differentiation. *In vitro* culture conditions are one of the factors that could affect these processes. Finding correlation between morphokinetic, lineage differentiation and culture conditions can potentially become a predictor of embryo viability.

Using time lapse microscopy we identify preimplantation rabbit embryo kinetic time points and their timing during *in vitro* culture (1) with different oxygen levels (5% and atmospheric) and with (2) addition of protein components (BSA, KSR) to evaluate their influence on rabbit embryo development and cell lineages differentiation.

Our results show that rabbit embryos cultured in atmospheric oxygen levels have higher percentage of cells that fail to express lineage-specific or pluripotency markers, and longer cleavage duration compared to embryos cultured in 5% oxygen.

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Poster Number: P34
Lineage segregation, X chromosome dynamics and regulation of pluripotency during pig embryogenesis revealed by single cell RNA-seq.

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Pre-implantation embryo development follows regulative processes of lineage segregation and transcriptional regulation that culminate with the formation of the epiblast, the cells of which give rise to all the fetal lineages. How these processes are regulated in large mammals is poorly understood. Here, we present the transcriptional map of pig embryo development following single cell RNA Seq. We show gradual segregation of the inner cell mass and trophectoderm in early blastocysts, followed by epiblast and hypoblast segregation in late blastocysts. In females, dosage compensation and X chromosome inactivation is accomplished in the late epiblast before lineage priming. We reveal the transcriptional circuitry and signaling effectors of pluripotency that define a short naïve pluripotent phase followed by a protracted primed stage. This detailed transcriptional analysis provides a blueprint for understanding early embryogenesis in the pig embryo that will impact the development of stem cell technologies in domestic animals.

Poster Number: P35
Chicken primordial germ cells require CXCR4 and c-Kit signalling for directed vascular migration and colonisation of the chick embryonic gonads

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Primordial germ cells (PGCs) are the precursors of the germ cell lineage that differentiate into mature spermatozoa and oocytes. In many organisms, PGCs are specified at a distant site and migrate actively to the developing gonads. The chemokine/receptor SDF1/CXCR4 signalling has been shown to provide directionality to migrating PGCs in mouse, zebrafish and Xenopus while SCF/c-Kit signalling maintains survival of migrating PGCs in mouse. Avian PGCs migrate through the vascular system in place of endoderm migration observed in mammals. Importantly, avian PGCs express similar cytokine receptors as their mammalian counterparts. To address the factors guiding avian PGC migration, we used CRISPR/Cas9 to create loss-of-function deletions in chicken PGCs. We show *in vivo* that CXCR4-knockout PGCs fail to migrate to the genital ridges whereas c-Kit-knockout PGCs colonise the developing gonads in reduced numbers. These results reveal essential roles for CXCR4 and c-Kit signalling in chicken PGCs for efficient gonadal colonisation and proliferation.

Poster Number: P36
Polo kinase is recruited to the mitotic pericentriolar material by Spd-2 to drive centrosome maturation in flies

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PLK1/Polo kinase is a major regulator of cell division that is recruited to multiple sites in mitotic cells by phosphorylated S-S/T(P) motifs. At the centrosome, Polo is key for correct centriole maturation and disengagement, and for the dramatic expansion of the pericentriolar material (PCM) during mitosis.

Here, we have used a screen based on mRNA injection into *Drosophila* embryos to study what protein(s) recruit Polo to its different centrosomal targets and so enable Polo to perform its various centrosomal functions. Our results highlight the importance of the centrosomal protein Spd-2 in Polo recruitment for formation of the scaffold over which the PCM organizes. Loss of Spd-2-mediated recruitment of Polo results in PCM defects and abnormal distribution of pericentriolar proteins Cnn and γ-tubulin. We have also used transgenic fly lines to further characterize the consequences of losing Spd-2-mediated Polo recruitment, including the effects on embryo development.

Poster Number: P37
Klf family genes expression in preimplantation rabbit embryos
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Klf family genes are known to be involved in proliferation, apoptosis, differentiation of cells, pluripotency maintanance of ES cells and embryo development. Klf4, one of seventeen genes from Klf family, was shown to be a crucial factor, together with *Sox2*, *cMyc* and *Oct4*, for reprogramming cells into iPSc.

Expression of Klf family genes in embryos has been confirmed in mouse, chicken and human. These studies revealed differences in expression of Klf factors. As the role of Klf family genes is known in mouse epiblast specification, little is known about their expression, localisation and role in rabbit embryo development.

Here we show profile of Klf family genes expression at consecutive stages of rabbit embryo development and detailed analysis of localisation of the best known Klf factor-Klf4. Research on Klf family genes and mechanisms responsible for maintaining pluripotency in other species than mouse brings us to reveal more general mechanism of mammalian development.

Poster Number: P38
Identification and characterisation of molecular networks driving mesoderm differentiation
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During development, muscle, bone, heart and blood arise from specific pools of mesodermal progenitors (MPs). Different signalling pathways and transcription factors provide the spatio-temporal information required to generate the variety of mesodermal types. However, how different progenitors acquire their specific mesodermal fate and what are the molecular networks governing this choice are still open questions.

Taking into account the different combinations of signalling cues present at gastrulation time, we established new *in vitro* protocols to differentiate mouse pluripotent stem cells into different MPs. Single-cell RNA-sequencing provided a detailed transcriptional snapshot of all different MPs produced. We are currently characterising their functional potential using *in vitro* and *in vivo* assays.

We believe that this combination of *in vitro* differentiation systems, single-cell profiling and *in vivo* genetic studies represents the best approach to get a deeper understanding of the mechanisms controlling mesoderm specification, that will open new avenues for therapeutic applications.

Poster Number: P39
The mirtron miR-1010 regulates the nAcRß2 to ensure synaptic homeostasis in *Drosophila*
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Synaptic homeostasis is critical to maintain postsynaptic excitability within an optimal range and is often altered in neurological diseases. Yet, the mechanisms underlying it remain poorly understood. Here, we reveal the existence of an intricate loop ensuring synaptic homeostasis via miR-1010. Homozygous miR-1010 mutant complete embryogenesis without any apparent defect. However, larvae do not grow as wild-type or heterozygous mutants. MiR-1010 mutant larvae retain a first instar larvae size and are unable to pupariate. We show that the nAcRß2 is overexpressed in the miR-1010 mutant. Our results indicate that the activation of the nAcRß2 boosts synaptic potentials and triggers transcription of new nAcRß2. The high permeability of nAcRs creates an influx of calcium which concomitantly activates Shal potassium channel and SKIP (host gene of miR-1010) transcription via CaMKII and Adf-1. Whilst Shal and SKIP temper synaptic potential, miR-1010 downregulates nAcRß2 to further retain synaptic potential within the normal range.

Poster Number: P40
Using fluorescence lifetime imaging of NAD(P)H and live confocal imaging of mitochondrial membrane potential to elucidate the developmental origins of cell metabolism in inner ear sensory epithelia
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In complex tissues, metabolic switching can instruct cell lineage choices. Defining the metabolic programs that instruct cell differentiation during development and regeneration is essential for developing new strategies to manipulate stem cell capacity to generate specific, fully functional cells.

Inner ear sensory epithelia comprise different cell types with unique metabolic properties. Using fluorescence lifetime imaging of NAD(P)H, we show metabolic switching in cochlear sensory cells between E14 and E16. We differentiate NADH and NADPH pools and quantify relative levels of the two cofactors in different cell types. We find that sensory hair cells but not supporting cells become more oxidative as they develop. Additionally, using TMRM to monitor mitochondrial membrane potential ($\Delta\Psi^{mt}$) we observe marked changes in mitochondrial activity and morphology as cells differentiate. At early embryonic stages mitochondria are spherical and become progressively branched as cells develop. These findings implicate metabolism as a driver of cell fate decisions in complex tissues.

Poster Number: P41
Insight into the phosphorylation and dual function of a rhomboid protease, RHBDL4
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Rhomboid-like proteins are a superfamily of membrane polytopic proteins which act as fate determinants of protein traffic in the secretory pathway. Reportedly, these rhomboid-like proteins show dual functionality when specifying the forward trafficking or degradation of membrane proteins. For example, RHBDL4 is an ER resident member of the superfamily and an active protease. RHBDL4 cleaves and allows secretion of APP, TGFα; while cleavage of pTCRα and opsonin specify the degradation via ERAD. Here, we present a forward-spatial proteome of RHBDL4 and a related protein iRhom2. In the screen, we found a phosphatase interacting with RHBDL4 and phosphopeptides mapping to the protease. Potential-function separation mutants were generated by targeting putative phosphosites of RHBDL4. Those mutants were tested against known substrates or our proteomic candidates. We hope to determine at the mechanistic level how the membrane-protein fate determinant, RHBDL4 exerts its dual function.

Poster Number: P42
Role of Pbx proteins in lineage choice and mesoderm specification
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The mesoderm is the embryonic germ layer that gives rise to muscle, bone, heart and blood. Mesodermal progenitors (MPs) are specified through the primitive streak (PS) during gastrulation and contribute to different mesodermal tissues. In the PS, the coordination of different signalling pathways and transcription factors (TFs) provides the spatial/temporal information that specify distinct mesodermal fates. Genes conferring positional identity, such as Hox and Pbx TFs, could be important for attributing to cells the required space and time coordinates to acquire a specific identity. However, what are the molecular networks regulating different MPs specification is still unclear. We found that Pbx proteins are expressed in the PS and regulate the identity of two distinct populations of lateral MPs. We hypothesize that Pbx control molecular networks critical for the specification of distinct MPs populations. Using *in vivo* and *in vitro* approaches we will characterize the Pbx-dependent molecular networks regulating mesoderm specification.

Poster Number: P43
De Novo DNA Methylation Secures Embryonic Lineage Determination during Pluripotent Phase Transitions
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The major wave of global DNA methylation in mammalian development occurs around implantation. While DNA methylation acquisition is essential to development, its function is unclear. We investigated progression from naïve embryonic stem cells (ESCs) to lineage specification using mouse ESCs lacking de novo DNA methyltransferases, Dnmt3a/3b. Dnmt3a/3b double knockout (dKO) ESCs are unable to specify all three germ layer lineages, but can commit to primordial germ cell fate. dKO cells aberrantly initiate trophectoderm lineage program. Nonetheless, dKO ESCs can be converted into post-implantation epiblast stem cells (EpiSCs) which are highly methylated. However, dKO EpiSCs can differentiate with low efficiency into all three germ layer lineages and germ cells. Single cell expression revealed that upon naïve state exit, dKO cells progress through aberrant expression states, co-expressing post-implantation, trophectorderm, germ cell and naïve pluripotency markers. The chaotic cellular states perturb the execution of developmental lineage specification and prohibit efficient cell fate transitions.

Poster Number: P44
Regulation of stem cell differentiation by ERK signalling
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Stimulation of the ERK/MAPK pathway is required for the onset of differentiation in mouse embryonic stem cells (mESCs). Many markers of pluripotency show heterogeneous expression under standard mESC culture conditions. Inhibition of the MAPK pathway causes much of this heterogeneity to be lost, as cells are forced into a more pluripotent state. However, the regulatory dynamics of ERK signaling during differentiation are not understood. Using a FRET based biosensor, we show ERK activity to be highly heterogeneous within a population. Quantification of ERK signaling dynamics, following the induction of differentiation, revealed distinct ERK signaling behaviours. By measuring the expression levels of pluripotent and differentiation markers, we have been able to determine how these distinct ERK signaling behaviours scale with the pluripotent state of a cell. This work furthers our understanding of how signaling dynamics regulate differentiation and how environmental modulation of these dynamics may influence pluripotency.

Poster Number: P45
Actomyosin driven tension at compartment boundaries orients cell divisions independently of cell shape *in vivo*
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During animal development, planar polarization of the actomyosin cytoskeleton underlies key morphogenetic events such as axis extension and boundary formation. Actomyosin is enriched along compartment boundaries during segmentation of the Drosophila embryo, forming supracellular contractile cables, required for keeping cells segregated at the boundaries. Here, we show that, whereas most epithelial cells divide according to cell shape or tricellular vertices distribution, cells dividing at compartment boundaries do not follow neither their cell shape nor vertex geometry. Instead, they require the contractile actomyosin cable. By locally perturbing actomyosin cable tension in vivo using laser ablation or, conversely, ectopically increasing tension using IR-laser wounding we found that localised subcellular force at the cable is necessary and sufficient to reorient mitoses. In summary, we demonstrate that subcellular-scale forces alone orient cell divisions independently of cell shape in an epithelium.

Poster Number: P46
Wingless acts as a long-range morphogen to pattern the proximo-distal axis of *Drosophila* renal tubules
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Wingless/Wnts are signalling molecules, traditionally considered to pattern tissues as long-range morphogens. However, more recently the long-range spread of Wingless was shown to be dispensable in diverse developmental contexts in *Drosophila* and vertebrates. Here we demonstrate that Wingless does act as a long-range morphogen, to pattern the proximo-distal (P-D) axis of *Drosophila* Malpighian tubules. Wingless signalling, emanating from the midgut, directly activates *odd skipped* expression several cells distant in the proximal tubule. Replacing Wingless with a membrane-tethered version, unable to diffuse from the Wingless producing cells, results in aberrant patterning of the Malpighian tubule P-D axis and to development of short, deformed ureters. This work directly demonstrates a role for Wingless as a long-range morphogen. As well as extending our understanding about the functional modes by which Wnts shape animal development, we anticipate this mechanism to be relevant to patterning epithelial tubes in other organs, such as the vertebrate kidney.

Poster Number: P47
Activation of mechanical forces to control neuronal polarisation
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During development, neurons extend one long axon and several short dendrites. This neuronal polarisation is fundamental for the functioning of the nervous system. Neuronal polarisation starts with the formation of several short processes (neurites). Eventually, one of these neurites starts growing faster and eventually becomes the axon. Despite the fundamental importance of this process, the molecular mechanisms driving axon formation have not been identified yet. Importantly, axon formation can be induced experimentally by applying a tensile (pulling) force to a neurite. As growth cones constantly pull on their neurite, differential regulation of these intrinsic pulling forces could be the driver of symmetry breaking and axon specification. To test this hypothesis, we are investigating whether forces exerted by growth cones correlate with the fate of their neurite (axon vs. dendrite). These results might also provide new insights into axonal regeneration, which fails in adult mammals.

Poster Number: P48
Mouse Blastocyst to Egg-Cylinder Transformation
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The mouse embryo radically changes shape and organisation upon implantation transforming from the mature blastocyst into the post-implantation egg-cylinder. This transition is achieved by polarisation of the inner cell mass into a highly polarised epithelium, the epiblast, and the specification and expansion of two extraembryonic tissues, which surround the epiblast. The extraembryonic ectoderm differentiates from the polar trophectoderm and expands into a multi-layered tissue at the proximal tip of the epiblast. Concomitantly, the visceral endoderm specifies from the primitive endoderm to envelope the epiblast and then also the extraembryonic ectoderm starting at the distal tip. The mechanisms and the dynamics governing the blastocyst to egg-cylinder transition remain elusive. In this study, using analysis of fixed samples and high resolution live imaging at peri-implantation stages as well as pharmacological perturbations, we shed light on the morphogenetic mechanisms governing the blastocyst to egg cylinder transition.

Poster Number: P49
5 of 27 Rab GTPases are needed for apical membrane morphogenesis in tracheal cells
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The tracheal system in Drosophila consists of branched tubes of different sizes. Single terminal cells grow the smallest tracheal branches by deforming their basal membrane domain. In parallel, their apical membrane

forms a branched lumen. A quantitative study of phenotypic defects in terminal cells led us to conclude that at least two distinct membrane trafficking pathways contribute to the morphogenesis of subcellular tubes. To obtain more comprehensive data on membrane trafficking in the tracheal system, we performed a YFP-mediated and therefore quantitatively cross-comparable RNAi screen of 27 endogenously YFP-tagged Rab GTPases. We found that only five Rab GTPases cause defects in terminal cells when knocked down, the most striking one being Rab8. Based on further data, we hypothesise that Rab8 is involved both in delivering membrane material to the apical membrane, and in preventing the apical secretion of basal-directed secretory cargo.

Poster Number: P50
Embryonic polarity during energy depleting conditions
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Polarity is regulated by PAR proteins, which define opposing membrane domains through a set of antagonistic interactions sustained by phosphorylation. Consequently, current models require constant energy consumption. Therefore, to probe the design principles of this network, we sought to explore its response to energy depletion.

We are using anoxic arrest of the *C. elegans* zygote as a model for energy depletion as embryos have previously been shown to enter a reversible state of suspended animation. Our data show that during anoxia, the zygote cell cycle halts, accompanied by a loss of asymmetry in polarity markers. When normal oxygen levels return, the cell cycle resumes and polarity is re-established. Strikingly, we find anterior PARs maintain residual asymmetry during anoxia. We are currently exploring how this asymmetry is maintained during anoxia and whether this population could provide a spatial memory of the polarized state.

Poster Number: P51
The role of primary cilia in controlling stem cells in the developing cerebral cortex
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We are interested in the function of primary cilia in stem cells of the developing cerebral cortex which is responsible for all higher cognitive functions. We characterize mice mutant for *Inpp5e* which controls ciliary stability and the Inositolphosphate composition of the cilium thereby regulating hedgehog and Akt signalling. Moreover, *INPP5E* is mutated in Joubert-Syndrome patients who show malformations of the cerebral cortex including heterotopias and polymicrogyri. Interestingly, *Inpp5e* mutant mice also develop microgyri and heterotopias. These findings correlate with a severe depletion of basal progenitor cells, one of the major cortical progenitor cell types. Reduced stability of the cilium also results in a severe reduction of the Gli3 repressor, a key factor in cortical development. Taken together, these findings establish *Inpp5e* mutant mice as an animal model of cortical malformations in Joubert Syndrome and provide important insights into how primary cilia control the proliferation and differentiation of cortical stem cells.

Poster Number: P52
Activation of the PAR polarity network in the *C. elegans* zygote
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Polarisation of the *C. elegans* zygote requires the segregation of PAR proteins into opposing anterior and posterior cortical domains in response to a centrosome-related cue. The activation and consequences of the cue are relatively well understood, and thought to temporally regulate symmetry breaking. However, little is known about PAR network activation itself, allowing it to respond to cues and form antagonistic protein domains. While the PAR proteins are present in the oocyte, initial experiments suggested that key PAR network interactions are not evident at this time. We therefore investigated the behaviour of PAR proteins from oocyte maturation to symmetry breaking, uncovering a highly orchestrated pattern of PAR localisation changes and network activations steps. Strikingly, the majority of this programme does not require fertilisation or meiosis progression. Oocyte maturation appears sufficient to trigger the activation process and drive symmetry breaking, despite the absence of normal cues or cell cycle events.

Poster Number: P53
Regulation of Crumbs trafficking in epithelia
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Crumbs is a transmembrane protein that serves as both a determinant of epithelial cell polarity and an upstream component of the Hippo signalling pathway. Crb is normally localised to apical cell-cell contacts, located just above E-cadherin based adherens junctions, but how apical trafficking of Crb is regulated remains unclear. Here we show that polarised membrane trafficking of Crb is mediated by transport along either microtubules or actin filaments to deliver Crb apically. Apical Crb/Sdt then promotes recruitment of Cdc42, which is required to polarise the entire cytoskeleton via aPKC and Pak-family kinases, delineating a positive feedback loop that simulations suggest is crucial for polarization.

Poster Number: P54
APC/C-Vihar regulates centrosome activity and stability in the *Drosophila* germline
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A universal feature of metazoan reproduction is the elimination of maternal centrosomes prior to the end of oogenesis. In animals that have a syncytial cyst stage of oocyte development, including *Drosophila* and mouse, the germline centrosomes undergo a migration to all reside within the oocyte. However, the functional significance of centrosome transport within the female germline and the mechanism orchestrating this event is still a mystery. The Anaphase Promoting Complex/Cyclosome (APC/C) is the multi-subunit ubiquitin ligase (E3) that temporally regulates progression of the cell and centrosome cycles. By altering the negative regulation of its cooperating ubiquitin conjugating enzyme (E2), Vihar/Ube2c, we show that temporal control of APC/C activity and subsequently Polo kinase levels ensures centrosome stability and migration during early *Drosophila* oogenesis. Considering the conserved roles of the APC/C and Polo throughout the animal kingdom, our results provide insight into the general necessity of gametic centrosome transport for female fertility.

Poster Number: P55
Regulation of the muscle cell differentiation program
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Cell differentiation programs drive the production of specialised tissues from progenitor cells during development. Understanding these programs is critical for directing stem cells to make specific cell-types. Key transcription factors co-ordinate gene expression in differentiation programs. We study the conserved transcription factor Mef2 in Drosophila muscle differentiation. Mef2 is significant both as a key player in muscle cell differentiation and as a model for how protein interactions modulate transcription factor output. Muscle is both important for human health and an established paradigm for cell differentiation.

The project builds on our previous work. Mef2 protein activity is regulated both to stop it activating differentiation genes in progenitor cells, and to produce sequential gene activation in the differentiation program. This regulation results from interactions with other proteins. We are analysing these interactions, with the aim of understanding of how Mef2 orchestrates the differentiation of muscle progenitor cells, including in remodeling and regeneration.

Poster Number: P56
Exploring polyploidy in the extraembryonic epithelia of the beetle *Tribolium castaneum* using two complementary methods
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In certain contexts, animal cells cease mitosis and switch to endoreplication, increasing DNA copy number

without cytokinesis (polyploidy). While the molecular effectors of this process are known, its physiological relevance remains an open question. Polyploidy has been implicated in maximizing rapid transcription, such as in *Drosophila* nurse cells, or in supporting tissue homeostasis, as in mammalian hepatocytes. Similarly, polyploidy is a defining feature of the extraembryonic epithelia of insects, where both transcriptional and structural roles may be relevant.

Our recent characterization of transgenic lines with tissue-specific EGFP expression in the beetle enables us to investigate the dynamics and genetics of polyploidy in these epithelia. Firstly, we extract the features of the nuclei from multiview time-lapse recordings to characterize the developmental progression of endoreplication. At the same time, we purify these tissues via FACS to assess the functional relevance of their polyploidy at genomic and transcriptomic levels.

Poster Number: P57
Cell-cell interactions during forebrain morphogenesis
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The establishment of cell identities and sharp boundaries between distinct populations during development is essential for morphogenesis. Abnormalities in these processes lead to birth defects, and pathologies such as metastasis. During neurulation, telencephalic cells converge towards the midline, above eye field progenitors that maintain a cohesive state before moving outwards to form the optic vesicles. Although the patterning mechanisms, giving rise to telencephalon and eye identity within the forebrain, begin to be understood, how these decisions translate into complex morphogenetic behaviours is still unknown. Recent work in the lab has identified two zebrafish mutants presenting cell segregation defects during forebrain neurulation. Combining high-resolution live imaging, high throughput genomics and functional analyses in zebrafish embryo, I start 1) deciphering the mechanisms of boundary maintenance during neurulation, 2) understanding the cellular dynamics underpinning complex forebrain neurulation, and 3) identifying the effectors of cell segregation.

Poster Number: P58
Decoding the dynamic behaviour of Ngn2 in neurogenesis
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Live single-cell imaging has shed new light onto the process by which cells make fate decisions. For example, in the developing nervous system, it has been shown that key regulatory proteins such as neurogenic transcription factors (Hes1, Ascl1, Ngn2) oscillate with a periodicity of a few hours. Importantly these dynamics have been shown to be functional. Indeed, these findings show that not just the presence or absence of a protein but also its expression dynamics are causally related to the biological outcome. However, the mechanisms of decoding protein expression dynamics for cell behaviour and fate decisions is poorly understood. I focus on decoding Ngn2's protein dynamics by examining the response of its downstream targets. I hypothesize that Ngn2's downstream target genes respond differently to dynamic vs steady protein expression of Ngn2, and that the response is due to differences in chromatin architecture around their regulatory regions.

Poster Number: P59
Multi-site phosphorylation of bHLH transcription factors regulates formation of nerve and muscle
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Basic Helix Loop Helix (bHLH) transcription factors are master regulators during development, but a greater understanding of these key proteins is also relevant to diseases such as cancer, and to enable manipulation for cellular reprograming. Previous work has established that bHLH proteins Neurogenin2 and Ascl1 undergo multi-site phosphorylation that directly reduces their ability to drive neuronal differentiation. Using the developmental system of *Xenopus laevis*, we now extend this model to include NeuroD4, acting downstream of Neurogenin2 in neurogenesis, and to MyoD, a master regulator of myogenesis. We have generated optimised phospho-mutant forms of NeuroD4 and MyoD that dramatically enhance *in vivo* reprogramming of embryonic tissue to nerve and muscle respectively. Furthermore, we have identified conserved mechanisms by which these mutant proteins exert their superior activity. Thus, our findings

indicate that multi-site phosphorylation is functionally and mechanistically conserved to regulate bHLH protein activity.

Poster Number: P60
A dynamic contractile actomyosin network in cells that transit from migratory to constrictive behaviour during abdominal morphogenesis in *Drosophila*
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During morphogenesis of the *Drosophila* adult abdominal epidermis, the larval epithelial cells (LECs) migrate directedly, then constrict apically and die. These behaviours need to be coordinated, but how such coordination is achieved remains elusive. This is, however, central to our understanding of morphogenetic processes. Using 4D microscopy and genetic manipulation, we have studied the mechanisms underlying the LECs' transition from migration to constriction. We show that LECs possess a pulsatile apical contractile actomyosin network and that a change in network polarity underlies behavioural change. The level of cell contractility impacts on the network's behaviour, as well as on overall cellular architecture and behaviour. We find that constriction can occur without pulsed contractions, which raises questions about the contribution of the contractile network and the cell cortex to constriction. Our findings furthermore suggest that the contractile network serves a second function, which is to maintain cell shape independently from pulsed contractions.

Poster Number: P61
Chemical and mechanical signals interact to direct axon growth
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During brain development, growing neurons navigate through a highly complex environment as they extend towards synaptic targets. Studies of this axon pathfinding process have focused primarily on chemical guidance signals; however, neurons also sense and respond to mechanical properties such as local tissue stiffness, which strongly impact neuron growth. Thus axons must integrate chemical and mechanical signals as they grow. We find that substrate stiffness modulates the response of *Xenopus laevis* CNS neurons to the chemical guidance cue Semaphorin3A (Sema3A), with a softer environment attenuating the Sema3A response. Calcium dynamics and cyclic GMP (cGMP) levels - both critical regulators of Sema3A signalling – were elevated on soft substrates. Pharmacological studies further indicate that cGMP levels play an important role in the stiffness-dependent modulation of the Sema3A response. Learning how neurons integrate different signals in complex environments will help us to better understand axon guidance during development and regeneration.

Poster Number: P62
Cross-talk between distal- and proximal-end proteins regulates centriole size
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Centrioles are barrel-shaped structures, comprising a characteristic central "cartwheel" and surrounding microtubule (MT) blades. Centriole size varies between different cell and tissue types, but within the same cell line is remarkably consistent; new centrioles (daughters) usually grow to reach the same length as the older centriole (mother). Cartwheel growth is stimulated by Polo-like kinase 4 (Plk4), while the growth of centriolar microtubules is restricted by a 'capping' complex of CP110 and Cep97. Curiously, while MTs grow at the distal-end of centrioles, our recent work has shown that the cartwheel grows from the proximal-end. How are these two processes reconciled to ensure that the centriolar MTs and the cartwheel grow in phase and reach the same size? We have found that, in developing Drosophila embryos, 'cross-talk' between Plk4 and CP110/Cep97 allows the spatially separated processes of cartwheel and microtubule growth to be coordinated so that daughter centrioles reach the correct size.

Poster Number: P63

How do calcium oscillations co-ordinate endothelial cell biology during angiogenesis *in vivo*? An essential role for the uncharacterised endoplasmic reticulum transmembrane protein Tmem33 in promoting VEGF-mediated endothelial calcium oscillations and angiogenesis

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Angiogenesis requires co-ordination of multiple signalling inputs to tightly regulate behaviour of endothelial cells (ECs) as they form vascular networks. Vascular Endothelial Growth Factor (VEGF) is essential for angiogenesis and induces downstream signalling pathways including cytosolic calcium oscillations. How ECs interpret calcium oscillations to co-ordinate angiogenesis remains unknown. Here we show that Transmembrane Protein 33 (*tmem33*) which has no known function in multicellular organisms, is essential to mediate effects of VEGF in both zebrafish and human ECs. *tmem33* localises to the endoplasmic reticulum in zebrafish ECs and is required for cytosolic calcium oscillations in response to Vegfa. *tmem33*-mediated endothelial calcium oscillations are critical for formation of endothelial tip cell filopodia and EC migration. Global or endothelial-cell specific knockdown of *tmem33* impairs multiple downstream effects of VEGF including ERK phosphorylation, Notch signalling and EC proliferation. These studies reveal a hitherto unsuspected role for *tmem33* and calcium oscillations in promoting vascular development.

Poster Number: P64

Mass spectrometry imaging of barrier lipids in *Drosophila*

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Lipids on the body surface form an important barrier protecting the skin from trans-epithelial water loss, bacterial infection, and UV damage. In *Drosophila*, a complex lipid mixture secreted onto the body surface (cuticle) of adult flies has beneficial barrier and pheromonal functions. However, our previous work found that the alkene hydrocarbon component of cuticular lipids can also have a detrimental (autotoxic) effect on the lifespan of the host producer and its neighbours. The amount of autotoxic alkenes produced by adult flies is strongly influenced by the protein (yeast) content of the diet during development. We have recently developed mass spectrometry imaging techniques to map non-hydrocarbon lipids such as wax esters with high spatial resolution. Surprisingly, this new methodology reveals that many non-hydrocarbon lipids are spatially patterned on the cuticular surface. We are now exploring which cells and enzymes generate these patterned surface lipids.

Poster Number: P65

Pegasus, a novel small extracellular regulator of Wingless signalling in *Drosophila*

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Wnt/Wingless (Wg) signalling ligands precisely orchestrate the development of various tissues, often by activating the expression of specific genes at different diffusion ranges. Here we describe a novel peptide, Pegasus (Peg), encoded by a small open reading frame gene, which facilitates Wg diffusion during the development of the *Drosophila* wing imaginal disc. CRISPR/Cas9-mediated mutations of *pegasus* generate wing margin phenotypes, and changes in target gene expression, consistent with a role of *peg* in Wg signalling. We find that Peg is secreted, and that it co-localizes and co-immunoprecipitates with Wg, suggesting that Peg directly binds Wg in order to enhance its extracellular transport and signalling. Our results unveil a new element in the regulation of the Wg signalling pathway, and shed light on the functional consequences of Wg diffusion miss-regulation, while also reminding us of the functional diversity, and relevance of small open reading frame genes.

Poster Number: P66
Integration of haemodynamic forces and endothelial signalling during zebrafish vascular remodelling
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Angiogenesis is controlled by interactions between Vascular Endothelial Growth Factor (VEGF) and Notch signalling. The mechanisms by which endothelial cells (ECs) co-ordinate vascular remodelling in response to mechanical shear stress are incompletely understood. We investigated these mechanisms in the zebrafish sub-intestinal vein (SIV), which undergoes blood flow-dependent remodelling. Lightsheet time-lapse imaging in zebrafish embryos showed increased EC number and frequency of leading SIV sprouts which failed to regress, in the absence of blood flow (*tnnt2* morphant). Moreover, blood flow provides directionality during collective EC migration which was less uniform in the absence of blood flow. Overexpression of *vegfa* mRNA overrides flow-dependent SIV regression, whereas inhibition of Notch signalling with DAPT did not impair SIV remodelling. Interestingly, Bmp receptor expression was increased in the absence of blood flow. Collectively, this suggests blood flow-mediated haemodynamic force is required for developmental vascular remodelling potentially via induction of VEGF- and Bmp-mediated vessel regression.

Poster Number: P67
Cell shape changes couple wing vein morphogenesis with BMP signalling
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Coupling mechanisms between dynamic morphogenesis and developmental signalling pathways play an important role in tissue development. Using the *Drosophila* pupal wing as a model we investigated the interplay between wing vein morphogenesis and the bone morphogenetic protein (BMP) signalling pathway. During vein morphogenesis cells apically constrict despite the lumen forming basally. BMP signalling regulates shape changes through the induction of apical constriction. To alter cell shape we disrupted the actomyosin machinery, doing so throughout the tissue resulted in a spread of BMP signalling range, however smaller clones caused a local loss of BMP signalling. The spread of BMP signalling is dependent on *crossveinless*, which is required for ligand transport, suggesting that signal regulation is at the level of extracellular ligand trafficking. We propose that cell shape changes caused by BMP signalling facilitate the refinement of signalling range by forming a ligand 'sink' and form a feed-forward loop promoting BMP signalling.

Poster Number: P68
Dopaminergic axon guidance defects and lack of striatal innervation in Zfp503 mutant embryos
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Midbrain dopaminergic neurons regulate important brain processes including locomotion, reward and emotions. Their axons follow long longitudinal trajectories to innervate the striatum and other forebrain areas. Several chemotrophic molecules located in the midbrain and hypothalamus are involved in guiding dopaminergic axons towards the striatum, but the influence of target tissue is less well explored. We found that transcriptional regulator Zfp503 expressed in both dopaminergic neurons and the striatum has a key role in establishing dopaminergic circuitry. Using a conditional gene targeting approach we demonstrate a cell non-autonomous role for Zfp503 in dopaminergic axon guidance. While the dopaminergic circuitry develops normally after selective ablation of Zfp503 expression in dopaminergic neurons, its striatal function is required to guide dopaminergic axons towards their target areas. Our results suggest an unexpected role of the developing striatum in dopaminergic axon guidance.

Poster Number: P69
Optogenetic Frizzled 7 reveals a solely permissive function of Wnt/PCP signaling in directed mesenchymal cell migration

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The Wnt/PCP pathway determines planar polarity of epithelial cells in both vertebrates and invertebrates. Overexpression studies demonstrated the capacity of Wnt/PCP signaling to polarize cell shape and migration in an instructive manner. Yet, how endogenous Wnt/PCP signaling functions in mesenchymal cells remains unclear. Here we developed a light-switchable version of the Wnt/PCP receptor Frizzled 7 (Fz7) to distinguish between an instructive or permissive role in the developing mesendoderm during zebrafish gastrulation. We show that prechordal plate (ppl) cell migration is defective in maternal-zygotic *fz7* mutant embryos, and that Fz7 functions cell-autonomously in this process by promoting protrusion formation and directed migration. We found that local activation of Fz7 can direct cell migration both *in vitro* and *in vivo*. Uniform activation, however, fully rescues the ppl phenotype in mutant embryos. Thus, we unambiguously demonstrate that permissive Wnt/PCP signaling is sufficient to maintain directed migration of mesenchymal cells during zebrafish gastrulation.

Poster Number: P70
Buffering transcriptional noise: Single cell quantitation of microRNA function during SOP specification

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MicroRNAs are short non-coding RNAs that primarily function to regulate gene expression by destabilising mRNAs or inhibiting their translation. The common observation that loss of function mutations in a single microRNA do not exhibit strong phenotypes led to the hypothesis that microRNAs often do not act as binary switches but as buffering factors. Here we have developed a system to investigate microRNA buffering activity at single cell level. *Drosophila melanogaster* provides a convenient model for quantifying buffering. Regulated cell differentiation requires cells to turn on and off specific genes and maintain proteins at specific levels. We have quantitatively characterised mRNA and Protein levels of *Senseless*, a gene involved in SOP specification that is targeted by dme-*mir-9a*. *Senseless* and *mir-9a* exhibit a dynamic relationship during differentiation. This system can be applied to different microRNA – target gene networks and used for single cell quantification in diverse developmental contexts.

Poster Number: P71
Rapidly diverging targets of a Bmp2/Wnt3a/Smad1 signalling network in mesoderm progenitors

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During gastrulation, mesoderm cells undergo ingression through the primitive streak followed by migration and further specification. Our aim is to investigate the regulation of these closely linked processes.

We previously showed that BMP2 and Wnt3a converge on Smad1 to alter cardiac progenitor cell (CPC) migration in the early chick gastrula; interestingly, ectopically located cells remained cardiogenic. In contrast, paraxial mesoderm progenitors (PMPs) at the mid-gastrula stage responded to elevated BMP2 by becoming lateralized without changing their migration. We use RNAseq to uncouple the differential responses of early and late mesoderm progenitors to BMP2/Wnt3a/Smad1 signalling.

CPC and PMP cells were exposed to BMP2, Wnt3a, or constitutively-active Smad1. RNAseq analysis identified candidate genes that were up- or downregulated in response to all treatments. Validation of candidate genes is ongoing, using qPCR and functional *in vivo* analyses. Some developmental regulators have been identified alongside more specific signal transducers and several novel genes.

Poster Number: P72
Dynamic basement membrane remodelling pre-patterns primitive streak in the murine embryo
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The early post-implantation mouse embryo undergoes rapid growth while being surrounded by a basement membrane (BM). We have observed that the BM underlying the epiblast is covered with multiple perforations that appear to be providing the plasticity to accommodate the growth of the embryo.

More importantly this architecture is being modulated during anterior-posterior (A-P) axis establishment by re-aligning these perforations along this A-P axis. Using cell models, we have investigated the extent by which an embryo can remodel an adjacent BM and have concluded that this is a process that requires the expression, secretion and processing of matrix metalloproteinases (MMPs) that can in turn be regulated by processes also involved in A-P axis establishment in the embryo.

This BM remodelling leads to a pre-gastrula BM with the future primitive streak domain at the posterior covered with small perforations foreshadowing its breaking during gastrulation, potentially important in primitive streak extension.

Poster Number: P73
***Drosophila* TNF, Eiger,modulates tissue tension in the embryo to facilitate macrophage invasive migration**
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Migrating cells penetrate tissue barriers during development, inflammatory responses and tumor metastasis. We study if migration *in vivo* in such three-dimensionally confined environments requires changes in the mechanical properties of the surrounding cells using embryonic *Drosophila melanogaster* hemocytes, also called macrophages, as a model. We find that macrophage invasion into the germband through transient separation of the apposing ectoderm and mesoderm requires cell deformations and reductions in apical tension in the ectoderm. Interestingly, the genetic pathway governing these mechanical shifts acts downstream of the only known TNF super family member in *Drosophila*, Eiger, and its receptor, Grindelwald. Eiger-Grindelwald signaling reduces levels of active Myosin in the germband ectodermal cortex through the localization of a Crumbs complex component, Patj (Pals-1-associated tight junction protein). We therefore elucidate a new molecular pathway that controls tissue tension and demonstrate the importance of such regulation for invasive migration *in vivo*.

Poster Number: P74
Temporal modulation of cell signalling state by re-assembly of the primary cilium during vertebrate CNS development
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Establishment of neuronal polarity is a critical event during CNS development. Differentiating neurons delaminate from the neuroepithelium, a process involving abscission of the apical membrane, dis-assembly of the primary cilium and subsequent cessation of Shh signalling and cell cycle exit. New-born neurons must rapidly repolarise in response to extracellular signals, leading to axonogenesis. Using high-resolution live-tissue imaging in the chick neural tube, we show that delaminating neurons strikingly inherit a procilium-like structure that acts as the site for primary cilium re-assembly prior to initiation of axonogenesis. Further analysis demonstrates that intraflagellar trafficking of Smoothened is re-established during cilium re-assembly, suggesting that the re-assembled primary cilium is actively transducing signals. This is maintained during axonogenesis and disrupting cilium function during this process leads to defects in axon extension. These results indicate that differentiating neurons undergo a temporal re-setting of their signalling state through disassembly and subsequent re-assembly of the primary cilium.

Poster Number: P75
Protein localisation, cell shape, and tissue remodelling: measuring morphogenesis across scales in the zebrafish hindbrain
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A significant challenge in developmental biology is to understand the relationships between molecular, cellular and tissue-level processes. The zebrafish hindbrain is a prime example of this conundrum; we know a lot about the molecular patterning of the neuroepithelium in this region of the brain, but relatively little about the remarkable morphogenetic transformations it undergoes during formation of the fourth ventricle, an elaborate lumenal space for cerebrospinal fluid. Constituent cells determine the form of a tissue, and their properties are, in turn, affected by intracellular components. To address this relationship, we have developed an analysis regime that allows measurement of protein localisation, cell shape and tissue form at well-defined anatomical locations in the hindbrain. Our results demonstrate that cellular force production is required for proper morphogenesis, and that spatiotemporal differences in cellular adhesion correlate with differences in tissue form.

Poster Number: P76
Dynamic protein expression of Her6-venus knock-in during zebrafish neural development
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Previous work revealed that miR-9 is essential for neurogenesis, an effect mediated by targeting and controlling the ultradian oscillations of Hes1 (master regulator of neural progenitors). We showed that pri-miR-9 is likely to oscillate in neural progenitors and that mature miR-9 builds over time, eventually terminating Hes1 oscillations. Therefore, we proposed that a mir-9/Hes1 regulatory loop controls oscillations in neural progenitors and forms a tunable timer for cell differentiation. To understand the mechanisms and significance of such oscillations we developed a Her6_venus (zebrafish Hes1 ortholog) knock-in line in order to study, *in vivo*, the dynamic regulation of protein expression during development in the context of the whole organism. After extensive characterisation of the knock-in line, we find Her6 protein is expressed dynamically in the tissue, and correlates with cell fate. Further, we have mutated the mir9-binding-site at the *Her6* 3'UTR to analyse the effect on dynamics and cell fate decisions.

Poster Number: P77
Contribution of oocyte-inherited DNA methylation to the regulation of the early embryo transcriptome
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In mammals, the sperm and oocyte genomes have strikingly different DNA methylation content and distribution. In consequence, the embryo inherits two parental sets of chromosomes with remarkably asymmetric methylomes. Abolition of oocyte-inherited DNA methylation, as exemplified by the *Dnmt3L* maternal mutation in mice, results in an obligate lethality at mid-gestation, illustrating the key role of maternal imprinting on embryonic development. However, the role of oocyte-inherited DNA methylation on the control of the transcriptome right after fertilization is unknown. By combining high throughput single-cell sequencing with detailed developmental analyses of maternal methylation deficient models, we assessed the net effect of oocyte-inherited DNA methylation on the regulation of the transcriptome and development of the preimplantation embryo. Our results highlight the sensitivity of specific cleavage stages to the lack of maternal DNA methylation, notably at the onset of the zygotic genome activation, which influence the normal developmental timing of the early embryo.

Poster Number: P78
iRhoms and the nervous system: A stressful relationship
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Defects in cellular quality control can contribute to the pathogenesis of various neurodegenerative diseases. iRhoms are a group of recently discovered pseudoproteases that, in *Drosophila*, function to regulate EGF signalling via ER associated degradation (ERAD). Interestingly, they are enriched in the fly nervous system. My project focuses on understanding the mechanisms by which iRhom acts, and its physiological significance in the nervous system. Work in this direction shows that a loss of *iRhom* in flies activates the Unfolded Protein Response (UPR) in an age dependent manner. Physiologically, the *iRhom* mutants also display an age associated retinal degeneration and defects in behavioural assays. A loss of mouse *iRhom2* in microglia cells of the aged mouse brain appears to recapitulate these effects suggesting an evolutionarily conserved relationship between iRhoms and the ER stress pathways. Future efforts are directed towards identifying the molecular mechanism of action of iRhoms in the nervous system.

Poster Number: P79
A statistical approach to mitigate the influence of noise on the detection of stochastic oscillations in 3D imaging data
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Understanding how gene expression is regulated at single cell level is an essential step in understanding how a multicellular system achieves a reproducible outcome during development. A major obstacle is that dynamics are obscured by noise both biological, i.e. stochasticity and experimental, i.e. technical. We used data from cells containing endogenous reporters of Hes proteins that exhibit oscillations during neural development. Using a sequential filtering technique, we estimated that noise in 3D single cell fluorescent data is higher than observed in 2D data, thus an adaptive strategy to mitigate the influence of noise is required. We incorporate information as prior distributions on noise in a Gaussian Processes framework (*Phillips et al. 2017 Plos Comp Biol*) and show that noise can be robustly estimated from synthetic data. Finally, we show that this approach significantly improves the ability to discriminate between oscillatory and randomly fluctuating activity in 3D data collected from embryonic tissue.

Poster Number: P80
The effect of hyperglycaemia on expression of let-7 microRNAs during macrophage differentiation and polarisation in tissue regeneration
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The let-7 microRNA family regulate cell differentiation in many biological contexts including haematopoetic stem cell differentiation and macrophage polarisation during tissue repair and regeneration. Macrophage differentiation and polarisation into pro-inflammatory and pro-healing phenotypes controls the transition between key stages of wound healing. This transition fails in ageing-related pathologies, such as diabetes. Here we examine the role of let-7 family members in macrophage polarisation in both low and high glucose environments as a model of the diabetic environment. Using a macrophage cell line and primary bone marrow-derived-macrophages we find that in high glucose conditions, macrophages exhibit significant changes in expression of all let-7 microRNAs, except let-7 g and i. Let-7b is markedly down-regulated in pro-inflammatory macrophages cultured in high glucose compared to those cultured in low glucose in both models. These findings suggest misregulated let-7b may result in defective macrophage polarisation associated with pathologies of diabetic chronic wound development.

Poster Number: P81
Transvection and pairing at *Drosophila* Hox long noncoding RNAs in the regulation of *Sex combs reduced*
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Long noncoding RNAs (lncRNAs) are emerging as key regulators of Hox expression in diverse animals. Here we have identified and characterized two adjacent lncRNAs *lincX* and *TIPX*, that comprise a regulatory unit involved in transcriptional initiation and maintenance of the *D.melanogaster* Hox gene *Sex combs reduced* (*Scr*). We find that *TIPX* overlaps a Polycomb/trithorax response element (PRE/TRE) and that *TIPX* RNAs function locally in maintenance of *Scr* expression. In contrast, early transcription through the *lincX* locus, but not the *lincX* RNA itself, facilitates initiation of *Scr* in *cis*. Direct visualization of allele specific transcription in mutant backgrounds reveals *lincX* and *Scr* transvection, whereby the mutant transcriptional state is relayed in *trans* between chromosomes to the wild-type homolog. We find that this transvection phenomenon is associated with increased chromosomal proximity. These results support a model where lncRNAs mediate long-range communication of regulatory information in *cis*, in *trans*, and across developmental time.

Poster Number: P82
Unappreciated subset of catecholaminergic neuronal cells play fundamental role in salivary gland branching morphogenesis
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It is well known that autonomic nerves are required for salivary gland (SG) development. It has been reported that cholinergic nerves are essential during mouse gland development, maintaining undifferentiated progenitor cells. During early development, studies showed the presence of heterogeneous neurones with different fate depending on signals received. This is however unknown in SG formation, and our aim is therefore to identify catecholaminergic neurones during murine SG development. We also propose to analyse their functional role in *ex vivo* explants by inhibiting their growth and survival. Neurones expressing Tyrosine Hydroxylase (TH) were observed from early stages within the submandibular ganglion, which then followed parasympathetic nerves reaching the secretory units. Further dopamine inhibition in developing glands resulted in branching defects. The phenotype was rescued by nerve growth factor, which improved branching morphogenesis after removing NGF. This unappreciated subset of catecholaminergic nerves may play essential role in branching morphogenesis that impairs bud formation.

Poster Number: P83
Investigating the role of cell size and cell polarity during asymmetric segregation of neuronal potential in *Caenorhabditis elegans*
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During asymmetric cell divisions, polarisation of the mother cell leads to asymmetric segregation of key cell fate regulators and the production of two differently fated daughters. Asymmetric cell divisions are often also volumetrically unequal, however it is unclear if size alone affects daughter cell fates. Through a 4D-lineage based genetic screen, we have identified that the Mediator complex component *let-19/MED13* is required for an unequal cell division in the C lineage of *Caenorhabditis elegans*, during which neural and non-neural ectoderm potential are segregated. In *let-19* mutants this division is volumetrically symmetrised with a concomitant loss of proneural bHLH transcription factor *hlh-14/ASCL1* expression and thus C lineage neurogenesis. This suggests a potential role of daughter size in asymmetric cell fate specification. To investigate the specific role of cell size in this asymmetric division we are using a temperature sensitive allele of *lin-5/NuMA* to alter cleavage plane position yet not cell polarity.

Poster Number: P84
Investigating glia-to-neuron cell fate switches in *C. elegans*
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We have discovered two cases in which stably differentiated glial cells display a remarkable degree of plasticity and undergo glia-to-neuron cell fate switches during sexual maturation in the nervous system of *C. elegans*. In one case this requires an asymmetric cell division and in the other it occurs through a direct cell fate switch. To uncover molecular regulators of this cell fate plasticity we performed a forward genetic screen. Gene expression studies have allowed us to classify mutants affecting sequential stages of the glia-to-neuron cell fate switch and begin to assess the role of dedifferentiation. We find that certain alleles of the cell-cycle regulator *cdk-4* specifically affect the glial cell division, suggesting specific regulation of cell-cycle re-entry in these cells. Using a temperature-sensitive *lin-5/NuMA* mutant and a battery of other cell cycle mutants we are assessing the role of DNA replication and cell division in these glia-to-neuron cell fate switches.

Poster Number: P85
Control of Pancreatic Endocrine Differentiation by the Planar Cell Polarity Pathway
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The PCP pathway is required in the developing mouse pancreas for the differentiation of endocrine cells from epithelial progenitors lining a network of ducts. We are investigating how the PCP components, conferring polarity information, control progenitor fates during embryogenesis. We demonstrate that Vangl1/2 protein is planar polarized in the ducts. We show that loss of function of Vangl1/2 exhibits ductal morphological defects and a 60% decrease of insulin cell number. Conversely, the Inversin mutant that displays an apical upregulation of Vangl1/2 protein, exhibits increased insulin cell numbers. These mutants enable us to clarify the mechanisms by which the PCP components link duct enlargement and differentiation. Moreover, using transgenic lines expressing a Vangl2-cherry fusion protein in the progenitors, we show that a mislocation of Vangl leads to apoptosis and epithelial exit via downregulation of ROCK pathway activity. This suggests that apical restriction of PCP components is important for epithelial integrity.

Poster Number: P86
Dchs1-Fat4 regulation of Yap/Taz activity within osteoblast progenitors
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Compound mutations of the protocadherins, Fat4 and Dchs1, result in Van Maldergem syndrome characterized, in part, by mental retardation, enlarged fontanelles and craniofacial abnormalities. Here we analyse the role of Dchs1-Fat4 signalling during bone development, and its link with the co-transcriptional "Hippo" effectors, Yap and Taz. We have shown that in the absence of either Fat4 or Dchs1, there is increased proliferation, expansion and delayed differentiation of the osteogenic progenitors. *In vitro* analysis of primary bone cells and osteogenic cell lines shows that Dchs1-Fat4 signalling increases the activity of the Yap/Taz and the Runx2-TGFβR1 reporters. In contrast, the activity of the Runx2-generic and Runx2-p21 reporters was decreased. Transfection of Fat4-intracellular domain shows that these effects are mediated by Fat4. We have determined how these alterations in Yap and Taz activity contribute to changes in the activity of the Runx2 promoters and cell proliferation in osteoblast progenitors.

Poster Number: P87

Histone H3 methylated at arginine 17 is essential for reprogramming the paternal genome in zygotes

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At fertilization, the paternal genome undergoes extensive reprogramming through protamine-histone exchange and active DNA demethylation, but the mechanism are largely unknown. We have reported that gonad specific expression gene (GSE) is essential for 5mC oxidation in the paternal genome. In this study, we showed that GSE interacted with Tet3 and maternal methyltransferase like 23 (Mettl23), a novel arginine methyltransferase which most likely catalyses the asymmetric demethylation of histone H3R17 (H3R17me2a), as indicated by *in vitro* assays and treatment with TBBD, an H3R17 PRMT inhibitor. Maternal histone H3.3, which is essential for paternal nucleosomal assembly, is unable to be incorporated into the male pronucleus when it lacks R17me2a. Depletion of Mettl23 from oocytes resulted in impaired accumulation of GSE, Tet3, and 5hmC in the male pronucleus, suggesting that Mettl23 may recruit GSE-Tet3 to chromatin. Our findings established H3R17me2a and its catalysing enzyme Mettl23 as key regulators of paternal genome reprogramming.

Poster Number: P88

mTOR Signalling During Epigenetic Reprogramming in Murine Primordial Germ Gells

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During embryonic development, primordial germ cells (PGCs), the precursors of egg and sperm cells, undergo epigenetic reprogramming in order to retain their unique ability to eventually form a new totipotent zygote. Of particular interest is the reprogramming process that is initiated upon entry of PGCs to the developing embryonic gonads. Currently, very little is known about how this process is triggered. For the first time, we describe activation of a key nutrient and hormone sensing pathway (mTORC1) in mouse PGCs immediately prior to gonadal epigenetic reprogramming. Analysis of mTORC1 signalling in wildtype PGCs at the RNA and protein level reveals that 4E binding protein 1, a translational repressor, is the most highly expressed downstream target of the mTORC1 signalling cascade. We will show characterization of knockout tissues depleted in various components of this signalling pathway and discuss a possible role of mTORC1 signalling in germ cell development and epigenetic reprogramming.

Poster Number: P269

Deciphering mechanisms underlying cellular identity maintenance and reprogramming *in vivo* in *C. elegans*

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Cellular reprogramming is one of the key processes in developmental biology. We are currently characterizing the intrinsic and extrinsic mechanisms underlying these mechanisms *in vivo* by using the *C. elegans* model. We gathered a large tool box and a detailed understanding of the transdifferentiation (Td) of a differentiated rectal cell, “Y”, into a perfectly functional and differentiated moto-neuron “PDA”. Indeed, an EM screen highlighted the genes involved in the process, among which the *lin-15A* gene coding for a THAP domain protein was found. A *lin-15A* mutation leads to loss of PDA. Interestingly, we found that specific conditions such as knocking-down of Rb and Tor pathway, but also caloric restriction, growth delay and virulence of pathogens lead to a complete suppression of this Td defect. Taking together, those results provide essential elements for further deciphering cellular identity maintenance and reprogramming mechanisms.

Poster Number: P272
Circadian-related gene expression in the suprachiasmatic nucleus of an R6/2 mouse model of Huntington's disease in response to a light pulse

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Huntington's disease (HD) is a neurodegenerative disease characterised by complex behavioural abnormalities, including circadian dysfunction. Circadian rhythms are synchronised by the light-dark cycle and regulated by the suprachiasmatic nucleus (SCN) in the hypothalamus and are abnormal in HD mice. To test whether circadian rhythms can entrain to photic cues, symptomatic HD mice (R6/2 line) were placed in constant darkness and subjected to light pulses at circadian time (CT)6, CT15 or CT23. Light pulses typically induce phase shifts in activity onset, which are diminished in symptomatic R6/2 mice. We found that expression of the light-inducible genes Period1 and *cfos*, was upregulated 1 hour after a light pulse in the SCN of both wild-type and R6/2 mice. Although the behavioural response is diminished, these results show that the SCN neurons in R6/2 mice can still respond to light and synchronise, and that the circadian abnormalities are not due to abnormal light reception.

Poster Number: P273
P53 and mTOR signalling determine fitness selection through cell competition during early mouse embryonic development

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Cell competition is a quality control mechanism that eliminates cells which are viable but less fit than surrounding cells, resulting in enhanced organismal fitness. Although this type of fitness selection has recently been described to occur during mammalian embryogenesis, the mechanisms underlying the process in this system remain poorly resolved. Here, we find that mTOR and p53 are key determinants of the competitive ability of pluripotent cells. First, p53-dependent repression of mTOR activity is sufficient and necessary for the elimination of cells with reduced relative fitness. Second, inhibiting p53 or constitutively activating the mTOR pathway generates 'super-competitor' cells which can eliminate wild-type neighbours, leading to tissue overgrowths and disruption of morphogenesis *in vivo*. Finally, around 35% of cells are eliminated through this mechanism during normal mouse development. Our results shed light on the mechanisms of cell competition but also highlight the importance of tight regulation of the process during embryogenesis.

Poster Number: P89
Triggering of cell differentiation in the mouse preimplantation embryo is driven by Notch at compaction

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The onset of cell differentiation in the mammalian embryo entails the loss of totipotency to favor the appearance of the first lineages. The regulation of *Cdx2*, key element in the trophectoderm, has been attributed to the differential activity of the Hippo pathway in polarized and unpolarized blastomeres. We have shown that Notch cooperates with Hippo in this regulation. Further analysis of Notch activity during preimplantation stages indicates that it is active at 4-cell stage. Notch affects the initial expression of *Cdx2* in the morula, which is reinforced by Hippo. Using an inducible mosaic model, we found that differences in Notch levels in the early embryo determines cell fate at blastocyst stage. Moreover, single embryo transcriptome profiling in *Rbpj* null morulae indicates that Notch regulates repressors that block naïve pluripotency markers. These findings suggest that Notch is boosting the trigger of initial differentiation that is then reinforced by other morphogenetic programs.

Poster Number: P90
Robust cell type proportioning by a noisy oscillator

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Cell-cell heterogeneity has puzzled developmental biologists because it might prevent cell populations from behaving in a coordinated fashion. On the other hand, cell-cell heterogeneity could increase the spectrum of differentiation possibilities of cells in a uniform environment. However, remarkably little is known about the origin of heterogeneity, or if it can be controlled to generate reproducible cell type proportioning *in vivo*. Our studies, using experimentation and modeling in *Dictyostelium*, have allowed us to address these questions. Firstly, we find cell cycle position is quantitatively linked to responsiveness to differentiation inducing signals. Secondly, variation in cell cycle length ensures cells are randomly distributed throughout the cell cycle. Finally, perturbation of optimal cell cycle heterogeneity is buffered by compensatory changes in global signal responsiveness. These studies represent a major mechanistic advance because they reveal heterogeneity in cell cycle position can be optimised and harnessed to generate robust cell-type proportioning during embryonic development.

Poster Number: P91
The role of Fgf4/MAPK signaling pathway in regulation of development of mouse chimeric embryo

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Molecular mechanisms underlying regulative abilities of the mouse embryo are not fully unravelled. Our previous research showed that in chimeric embryos constructed by microinjection of embryonic stem cells (ES cells) into the cleaving 8-cell mouse embryo the interactions between blastomeres of the host embryo and the introduced ES cells are responsible for the pattern of their cleavage and specification of the first cell lineages. Our results suggest the existance of a controlling mechanism, based on the communication between the cells of the embryo and ES cells, which regulates the plasticity of chimeric mouse embryos. We postulate that Fgf4 - fibroblast growth factor 4 is a candidate involved in these interactions. Thus the aim of this project is thus to determine the role of Fgf4/MAPK signaling pathway in development of chimeric mouse embryo.

Poster Number: P92
Control of primitive hematopoiesis by the pluripotency factor NANOG that directly regulates Tal1
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Progenitors of the first hematopoietic cells in the mouse arise in the early embryo, but the mechanisms that specify primitive blood cells are still largely unknown. Pluripotency factors maintain uncommitted cells of the blastocyst and embryonic stem cells in the pluripotent state. However, little is known about the role played by these factors during later development, despite their being expressed in the postimplantation epiblast. Here we show that Nanog blocks primitive hematopoiesis in the gastrulating embryo, resulting in a loss of red blood cells and downregulation of erythropoietic genes. Accordingly, Nanog deficient embryonic stem cells are prone to erythropoietic differentiation. By analysis of previous data for NANOG binding during stem cell differentiation and CRISPR/Cas9 genome editing, we found that Tal1 is a direct NANOG target. Our results show that Nanog regulates primitive hematopoiesis by directly repressing critical erythroid lineage specifiers.

Poster Number: P93
Mapping the Embryological Origins of the Radius and Ulna
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Fate mapping involves tracing the embryological origins of cells and can give a wealth of information on the lineage and movements of cells between early and late embryonic stages. There have been several fate maps of the limb bud created over the past 70 years each building on previous studies as new techniques became available. Here we present the next generation of limb bud fate mapping using novel transgenic chicken embryos that have a Cre-inducible multi-fluorescent Cytbow construct. Through application of an latex bead soaked in Cre protein we can induce recombination in early limb bud cells causing mutually exclusive expression of one of three fluorescent proteins. Employing this technique we create a fate map of the early limb bud and focus in particular on the origin of the radius and ulna. This will then permit us to explore the anterior-posterior patterning of the forearm in greater detail.

Poster Number: P94
Combinatorial Smad2/3 activities downstream of Nodal signalling maintain the embryonic/extra-embryonic barrier during lineage priming in mice
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Epiblast cells in the early post-implantation stage mammalian embryo undergo a transition described as lineage priming prior to cell fate allocation, but signalling pathways acting upstream remain ill-defined. Genetic studies demonstrate that Smad2/3 double mutant mouse embryos die shortly after implantation. To learn more about the molecular disturbances underlying this abrupt failure, here we characterized Smad2/3-deficient embryonic stem cells (ESCs). We found that Smad2/3 double knockout ESCs induced to form primed epiblast-like cells (EpiLCs) display changes in naïve and primed pluripotency marker gene expression, associated with the disruption of Oct4-bound distal regulatory elements. In the absence of Smad2/3 we observed enhanced Bmp target gene expression and de-repression of extra-embryonic gene expression. Cell fate allocation into all three embryonic germ layers was disrupted. Collectively these experiments demonstrate that combinatorial Smad2/3 functional activities are required to maintain the embryonic/extra-embryonic barrier during lineage priming in the epiblast prior to gastrulation.

Poster Number: P95

Single cell expression profiling identifies pigment cell differentiation trajectories from unexpectedly multipotent intermediate pigment progenitor cell

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The neural crest (NC) is a major model for understanding how multipotent progenitors generate a balance of derivative cell-types. There is long-standing controversy over whether NC fate choice proceeds via a Direct Fate (no intermediates) or Progressive Fate Restriction (partially-restricted intermediates) model. Zebrafish NC generates three distinct pigment cell types (melanocytes, iridophores and xanthophores), proposed to share a common cellular origin, either a partially-restricted *ltk*-expressingchromatoblast, or a bipotent melanoiridoblast. Fate-mapping of *ltk*-expressing cells confirms their multipotency, but reveals their unexpected peripheral neuron potential. NanoString expression profiling of single NC-derived cells identifies a likely course of differentiation of pigment cells via intermediates. These intermediates again identify a highly multipotent partially-restricted intermediate in vivo, a finding supported by single cell qRT-PCR profiling. Surprisingly, we find no evidence for a bipotential melanoiridoblast. Together these data give us a novel and unexpected view of the mechanisms of pigment cell development *in vivo*.

Poster Number: P96

Neural induction by the node and placode induction by head mesoderm share an initial state resembling neural plate border and ES cells

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During development, instructive signals from inducing tissues cause fate changes in responding cells. We explored the transcriptional responses to two such events- neural plate induction by Hensen's node and placode induction by lateral Head Mesoderm (lHM), and reveal that initial responses are largely identical. They define a distinct state, strikingly similar to the pre-gastrulation epiblast and neural plate border.

Demonstrating that this "pre-border" state is common to neural and placodal development, we show that its induction by the node, lHM, or hypoblast (extraembryonic endoderm), can be subsequently directed towards specific fates by exposure to the appropriate tissue. Furthermore, in the absence of signals, early epiblast explants differentiate into neural plate border derivatives: lens, neural crest and neural plate.

We propose that inductive events begin with a reprogramming step where cells acquire a "pre-border"-like state similar to early epiblast and ESCs. Specific lineages diverge later under the influence of additional signals.

Poster Number: P97

Unique Dll4/Notch function in regulating the Horizontal cell fate in the developing mouse neural retina

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Two Notch ligands, Dll1 and Dll4, are expressed in the developing mammalian neural retina. Using transgenic mice carrying conditional alleles of *Dll1* or *Dll4*, we are addressing the function of Dll1 and Dll4 in the developing neural retina. Our results show that Dll1 and Dll4 exhibit non redundant roles in retinal neurogenesis. Dll1 is involved in the control of RGC generation, whereas Dll4 regulates the generation of Cone photoreceptors and Horizontal cells. Our data supports a model in which both Dll1 and Dll4 control the pool of multipotent RPCs, while Dll4 acts upon a subsequent stage of RPC competence to regulate the acquisition of Cone and Horizontal fates. Surprisingly, our results show that Dll4 acts through different mechanisms to control these two fates: it inhibits the transition from multipotent RPCs to bipotent RPCs, and promotes the Horizontal fate by activating an RBPj/Ptf1A auto-regulatory loop, necessary to impose this fate on RPCs.

Poster Number: P98
High glucose modulates phenotype of human arteriolar smooth muscle cells
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Diabetes remains a major contributor to morbidity and mortality worldwide. Although high glucose milieu is known to promote development of atherosclerosis as well as modulate behavior of vascular smooth muscle cells (SMCs) of large arteries, very little is known about the impact of a diabetic-like condition on SMCs from microvessels. Here we show that treatment with high glucose (HG; 25 mM) up to 3 weeks reduces proliferation of human arteriolar SMCs. Moreover, HG increased migration as well as phosphorylation of ERK1/2 and FAK. Interestingly, pretreatment with GF 109203X, a PKC inhibitor, or PD98059, an ERK1/2 inhibitor, abolished HG-induced decrease in cell proliferation. In contrast, phorbol 2,13-dibutyrate, a PKC activator, reduces cell proliferation. Taken together, our data show for the first time that high glucose modulates phenotype of human microvascular SMCs via a mechanism that is dependent on ERK1/2 and PKC. This highlights potential targets in treating diabetes-associated microvascular complications.

Poster Number: P99
A diffusion model of interkinetic nuclear migration in the zebrafish retina
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A major hallmark of neural development is the oscillatory movement of nuclei between the apical and basal surfaces of the neuroepithelium during the process of interkinetic nuclear migration (IKNM). The precise function of IKNM in creating the organized diversity of the neuroepithelium is still unknown. Long-term, rapid imaging of whole zebrafish retinas during early stages of development reveal the physical processes that govern the behavior of nuclei during IKNM. We image the retina at a high temporal resolution and produce reliable tracks of nuclear movements and division using automated tracking software and manual curation. Subsequently, we have used these tracks to create a model of retinal IKNM as a simple one dimensional diffusion process in a nuclear concentration gradient across the retina. The model is based on the observed stochastic movement of the nuclei during IKNM and produces a diffusion constant in line with those previously reported in the literature.

Poster Number: P100
Neurotransmitter specification in the *Drosophila melanogaster* ventral nerve cord
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Neuroblasts constitute the fundamental developmental units of the insect nervous system, each generating a unique lineage. Our understanding of neuroblast lineages at the anatomical level contrasts sharply with a conspicuous lack of understanding of their neurotransmitter phenotypes, overlooking a critical, function-determining attribute of individual neurons. We assembled a recombinant Drosophila stock which, when combined with immunological reporters, allows us to visualize the three key neurotransmitters of the ventral nerve cord simultaneously (GABA, acetylcholine, and glutamate). When this stock is used in conjunction with a collection of neuroblast-specific GAL4 lines, we can identify neurotransmitter phenotype in a variety of neuroblast lineages. Thus far, we have shown that neuroblast 5-3 generates GABAergic neurons, where neuroblast 3-5 generates both cholinergic and GABAergic neurons. For examining mechanisms of neurotransmitter patterning, we are focusing on the roles of birth order and apoptosis via live imaging and apoptosis mutants respectively.

Poster Number: P101
Elucidating the molecular signals guiding the formation of inner ear sensory organs
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The inner ear comprises distinct sensory organs responsible for sound detection and the perception of balance and head movements. The mechanisms controlling their formation remain unclear. Our recent work has shown that several of the sensory organs arise by progressive segregation from a common prosensory domain. During this process, Notch signalling uses lateral induction to propagate and maintain sensory identity among interacting cells. To further characterise the molecular signals regulating the specification and segregation of sensory organs, we performed a transcriptome profiling of chicken inner ears after gain- and loss-of Notch function. Our results identified a number of candidate Notch targets. Among these, we found a significant enrichment of key elements of Wnt signalling pathway. Our functional studies confirm that the Wnt signalling is critical for the normal morphogenesis of sensory organs, suggesting that it could mediate at least in part the prosensory effects of Notch signalling in the ear.

Poster Number: P102
Wnt/b-catenin signalling influences cell fate decision making in the early mouse embryo
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At embryonic day 3.5 (E3.5), inner cell mass (ICM) cells co-express the transcription factors NANOG and GATA6. Between E3.5 and E4.5, cells of the ICM differentiate into epiblast (Epi) and primitive endoderm (PrE). These two lineages are distinguished by the differential expression of the previously co-expressed transcription factors, Epi cells express NANOG while PrE cells GATA6. FGF/ERK signalling is responsible for Epi/PrE differentiation but does not explain the initial co-expression of both factors. β-catenin is the downstream effector of Wnt signalling, and also found forming a complex with E-cadherin in the membrane. Our hypothesis is that changes in both cellular pools of β-catenin are involved in ICM differentiation. Our results indicate that increases in nuclear β-catenin levels allow the cells to move further into the PrE fate, determined by an earlier appearance of mutually exclusive expression of GATA6 and NANOG *in vitro*, *ex vivo* and in *β-catenin* mutant embryos.

Poster Number: P103
Enrichment of left ventricle cardiomyocytes from human pluripotent stem cells
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Myocardial infarction often results in dramatic loss of cardiomyocytes, particularly in the left ventricle (LV). As a result, the heart is remodelled, leading to impaired function. Adverse remodelling might be ameliorated if the LV were to be repopulated by functional cardiomyocytes with the electrophysiology properties of the left ventricle. To this end, attempts are under way to reprogram, in an efficient manner, endogenous or exogenous cells to a LV identity. To better understand the formation of the LV *in vivo*, mouse hearts from several embryonic developmental time-points were micro-dissected into distinct anatomical regions and analysed by mRNA-sequencing. We have identified candidate genes and signalling pathways which are specifically up- or down- regulated in the LV myocardium during heart development. Some of these identified candidate genes, which represent an array of biological functions, have been modulated to optimise *in vitro* differentiation of hESC into a homogenous LV cardiomyocyte fate.

Poster Number: P104

SCL/TAL1 cooperates with Polycomb RYBP-PRC1 and co-repressor ETO2 to suppress alternative lineages in blood-fated cells

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During development, it is unclear if lineage-fated cells derive from multilineage-primed progenitors and whether active mechanisms operate to restrict cell fate. We investigated how mesodermal cells specify into blood-fated cells. We document temporally restricted co-expression of blood (SCL/TAL1), cardiac (MESP1) and paraxial (TBX6) lineage-affiliated transcription factors in single cells, at the onset of blood specification, supporting the existence of common progenitors. At the same time-restricted stage, absence of SCL results in expansion of cardiac/paraxial cell populations and increased cardiac/paraxial gene expression, suggesting active suppression of alternative fates. Indeed, SCL normally activates expression of co-repressor ETO2 and Polycomb-PRC1 subunits (RYBP, PCGF5) and maintains levels of Polycomb-associated histone marks (H2AK119ub/H3K27me3). Genome-wide analyses reveal ETO2 and RYBP co-occupy most SCL target genes, including cardiac/paraxial loci. Reduction of *Eto2* or *Rybp* expression mimics *Scl*-null cardiac phenotype. Therefore, SCL-mediated transcriptional repression prevents mis-specification of blood-fated cells. Active repression mechanisms are central to fate determination processes.

Poster Number: P105

Protrusion activity regulates neuronal spacing pattern in the zebrafish spinal cord

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During early stages of zebrafish embryonic development, neuronal subtypes appear regularly spaced along the spinal cord. It remains unknown how this periodic pattern is achieved. To determine the mechanisms that regulate neuronal differentiation in space and time, we used live-imaging in zebrafish embryos to monitor neurons differentiating *in vivo*. We observe that all differentiating neurons in the spinal cord transiently form two long cellular protrusions that remain extended for several hours at the basal surface of the neuroepithelium. Our experimental and *in silico* data suggest that these long basal protrusions may regulate neuronal spacing via a Delta/Notch lateral inhibition mechanism. When we prevent the elongation of basal protrusions through the reduction of laminin expression, we find the neuronal periodic spaced pattern becomes abnormal. The present work demonstrates the first association between a cellular behaviour and the spatial-temporal regulation of neurogenesis in a vertebrate embryo.

Poster Number: P106

When Turing meets Waddington: a theory of pattern formation in active multicellular tissues

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The formation of self-organized patterns of cell differentiation is key to the morphogenesis of multicellular organisms, and while a general theory of biological pattern formation is still lacking, we introduce a generalisation of Turing's work on pattern formation in monophasic systems to biphasic multicellular tissues. Our model incorporate morphogen production and transport, cell differentiation and tissue mechanics in a single framework, where a first tissue phase consists in a three-dimensional viscoelastic network made of cells, and a second phase composed of extracellular fluid, both compartments being separated by cell membranes, actively regulating interfacial water and morphogens exchanges. Coupling reaction-diffusion, active membrane transport and tissue poroelasticity, we show that tissue spatial organisation and mechanics can control developmental pattern formation. Overcoming crucial limitations of other models, we demonstrate the possibility of generating robust spatial patterns of cell differentiation using biochemical signalling pathways and gene regulatory networks involved in cell fate decision.

Poster Number: P107
Complete cell lineages inferred by *in situ* sequencing of induced somatic mutations
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Complex animals consist of millions of cells that derive from a single cell, the zygote. A long-standing aim in developmental biology has been to unravel an organism's cell lineage, i.e., how every cell relate to each other. Recently, CRISPR-Cas9 "recorders" have been generated, which accumulate mutations as cells divide during development. These mutations are then used to retrospectively infer the relationships between cells.

I will present the SEQuoia project, which aims to reconstruct the whole cell-lineage of a *Drosophila* larva using using a CRISPR recorder and in situ sequencing. Using computer simulations we first determined optimal mutation rates for CRISPR arrays, which then were fined tuned *in vivo*. We then simulated how several non-ideal scenarios, or using different sequencing technologies, could affect the cell-lineage accuracy. Our results highlight the importance of optimising the different parameters of the CRISPR recorder system and of being cautious when interpreting a reconstructed lineage.

Poster Number: P108
Trophectoderm and primitive endoderm specification in preimplantation rabbit embryos
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Preimplantation development of mammalian embryos is dedicated to specification of first three cell lineages: epiblast, primitive endoderm and trophectoderm. Scarce data available from primate and other non-murine eutherian mammals suggest differences in early lineage specification between species. Here we assess lineage specification in rabbit embryo and highlight differences and similarities in preimplantation development of the rabbit and the mouse, including timing of early developmental events, lineage-specific transcription factors expression, and role of FGF and GSK3 signalling. Major differences observed include the role of MEK signalling in primitive endoderm versus epiblast differentiation and the expression of transcription factors during early stages of trophectoderm formation. Our data indicate that the rabbit can be a robust model representative of preimplantation mammalian development. This work is supported by National Science Centre (NCN) grants number 2011/03/D/NZ3/03992 and 2011/01/N/NZ3/0060, and KNOW–The Leading National Research Centre, Scientific Consortium "Healthy animal-safe food".

Poster Number: P109
Single-cell Gene Expression Analysis of a Human ESC model of Pancreatic Endocrine Development
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The production of β cells from human embryonic stem cells in vitro represents a promising strategy for a cell-based therapy. We performed single-cell qPCR cells isolated from several stages of in vitro differentiation of hESCs and compared them with adult human islets. We reveal distinct subpopulations along the endocrine differentiation path and early lineage bifurcation towards either polyhormonal cells or β-like cells. Using cells isolated with stage-specific markers, we also analysed samples from from human fetal pancreata at a specific time point and we have verified the occurrence of different stages of maturation along the endocrine path showing that cells at different steps of differentiation activate different transcription factors sequentially also in vivo. We see that in vitro cells cluster homogeneously compared to in vivo cells. Combining the strengths of in vitro and in vivo data, we would like to shed light on fate allocation towards different pancreatic endocrine cells.

Poster Number: P110

The effect of mechanical cues on post-migratory neural crest cells in embryogenesis

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Neural crest cells (NCC) are a unique population of multipotent cells, contributing to the development of the vertebrate head. Cranial NCC give rise to a variety of hard and soft tissue cells including osteoblasts, chondrocytes, odontoblasts and neuronal cells. In adult tissues, there is substantial evidence that mechanoregulatory cues are sufficient, or synergise with chemical signals, to direct stem cell behaviours including cell fate. During development, NCC are exposed to different mechanoregulatory influences from local matrices and adjacent cells. To determine how these mechanoregulatory cues influence NCC differentiation, cell shape and density are being measured within mTmG mouse embryos, and recapitulated via micro-patterning *in vitro*. This will determine how *in vivo* NCC shapes influence cell fate decisions. In addition, Atomic Force Microscopy is being used to measure the stiffness within the developing mouse face in which NCC are differentiating. This research will reveal how the mechanoregulatory niche around NCC influences cell fate decisions.

Poster Number: P111
Dissecting the upstream regulation of the GATA genes during heart development
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The cardiac GATA transcription factors (TFs) play vital roles in cardiogenesis. While their function as cardiac effectors has been well studied, precise molecular mechanisms driving their activity have yet to be parsed. Using ATAC-seq we identified putative enhancers, accessible during development and regeneration, around the *gata4, 5 and 6* loci in cardiomyocytes. We tested the activity of these *cis*-regulatory elements using a novel, highly efficient reporter system in zebrafish.

Analysis of the enhancer-driven reporter activity showed high specificity: Gata5-enh5 drives activity in a subset of cells that co-localize with second heart field progenitors, while Gata5-enh12 drives activity restricted to the ventricle.

We zoomed into these enhancer sequences, identifying TF binding site motifs, and tested the requirement of overrepresented regulators by mutating their binding sites. These direct interactions are being tested by ChIP-PCR. Capture-C is currently being performed to reveal topologically associating domains, ultimately revealing the functional interaction between these enhancers and their regulated genes.

Poster Number: P112
Function, cooperation and evolution of multiple enhancers governing the expression of a vertebrate developmental gene
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Developmental genes harbour multiple transcriptional enhancers that act concomitantly to achieve precise spatiotemporal expression. To provide insights into the mechanisms involved in the regulation of a vertebrate gene, we investigated the case of *Krox20* gene required for the specification of rhombomeres 3 and 5. We have functionally characterized, by in vivo deletions, 6 elements, spread on a large distance, that cooperate during the initiation and the maintenance of *Krox20* expression. By investigations of chromatin organisation, we show that besides its classical enhancer function, one initiating element is permanently required in *cis* to potentiate the autoregulatory activity of an enhancer by increasing its accessibility. Additionally, despite having the same profile of expression, the *cis*-regulation of *Krox20* differs between zebrafish and mice. This study reveals both a strong enhancer redundancy for the expression of a developmental gene, and an unexpected plasticity in the function and number of enhancers throughout vertebrate evolution.

Poster Number: P113
Capture Hi-C reveals the chromatin interactome and long-range gene regulatory landscape of cerebellar granule neuron progenitors
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Cellular differentiation and cell type-specific gene expression are under the control of distal regulatory elements in the genome. GNPs are transit amplifying, lineage committed neural progenitors that are responsible for the postnatal growth and the formation of the characteristic foliated structure of the cerebellum. Using Capture Hi-C, we identified over 80,000 promoter-interacting regions for >18,000 gene promoters throughout the genome. Integration with ATAC-seq and ChIP-seq data identified approximately 4,200 putative canonical, active enhancer elements. Many regulatory factors that control GNP proliferation and differentiation primarily localize to distal regulatory regions. One such factor is the chromatin remodeling factor CHD7 (chromodomain helicase DNA binding factor 7). We have used our data to identify the CHD7-regulated enhanceosome and *Zic1/4* enhancers in GNPs. Together, our findings provide fundamental

insights into the long-range gene regulatory landscape of cerebellar GNPs and will form the basis of future studies aimed at elucidating chromatin reorganization during GNP differentiation.

Poster Number: P114
Imprinted genes linking fetal growth and adult metabolic health
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The control of body size and proportions remains poorly understood, despite being a fundamental aspect of development. Perturbations of growth during early life are linked with adverse metabolic health later on. The delta-like 1 gene (*Dlk1*) encodes a putative ligand that promotes fetal growth and in adults restricts adipose deposition. Conversely, *Grb10* encodes an intracellular signalling adaptor protein that, when expressed from the maternal allele, acts to restrict fetal growth and is permissive for adipose deposition in adulthood. Here, we present genetic and biochemical evidence that *Dlk1* and *Grb10* act in a common signalling pathway that is separate from the IGF pathway. As such, they may be considered only the second clear example of a directly antagonistic imprinted gene pair, after the archetypal imprinted genes *Igf2* and *Igf2r*. We propose that *Dlk1* and *Grb10* define a mammalian growth axis that may be involved in early life programming of health.

Poster Number: P115
Lifting the veil of HOX specificity: Comparing HOXA2 and HOXA3 binding profiles in the developing embryo
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HOX transcription factors are essential for embryonic development. HOXA2 and HOXA3 confer identities to cells in the second and third branchial arch, respectively. Because these evolutionarily conserved proteins bind DNA with low sequence specificity, how they execute their specific functions *in vivo* remains unclear.

To address this question, we mapped binding of HOXA2 and HOXA3 in the second and more posterior branchial arches, respectively. We report that though their binding profiles partially overlap, many binding events are unique to either HOXA2 or HOXA3. Moreover, we show that the binding of these transcription factors preferentially coincides with active enhancer marks, and is associated with hundreds of genes involved in embryonic development.

This comprehensive mapping of HOXA2 and HOXA3 binding sites provides a framework to understand the basis of HOX functional specificity in vertebrate embryos and also to identify their shared functions.

Poster Number: P116
Depletion of maternal Cyclin B3 contributes to zygotic genome activation in the *Ciona* embryo
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Most animal embryos display a delay in the activation of zygotic transcription during early embryogenesis. This process is thought to help coordinate rapid increases in cell number during early development. The underlying basis of zygotic genome activation (ZGA) during the maternal-to-zygotic transition is unknown, despite extensive efforts. We explore ZGA in the simple protovertebrate, *Ciona intestinalis*. Single-cell RNA-seq assays identified *Cyclin B3* (*Ccnb3*) as a potential mediator of ZGA. Maternal *Ccnb3* transcripts exhibit rapid diminishment in abundance during the onset of zygotic transcription at the 8-cell and 16-cell stages. Disruption of *Ccnb3* activity results in precocious activation of zygotic transcription, while overexpression abolishes activation. These observations suggest that ZGA is enabled by the depletion of maternal *Cyclin B3* products. Moreover there is evidence that this mechanism might play a conserved role in the MZT of other metazoans, including mice and humans.

Poster Number: P117
Comparative functional analysis of the atypical Notch ligands DLK1 and DLK2 in vertebrate development
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The atypical, vertebrate specific Notch ligand, Delta-like homologue 1, *Dlk1* possesses secreted and membrane-tethered isoforms, and can act as an autocrine, paracrine and endocrine factor.

Dlk1 has diverse mammalian functions regulating stem and progenitor cells during the development of multiple lineages both before and after birth. Furthermore, secreted by the conceptus, the protein regulates maternal metabolic partitioning including in human pregnancy, with important implications for fetal growth. DLK1 is additionally implicated in diabetes, obesity and cancer.

Dlk1 has an orthologue, *Dlk2*. Despite homology with *Dlk1*, virtually nothing is known about *Dlk2*. Bioinformatic analysis suggests that *Dlk2* is the ancestral version of *Dlk1*.

Assessment of the function of both genes and the evolutionary relationship between them is ongoing in wild type and mutant zebrafish and mice. Progress will be presented.

Poster Number: P118
Epigenetic Plasticity: Integrating signalling with chromatin regulators to direct tissue regeneration or tumorigenesis
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[1]Department of Biosystems Science and Engineering, ETH Zurich, Basel, Switzerland; [2]Faculty of Science, University of Basel, Basel, Switzerland

Signalling pathways modulate developmental and regenerative processes, but can also be exploited by cancer cells to promote growth and tissue invasion. Motivated by the parallels between both processes, we identified context-specific features that discriminate regenerative from tumorigenic states. We dissected the contribution of ectopic signalling pathways (JNK, JAK/STAT, Notch, and also developmental transcription factors) to promote tumour development upon impaired Polycomb silencing, revealing a signalling hierarchy that is distinct from regeneration.

We also established novel low-input methods for tissue-specific chromatin profiling of rare cell populations. Overcoming current limitations, it is broadly applicable to a diverse array of cell types, organisms and developmental stages. To understand how tissues respond to stress by directing regeneration or tumorigenesis, we are investigating how chromatin state modulates the response to context-specific signalling. The combination of emerging genomic technologies with powerful genetics in real tissues will support mechanistic insights driving chromatin alterations during development and homeostasis.

Poster Number: P119
Discrete Functional Domains and Intrinsic Redundancy in a Conserved Sonic Hedgehog Enhancer Contributes to Spatial Specific Expression
LA Lettice, P Devenney, C De Angelis, RE Hill

MRC Human Genetics Unit, IGMM, University of Edinburgh, Edinburgh, UK

Expression of sonic hedgehog (*Shh*) in the limb bud is regulated by a single enhancer called the ZRS which in evolution belongs to an ancient group of highly conserved *cis*-regulators found in all classes of vertebrates. Here, we examined the endogenous ZRS in mouse using genome editing to establish the relationship between enhancer composition and embryonic phenotype. We show that enhancer activity is a consolidation of distinct activity domains. Spatial restriction of *Shh* expression is mediated by a discrete repressor module; whereas, levels of gene expression are controlled by large overlapping domains containing varying numbers of HOXD binding sites. The number of HOXD binding sites regulate expression levels incrementally. Substantial portions of conserved sequence are dispensable indicating the presence of sequence redundancy. We propose a collective model for enhancer activity in which function is an integration of discrete expression activities and redundant components that drive robust expression.

Poster Number: P120
***Shh* has a dual role in jaw development**
Z Crane-Smith[1], E Anderson[2], P Devenney[1], L Lettice[1], RE Hill[1]

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The requirement for the morphogen Sonic Hedgehog (SHH) in mandibular formation has long been established; however, the exact mandibular developmental mechanisms affected by *Shh* are still unclear. Through the use of RNA-seq and ATAC-seq on mandibular prominences I have established a dual role for *Shh* in mandibular development. At early jaw development stages, E10.5, lack of *Shh* leads to a loss of expression of cell cycle and metabolic genes, including the Fox gene family. However, later in development, at the beginning of cell fate specification, *Shh* is required to instruct cells to adopt bone like phenotypes. Moreover, at both early and late mandibular developmental stages loss of *Shh*, and downstream gene expression, leads to a vast change in the regulatory landscape. Such as, loss of Fox gene binding at E10.5 and loss of ETS family member binding at E12.5.

Poster Number: P121
The Shh topologically associated domain adopts a novel chromatin conformation in the embryonic forebrain mediated by CTCF binding sites
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MRC Human Genetics Unit, University of Edinburgh, Edinburgh, UK

Mammalian genomes are organised at the sub-megabase level into topologically associated domains (TADs) and chromatin loops. TAD boundaries are highly enriched for CTCF binding sites; consequently, CTCF has been proposed to be one of the major factors organising the genomes into TADs by constraining the extent of cohesin-mediated loop extrusion. Structuring of chromatin in these highly conserved TADs is believed to be essential for gene regulation by bringing distal enhancers and their target promoters into close proximity whilst insulating enhancer activity at TAD boundaries. The *Shh* regulatory domain is arranged into a 1Mb TAD that contains all known *Shh* enhancers and has been previously proposed to form a invariant chromatin loop structure across various tissue types. We found that the *Shh* TAD adopts a novel chromatin conformation in the developing embryonic forebrain, mediated by CTCF, that we believe is important for facilitating Shh regulation by a distal forebrain enhancer.

Poster Number: P122
Genomic dissection of cell identity reveals the timing of AP identity during neural induction
V Metzis[1], S Steinhauser[1], E Pakanavicius[1], M Gouti[1,2], D Stamataki[1], R Lovell-Badge[1], NM Luscombe[1,3,4], J Briscoe[1]

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Neural induction in vertebrates generates a central nervous system that extends the rostral-caudal length of the body. The prevailing view is that neural cells are initially induced with anterior (forebrain) identity; caudalising signals then convert a proportion to posterior fates (spinal cord). To test this model, we used chromatin accessibility assays to define how cells adopt region-specific neural fates. Together with genetic and biochemical perturbations this identified a developmental time window in which genome-wide chromatin remodeling events preconfigure epiblast cells for neural induction. Contrary to the established model, this revealed that cells commit to a regional identity before acquiring neural identity. This “primary regionalization” allocates cells to anterior or posterior regions of the nervous system, explaining how cranial and spinal neurons are generated at appropriate axial positions. These findings prompt a revision to models of neural induction and support the proposed dual evolutionary origin of the vertebrate central nervous system.

Poster Number: P123
Gene regulation dynamics during somitogenesis
E Thierion[1], X Ibarra-Soria[1], JC Marioni[1,2], DT Odom[1]

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During vertebrate development gene expression is intricately regulated to achieve precise and robust spatio-temporal dynamics, critical for tissue identity specification. Detailed understanding of these processes are lacking in most systems. To this end we are studying somitogenesis. Somites contain the precursors of vertebrae and skeletal muscles. They form periodically, in pairs on either side of the neural tube in an anterior-to-posterior manner. We have optimized a protocol to dissect individual somites from mouse embryos, keeping both somites from each pair. We then perform RNA- and ATAC-sequencing on each to characterize the transcriptional profile and the associated chromatin landscape. We perform this on somites along the embryo axis and at different developmental stages. An in-house developed analytical framework (see abstract by Ibarra-Soria et al.) will allow us to characterize the gene expression dynamics across time and space along with the putative regulatory elements driving these changes.

Poster Number: P124
Gene regulation dynamics during somitogenesis
X Ibarra-Soria[1], E Thierion[1], DT Odom[1], JC Marioni[1,2]

[1]Cancer Research UK Cambridge Institute, University of Cambridge, Cambridge, UK; [2]EMBL-European Bioinformatics Institute, Wellcome Genome Campus, Cambridge, UK

During vertebrate development gene expression is intricately regulated to achieve precise and robust spatio-temporal dynamics, critical for tissue identity specification. Detailed understanding of these processes are lacking in most systems. To this end we are studying somitogenesis. Somites contain the precursors of vertebrae and skeletal muscles. They form periodically, in pairs on either side of the neural tube in an anterior-to-posterior manner. We have dissected individual somites and performed RNA- and ATAC-sequencing on each pair (see abstract by Thierion *et al.*). We are developing a bioinformatics analytical framework capable of integrating: 1) the gene expression dynamics with the chromatin landscape state; 2) positional information along the embryonic axis; 3) temporal information from different developmental stages. The integration of these data will provide a detailed picture of the processes driving somitogenesis, as well as their key genes and regulatory elements.

Poster Number: P125
Redundancy in microRNA regulation and microRNA deletion phenotypes
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MicroRNAs are small non-coding RNAs that acts as gene expression regulators. The misexpression of most individual microRNAs has been found to have major phenotypic consequences, however loss of a single microRNA seldom results in significant phenotypic change. This suggests that there may be a high degree of redundancy in the microRNA regulatory network. We wish to understand how redundant targeting by microRNAs regulates gene function during development. To this end, we predicted targets of microRNAs in *Drosophila melanogaster* 3' UTRs, and constructed a set of 602 miRNA redundancy networks. We focused on gene family members that conserve the redundant targeting. We also discovered that larger paralogous gene families, as well as genes with longer 3'UTR, are regulated by more numbers and distinct types of miRNA, which suggests greater redundancy. We are investigating the regulation of these networks by looking at the miRNA gene expression and quantifying mRNA and protein levels.

Poster Number: P126
Transcriptome profiling of piRNAs during *Parasteatoda tepidariorum* embryogenesis
L Tincopa-Marca, S Griffiths-Jones, M Ronshaugen

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PIWI-interacting RNAs (piRNAs) are small-RNA molecules that inhibit the transcription of transposons. In *Drosophila melanogaster* this activity appears to be largely limited to the germ line but is found in somatic

tissue of some other arthropods. Here we examine piRNA expression in the common house spider, *Parasteatoda tepidariorum*. piRNA expression has been reported in the germline of *P. tepidariorum* but has not been characterised in the embryo. Here we examine the developmental profile of piRNA expression during *P. tepidariorum* embryogenesis and find piRNA production throughout all stages of embryonic development. Furthermore, we present an analysis of the temporal profile of piRNAs across embryogenesis and profile the presence of both primary and secondary piRNAs.

Poster Number: P127

Transient early gestational antithyroid treatment in mice results in behavioural deficits in adult offspring

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Hypothyroidism in early gestation is associated with cognitive deficits in offspring including Autistic Spectrum Disorder. Our previous work had shown that early hypothyroidism disrupts the formation of the major cerebellar nuclei in the chick model. We therefore hypothesised that thyroid-dependent cerebellar disconnection may underlie cognitive deficits in later life. We used a mouse model and treated pregnant dams with Methimazole from E0 to E14. ELISA analysis at E14 showed significant drop in T3 and T4 levels. The gross morphology of experimental and control groups was broadly similar, as analysed by X-ray micro-CT scan, suggesting that the behavioural phenotype results from relatively subtle changes in cell number, physiology or connectivity. Significant differences in behaviour were detected in open-field test of anxiety and a three-chamber test for sociability at P64. This suggests that the findings in studies of human cohorts can be simulated in a model of gestational hypothyroidism in mice.

Poster Number: P128

From Pioneer to Repressor: Bimodal foxd3 Activity Dynamically Remodels Neural Crest Regulatory Landscape *in vivo*

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The neural crest (NC) is a multipotent embryonic cell population that gives rise to a broad range of derivatives in the vertebrate embryo. Core NC transcription factor foxd3, known to mediate late NC lineage decisions via transcriptional repression, is also pervasively expressed in the pre-migratory NC progenitors, where its putative role remains elusive. To elucidate the mechanistic and temporal mode of foxd3 action, we analysed its genome-wide binding profiles across multiple stages of zebrafish development. To this end, we used our novel biotagging approach allowing to specifically biotinylate foxd3 protein *in vivo*. Foxd3 binding maps interpreted within the context of NC-specific transcriptional and epigenomic profiles of foxd3-mutant and control cells reveal that foxd3 acts bimodally throughout the NC ontogeny. We show that foxd3 first functions as a chromatin pioneer, priming NC *cis*-regulatory elements and gradually shifts towards its canonical repressive mode to maintain NC pluripotency and define cell fates.

Poster Number: P129

Genome-wide analysis of gene expression and chromatin architecture *in vivo* reveals intricate gene regulatory networks underlying cranial neural crest development

RM Williams[1], D Gavriouchkina[1], I Candido-Ferreira[1], E Repapi[2], U Senanayake[1], J Telenius[2], J Hughes[2], T Sauka-Spengler[1]

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The neural crest (NC) is a multipotent embryonic population that gives rise to a wide range of derivatives in the vertebrate embryo. The process of NC formation is orchestrated by an intricate network of gene regulatory interactions, previously proposed as the NC gene regulatory network (NC-GRN). Here we decipher NC-GRN circuits genome-wide using chromatin and cis-regulatory profiling of the cranial NC cells. By conducting a comprehensive survey of their chromatin and transcriptional landscapes, we uncover accessibility dynamics and chromosome conformation thus identifying a full complement of active NC enhancers. Analysis of enhancer organisation genome-wide, together with a survey of their mediator complex occupancy and H327Ac modifications reveals a 'super-enhancer'-like signature of clustered elements controlling key NC regulators. The identified single-cell transcriptional signatures of cranial NC cells in combination with global enhancer profiling allows us to propose, for the first time, a high-resolution representation of the cranial NC GRN.

Poster Number: P130

Linking self-renewal and differentiation:

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Embryonic stem cells (ESCs) are supported by a network of transcription factors (TFs) known as the pluripotency network. While the population of ESCs that expresses these factors is closest to embryonic epiblast, expression *in vivo* indicates additional roles in lineage specification. Is there a role of specific pluripotency factors in lineages specification and how does this relate to their support of ESC self-renewal? Here we explore these questions with respect to the pluripotency TF Esrrb. Based on analysis of Esrrb's behavior in Nanog mutants, we suggest that it has two roles; to stimulate self-renewal while preserving competency for primitive endoderm differentiation. Thus, in the presence of Nanog, Esrrb inhibits differentiation and supports pluripotency, but in its absence, promotes differentiation. Moreover, Nanog and Esrrb ratio was found to be regulated by Fgf/ERK signaling, suggesting a model in which signaling modulates the relative stoichiometry of these two TFs to mediate lineage choice.

Poster Number: P131

Cdx2 is an essential gatekeeper of murine trophoblast pluripotency

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Cdx2 is crucial for the establishment of the murine trophoblast lineage, but the effect of Cdx2 loss on established trophoblast cells is unknown. We have generated ATACseq and RNAseq libraries from wild-type (WT) and Cdx2 knockdown (KD) trophoblast stem cells (TSCs) in vitro. Cdx2 KD triggers increased chromatin accessibility, which is reminiscent of what happens upon TSC differentiation. Consistent with this observation, the peaks with increased accessibility in our KD cells are enriched for the Tfap2c consensus motif, a key player in TSC differentiation. Tfap2c likely contributes for the activation of newly accessible cis-regulatory elements given that many of these sites display Tfap2c occupancy. Our RNAseq data further shows that Tfap2c is significantly upregulated in KD cells, and we found a significant overlap between our KD cells and TSC-differentiating cells. Moreover, KD cells terminally differentiate into trophoblast giant cells, suggesting that Cdx2 prevents TSC differentiation and thus maintains pluripotency.

Poster Number: P132
Network mapping of genome organisation reveals the formation of large co-regulated hubs upon the transition from naïve to primed human pluripotency
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Naïve and primed human pluripotent cells hold distinct developmental and molecular identities. To compare their 3D genome organisation, we used promoter-capture HiC to generate a high-resolution atlas of DNA interactions in these two pluripotent states. We also developed new computational approaches allowing us to interrogate the atlas at multiple scales, ranging from a global overview to local communities that recapitulate TADs, down to individual promoter-enhancer interactions. We uncovered numerous, large highly connected hubs that changed substantially in interaction frequency and in transcriptional co-regulation between naïve and primed states. Small interaction hubs frequently merged to form larger networks during naive to primed transition, and these were typically linked by newly acquired Polycomb-bound long-range interactions. We also identified changes in enhancer activity and interactivity that associated with state-specific transcription of their target genes. Investigating chromatin topology in human pluripotent states offers new insights into features of gene regulatory control during human development.

Poster Number: P133
Quantitative and dynamic analysis of neurogenesis with single cell resolution at the tissue level
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In recent years, our understanding of how cells make cell state transitions has been transformed by the application of single cell technologies. This is well exemplified by the short-period oscillations of Hes gene expression in neural development. Here, we take a quantitative approach to analyse single-cell expression dynamics in the developing spinal cord of Venus-Hes5 knock-in mice. Direct protein quantitation using fluorescence correlation spectroscopy (FCS) in live E10.5 spinal cord slices shows that Hes5 expression has a 10-fold range between cells. Live imaging of spinal cord ex-vivo shows that Hes5 expression is fluctuating and 30-40% of cells show periodic expression. We use hierarchical clustering to define distinct Hes5 dynamics and use cell position and division properties to infer cell state. We find that neural progenitor cells have fluctuating and aperiodic Hes5 expression whereas cells transitioning towards differentiated neurons show a slow decrease in Hes5 and are more frequently periodic.

Poster Number: P134
Understanding ear development and disease: a gene regulatory network approach
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The vertebrate inner ear is responsible for hearing and balance, and during development arises from sensory progenitors located in the ectoderm outside the central nervous system. Using a combination of developmental, molecular and computational approaches we have established the signalling and transcription factor networks that control specification of sensory progenitors and their commitment to the ear lineage. These epigenetic networks reveal the regulatory regions that control gene expression, their hierarchical relationships and thus provide a 'road map' for ear commitment. This approach has allowed us to identify Sox transcription factors as 'master regulators' for ear identity, as well as the epigenetic modifiers that maintain the regulatory module at the top of the ear hierarchy. In addition, we have used these networks to uncover targets of the Six1 transcription factor, which in turn represent new candidate genes for Branchio-Oto-Renal Syndrome.

Poster Number: P135
The LINE1 retrotransposon regulates early embryonic cell identity
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Transposons comprise half of mammalian genomes and are often described as 'junk DNA'. LINE1 retrotransposons are the most abundant class and their expression is thought to be deleterious for cells. However paradoxically, LINE1 is highly expressed during early development. Here we reveal essential roles for LINE1 in mouse embryonic stem (ES) cells and embryos. In ES cells, LINE1 RNA acts as a nuclear scaffold that recruits Nucleolin and Kap1/Trim28 to repress *Dux*, master activator of a transcriptional program specific to the totipotent 2-cell embryo. LINE1 depletion causes inappropriate activation of *Dux*, along with transcripts driven by the 2-cell-specific LTR retrotransposon, MERVL. In parallel, LINE1 mediates association of Nucleolin/Kap1 with rDNA, promoting rRNA synthesis and ES self-renewal. In embryos, LINE1 knockdown prevents *Dux* silencing, rRNA synthesis, and exit from the 2-cell stage. We reveal an essential partnership between LINE1 RNA and chromatin factors that regulates transcription, developmental potency and ES self-renewal.

Poster Number: P136
Investigating the mechanism of Groucho co-repressor function
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Groucho/Transducin-Like Enhancer of split (Gro/TLE) proteins act as co-repressors and act in several key pathways during development and cancer (including Notch and Wnt signalling). *Drosophila* Groucho interacts with transcription factors that are involved in development including Hes and LEF1/Tcf protein families. Although it is well established that Groucho acts as a co-repressor in vivo, the mechanisms through which it acts remain unclear. ChIP-seq revealed that despite acting as a co-repressor, Groucho recruitment is enriched in "active" chromatin. Groucho is enriched at genes that exhibit RNA polymerase pausing in both cell culture, and embryos and depletion of Groucho in Kc167 cells leads to release of RNA polymerase pausing and increased transcript production from a bone fide target gene. We are currently pursuing a number of strategies to understand the molecular mechanisms underlying Groucho repression in *Drosophila*. A current review of our analysis will be presented.

Poster Number: P137
miR-133 mediated regulation of the Hedgehog pathway orchestrates embryo myogenesis
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Skeletal myogenesis serves as a paradigm to investigate molecular mechanisms underlying exquisitely regulated cell fate decisions in developing embryos. The microRNA miR-133 is expressed in the myogenic lineage but how it acts remains incompletely understood. Here we performed genome-wide differential transcriptomics of miR-133 knock-down (KD) embryonic somites, the source of vertebrate skeletal muscle. This revealed extensive down-regulation of Shh pathway components: Ptc receptors, HHIP, and the transcriptional activator, Gli1. By contrast Gli3, a transcriptional repressor, was de-repressed and confirmed as a direct miR-133 target. miR-133 KD impaired myotome formation and growth by disrupting proliferation, extracellular matrix deposition and epithelialization. Together this suggests that miR-133 mediated Gli3 silencing is critical for embryonic myogenesis. Consistent with this idea we found that either activation of Shh signalling by purmorphamine or Gli3 KD by morpholino rescued the miR-133 KD phenotype. We identify a novel Shh/MRF/miR-133/Gli3 axis that connects epithelial morphogenesis with myogenic fate specification.

Poster Number: P138
How to build a spider: the regulation of segment addition in *Parasteatoda tepidariorum*
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It has been shown that Wnt and Delta-Notch signalling probably regulated posterior segmentation ancestrally in arthropods. However, it remains unclear how these signalling pathways interact and regulate putative downstream segmentation genes. We studied the regulatory interactions between *Delta*, *Notch*, *Wnt8*, *caudal*, *even-skipped*, *runt-1*, and *odd-skipped* during posterior segmentation in *Parasteatoda tepidariorum*. We showed that *Delta* initially activates *Wnt8* in the posterior SAZ, but conversely inhibits *Wnt8* expression in the anterior SAZ. This shows that the SAZ can be divided into at least two regions: a posterior region of uncommitted cells and an anterior region where cells become committed to forming a new segment. Furthermore, the dynamic expression of *even-skipped*, *runt-1* and *odd-skipped* in forming segments is regulated by the read-out of Delta-Notch and Wnt signaling *via caudal*. However, unlike the other pair-rule gene orthologs, it appears that *hairy* is part of the oscillatory mechanism rather than a read-out from it.

Poster Number: P139
ABSTRACT WITHDRAWN

Poster Number: P140
Investigating enhancer evolution in *Drosophila*: Learning the rules of regulatory logic
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Enhancers are cis-regulatory elements that play a crucial role in gene regulation. Mutations in enhancers is one of the principal mechanisms underlying phenotypic evolution. However, enhancers can also turnover while maintaining the same output, a process called developmental systems drift (DSD). The aim of this project is to better understand how enhancers evolve by studying DSD of the P2 enhancer of *hunchback* in *Drosophila* species. We first surveyed natural variation in the P2 enhancer, and then tested the functional equivalence of enhancers from different species in *D. melanogaster*, through replacement of the endogenous P2. We have found that the P2 from *D. pseudoobscura* and *D. yakuba* is functionally equivalent to that from *D. melanogaster*. We are currently using the MS2-MCP system to qualitatively measure live expression driven by enhancer variants. This study will improve our understanding of the evolution of cis-regulatory sequences and the design of synthetic enhancers.

Poster Number: P141
Characterising novel zebrafish enhancers in migratory neural crest function
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The neural crest (NC) is a transient and multipotent cell population in vertebrates that give rise to a plethora of tissue types including the craniofacial skeleton, sensory neurons, melanocytes and glia. Extensive research in the elucidation of the NC gene regulatory network (NC-GRN) uncovered key players in NC ontogeny from the *pax*, *soxE*, *fox*, *zic*, *tfap2*, and *snail* families of transcription factors. We previously reported an in depth look into the nuclear transcriptome of migratory neural crest, using the *biotagging* method developed for zebrafish to isolate subcellular compartments from specific cell populations. This study revealed a high confidence cohort of putative *cis*-regulatory elements that are bidirectionally transcribed and recapitulated NC molecular identity after functional annotation. Here, we present biologically active and previously uncharacterised enhancers for two NC players, *pax3a* and *sox10*, including those identified previously to be bidirectionally transcribed. We are currently characterising these enhancers in zebrafish using CRISPR/Cas9 technology.

Poster Number: P142
Networking opportunities: Integrating properties of biological oscillators in a bioinformatic screen reveals novel periodically expressed human genes
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Oscillatory gene research is an emerging area of focus across many fields. To date we only know of a handful of genes which have oscillatory expression. Identification of oscillatory genes is important to furthering our understanding of the mechanisms gene regulation. Here we integrate expression, transcription factor (TF) binding-site and microRNA target data into a computational gene interaction network. This network was interrogated for oscillatory type structures previously identified in systems biology research. Auto-regulation was identified in 73% of TFs investigated and 67% of TFs studied were identified in incoherent feedback involving a microRNA; both motifs were found more often than expected by chance within the network ($p<0.001$ and $p=0.01$ respectively, by simulation). Experimental investigation of the targets identified should validate our approach. The network-motifs studied include microRNA regulation, manipulation of these interactions will reveal new insights into the role of microRNAs in oscillatory protein expression.

Poster Number: P143
Live visualization of native gene transcription reveals an exclusive transcription compartment forming before global zygotic genome activation
Y Hadzhiev[1], H Qureshi[1], L Wheatley[1], J Wragg[1], A Jasiulewicz[1], H Nguyen[2], A Gambus[1], L Tora[3], J Fossey[2], **F Mueller**[1]

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In externally developing metazoan embryos a series of extremely fast and synchronous cell cycles precedes global zygotic genome activation. However, a small group of genes are activated well before global genome activation. How do these genes escape the global repression of the genome and how transcription proceeds during the short cell cycles without gap phases remains unknown. We developed a novel live imaging tool for detection of native, nascent gene transcription and show spatio-temporal dynamics of the first wave of genome activation in S phase of metasynchronous cell cycles in zebrafish. Simultaneous 4D imaging of native expression of genes on different chromosomes reveals the formation of a transcription compartment shared by active chromosomes. The transcription compartment offers an escape from global repression of transcription whereas the observed inter-chromosomal organisation indicates a novel transcription regulatory function for nuclear topology in early development.

Poster Number: P144
Dynamics of transcription from Notch responsive enhancers
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Transcriptional changes elicited by signalling are highly dynamic. Though static patterns of gene expression have been studied extensively, we know little about how dynamic signals are interpreted. In the Notch signalling pathway, the Notch intracellular domain (NICD) itself transduces the signal directly to the nucleus. To discover how these highly stochastic signals are read-out by enhancers we are using the MS2/MCP system to analyze the dynamics of transcription from two Notch responsive enhancers active in *Drosophila* blastoderm embryos. Remarkably, both enhancers confer the same temporal profiles of activity, including a marked increase in levels at the onset of gastrulation. Placing different promoters downstream of these enhancers changes the mean levels of transcription but not the overall profile. In contrast, providing ectopic Notch results in ectopic responses with different temporal dynamics. By applying a simple mathematical model of transcription to these behaviours we infer underlying mechanisms regulating transcription and promoter activity.

Poster Number: P145
The Gene Regulatory Network Underlying the Neural-to-Glial Fate Transition in the Developing Spinal Cord
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Neurons and glia are generated sequentially in the central nervous system. In vivo, this process is under tight spatial and temporal control. Although several factors have been defined, the underlying gene regulatory network mediating the transition remains unclear. We have developed an *in vitro* model system using embryonic stem cells that reproduces the dynamics observed *in vivo*. Using single-cell transcriptomics, we define the transcriptional changes that accompany the transition and identify novel candidate genes involved. Using CRISPR-Cas9 and lentiviral technologies, we test these candidates and investigate their effect on the transition. Through this approach we reveal a novel player in the activation of the glial lineage. Our work provides new understanding of how gene regulatory networks instruct cell fate decisions in the developing spinal cord.

Poster Number: P146
Memory functions reveal structural properties of gene regulatory networks
EHD Herrera Delgado[1,2], RPC Perez Carrasco[1,3], JB Briscoe[1], PS Sollich[2]

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Gene regulatory networks are essential for cell fate specification and function. But the recursive links that comprise these networks often make determining their properties and behaviour complicated. Computational models of these networks can also be difficult to decipher. To reduce their complexity we employ a Zwanzig-Mori projection approach which reduces a system of ordinary differential equations, representing a network, to an arbitrary subnetwork with additional memory functions. These memory functions account for the bulk by describing signals that return to the subnetwork after some time, having passed through the bulk. Applying the method to a transcriptional network in the vertebrate neural tube reveals previously unappreciated properties of the network. By taking advantage of the structure of the memory functions we identify interactions within the network that are unnecessary for sustaining correct patterning. Upon further investigation we find that these interactions are important for conferring robustness to variation in initial conditions.

Poster Number: P147
Molecules that count: molecular insights into precise cell fate decisions in the vertebrate neural tube
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Pattern formation and cell fate specification in developing tissues are remarkably reproducible. In each fate decision a cell has to compute internal molecular events to produce a specific output, represented by gene expression, as part of a process controlled by gene regulatory networks. One well-studied example is the vertebrate neural tube, where neural progenitors are allocated in molecularly distinct domains arrayed along the dorsoventral axis. To understand how accuracy in gene expression is achieved in this tissue, we are undertaking measurements with single-molecule resolution to quantify the dynamics and precision of a bistable switch comprising the transcription factors Irx3 and Olig2. These quantifications include the estimation of molecule number and rates of production and degradation, for both mRNAs and proteins. Furthermore, we are developing mathematical models using this data with the aim of understanding how intrinsic molecular properties influence cell fate transitions.

Poster Number: P148

Interrogation of the combinatorial *cis*-regulatory code in the cranial neural crest

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The cranial neural crest (CNC) is a transient population of embryonic cells with remarkable multipotency and migratory behaviour. Our recent description of CNC regulatory landscape using spatiotemporal chromatin profiling revealed the presence of enhancer clusters displaying 'super-enhancer'-like features, including H3K27Ac enrichment and Mediator complex occupancy. Here, we performed *k*-means clustering to identify dynamic changes in chromatin accessibility followed by downstream motif enrichment analysis as a means of identifying core transcription factors and their potential co-binding activities controlling CNC enhancers. We detected differential enrichment in Sox10 and TFAP2a/c motifs, suggesting that CNC enhancer activity is primarily dictated by their heterotypic binding, likely via feed-forward loops. *In vivo* biotinylation of Avi-tagged transcription factors followed by biotin-ChIP-sequencing revealed Sox10 occupancy in CNC specific-loci consistent with chromatin accessibility dynamics, defining at high-resolution the pivotal role of Sox10 in the regulatory landscape of CNC.

Poster Number: P149
What's under the kilt? *tartan* is a likely causative gene for rapid male genitalia divergence between *Drosophila* species
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Although *Drosophila simulans* and *Drosophila mauritiana* diverged only 240 thousand years ago, there are already striking differences in the morphology of the male genitalia. The claspers, which are important for correct positioning of the male during copulation, are twice as large in *D. mauritiana* than in *D. simulans*. In order to unravel how this rapid trait evolution is facilitated in the genome, we performed Quantitative Trait Loci and introgression mapping. This revealed a 177kb candidate region on the left arm of the third chromosome underlying 16.6% of clasper size divergence between the species. An RNAi screen in *D.melanogaster*, differential gene expression analysis and *in situ* hybridisation has identified *tartan*, a LRR transmembrane protein, as the likely causative gene. To prove *tartan* is the divergent gene, we are currently using CRISPR/Cas9 to generate reciprocal hemizygotes. If correct, this would indicate novel roles for LRR proteins in regulating organ size development, morphological evolution and potentially reproductive isolation between closely related species.

Poster Number: P151
Evolution and Function of Young Homeobox Genes in Preimplantation Development
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Evolutionary changes to embryonic development underpins evolutionary change to complex organisms. The homeobox gene superclass encode DNA-binding proteins, many of which possess important functions in embryogenesis. Most homeobox genes are highly conserved, but there are exceptions. For example, ETCHbox (Eutherian Totipotent Cell Homeobox) genes are eutherian (placental) mammal specific, and they show many instances of gene loss and duplication. Mouse and human have very different sets of ETCHbox genes, with human retaining five (*ARGFX*, *LEUTX*, *TPRX1*, *TPRX2*, *DPRX*) and mouse only two (*Crxos*, *Obox*), although with multiple duplications. These genes are expressed specifically in the pre-implantation embryo when the cells are preparing for and undergoing the first cell lineage decisions. Using cell culture and transcriptomics, we are beginning to unravel the role of ETCHbox genes in preimplantation development with findings which increase our understanding of how repeated loss and divergence of ETCHbox genes contributes to mammalian evolution and development.

Poster Number: P152
Modelling the ancestral Hedgehog signalling pathway
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Hedgehog (Hh) signalling is crucial for the proper development of most animals and dysfunction of Sonic hedgehog signalling underlies a number of severe birth defects, ciliopathies, and cancers in humans and animals. A mechanistic understanding of Hh function is therefore of significant fundamental and therapeutic interest. Although Hh signalling is well described in several model systems, differences between Drosophila and vertebrate models means that parts of the pathway remain enigmatic.

The most recent common ancestor to have a full complement of "core" Hedgehog pathway genes is shared between bilaterians and Cnidarians. Comparison of functional data between bilaterians and Cnidarians should allow the reconstruction of the ancestral mechanism of Hh signalling, and hence give insights into its divergence during evolution. Using a combination of bioinformatics, genetic and molecular approaches we are developing a Cnidarian model of Hh signalling using the sea anemone, Nematostella vectensis.

Poster Number: P153
A Sox gene is a key player in the spider embryogenesis
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The Sox gene family encodes a HMG-containing domain similar to the SRY (Sex-Determining Region Y) of eutherian mammals. These genes regulate many processes during embryogenesis in metazoans. In insects, *Dichaete* is the only Sox gene known to be involved in segmentation. To determine if similar mechanisms are used in other arthropods, we investigated the role of Sox genes during segmentation in the spider *Parasteatoda tepidariorum*. While Dichaete does not appear to be involved in spider segmentation, RNAi knockdown of *Sox 21-B1* (a *Drosophila* Sox 21-B orthologue) perturbed the sequential addition of prosomal segments and the expression of segmentation genes. Thus, we have found that segmentation in other arthropods is also regulated by a Sox gene, but that spiders employ a different gene from insects. Our work provides new insights into the function of an important and conserved gene family across arthropods and the evolution of the development of these animals.

Poster Number: P154
Weird gene in a weird mammal: A highly divergent pancreatic duodenal homeobox 1 (Pdx1) gene in the fat sand rat
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Pancreatic duodenal homeobox 1 (Pdx1) is a highly conserved protein regulator of pancreatic development during embryogenesis and a maintainer of β-cell function in adults. *Pdx1*$^{-/-}$ mice fail to develop a pancreas, while *Pdx1*$^{+/-}$ mice form a pancreas but show type II diabetes symptoms. *Psammomys obesus* (fat sand rat) is a desert rodent prone to type II diabetes, and it possesses a highly divergent *Pdx1* gene. Currently, only members of the Gerbillinae subfamily have been found to carry these drastic mutations in *Pdx1*. Functional analysis has shown that sand rat Pdx1 has a longer protein half-life than mouse Pdx1, and under high glucose conditions, sand rat Pdx1 is unable to induce insulin expression to the same degree as mouse Pdx1. The high levels of GC in sand rat Pdx1 and its surrounding genomic regions indicate that this genome region may be a mutational hotspot, however how this hotspot arose remains unexplained.

Poster Number: P155
From Hippocrates to gerbils – asymmetry in reproduction and development
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The internet abounds with claims that foetal gender can be predicted based on whether the placenta is localised on the left or right, echoing Hippocrates that “the male embryo is usually on the right, the female on the left”. In the Mongolian gerbil (*Meriones unguiculatus*) at least, it seems that Hippocrates might have been right. Gerbils exhibit an intrauterine sex bias, where male fetuses are more common in the right uterine horn, and females more common in the left. Whilst this asymmetry has been known to exist for several decades, we do not know why, when and how it might be established. We suggest that altered sex bias is an adaptation for improved offspring quality, through reduction of intrauterine position effects. We further suggest that sex bias results from an interaction between the developing ovaries and adrenal glands.

Poster Number: P156
Remodeling of the stapes and otic capsule in post-natal development
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The stapes is the last bone in the ossicular chain of the middle ear inserting into the otic capsule and is crucial in transmitting sounds to the cochlea. The stapes and capsule initiate as a cartilaginous template that ossifies due to the action of osteoblasts. Following ossification, the stapes must then be remodeled from its initial form by osteoclasts, moving from thick crura and a small foramen, to thin crura with a large foramen in the adult. In contrast the otic capsule appears not to remodel; inappropriate remodeling being

associated with hearing loss.

Using the mouse, stapes and otic capsule remodeling has been followed over post-natal development. This is compared with c-Fos mutant mice, which lack osteoclasts necessary for remodeling. A combination of histochemical and 3D imaging techniques has been used to achieve this. The different patterns of ossification and remodeling are compared in these two adjacent bones.

Poster Number: P157
Investigating transcription factor hierarchies underlying the formation of hair cells versus electroreceptors in the lateral line system

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In fishes and aquatic-stage amphibians, local water displacement is detected by lateral line placode-derived 'neuromasts' containing mechanosensory hair cells. In all lineages except frogs and neopterygian fishes (gars, bowfin, and teleosts), some neuromast lines on the head are flanked by fields of lateral line placode-derived 'ampullary organs', containing electroreceptors which detect low-frequency electric fields (primarily used for hunting). The presence of two different but related sensory cell types deriving from the same lateral line placode within a single organism represents a unique opportunity for studying sensory cell-type specification. We previously used differential RNA-seq to generate a lateral line organ-enriched gene-set from late-larval paddlefish (Polyodon spathula) (Modrell *et al.*, 2017, eLife 6: e24197). Building on this, we are now using another, more easily accessible chondrostean fish, the sterlet (Acipenser ruthenus), as a functional model for investigating the transcription factor hierarchies underlying the formation of lateral line hair cells versus electroreceptors.

Poster Number: P158
The Genetic Basis of Eye Size Natural Variation in *Drosophila melanogaster*

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The compound eyes of Diptera exhibit remarkable morphological diversity often associated with behavioral adaptations. We have observed inter- and intra-specific variation in eye size among wild strains of the *Drosophila melanogaster* species subgroup and determined the heritability of this and other head traits. Using an interval mapping approach, we have mapped quantitive trait loci underlying eye size variation within *Drosophila melanogaster* and *Drosophila simulans* and validated the mapped effects using reciprocal introgressions. We further focused on fine scale mapping of QTL detected on similar regions of the 3rd chromosome of both species. Additionally, we describe differences in eye development of the analysed strains, namely related to the size of the eye primordium expressing the determinant Eyes Absent and to cell proliferation differences. Finally, I will discuss how these developmental differences may relate to the molecular function of candidate genes underlying the detected QTLs.

Poster Number: P159
Functional studies in 2D and 3D stem cell systems of candidate genes underlying human-specific features of cerebral cortex development

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Sequencing of primate genomes and comparative studies of primate cerebral cortex have generated numerous hypotheses on the genetic bases for evolutionary differences in cortical development; however, the contribution of selected genes has seldom been tested functionally. Cortical cultures and organoids derived from pluripotent stem cells can recapitulate *in vitro* key features of human and NHP cortical development, therefore we used these models to test how cortical development might be affected by evolutionary differences in gene expression. Among the genes differentially expressed between humans and macaques, we found several known to cause microcephaly or megalencephaly when mutated in humans. For a few of these, modification of their expression levels in macaque cortical cultures to human-like expression resulted in more human-like progenitor behaviour, including increased progenitor expansion and decreased early neuronal

differentiation. Our results highlight the importance of regulation of gene expression as a mechanism contributing to evolutionary change in cortical development.

Poster Number: P160
Using CRISPR/Cas9 to investigate the role of neuropeptides in the development of the sea urchin *Strongylocentrotus purpuratus*

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My project focuses on the role neuropeptides have in the development of the sea urchin, Strongylocentrotus purpuratus with the possibility to uncover new important function(s) for this exciting class of signalling molecules.

Neuropeptides are ancient neuronal signalling molecules that bind to receptor proteins on target cells. Preliminary data in the purple sea urchin, S. purpuratus has suggested a developmental role of neuropeptides. Thirty-eight neuropeptide genes have so far been identified in the sea urchin genome and at least sixteen are expressed in the early phase of embryogenesis. Further some of these are spatially localised. A pedal peptide-like neuropeptide (PPLN1) shows oral-aboral asymmetric expression, suggesting a role in early axis specification.

Deducing their innovative function(s) will help to elucidate the evolutionary history of these molecules. To identify the putative function of these molecules we are undertaking knock- down/out experiments using morpholino antisense oligonucleotides and the CRISPR/Cas9 system.

Poster Number: P161
Functional genomics and the evolutionary diversification of the artiodactyl limb

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Morphogenesis of the vertebrate limb is a genetically well-studied process that can be used as a paradigm to gain insight into the mechanisms of transcriptional regulation during both developmental and evolutionary processes. The pig (*Sus scrofa*) has, as other terrestrial artiodactyls, extremities specialized for cursorial locomotion thanks to various modifications of the distal limb skeleton. Here, we report a detailed morphological and molecular analysis of pig limb development. These studies reveal that the pig limb bud displays a loss of anterior-posterior (AP) polarity at the molecular level in the distal mesenchyme, where digit progenitors are located. This loss of AP polarity mirrors the morphological loss of symmetry observed in the handplate. To gain mechanistic insight into these evolutionary processes, we are also using functional (eg. ATAC-seq, RNA-seq, etc) genomics in mouse and pig embryos to map and identify divergent regulatory strategies during limb bud development.

Poster Number: P162
Investigating the function and evolution of *Wnt* ligands in *Drosophila melanogaster*

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Wnt genes encode secreted glycoproteins that play many important roles in development of metazoans. There are thirteen subfamilies of Wnt ligands in metazoans, but only seven are represented in *Drosophila melanogaster*. While *wingless* (*wg*) is the best understood and widely studied Wnt gene in *Drosophila*, the functions of the other ligands are less well understood in this fly. *Wnt6* is the most closely related Wnt gene to *wg* and it was previously shown that this ligand is involved in the development of the maxillary palps. We generated a new mutant allele of *Wnt6* using CRISPR/Cas9 and we have found that *Wnt6* is not only involved in maxillary palp formation but also appears to regulate larval growth. We are also currently testing the ability of *wg* and *Wnt6* and other Wnt ligands to replace each other in different developmental contexts and to map the amino acids that confer their functional specificity.

Poster Number: P163
Gut-like ectodermal tissue in a sea anemone challenges germ layer homology
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Cnidarians (e.g. sea anemones) develop from two germ layers (outer ectoderm and inner endoderm), while bilaterians (e.g. flies, vertebrates) additionally develop the intermediate mesoderm. Since their discovery, cnidarian and bilaterian endodermal layers are considered as evolutionary homologous. We have tested this long-standing hypothesis by a comparative fate map, cell type and transcription factor expression study in the sea anemone *Nematostella vectensis*. Using transplantation of transgenically labelled cells, we generated the first cnidarian germ layer fate map and found an ectodermal origin of the inner cnido-glandular epithelium. Strikingly, this ectodermal part displays a developmental transcription factor expression profile (e.g. *foxA*, *hhex*) and a specific cell type complement (e.g. exocrine) reminiscent of the developing bilaterian endodermal midgut. The endodermal derivatives, in contrast, display cell functions and transcription factor profiles shared with bilaterian mesodermal derivatives (e.g. cardiomyocytes). Our data thus refutes the generally accepted model of germ layer homology between cnidarians and bilaterians.

Poster Number: P164
Organizing the organizer: A novel role for *Ets4* in axis specification and cell migration in the spider *Parasteatoda tepidariorum*
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Axis determination is a fundamental process during animal development. In vertebrates as well as in spiders an organizing centre plays an important role during this process. In spiders the organizer is composed of a cluster of migratory cells (the cumulus) that induce the dorsoventral body axis via the secretion of Decapentaplegic (the ligand for the BMP receptor). This study reveals that the transcription factor *Ets4* is required to keep cumulus cells in the cluster and to activate the expression of cumulus specific genes like *hunchback* and *twist*. Loss of *Ets4* expression is leading to ventralized spider embryos. Interestingly, ectopic expression of *Ets4* is sufficient to induce cell delamination and migration by inducing a mesoderm-like cell fate.

Poster Number: P165
A genome-wide assessment of the ancestral neural crest gene regulatory network
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The neural crest (NC) is an embryonic cell population that contributes to key vertebrate-specific features. We examine the transcriptional profiles and chromatin accessibility of NC cells in the sea lamprey to gain insight into the ancestral NC gene regulatory network (GRN). Transcriptome analyses reveal clusters of co-regulated genes during NC specification and migration that show high conservation across vertebrates for dynamic programmes like Wnt modulation, but also reveal novel transcription factors and cell-adhesion molecules not previously implicated in NC migration. ATAC-seq analysis refines the location of known cis-regulatory elements at the *Hoxa2* locus and uncovers novel cis-regulatory elements for *Tfab2b* and *SoxE1*. Moreover, cross-species analysis reveals that the lamprey *SoxE1* enhancer activity is deeply conserved, mediating homologous expression in jawed vertebrates. Our data provide insight into the core elements of the NC GRN that are conserved to the base of the vertebrates, as well exposing elements that are unique to lampreys.

Poster Number: P166
The origin and evolution of vertebrate head mesoderm: *Alx* homeobox gene and amphioxus first somite
H Wang, **T Takahashi**

Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

The head is the most elaborate and characteristic structure in the vertebrate body, and its evolutionary origin has long attracted the interests of scientists. This question has often been addressed by comparing vertebrates with amphioxus: a marine invertebrate closely related to vertebrates. Previous studies indicate that the vertebrate head has evolved through the elaboration of a pre-existing structure, with evolutionary inventions of cranial neural crest cells and epidermal placodes, to establish the "New" head. What still remains unresolved is the evolutionary origin of the head mesoderm of vertebrates. This is mainly because the head mesoderm is unsegmented in vertebrates whereas the comparable region in amphioxus is explicitly segmented.

We found that amphioxus *Alx* homeobox gene is exclusively expressed in the most anterior somite, and with other marker genes for head mesoderm, we investigate the homologous relation between the head mesoderm in vertebrates and the anterior somites in amphioxus.

Poster Number: P167
Investigating microRNA function in the evolution of arthropod segmentation
LI Calvo Gonzalez, S Griffiths-Jones, M Ronshaugen

School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

Among arthropods two different modes of segmentation coexist. The ancestral mode is short-germ where segments are formed sequentially. The other is the derived long-germ where segment form simultaneously. The evolutionary transition between these modes of segmentation remains poorly understood. Interestingly, there are several similarities between short-germ segmentation and vertebrate's somitogenesis such as the involvement of some conserved signaling pathways (eg. Notch) and the apparent involvement of oscillatory regulatory genes. microRNA's are becoming recognized as key modulators of oscillatory behaviors with the potential to modulate the period of oscillatory genes during short-germ segmentation. Therefore, evolution of microRNA function may contribute to the transition between these distinct modes of segmentation. Using small RNA-Seq we are profiling microRNA expression in the short-germ arthropod *T.castaneum* and *P. hawaiensis* during segmentation. We are also using nascent transcriptional FISH to assess oscillations of clock-like genes and the expression pattern of potential regulatory microRNAs.

Poster Number: P168
Orthologs of the U-shaped-group transcription factors play multiple, topologically distinct roles in insect epithelial development
F Pridoehl[1], M Pentzien[2], KA Panfilio[1,2]

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Extraembryonic (EE) membranes are dynamic epithelia that protect the egg and help to shape embryonic form. Most insects, like the flour beetle *Tribolium*, retain the ancestral situation of two distinct EE membranes: the well-characterized serosa and the poorly studied amnion. In order to identify new genes relevant in the amnion, we are investigating orthologs of the Drosophila U-shaped-group genes, which are necessary in the single amnioserosa of fruit flies. To our surprise, two U-shaped members with EE tissue maintenance roles in the fly are rather required for EE morphogenesis in the beetle. To continue these functional analyses, we are now investigating the beetle orthologs of *tailup* and the eponymous *u-shaped*. To date, we find that both of these candidates have essential early functions, prior to either morphogenetic or maintenance functions, widening the scope for how U-shaped orthologs may play distinct roles in different EE tissue organizations.

Poster Number: P169
Segmentation in Arthropods: a study investigating regulatory relationship between gap genes and pair-rule genes in the beetle *Tribolium castaneum*
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In *Drosophila*, segments are patterned simultaneously via a gene cascade involving regulation of pair-rule genes by gap genes. The beetle *Tribolium castaneum* exhibits the ancestral condition of sequential segmentation using a segmentation oscillator/clock thought to comprise a negative feedback loop involving three pair-rule gene homologues (*Tc-even-skipped*, *Tc-odd-skipped* & *Tc-runt*). Gap gene knockdown in *Tribolium* does not result in gap phenotypes, and therefore gap homologues cannot regulate periodic pair-rule gene expression as in *Drosophila*. We have studied gap and pair-rule genes in *Tribolium*. We find that, contrary to previous reports, a pair-rule phenotype is observed in *Tc-odd*$^{\text{-RNAi}}$ and *Tc-odd*-CRISPR mutant embryos, and periodic expression of *Tc-eve* is abolished in this context. In addition, the expression domains of gap genes are altered. This suggests that pair-rule genes regulate gap genes in *Tribolium*, and that primary segmentation is driven by a segmentation clock involving more than just a single three-gene negative feedback loop.

Poster Number: P170
Acoel regeneration mechanisms indicate an ancient and widespread role for muscle in regenerative patterning
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Positional information is required for animal regeneration, yet how it is harbored in adult tissues is poorly understood. In planarians, positional control genes (PCGs) control regeneration outcomes and are regionally expressed predominately in the musculature. Acoels are early diverging bilaterally symmetric animals, having separated from other bilaterians >550 million years ago. Here, we find that PCGs in the acoel *Hofstenia miamia* are expressed together and specifically in a primary differentiated cell type: muscle. The vast majority of *Hofstenia* muscle cells in regions tested express PCGs, suggesting positional information is a major feature of muscle. PCG expression domains are dynamic in muscle after injury, consistent with known PCG roles in guiding regeneration. These data demonstrate an instructive positional role for *Hofstenia* muscle and this similarity with planarians suggests mesodermal muscle originated at the base of the Bilateria not only for contraction, but also as the source of positional information guiding regeneration.

Poster Number: P171
Hedgehog-like signalling in *C. elegans*?
EA Baker[1], AC Woollard[1], SM Shimeld[2], SPR Gilbert[1]

[1]Department of Biochemistry, University of Oxford, Oxford, UK; [2]Department of Zoology, University of Oxford, Oxford, UK

Hedgehog is one of a handful of signal transduction pathways that underpins the development of bilaterian animals. Having a single origin in the bilateria, Hedgehog has been conserved throughout all phyla exhibiting little divergence, with the exception of nematodes. Whilst the model nematode *Caenorhabditis elegans* has lost the Hedgehog pathway, the worm has around 60 'Hedgehog-like' genes, 10 of which reside within the Warthog family. This immense repertoire of Hedgehog-like genes has evolved over eons of duplication in the nematodes which we have mapped using a range of phylogenetic techniques. Using the phylogeny to inform their function in *C. elegans*, we have found several clade-specific roles of the Wrt genes including three (*wrt-2*, *wrt-4*, *wrt-8*) involved in the generation of left-right asymmetry, suggesting homoplasy with the same role of Sonic Hedgehog in mammals. As such, this work represents one of the most experimentally rigorous determinations of Duplication-Degeneration-Complementation dynamics to date.

Poster Number: P172
Investigating microRNA function in the evolution of arthropod segmentation
LL Calvo Gonzalez, S Grifiths-Jones, M Ronshaugen

School of Biological Sciences Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

Among arthropods two different modes of segmentation coexist. The ancestral mode is short-germ where segments are formed sequentially. The other is the derived long-germ where segment formation occurs simultaneously. The evolutionary transition between these modes of segmentation is poorly understood. Interestingly there are several similarities between short-germ segmentation and vertebrate's somitogenesis such as the involvement of conserved signaling pathways (eg. Notch). Both modes also involve oscillatory clock-like transcription of key regulatory genes. MicroRNAs are becoming recognized as key modulators of oscillatory behaviors, and have conserved functions in the regulation of Notch. There is therefore significant potential that microRNAs are involved in ensuring the periodic nature of oscillatory genes during short-germ segmentation. Using small RNAseq we are profiling microRNA expression in the short-germ arthropod *T.castaneum* and *P. hawaiensis* during segmentation. We are also using nascent transcriptional FISH to assess oscillations of clock-like genes and the expression pattern of potential regulatory microRNAs.

Poster Number: P173
ABSTRACT WITHDRAWN

Poster Number: P174
Patterning of a telencephalon-like region in the adult brain of amphioxus
E Benito-Gutierrez

Zoology, University of Cambridge, Cambridge, UK

The evolutionary origin of the vertebrate brain is still uncertain, as no homologous brain partitions have been found outside vertebrates in chordates. We have found a compelling homologue of the vertebrate telencephalon in amphioxus, the most basally branching chordate. This telencephalic region is characterised by a broad FoxG1 domain, molecularly sub-regionalised into a dorsal Emx-Lhx2/9-Pax4/6 domain, and a ventro-medial Hh-Nk2.1 domain. The unprecedented finding of Hh in the adult amphioxus brain suggests that molecules with organising properties might regionalise the amphioxus brain, as in vertebrates, but only late in development. This is congruent with our results on neuronal profiling using neurotransmitters and neuropeptides, which clearly show sustained neurogenesis and growth beyond metamorphosis. Metamorphosis in amphioxus re-shapes their body plan into a vertebrate-like one, further triggering a complete change in their life-style. Our results indicate that this life-style change might be also related to the development of a vertebrate-like brain.

Poster Number: P175
Sea lamprey Hox genes: insights into *cis*-regulatory evolution of neural crest patterning in vertebrates
HJ Parker[1], B De Kumar[1], ME Parrish[1], C Hess[2], SA Green[3], LM Wiedemann[1], C Mosimann[2], ME Bronner[3], R Krumlauf[1]

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The origin of vertebrates was accompanied by invention of the neural crest, a novel cell type characterised by its migratory ability and multipotency. Neural crest cells emerging from the hindbrain are patterned along the anterior-posterior axis by nested domains of *Hox* gene expression, which specify pharyngeal arch derivatives in the head and neck. Neural crest cells played a particularly important role in vertebrate evolution since they contribute to jaws and elements of the feeding apparatus of jawed vertebrates. Here, we use cross-species enhancer analysis in zebrafish and the jawless sea lamprey to investigate the evolution of *Hox* gene expression in the vertebrate neural crest. Importantly, we uncover conservation of key transcription factor binding sites between jawed vertebrate and lamprey *Hox2* neural crest enhancers. These results illuminate ancestral features of neural crest patterning in vertebrates and illustrate how duplication and divergence enabled independent and tissue specific *Hox* gene regulation.

Poster Number: P176

***In toto* live imaging in scuttle fly *Megaselia abdita* reveals transitions towards novel extraembryonic architecture**

F Caroti[1], E González Avalos[1], P González Avalos[1], D Kromm[2,3], V Noeske[1], M Wosch[1], L Schütz[1], L Hufnagel[2], **S Lemke**[1]

[1]Centre for Organismal Studies Heidelberg, Heidelberg University, Heidelberg, Germany; [2]European Molecular Biology Laboratory, Heidelberg, Germany; [3]Faculty of Biosciences, Heidelberg University, Heidelberg, Germany

To elucidate gradual genetic transitions that underlie developmental novelty, we study the evolutionary origin of the Drosophila amnioserosa. To better understand how the amnioserosa differed and evolved from the two extraembryonic tissues present in most other insects, we used quantitative whole-mount time-lapse recordings in the scuttle fly Megaselia abdita. Our findings suggest that the amnioserosa did not evolve by transformation of autonomous developmental programs in either serosa or amnion, but rather from genetic changes in an unrelated but tightly associated extraembryonic membrane, the yolk sac. Our results imply that the amnioserosa has retained properties of the ancient serosa and, more generally, suggest specific transitions in a continuous and gradual evolution of extraembryonic tissues since the last common ancestor of flies and beetles.

Invited speaker

Poster Number: P150

Wnt signaling regulates head regeneration in the starlet sea anemone *Nematostella vectensis*

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Biochemistry & Cell Biology, Stony Brook University, Stony Brook, USA

We are using the anthozoan cnidarian *Nematostella vectensis* to investigate regenerative mechanisms and the evolution of regeneration. The aboral fragment (physa) of an adult Nematostella polyp regenerates an entire body, and we find that all *wnts* in the genome are expressed sequentially in the amputated physa as new head and body structures reform. In contrast, *wnt* genes are not activated at the complementary aboral-facing cut site on the polyp “amputee”, thus indicating that the wnt response is polarized to the prospective site of head formation. MAPK signaling induced by wounding is required to initiate *wnt* expression during head regeneration, and blocking Wnt signaling inhibits head regeneration and associated blastema-like cell proliferation. Our findings demonstrate that polarized Wnt signaling is essential for regeneration of head and body structures in the amputated physa. Moreover, Hydrozoan and Anthozoan cnidarians appear to share a conserved, Wnt-dependent mechanism for oral regeneration.

Poster Number: P177
Embryonic geometry underlies phenotypic variation in decanalized conditions
A Huang[1], TE Saunders[1,2,3]

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In the process of development, many mutations cause increased variability in phenotypic outcomes, a phenomenon termed decanalization. While many of such variations can be attributed to genetic and environmental perturbations, phenotypic discordance remains even in isogenic model organisms raised in homogeneous environments. To understand the mechanisms underlying phenotypic variation, we used Drosophila embryonic patterning as model and identified embryonic geometry as one factor predetermining patterning outcomes in decanalized conditions. By simultaneously manipulating the morphogen Bicoid and embryonic geometry, we found that while in wild-type embryos, the patterns formed always scale in proportion to embryonic size, the segmentation gene boundaries shift away from the scaled positions according to the total embryonic length under manipulated conditions. Further analysis of the gene regulatory network acting downstream of the morphogen shows that, patterning defects are introduced at the vulnerable points of the gene network in the face of limited absolute physical space.

Poster Number: P178
A novel role for Gremlin in neural crest induction and its regulation by heparan sulfate proteoglycans
J Pegge[1], AJ Tatsinkam[2], CC Rider[2], E Bell[1]

[1]Centre for Developmental Neurobiology, King's College London, London, UK; [2]Centre for Biomedical Sciences, Royal Holloway University of London, Egham, UK

Gremlin (Grem1) is a secreted bone morphogenetic protein (BMP) antagonist involved in limb, kidney, and lung development. Originally identified in *Xenopus laevis*, its functions have been characterised primarily in chickens and mice. Consequently, potential roles in the earliest developmental stages remain unknown. BMP signalling is known to be a key player in neural crest induction with levels intermediate to those in prospective neural plate and surface ectoderm acting in concert with Wnt activation. Grem1 is expressed early in *Xenopus* development and we are investigating its role in neural crest induction by gain and loss of function approaches. Heparan sulfate proteoglycans (HSPGs) are a class of cell surface and extracellular matrix macromolecules with emerging roles in regulating distribution and availability of signalling molecules including BMP ligands and antagonists. We are comparing the activity of Grem1 to mutant forms with impaired HSPG binding in order to determine their impact on its function.

Poster Number: P179
Size-reduced embryos reveal a gradient scaling mechanism for zebrafish somite formation
K Ishimatsu[1], **TW Hiscock**[1], ZM Collins[1], DWK Sari[2,3], K Lischer[2], D Richmond[4], Y Bessho[2], T Matsui[2], SG Megason[1]

[1]Department of Systems Biology, Harvard Medical School, Boston, USA; [2]Gene Regulation Research, Nara Institute of Science and Technology, Nara, Japan; [3]Department of Fisheries, Universitas Gadjah Mada, Yogyakarta, Indonesia; [4]Image and Data Analysis Core, Harvard Medical School, Boston, USA

Animals vary greatly in the relative proportions of their body parts yet little is known about how their size is controlled. Somite size varies widely both within an individual and across species, but how the well-studied segmentation clock relates to somite size is unknown. Here we use surgical size reduction, quantitative imaging, and mathematical modeling to investigate somite size control. We find that somite size scales with the length of the presomitic mesoderm (PSM) despite considerable variation in PSM length across developmental stages and between different size embryos. Measurement of clock period, axis elongation speed, and clock gene expression patterns shows that existing models cannot explain scaling. We propose a new model in which dynamic scaling of a morphogen gradient in the PSM plays a central role both in progression and size control of somite formation, while the clock ticks at a constant rate.

Poster Number: P180
Long-Range Communication through the Embryo Governs Symmetry Breaking in the Chick
HC Lee, NMM Oliveira, CD Stern

Department of Cell and Developmental Biology, University College London, London, UK

Chick embryos are 'regulative', as shown by spontaneous formation of a new primitive streak (PS) when the embryo is cut experimentally, removing the posterior part. An isolated anterior half always generates a single PS at one edge, left or right. Here, we study how the embryo ensures that a single PS forms, both during normal development and after experimental manipulation. Time-course experiments suggest the spread of positional information over a long distance. Using microsurgical experiments we show that positional information spreads exclusively within the extraembryonic marginal zone. By manipulating exposure to signals in time and space, we provide evidence that long-range communication can't be explained by a simple morphogen gradient and propose that cells assess their position by comparison to their immediate neighbours. Finally we implicate the combined action of different signal pathways, including TGF beta, WNT and NOTCH in this process.

Poster Number: P181
Anterior-posterior patterning of in vitro derived human neural crest cells reveals that a trunk fate depends on the acquisition of a multipotent axial progenitor identity
TJR Frith[1], E Stout[1], O Thompson[1], D Stavish[1], P Heath[2], M Gouti[3], J Briscoe[4], V Wilson[5], PW Andrews[1], A Tsakiridis[1]

[1]Centre for Stem Cell Biology, University of Sheffield, Sheffield, UK; [2]Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, UK; [3]Max Delbrück Center for Molecular Medicine, Berlin, Germany; [4]Francis Crick Institute, London, UK; [5]MRC Centre for Regenerative Medicine, Institute for Stem Cell Research, University of Edinburgh, Edinburgh, UK

The predominant model of embryonic neural patterning involves the posteriorisation of a default anterior progenitor via the action of signals such as retinoic acid (RA). This model has carried over to neural crest (NC), a multipotent cell population that arises at the neural plate border producing a range of derivatives. Here we show, through the use of human pluripotent stem cells (hPSCs), that RA posteriorises cranial NC progenitors to a cardiac/vagal NC identity but fails to induce a trunk fate. This can only be achieved via a transition through a posterior axial progenitor state. We show that hPSC- derived axial progenitors express early NC markers and are competent to generate trunk NC, neurectoderm and paraxial mesoderm. Our data indicate a model whereby cranial NC is patterned to a hindbrain identity by RA, whereas trunk NC cells arise from a separate progenitor population that segregates from the anterior early during gastrulation.

Poster Number: P182
Matching gene expression with cell history, the computational challenge
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Early mammalian development is not governed by any known maternal determinants, and yet a robust system of cell division, fate allocation and reorganisation ensures embryo priming for implantation. Following the history of embryonic cells during development could identify early heterogeneities within the embryo, which in turn correspond to different cell fates. Live cell imaging provides cell history information, whereas immunostaining provides gene expression levels. These two modalities cannot be linked at a single cell level with an associated confidence. Using simulated embryonic coordinates, we have developed a programme which utilises Markov chain Monte Carlo methods to identify correct mapping of the cell coordinates, in two dimensions. Once the programme has identified this matching, cells can be matched and their history and gene expression correlated. Cell neighbourhood characteristics can be interrogated in greater depth and the effect this may have on pluripotency factor expression and thus cell fate.

Poster Number: P183
Engineering a long-range morphogen gradient
KS Stapornwongkul, JP Vincent

Epithelial Cell Interactions Laboratory, Francis Crick Institute, London, UK

Morphogens are secreted signalling molecules that diffuse from their site of production to induce concentration-dependent cellular responses in target tissues. During larval development, the Drosophila BMP2/4 homolog Decapentaplegic (Dpp) forms a concentration gradient along the basolateral region of the wing disc epithelium. This gradient is believed to specify the position of pattern elements such as veins. How the Dpp gradient forms remains an outstanding and controversial question. We are aiming to uncover the basic attributes that a generic secreted protein must have to form a concentration gradient in wing imaginal discs. Our approach is to modify an inert protein, GFP, and transform it into a molecule that forms a long-range concentration gradient. In parallel, we are designing a synthetic signalling pathway that responds to extracellular GFP. This will allow us to test functionally whether the engineered forms of GFP that we create can act as a bona fide morphogen.

Poster Number: P184
Cortical patterning anomalies in a mouse model for CHARGE syndrome
APA Donovan[1], C Mohan[1], J Ellegood[2], JP Lerch[2], MA Basson[1]

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Dominant mutations in the gene encoding the ATP dependent chromatin remodeling factor CHD7 cause CHARGE syndrome (Coloboma, Heart defects, Atresia of the choanae, Retardation of growth, Genital anomalies and Ear defects). Individuals with CHARGE syndrome have been reported to have deficits in executive functioning. The neurodevelopmental and neuroanatomical underpinnings of these defects are not yet known. However, functional studies in human and mouse have identified the prefrontal cortex as the principal brain region governing executive function.

Our initial MRI studies in *Chd7*$^{+/-}$ mice have identified pronounced and widespread cortical abnormalities. To investigate the underlying mechanisms, a genome-wide comparison of gene expression in *Chd7*$^{+/-}$ and *Chd7*$^{+/+}$ embryonic neocortices was carried out. Gene expression changes suggestive of abnormal cortical patterning were identified and validated using in situ hybridization. Together, these studies begin to provide insights into developmental alterations that could underlie executive dysfunction in CHARGE syndrome patients.

Poster Number: P185
In vitro generation of human axial progenitors and their derivatives
A Tsakiridis, M Wind, T Frith, E Brudenell, E Stout

Centre for Stem Cell Biology, Department of Biomedical Science, University of Sheffield, Sheffield, UK

Embryonic axis elongation in amniote embryos is driven by posteriorly-located progenitors which include a bipotent stem cell-like population that generates both the spinal cord neurectoderm and paraxial mesoderm. Here we describe the efficient in vitro generation of axial progenitors from human pluripotent stem cells (hPSCs) following combined stimulation of the WNT and FGF signalling pathways. Transcriptome analysis revealed that human axial progenitors closely resemble their mouse embryonic counterparts. We also show that hPSC-derived axial progenitors can be directed to produce a high yield of thoracic spinal cord progenitors and motor neurons as well as paraxial mesoderm cells. Collectively, our data indicate that human axial progenitors are the optimal starting cell population for generating cell lineages of a posterior axial identity, which are currently difficult to derive using conventional hPSC differentiation protocols.

Poster Number: P186
Community signaling maintains positional information in the hindbrain
M Addison, Q Xu, **DG Wilkinson**

Neural development lab, The Francis Crick Institute, London, UK

Positional information mediated by graded retinoid signalling in the hindbrain generates segments with distinct and homogeneous identity, but this pattern is potentially disrupted by cell intermingling. Cells that are transplanted into another segment can change identity, but it was unclear whether cell intermingling and switching occurs during normal development. We show that intermingling and identity switching occurs in the zebrafish hindbrain and is mediated by feedback between segment identity and the retinoic acid degrading enzymes, cyp26b1 and cyp26c1. Cells that intermingle into an adjacent segment encounter a different level of retinoid signalling, which changes their identity to match the new neighbours. Furthermore, segmental identity is regulated non-autonomously and depends upon the number of neighbours with the same or different identity. Our findings reveal that community regulation of retinoid signalling maintains homogeneous segments.

Poster Number: P187
A predictive model of asymmetric morphogenesis from 3D reconstructions of mouse heart looping dynamics
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Establishment of left-right patterning in the node is well characterized. However, how the initial molecular bias is transposed into asymmetric morphogenesis remains unclear. Heart looping is the first sign of left-right asymmetric morphogenesis and is essential for the establishment of the double blood circulation. It corresponds to a rapid change in heart shape, from a straight to a helical tube.

From 3D reconstructions by HREM, we quantified shape changes in the mouse, which are compatible with a buckling mechanism of heart looping. In combination with cell labelling and live-imaging, we identified sequential left-right asymmetries at the tube poles. A computer model was developed, which can predict the shape of the heart loop, and not just its direction, from initial asymmetries and mechanical constraints at the sites of attachment of the heart. Our work provides novel insight into the contribution of different factors to heart looping, with relevance to congenital heart defects.

Poster Number: P188
Long-range signaling activation and local inhibition separate the mesoderm and endoderm lineages
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One of the first and most fundamental processes in embryonic development is the specification of the three germ layers: ectoderm, endoderm and mesoderm. In zebrafish, endoderm is specified by the TGFβ related signaling ligand Nodal, within the most marginal cells of the embryo during late blastula stages. The prevailing model for endoderm specification is that Nodal acts as a morphogen, forming a signaling gradient from the margin, with cells receiving the highest levels becoming endoderm. In addition, it is known that Fgf signaling inhibits endoderm specification. However, Nodal induces Fgf signaling through transcriptional regulation of Fgf ligands and, therefore, endoderm is specified in cells receiving the highest levels of this inhibitory signal. Here, we resolve this apparent paradox by showing that as well as inducing Fgf ligands, Nodal simultaneously induces the intracellular Fgf signaling inhibitor Dusp4, which allows the most marginal blastomeres to differentiate into endoderm over time.

Poster Number: P189
Using single-cell technologies and planarians to study stem cells, their differentiation and their evolution
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Single cell transcriptomics methods will revolutionize the way we study stem cells and developmental processes such as regeneration. We applied single cell transcriptomics to the planarian *Schmidtea mediterranea*, which contains pluripotent stem cells that continuously differentiate to all adult cell types. By obtaining thousands of single cell profiles we provide the near-complete cell type atlas of the whole adult stage. We characterize all major lineages of planarian differentiated cells, including previously uncharacterized types. Using a combination of single cell sequencing and RNAi for the first time we identify progenitors for most of these lineages. By applying lineage reconstruction algorithms we elucidate their differentiation tree into all their differentiation products. Our study shows the advantages of using single cell sequencing to analyse stem cells and developmental processes and pave the way for the identification of stem cells and the reconstruction of complete lineage trees in other organisms.

Poster Number: P190
Phosphoproteomics Identifies a Bimodal EPHA2 Receptor Switch that Promotes Embryonic Stem Cell Differentiation
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Embryonic Stem Cell (ESC) differentiation is associated with dynamic remodelling of cellular signalling networks, although it remains a major challenge to pinpoint key molecular events driving this process. Here, we use phosphoproteomic profiling to identify an FGF4 mediated phosphorylation switch centred upon the Ephrin receptor EPHA2 in differentiating ESCs. Quantitative proteomics reveals EPHA2 as the major trans-membrane kinase in ESCs, which functions to support pluripotency gene expression and restrain lineage commitment by antagonising ERK1/2 signalling. Upon ESC differentiation, FGF4 utilises cooperative strategies to disable EPHA2. FGF4-dependent RSK activation inhibits EPHA2 via Ser/Thr phosphorylation, whilst FGF4-ERK1/2 signalling disrupts a core pluripotency circuit required for *Epha2* transcription. In vivo, EPHA2 expression is established upon assembly of the pluripotency gene regulatory network in the embryonic epiblast. Our data thereby uncover a role for EPHA2 in pluripotency maintenance, and identify a bimodal mechanism by which FGF4 signalling inhibits EPHA2 to reinforce transition from pluripotency towards differentiation.

Poster Number: P191
Development of Functional Nanoparticles for Targeted Joint Repair *in situ*
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Mesenchymal stromal cells (MSCs) are an adult stem cell population with the capacity to self-renew and differentiate. We aim to use magnetic nanoparticles (MNPs) that have been surface-functionalised with a temperature-sensitive polymer as a delivery system to functionally activate MSCs *in situ*. The magnetic and temperature-responsive properties of the functionalised particles will be used to trigger release of bioactive molecules at the target cells in a controlled fashion *in vivo*.

We have synthesised superparamagnetic iron oxide nanoparticles with a diameter of 6.2 ± 0.8nm which are surface coated with temperature-responsive polymer poly(*N*-isopropylacrylamide) (PNIPAM). PNIPAM-coated particles were able to encapsulate model test protein apotransferrin and release could be seen following magnetic nanoparticle heating. Heating could release the growth factor Wnt3a and stimulate an MSC Wnt reporter line response. This work promises to enable magnetically driven bioactivation of cells to promote differentiation *in situ*.

Poster Number: P192
Mitochondrial dynamics determines human embryonic stem cell fates
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Human embryonic stem cells (hESCs) undergo self-renewal, apoptosis or commit to differentiation into multiple cell types. Mitochondria are essential for energy metabolism and apoptosis, yet little is known about the role of mitochondrial dynamics during stem cell fate decisions. Mitochondrial dynamics refers to the shape and size of mitochondria, which is regulated by mitochondrial fusion and fission. In order to study the mechanisms underpinning mitochondrial dynamics in hESCs, we have used CRISPR-Cas9 genome editing to generate knock out cell lines of the mitochondrial fusion (*MFN1*, *MFN2* and *OPA1*) and fission (*DRP1*) factors. We show that deletion of *MFN1*, *MFN2*, *OPA1* and *DRP1* generates distinct mitochondrial fragmentation and fusion phenotypes. Our preliminary data supports the hypothesis that mitochondrial shape impacts stem cell fate decisions. Our findings will provide important insights into the underlying mechanisms of stem cell maintenance, which has implications for the translational goals of hESC research for regenerative medicine.

Poster Number: P193
Development of the cardiac lymphatic system in the adult zebrafish and its role in homeostasis and repair
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An intricate network of cardiac blood and lymphatic vessels provide cardiac tissue with oxygen and nutrients while eliminating excess fluid from the interstitium. Lymphatic vessels are required to maintain normal heart function and their blockage or destruction leads to cardiac oedema, fibrosis and inflammation. Despite their critical roles in physiology and pathology, little is known about lymphatic vessel growth and development in the heart. Building on our recent work on coronary vessel development, we have described the formation of the lymphatic vasculature system in adult zebrafish. This second wave of cardiac vascularization is depended on the completion of coronary vessel development first and failure of both results in a loss of the heart's regenerative potential. We have extended our developmental studies to study the function of the cardiac lymphatic vessels during homeostasis and repair, including a role in blood perfusion in response to increased cardiac output.

Poster Number: P194
Inflammatory cytokine IL-1β inhibits tendon formation by equine adult and fetal tenocytes, but ESC-derived tenocytes are protected
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Equine tendon injuries are common and re-injure frequently. We investigated the mechanisms detrimental to tendon regeneration and highlight potential molecular interventions. Inflammatory cytokine IL-1β is upregulated in the injured tendon. Culturing adult or fetal tenocytes with IL-1β upregulates matrix metalloproteinase expression. Tendon associated gene expression is also altered in response to IL-1β, with a downregulation of *Scleraxis* and *COMP* and upregulation of *Tenascin-C*. In contrast, IL-1β has no effect on gene expression in embryonic stem cell derived tenocytes (ESC-tenocytes). The addition of IL-1β to three-dimensional (3D) adult/fetal tenocyte cultures decreases the rate of matrix organisation and reduces the storage modulus of the resulting artificial tendons. This effect can be rescued in the presence of IL-1 receptor antagonist. IL-1β has no detrimental effect on the functional ability of ESC-tenocytes to form artificial tendons. Therefore ESC-tenocytes may offer novel insights into mechanisms protecting tendon cells from the detrimental impact of inflammation.

Poster Number: P195
Generation of a reporter cell line to identify determinants of cortical interneuron fate
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Cortical interneurons are inhibitory gamma-amino butyric acid (GABA) cells in the cerebral cortex, where they connect different cortical neurons and regulate the excitatory/inhibitory input on cortical networks. Cortical interneuron dysfunction is believed to underlie neurodevelopmental diseases such as autism, schizophrenia and epilepsy. Human pluripotent stem cells (hPSCs) can give rise to any cell type of the body and thus serve as a powerful tool for modelling the development of cortical interneurons in healthy and disease conditions. Such application is greatly benefited by reporter cell lines, which allow the identification of specific cell populations by direct visualising reporter (eg. GFP) expression. Here we described the generation and preliminary characterisation of a LHX6:mCherryreporter cell line via CRISPR/CAS9 mediated homologous recombination. Faithful expression of mCherry into LHX6-expressing-cells has been observed, providing the bases for using this cell line for identifying novel interneuron determinants.

Poster Number: P196
Mapping the cellular dynamics of liver regeneration using targeted photoactivatable cell ablation
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The liver has an intricate tissue architecture which is essential for its function. In the event of injury, the liver has the remarkable capacity to regenerate and restore both lost mass and architecture. However, our current understanding of the dynamic, cellular basis of liver regeneration is sadly lacking. We employ real-time high-resolution light microscopy of zebrafish liver injury models to determine the cellular dynamics of liver regeneration and understand how the tissue architecture of the liver is re-established after damage. Here we report the development of a new optogenetic, reactive oxygen species- (ROS-) mediated hepatocyte ablation tool. Mimicking the ROS stress inherent of liver damage *in vivo*, a two-component photosensitizer system inducible by far red light illumination is employed to generate toxic levels of ROS in hepatocytes. This tool provides rapid, tissue-specifc cell ablation in deep tissues such as the liver with a precise spatiotemporal control unattainable by currently available methods.

Poster Number: P197
Probing the skeletal stem cell niche through functional investigation of Prx1 expressing cells
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Prx1 marks an early population of mesenchymal cells in the developing limb buds and becomes restricted to the periosteum in the adult, contributing to callus formation during fracture repair. We have produced a Prx1 reporter mouse that expresses GFP in the mesenchymal cells of the limb bud at E10.5 and in the periosteum postnatally. I have established methods to isolate Prx1eGFP expressing cells and culture them *in vitro*. In parallel I have begun characterisation of the expression of the Prx1eGFP transgene *in vivo*. My results have demonstrated Prx1eGFP becomes restricted to the newly formed perichondrium by E15.5 in the developing hand plate. In the adult, Prx1eGFP is expressed in both fibrous and cambium periosteal layers, and is enriched in areas of muscle insertion, suggesting mechanical loading may play a role in the expansion and/or activation of these cells *in vivo*.

Poster Number: P198
Alternative splicing control over naïve and primed pluripotency throughout mammalian embryo development

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During mammalian development, the embryo goes through sequential pluripotency states before lineage commitment. These cell identities have been defined by their contrasting ability to initiate differentiation. While naïve pluripotent stem cells found in pre-implantation embryos, are not yet competent to differentiate, primed pluripotent stem cells, found later in post-implantation embryos have the ability to initiate this process. Alternative splicing is tightly regulated in stem cells and is crucial for promoting a pluripotent cell identity, however its role during the transition between the naïve and primed pluripotency states, both in vitro and in vivo, remains largely unexplored. We have performed ultra-deep coverage RNA sequencing on pre- and post-implantation embryos and embryo-derived stem cells, and identified over 600 exons that are differentially spliced in the naïve and primed states. We are currently uncovering the functional impact of these isoform switches in the establishment of pluripotency and identifying master regulators responsible for them.

Poster Number: P199
Regulation of the proliferation of neural stem cells in the adult hippocampus by Shh signalling

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Shh is proposed to control proliferation of neural stem cells (NSCs) in the adult hippocampus, but the stage regulated by Shh in this adult neurogenic lineage has not been defined. We use mouse genetics and tissue culture experiments to address this question. We find that hippocampal NSCs are heterogeneous in their response to Shh signalling, with a quarter of them expressing a Shh signalling reporter, and being enriched in the anterior hippocampus. Conditional deletion of the Shh co-receptor Smoothened reduces the number of proliferating NSCs. We are currently performing experiments to determine whether Shh activates quiescent NSCs or whether it extends the proliferation of already cycling NSCs. We also examine the transcriptional programme induced by Shh using a cell culture model of proliferating and quiescent adult hippocampal NSCs. With this project, we hope to shed light on the poorly understood mechanisms that activate quiescent stem cells in the adult hippocampus.

Poster Number: P200
Mechanisms of Selective Advantage in Cultures of Human Pluripotent Stem Cells

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The observation that hPSCs may acquire non-random genetic changes during prolonged culture is a major concern for their use in regenerative medicine and disease modelling. The predominant genetic changes observed in hPSCs include gains of whole or parts of chromosomes 1,12, 17 and 20, which are also frequently gained in embryonal carcinoma cells, the stem cells of germ cell tumours.

Genetically variant cells possess different growth characteristics compared to normal cells including improved survival and proliferation capacity. Previous work in our lab has shown that genetically variant hPSCs overtake normal cells in culture indicating variant cells possess a selective advantage over genetically normal cells. Current observations suggest that the presence of variant cells has a negative impact on normal cell growth. Therefore, we are investigating if the mechanisms of selective advantage involve active elimination of normal cells.

Poster Number: P201

Defining pluripotency in 3D: from embryonic stem cell identity to morphogenesis

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Pluripotency refers to the capability of a single cell to generate all the cell types of the organism. However, it is not a single condition as different pluripotent states can be identified *in vivo* and *in vitro*, based on transcriptional, epigenetic and metabolic patterns. The biological significance of these states with respect to embryo morphogenesis remains unclear. We now show that exit from an unrestricted naïve pluripotent state is a pre-requisite for epithelialization in mouse and human embryonic stem cells and embryos. Naïve cells are able to polarize but fail to open a lumen and to establish the pro-amniotic cavity. Our data shows that lumen formation is transcriptionally controlled downstream of naïve pluripotency exit by the transcription factor Oct4, which mediates expression of sialomucin proteins, required for lumen opening. The developmental arrest of mouse and human embryos upon deregulation of the pluripotency network supports the physiological relevance of these findings.

Poster Number: P202

Reprogramming pancreatic ductal organoids into insulin-producing β-cells

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During pancreatic development, the bHLH transcription factor Neurogenin3 (Ngn3) drives differentiation towards the endocrine lineage. Our previous work has shown that Ngn3 undergoes phosphorylation on multiple serine-proline sites and prevention of this phosphorylation increases protein stability and endocrine differentiation.

Here, we aim to exploit our recent data to investigate whether manipulation of Ngn3 phosphostatus might improve *in vitro* generation of β-cells for cell replacement therapies in diabetes. A potential source of β-cells comes from fate conversion of exocrine pancreatic cells into the endocrine lineage, by overexpression of 3 transcription factors, namely Ngn3, Pdx1 and MafA (Zhou *et al.*, *Nature* 2008). Using this approach we show that pancreatic ductal cells grown *in vitro* as 3D organoids can be reprogrammed to express insulin. Moreover, when substituting Ngn3 with a more active form that cannot be phosphorylated, the reprogramming efficiency increases and mono-hormonal insulin + β-like cells are generated.

Poster Number: P203

Tissue Mechanics Partition the Stem Zones Fuelling Axial Elongation

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Most animal embryos and adult regenerating tissues grow by the action of stem zones. In amniote embryos, two clonally realated, adjacent epithelial stem zones drive axial elongation: the mature Organiser generates dorsal mesoderm, while the adjacent neuralised ectoderm fuels the extension of neural tissue. What regulates cell fate allocation? Using the chick, we identify a molecular signature of the mesodermal stem zone, distinguishing it from the Sox2-expressing neural stem zones. We also examine the lineage relationships and stem zone separation using time-lapse, multi-photon imaging of live embryos. Precursors of either stem zone are found mingled with common progenitors, in a region subjected to divergent morphogenetic movements. If transplanted downstream of these collective cell flows, cells from this mingled region adopt the molecular identity and clonal behaviour of their new niche. We propose that tissue mechanical forces act extrinsically to determine the fate of pluripotent cells maintained during development.

Poster Number: P204
Identification of SIRT1 activation-mediated pancreatic β-cell regeneration and function as a therapeutic potential for diabetes
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Restoration of functional β-cells via an induction of endogenous β-cell regeneration is a promising alternative to treating diabetes. We thus sought to utilize an animal model of streptozotocin-induced β-cell regeneration in neonatal rats and cultured mouse pancreatic rudiments to examine the role of SIRT1 in the regulation of β-cell regeneration and the differentiation of pancreatic endocrine progenitors. Our in vivo data showed that SIRT1 activator SRT1720, but not SIRT1 inhibitor EX527, significantly ameliorated the hyperglycemia with increases in the level of serum insulin and β-cell area as well as improved islet morphology. These beneficial effects were mediated via the activation of Neurogenin 3 (NGN3) driven β-cell regeneration but not the proliferation of existing β-cells. Consistently, the differentiation of endocrine lineage was also promoted by SRT1720 as evidenced by the cultured pancreatic rudiments. Taken together, our study findings provide a scientific basis for SIRT1 activation as a potential for treating diabetes.

Poster Number: P205
Capturing formative pluripotency
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Pluripotency is a continuum from the pre-implantation epiblast until the end of gastrulation. ES cells and EpiSCs are alternative pluripotent stem cell cultures representing the initial naïve and the late primed phases of pluripotency. Between these two phases is an incompletely characterised intermediate stage that we have termed “formative” pluripotency. This corresponds to E5.0-E6.0 epiblast in the mouse embryo. During this period naïve epiblast cells acquire epithelial character and expand without overt regionalization or expression of lineage-specific markers. They also become competent to respond to germ cell induction signals, unlike either naïve or primed epiblast. Here we discuss features and significance of formative pluripotency and the potential for capturing a distinct type of epiblast stem cell.

Poster Number: P206
How Do Stem Cells Find Thier Niche?
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Localized niche Wnt signals orient asymmetric stem cell division (ACD) to produce one stem cell and another linage restricted daughter cell, a process that is essential for tissue formation and repair. The detection mechanisms of niche signals by stem cells remain largely elusive. We found that stem cells detect and recruit localised Wnt proteins by actin and β-catenin dependent protrusions. We employed the theory of simple liquids and determined that β-catenin controls the cellular affinity, location and duration of the interaction between localized Wnt and the plasma membrane. Consequently Wnt signals increase the membrane stiffness locally and recruit the ACD machinery. In this process, β-catenin is dispensable for polarizing the receptor lrp6 but essential for polarizing the down stream effector APC, spindle orientation and ACD. Our results provide a novel mechanism of the niche detection and cellular response and can be extended to other stem cell types and niche signals.

Poster Number: P207
Antioxidant role of lipid droplets in the neural stem cell niche of *Drosophila*
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Neural stem cells of *Drosophila*, called neuroblasts, proliferate within a niche composed of glial cells. Here, we investigate the role of the glial niche in regulating the remarkable ability of neuroblasts to sustain proliferation during oxidative stress. We previously found that lipid droplets (LDs) in glia are required to protect neuroblasts from oxidative damage, thus allowing them to proliferate. The underlying antioxidant

mechanism involves the sequestration of polyunsaturated fatty acids inside the droplet core, where they are less vulnerable to peroxidation chain reactions. We now find that the ability of niche glia to induce LDs is acquired only after the last larval moult and that it requires a prolonged exposure to oxidative stress. In contrast to some other biological contexts, induction of glial LDs does not require JNK signalling. Finally, we will present evidence suggesting that stress induction of glial LDs is linked to changes in the morphology of mitochondria.

Poster Number: P208
Determining the Metabolic Underpinnings of Totipotency
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Conventional Embryonic Stem Cells (ESC) are characterized as pluripotent, able to generate all embryonic lineages. Using a sensitive reporter for the extra-embryonic endoderm gene H*hex*, we identified a fraction of ESCs that co-express embryonic and extra-embryonic markers and are totipotent. Based on transcriptomic analysis of this totipotent fraction, we identified lipid metabolic regulators as a unique signature of this cell state. We found that culture conditions that promote totipotency also induced ESCs to exhibit higher rates of oxidative phosphorylation (OXPHOS) and that forcing ESCs to increase OXPHOS levels induced totipotent characteristics. Based on the transcriptomic signature of totipotent ESC fractions, we identified the mitochondrial protein Cpt1a as signature marker of “metabolic” potency. We found Cpt1a reporters an effective tool to assess lineage potency and metabolic states in different culture conditions, enabling us to probe the role of lipid metabolism in ESC potency for both embryonic and extra-embryonic development.

Poster Number: P209
Oct4 Coordinately Regulates Cell Cycle Determinants to Promote Embryonic Stem Cell Fitness
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Embryonic stem cells (ESCs) maintain pluripotency through an indefinite number of cell divisions, a process known as self-renewal. Here we explore how a key member of the pluripotency network, Oct4, regulates self-renewing cell divisions. Oct4 is a dose-dependent regulator of pluripotency, therefore we asked how distinct endogenous levels of Oct4 are linked to pluripotency. We identified $Oct4^{Hi}$ and $Oct4^{Lo}$ populations of ESCs using post translational Oct4 reporters. The $Oct4^{Hi}$ population showed enhanced fitness for both self-renewal and differentiation, although when left on its own, this population reverted to unsorted levels in standard ESC culture conditions. We determined the proteome of $Oct4^{Hi/Lo}$ cells, and found $Oct4^{Hi}$ cells enriched in mitotic proteins. We confirmed the coordination between Oct4 and mitotic proteins with an ESC cell cycle proteome, suggesting that peak levels of Oct4 promote efficient G2/M progression and restoration of the ESC cell state with each cell cycle.

Poster Number: P210
A single-cell screening approach to brain tumour initiation
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Neural stem-like cells have been found in brain tumours and are probably responsible for tumour initiation and growth. *brat* is a *Drosophila* brain tumour suppressor. Loss of *brat* or its human orthologue, *Trim3*, promotes brain tumour growth in both fly brain and human glioblastomas (GBMs). We performed a single-cell transcriptome screen comparing *brat* tumour-initiating cells to normal neural cells, harvested directly from *Drosophila* brains. The majority of identified regulated transcripts have highly conserved human orthologues. Gene ontology analysis indicates main dysregulation of translation and rRNA-related processes. We selected *HeatR1*, highly upregulated in both brat tumour initiation cells and human GBM biopsies for further analysis. We show that *HeatR1* knockdown prevents brain tumour growth in vivo in the

brat model and hampers cell cycle progression, ribosome biogenesis and protein synthesis in human GBM cell lines. We suggest *HeatR1* as a conserved potential novel player in brain tumourigenesis.

Poster Number: P211
Monitoring the origin and progression of neural stem cell (NSC) derived tumours using a Drosophila model
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Many solid tumours (e.g glioblastomas,neuroblastomas) are comprised of heterogeneous cell populations, which include cancer stem cells(CSCs). These drive tumour growth by deploying programs normally used by stem cells for tissue development. However, the mechanisms underlying CSC emergence during tumorigenesis remain elusive. Drosophila NSCs are a simple model to study the onset of tumorigenesis, dividing asymmetrically so that one daughter cell retains NSC identity and the other is routed to differentiate. Perturbations like excessive Notch signalling result in aberrant NSC proliferation. We have established NSC cultures and a tracking system to monitor live the expression of an early NSC marker in NSCs and their progeny during normal development and at the onset of Notch driven hyperplasia. The CSCs arise from a reactivation of the NSC programme in progeny, rather than an expansion of the NSCs themselves, and the normal process of NSC fate attenuation is initiated but subsequently suppressed.

Poster Number: P212
Whole organ liver architecture and homeostasis in adult zebrafish
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The liver, as the largest metabolic organ in vertebrates, has key functions in maintaining body homeostasis according to its respective needs. It relies on an intricate architecture that allows for all the cell types to fulfill their functions in a coordinated manner. Zebrafish has been used as a model to study liver development and regeneration mostly using larvae, while little is known about the adult liver. To bridge this gap and investigate the processes driving organ and tissue maturation, we aim to resolve the adult liver architecture in zebrafish and evaluate its similarities with mammalian systems. By using a whole organ approach and microscopy at a cellular resolution coupled with clearing strategies, we will examine how the different cell types interact both spatially and molecularly to maintain adult tissue mass and architecture.

Poster Number: P213
Investigating the role of a novel Nanog interacting partner in mESCs self-renewal
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The homeodomain protein Nanog is required for establishment of the epiblast of preimplantation embryo and for efficient generation of primordial germ cells (PGCs). Together with Oct4 and Sox2, Nanog is a key regulator of embryonic stem cell (ESC) identity. Overexpression of Nanog enhances ESC self-renewal efficiency and confers leukemia inhibitory factor (LIF)-independent self-renewal. This function is dependent on the Nanog tryptophan repeat (WR). Here we identify KIAA1551 as a novel partner of Nanog that interacts via the WR. KIAA1551 is an uncharacterized protein without known functional domains. Orthologues of KIAA1551 are found among Mammalia, Aves and Reptilia. By a genetic deletion we show that KIAA1551 is not required for mESC self-renewal. However, KIAA1551 deletion abolishes the ability of Nanog to confer LIF-independent self-renewal when overexpressed. We are currently assessing the differentiation potential of KIAA1551-/- ESCs. We hypothesise that KIAA1551 is a novel component of the ESC transcriptional regulatory network.

Poster Number: P214
A robust and dynamic macrophage transcriptional response after injury is dependent upon the local environment during zebrafish heart regeneration
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Efforts to restore lost tissue after a heart attack have paid little attention to the local environment of pro-inflammation and ensuing fibrosis. In the neonatal mouse, which regenerates its injured heart during the first week of life, immune cells are indispensable for the regenerative process. This suggests a tight modulation of the immune response may dictate the regeneration of adult heart tissue. We present a comprehensive transcriptomics analysis of macrophages during adult zebrafish heart regeneration, directly comparing two injury models, scar-inducing cryoinjury and scar-free resection. By employing biotagging of nuclei and RNA-Seq, we reveal active molecular programmes underpinning macrophages ability to initiate, maintain and resolve pro-inflammatory and anti-inflammatory responses to the distinct post-injury environments, which in-turn dictate the kinetics of scar resolution and regeneration. We provide evidence for how a scar-inducing environment can change the phenotype and function of macrophages, eliciting responses that can be finely tuned towards successful regeneration.

Poster Number: P215
Isolation of skeletal stem cells and progenitors from embryonic limb cartilage
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During endochondral ossification a cartilage template is converted into bone. The aim of developmental bone tissue engineering is to make an intermediate cartilage template that will be replaced by bone to heal fractures. Currently, a major challenge is the identification of the cells efficiently executing this program. Our aim is to identify these cells by studying growing embryonic cartilage. Using a panel of previously published markers, we identified mouse skeletal stem cells and skeletal progenitors in cells derived from 14.5 dpc femurs. Both populations, when encapsulated in hydrogel are able to form bone ectopically. Furthermore, we identified culture conditions for embryonic limb cartilage that enriches for the stem cells and progenitors. The findings of this study will be used as a tool to purify and select for adult stem cells from different sources with a high biological potency for bone formation.

Poster Number: P216
Deciphering integrin adhesion and signalling in *Drosophila* intestinal stem cells
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To maintain homeostasis of vital functions, stem cells (SC) constantly renew damaged and aging cells. SC behaviour is regulated by the niche, a local environment comprising neighbouring cells, secreted factors and extracellular matrix (ECM). Integrin family members are transmembrane receptors, they fulfil an adhesive role, by linking the cytoskeleton to the ECM, but they also are able to sense variations in the environment and induce signalling. Their adhesive role is essential to SC maintenance, but much less is known about the importance of the signalling events in SC function. In the *Drosophila* gut, integrins have been proposed to regulate intestinal SC proliferation, but how is unclear. To clarify integrin function, we will investigate the respective contribution of the adhesion-dependent and independent roles of integrins in the intestinal SC. We will also seek to identify the downstream effector(s) sustaining proliferation during homeostasis and tumour growth.

Poster Number: P217
Epigenetic and genetic effects of gender on reprogramming and pluripotency
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Pluripotent stem cells have unprecedented potential for regenerative medicine. However, our lack of comprehensive understanding of pluripotency currently limits applications. Gender is an increasingly important aspect of naïve pluripotency, but its relevance for induced pluripotent stem cells (iPSCs) remains enigmatic. Here, I will present new studies combining profiling of DNA methylation, transcription, open chromatin landscapes, and functional experiments to investigate the molecular effects of gender on pluripotency. I will show that transcriptional states, DNA methylation, open chromatin landscapes, exit from pluripotency and growth in mouse female iPSCs differ from male iPSCs, correlating with the presence of two active X chromosomes. I will present evidence that heterozygous deletion of *Dusp9* in female ESCs induces male-like DNA methylation, but, unexpectedly, maintains delayed pluripotency exit, indicating that distinct pathways regulate DNA methylation and delayed pluripotency exit in female ESCs. Defining how gender modulates pluripotency will have important implications for disease modeling.

Poster Number: P218
Initiation and interpretation of transcription factor dynamics during embryonic neurogenesis
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The control and downstream interpretation of gene expression dynamics is poorly understood. For example, gene expression oscillations of the bHLH transcription factor Hes1 in cultured neural progenitor cells have been proposed to control the timing of differentiation. Data from our lab show that Hes5 exhibits oscillatory dynamics in three-dimensional embryonic spinal cord tissue that are distinct from previously reported oscillations. It is unclear what processes may generate these novel gene expression dynamics and how experimentally observed transitions from noisy to oscillatory dynamics can emerge. By combining mathematical modelling and quantitative experimental data we show that the dynamics of Hes5 gene expression can be explained using a simple model of gene autorepression with transcriptional delay. We show that oscillations can be initiated by increased protein degradation and consider mechanisms that may enable the interpretation of small-amplitude oscillations. Our analysis illustrates how quantitative modelling can help unravel fundamental mechanisms of transcriptional regulation.

Poster Number: P219
WNT signalling maintains ductal progenitor cells in adult salivary glands
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We have investigated the role of Wnt signalling *in vivo* during salivary gland homeostasis and injury/repair. Using two distinct WNT reporter mouse lines, we show that during homeostasis, some intercalated duct (IDs) cells exhibit active WNT/β-catenin signalling. IDs are located between secretory acinar cells and granular convoluted tubules (GCTs). Lineage tracing assays following the progeny of cells with active WNT/β-catenin signalling show an increase in the number of labelled cells in both IDs and GCTs suggesting ID cells are progenitor cells for GCTs. Crucially, the progeny of cells with active WNT/β-catenin signalling is not found in secretory acini during both homeostasis and injury/repair, revealing these cells act *in vivo* as ductal stem/progenitor cells only. Expression of stem/progenitor cell markers is lost in ID cells after inhibition of WNT signalling, suggesting this pathway maintains a population of progenitor cells in salivary gland ducts.

Poster Number: P220
The effect of hyperglycaemia on expression of let-7 microRNAs during macrophage differentiation and polarisation in tissue regeneration
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The let-7 microRNA family regulate cell differentiation in many biological contexts including haematopoetic stem cell differentiation and macrophage polarisation during tissue repair and regeneration. Macrophage differentiation and polarisation into pro-inflammatory and pro-healing phenotypes controls the transition between key stages of wound healing. This transition fails in ageing-related pathologies, such as diabetes. Here we examine the role of let-7 family members in macrophage polarisation in both low and high glucose environments as a model of the diabetic environment. Using a macrophage cell line and primary bone marrow-derived-macrophages we find that in high glucose conditions, macrophages exhibit significant changes in expression of all let-7 microRNAs, except let-7 g and i. Let-7b is markedly down-regulated in pro-inflammatory macrophages cultured in high glucose compared to those cultured in low glucose in both models. These findings suggest misregulated let-7b may result in defective macrophage polarisation associated with pathologies of diabetic chronic wound development.

Poster Number: P221
Implementation of the three body axes and axial extension ex vivo in Gastruloids
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During mammalian development, the process of gastrulation leads to the unfolding of the body plan with three orthogonal axes and a population of progenitor cells at the posterior most region that will fuel the growth of the embryo. Using mouse Embryonic Stem Cells (ESCs) we have developed an ex vivo experimental system that mimics many of the early events of embryogenesis. We show that, under controlled conditions, small aggregates of ESCs are able to undergo gastrulation-like movements and elongation and organise an axially integrated post-occipital pattern of neural, mesodermal and endodermal derivatives mimicking that of the embryo in terms of gene expression. These results reveal an unanticipated self-organising capacity for aggregated ES cells and we show with some examples that gastruloids may be used as a complementary system to study early developmental events in the mammalian embryo.

Poster Number: P222
Regulated mRNA stability of the proto-oncogene, *myc*, by the RNA binding protein Imp determines neural stem cell size in the developing *Drosophila* brain
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The proliferation potential of neural stem cells (neuroblast) is limited by the extent of their regrowth between divisions, which is thought to be regulated by signalling pathways modulated by nutritional status and hormone levels. We have uncovered an additional mode of regulation of neuroblast cell size, through post-transcriptional regulation of the transcription factor and proto-oncogene, *myc*, by the RNA binding protein Imp. Imp binds to the long extended 3' UTR of *myc*, thus stabilising the transcript, leading to higher levels of Myc protein, and larger neuroblasts. Imp levels are an intrinsic indicator of neuroblast age, which varies between lineages and in turn are post-transcriptionally regulated by the RNA binding protein Syncrip. We propose that these post-transcriptional modes of regulation allow individual cells to bypass systemic signals for growth, once a threshold level of Imp is crossed.

Poster Number: P223
Developmental transition from naïve pluripotency to lineage specification
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Naïve pluripotent state refers to the cells of pre-implantation epiblast in the embryo. After implantation, epiblast cells undergo progressive transcriptional and epigenetic transformation until gastrulation stage, when lineage specification begins. Human naïve pluripotent stem cells (PSC) express transcription circuitry resembling pre-implantation epiblast and can be propagated *in vitro* retaining normal karyotype. Naïve PSC remain refractory to differentiation signals if applied directly to this state. In these conditions they loose naïve pluripotency factors without upregulation of lineage markers or generate unspecific cell types. We suggested that correct specification requires initial phase recapitulating developmental post-implantation transition and established culture requirements for this step. The cells changed their characteristics to that of pre-gastrulation epiblast (loss of naïve markers KLF4, KLF17, TFCP2L1, reduced NANOG, epithelial morphology) within 7-10 days, and acquired competence for multilineage differentiation. Recapitulation of post-implantation events using human PSC is fundamental to understanding how developmental programme is executed in early embryos.

Poster Number: P270
Modelling MAPK pathway overactivation in the mouse brain
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Overactivation of the Mitogen-Activated-Protein-Kinase (MAPK) signalling cascade drives tumourigenesis in numerous contexts. Our aim is to generate genetically engineered mouse models of MAPK overactivation to investigate the etiology of developmental brain tumours and conduct preclinical pharmacological trials. We have overactivated MAPK by conditional genetic B-RAF^{v600e} expression in the early mouse embryo brain, resulting in prenatal lesions in the telecephalon and diencephalon. Immunohistochemical analysis indicates that these comprise proliferative stem cells. And using an inducible model we have identified the cell-of-origin of these lesions to be neuroepithelial stem cells. The lesions generated share genetic etiology with Paediatric-Low-Grade-Glioma and also share histological characteristics with the aggressive CNS tumour Embryonal-Tumour-with-Multi-layered-Rosettes (ETMR). Immunological analysis of human ETMR samples identified overactivation of the MAPK pathway and ectopic proliferative stem cells. We are currently conducting *ex-vivo* brain slice culture and *in-vivo* experiments to determine the effects of inhibiting MAPK (using the FDA approved MEK inhibitor, Trametinib).

Poster Number: P271
The role of cellular senescence and its associated secretome in paediatric Adamantinomatous Craniopharyngioma (ACP)
S Manshaei[1], S Haston[1], JM Gonzalez-Meljem[1,2], J Gil[3], JP Martinez-Barbera[1]

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ACP is the most common non-neuroepithelial developmental brain-tumour. Mouse models generated in our group have demonstrated that mutations in *CTNNB1* during development can drive this tumour-formation. SOX2+ve pituitary stem cells targeted with oncogenic beta- catenin form senescent cell clusters that can induce tumourigenesis non-cell-autonomously, through a senescent-associated-secretory-phenotype (SASP), comprised of cytokines, chemokines, growth factors, etc. To elucidate the role of senescence in ACP I am generating a mouse model (*p21*$^{FDR/+}$) allowing detection and ablation of senescent cells *in-vivo*. Selective ablation of cluster cells at time-points during tumour formation will determine whether the cells are required for tumour initiation, or solely in tumour maintenance and growth. Additionally a *Rosa2*$^{STOP\text{-}mBRF1/+}$ mouse will attenuate activities of SASP genetically, to determine the crucial secretory drivers of tumourigenesis, as well as to determine the developmental roles of cytokines and chemokines in the pituitary. This will provide insight into senescence in ACP pathogenesis and pituitary development.

Poster Number: P224
Signalling and metabolic mechanisms for selective organ growth during starvation
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The growth of developing animals is tightly coordinated with nutrient availability. Some organs, however, are able to grow during starvation because their growth is spared at the expense of other tissues. Here we investigate the control of growth sparing in the wing imaginal disc of *Drosophila*. We find that, surprisingly, the insulin receptor is required for wing growth during starvation and this receptor is activated by Ilp6 secreted from fasted adipose tissue. This indicates that starvation switches off the insulin-like peptides that promote the growth of all organs but switches on Ilp6, which selectively stimulates the growth of spared tissues. Furthermore, we show that wing disc sparing relies upon glycogenolysis, lipolysis, autophagy and, most critically, the transcription factor Foxo in non-spared adipose tissue. We propose a dual role for Foxo in nutrient mobilization and Ilp6 production to ensure a balance between nutrient supply and growth factors during starvation.

Poster Number: P225
A role for *PRDM1* in cell fate decisions in the ectoderm
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The pre-neural ectoderm gives rise to the neural plate, the neural crest, and the pre-placodal ectoderm, which ultimately form the central and peripheral nervous system. Here we show that the transcription factor *Prdm1* is expressed in the pre-neural ectoderm, but is lost as neural, neural crest and placode-specific genes are initiated. Loss-of-function reveals that Prdm1 is required for all three fates, but normally inhibits pluripotency genes. In contrast, misexpression of Sox2 (neural), Foxd3 (crest), or Six1 (placodal) causes *Prdm1* reduction suggesting that these factors interact in a negative feedback loop. We also show that Prdm1 binds to the promoters of neural, neural crest and placodal genes and mediates the removal of repressive histone marks by recruiting histone demethylases. Our model suggests that Prdm1 facilitates fate decisions in the early nervous system by controlling histone modifications at the promoter regions of key fate determinants.

Poster Number: P226
Biomechanics of neural tube formation in mammals
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Mammalian neurulation requires the generation and transmission of mechanical force to enable neural tube closure. Using laser-ablation of living mouse embryos, and mosaic reporter-gene expression, we created strain-maps around the active spinal closure site. The entire caudal region is biomechanically coupled, via rostro-caudal F-actin cables that extend along the neural fold tips from the 'zippering point'. These cables transmit force for closure that is generated by medio-lateral F-actin/myosin profiles within the flat neuroepithelium. Late in closure, the F-actin cables come to encircle the closing region (neuropore) and a new closure point arises at the caudal-most extremity of the neuropore. Laser ablation shows that the new closure point diminishes stress experienced by the main zippering point, providing 'stress accommodation' that facilitates final closure. Genetic (e.g. Vangl2, Zic2 mutations) and non-genetic (e.g. valproic acid) influences that cause spina bifida disrupt specific elements of this biomechanical network.

Poster Number: P227
The role of Sox9 in the initial stages of salivary gland development and regeneration
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There is an increasing need to identify factors that determine the fate of salivary gland progenitors due to their application in regeneration as a treatment of xerostomia. We have identified Sox9 as a key factor for the proximo-distal patterning of salivary gland epithelium, one of the earliest specification events in the developing salivary gland. The distal part (tips of the gland) branches to produce acini and smaller ducts while the proximal part (the stalk) forms the excretory duct. We found that in the absence of Sox9 the distal epithelium is lost resulting in failure of branching and inhibition of growth. During development Sox9 is positively regulated by mesenchymal Fgf10 through the Erk pathway. In the adult regenerating salivary gland Sox9-positive cells are a major source of proliferating cells. Sox9 expression is also elevated in the excretory duct of regenerating glands one of the proposed locations of adult progenitor cells.

Poster Number: P228
Investigating the role of macrophages in the development of the cardiac lymphatic vasculature
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Macrophages are key components of the innate immune system and have been implicated in organogenesis. Importantly, the role of macrophages in the developing heart remains poorly characterised.

Here, we investigate the identity, timing, and localisation of macrophages in the murine embryonic heart. Macrophages were observed from embryonic day (E) 12.5, and a subset associated with the developing lymphatic vasculature. Macrophages did not act as progenitor cells giving rise to the lymphatics, although a $CSF1R^{+}$ myeloid-like progenitor was shown to incorporate into the lymphatic endothelium. To gain functional insight, heart formation was analysed in the *Pu.1*$^{-/-}$ mouse, which lacks macrophages. The absence of macrophages in this model was associated with defects in vessel branching, length and calibre, suggesting that a key role of macrophages in the developing heart is to pattern the lymphatic vasculature.

Poster Number: P229
Foxp1 controls neural stem cell maintenance and demarcates the early phase of cortical neurogenesis
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The laminar architecture of the mammalian neocortex depends on the orderly generation of distinct neuronal subtypes by apical radial glia (aRG) during embryogenesis. Here, we identify a critical role for Foxp1 in gating the temporal window for deep layer (DL) neurogenesis. Foxp1 is initially expressed at high levels by aRG and declines as upper layer neurogenesis commences. Loss and gain-of-function experiments in mice demonstrate that Foxp1 influences cell division symmetry, favoring expansion of the aRG pool and permitting DL neuron production into postnatal life. Sustained Foxp1 expression can preserve a population of cells with aRG identity within the adult brain and also elicit the generation of basal radial glia (bRG), a progenitor cell type associated with corticogenesis in higher species. Foxp1 is highly expressed by bRG in the human cortex, suggesting that its function may contribute to bRG production, and thereby influence the growth and development of the human brain.

Poster Number: P230
Working towards cell therapies for diabetes: identifying conditions to better induce and expand pancreatic endocrine progenitors in vitro
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Type I diabetes is becoming more prevalent, with a 3.9% annual increase in incidence in parts of Europe. Transplanting pancreatic islets from cadavers into diabetic patients is a promising cell therapy approach that can abrogate the need for insulin injections, but which is seldom utilized due to a shortage of donor material. hESCs could be used as a tool to overcome this shortage; hESCs have been successfully differentiated to pancreas progenitor cells in vitro, but expansion and subsequent differentiation of these cells is inefficient. Using foetal pancreas as an endogenous source of authentic pancreas progenitors, we show that these cells can be expanded in vitro and aim to screen a library of small molecules to identify conditions which can efficiently generate and expand endocrine progenitors. These small molecules could be used to improve production of therapeutically useful cells in culture.

Poster Number: P231
Regulation of neural tube growth by the morphogens Shh and BMP
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In the developing vertebrate neural tube a dorsoventral pattern of neural progenitor subtypes is established in response to the opposing morphogen gradients of Sonic hedgehog (Shh) and Bone Morphogenetic Proteins (BMP). Perturbations in Shh or BMP signaling lead to defects in neural tube size. However, how these pathways coordinately control neural tube growth is still poorly understood. To address this question, we are using mouse genetics and ex vivo assays to perturb Shh activity, BMP activity or both in a temporally controlled manner. We are obtaining high resolution datasets of cell proliferation, cell cycle exit and cell survival in these conditions. Our preliminary data indicates that loss of Shh activity does not affect progenitor proliferation, but induces a transient burst of apoptosis across the dorsoventral axis. Using genetics and genomics, we are investigating what factors contribute to this effect at the tissue level, and what is the underlying molecular mechanism.

Poster Number: P232
Epithelial cell rearrangement dynamics during mouse neural tube development
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Spinal cord formation in amniotes starts from a flat epithelial sheet, the neural plate, which extends and folds at the midline to form a closed neural tube. This morphogenetic transition is accompanied by a decrease in epithelial cell rearrangements and dispersion of clonally labeled cells over time. How this temporal change in epithelial dynamics is regulated is poorly understood. In particular, the roles of cell proliferation, changes in cell geometry, and mechanical forces remain unclear. I am developing live imaging protocols and a lineage tracing assay based on photoconversion to measure with high resolution the cell behaviors during mouse neural tube formation. I will combine experimental measurements with a computational model in order to evaluate the influence of the different cell behaviors to tissue dynamics. This quantitative description of cell rearrangement dynamics in the neuroepithelium will be relevant for understanding how cell rearrangements may affect pattern formation in the neural tube.

Poster Number: P233
ABSTRACT WITHDRAWN

Poster Number: P234
ABSTRACT WITHDRAWN

Poster Number: P235
Bridging structure and function in multicellular organ design using network science
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Multicellularity arose as a result of adaptive advantages conferred to complex cellular assemblies. The arrangement of cells within organs endows higher-order functionality through a structure-function relationship, though the organizational properties of these multicellular configurations remain poorly understood. We investigated the topological properties of complex organ architecture by digitally capturing global cellular interactions in the plant embryonic stem (hypocotyl), and analyzing these using quantitative network analysis. This revealed the presence of coherent conduits of reduced path length across epidermal non-hair (atrichoblast) cell files. The preferential movement of small molecules along this cell type was demonstrated using fluorescence transport assays.This suggests a division of labour is present between hair cells that acquire solutes, and their adjacent non-hair cells which are topologically optimized for long distance longitudinal transport. This network-based topological analysis of multicellular structural organization reveals higher order functions for patterning and principles of complex organ construction.

Poster Number: P236
The role of Stem Cells in Tooth Root Development
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The mammalian tooth root is the submerged part of the tooth providing support and anchorage. Although the initial stages of tooth development are well studied, little is known about root development, specially the apex which forms a crucial channel through which the blood vessels and nerves enter the vital dental pulp. It has been shown that a localised population of stem cells is located apical to the developing root although its role in root development remains unknown. Our investigation aims to identify potential stem/progenitor cell populations that are involved in late stages of root development. For this, we take advantage of transgenic reporter mice (Gli1CreERT2, Axin2LacZ) to label specific progenitor cell populations with the potential for lineage tracing experiments. Here we have followed a developmental time course of murine root development, concentrating on the stages when the root apex develops, and have investigated how putative stem cell populations are established.

Poster Number: P237
Apnoia, a new Crumbs regulator for proper breathing in flies
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The Drosophila tracheal system is a model to study the development and function of tubular organs. Maturation of tracheae has been extensively studied, however mechanisms such as tracheal inflation or tracheal growth in response to oxygen still remain elusive. Here we characterized apnoia (apn), a gene that encodes a transmembrane protein and localizes to the apical plasma membrane of epithelial cells, predominantly in the tracheal system. *apn* mutant animals show defects in tracheal inflation at larval stages. Tracheal tubes in mutant larvae are twisted, although tracheal maturation appears normal during development. We found Apn as a partner of Crumbs in a Y2H screen. In *apn* mutant tracheae Crumbs is mislocalized and trapped in large vesicles within the cell. We are currently studying the connection between Apn and Crumbs at the molecular and cellular level necessary for trachea development.

Poster Number: P238
The Development of Olfactory Ensheathing Cells from the Neural Crest
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Olfactory ensheathing cells (OECs), the glia of the olfactory nerve, are promising candidates for cell-mediated repair of spinal cord injuries. Our lab's discovery that OECs are neural crest-derived potentially means that homogeneous populations of patient-specific OECs for spinal cord repair could be expanded in culture from neural crest stem cells persisting in skin and hair follicles. Our goal is to identify molecular mechanisms underlying neural crest differentiation into OECs, as opposed to Schwann cells, which are less effective in spinal cord repair. To achieve this, we took an unbiased transcriptome profiling approach, using laser-capture microdissection on mouse embryos carrying a *Sox10:H2BVenus* transgene to isolate OEC subpopulations and Schwann cells (both of which express Sox10) at different stages of their development, for RNAseq and cross-wise comparison of transcriptomes. This approach has allowed the identification of candidate genes that may be important specifically for OEC differentiation and that distinguish different OEC subpopulations.

Poster Number: P239
Selective Filopodia Adhesion Ensures Robust Cell Matching in the *Drosophila* Heart
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The ability to form specific cell-cell connections within complex cellular environments is critical for multicellular organisms. However, the underlying mechanisms of cell matching that instruct these connections remain elusive. Here, we quantitatively explored the dynamics and regulation of cell matching processes utilizing *Drosophila* cardiogenesis. We found that cell matching is highly robust at boundaries between cardioblast (CB) subtypes, and filopodia of different CB subtypes have distinct binding affinities. Cdc42 is involved in regulating this selective filopodia binding adhesion and influences CB matching. Further, we identified adhesion molecules Fasciclin III (Fas3) and Ten-m, both of which also regulate synaptic targeting, as having complementary differential expression in CBs. Altering Fas3 expression changes differential filopodia adhesion and leads to CB mismatch. Furthermore, only when both Fas3 and Ten-m are lost is CB alignment severally impaired. Our results show that differential adhesion mediated by selective filopodia binding efficiently regulates precise and robust cell matching.

Poster Number: P240
Maternal transmission of an *Igf2r* domain 11: IGF2 binding mutant (*Igf2rI*^{1565A}) results in partial lethality, overgrowth and intestinal adenoma progression
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M6P/IGF2R or IGF2R traffics IGF2 and M6P ligands. Internalisation of IGF2 occurs by binding to IGF2R domain 11. Maternal transmission of imprinted *Igf2r* knock-out allele results in overgrowth and lethality. It remains unknown if this phenotype is due to increased IGF2 alone. We evaluated the phenotypic consequences of specific loss of IGF2 binding to IGF2R domain 11. A knock-in point mutation converted isoleucine to alanine in the hydrophobic CD loop of domain 11 (I1565A). Maternal allele *Igf2r*$^{I1656A/+p}$ resulted in partial neonatal lethality (<60%) and embryonic over-growth. Homozygotes developed perinatal mortality (90%) suggesting that paternal allele expression attenuates the heterozygote phenotype. To investigate tumour suppressor function, bi-allelic *Igf2r* expression reduced intestinal adenoma (*Apc*^{Min}). Combination of *Lgr5-Cre*, *Apc*$^{loxp/loxp}$ and *Igf2r*$^{I1656A/+p}$ resulted in adenoma progression. In conclusion, perinatal lethality following *Igf2r* maternal allele disruption appears to be mainly due to increased IGF2 supply, and *Igf2r* can act as an IGF2 dependent tumour suppressor.

Poster Number: P241
Mechanical strain regulates the Hippo pathway in *Drosophila*
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Animal cells are thought to sense mechanical forces via the transcriptional co-activators YAP/TAZ, whose sole *Drosophila* homolog is Yorkie. In mammalian tissue culture, artificial mechanical forces induce nuclear translocation of YAP/TAZ. Here we show that physiological mechanical strain can also drive nuclear localisation of Yorkie and activation of Yorkie target genes in the follicular epithelium. Mechanical strain activates Yorkie by stretching the apical domain, reducing the concentration of apical Crumbs, Expanded, Kibra and Merlin and reducing Hippo kinase dimerisation. Overexpressing Hippo to induce ectopic activation in the cytoplasm is sufficient to prevent Yorkie nuclear localisation even in flattened follicle cells. Conversely, blocking Hippo signalling in *warts* clones causes Yki nuclear localisation even in columnar follicle cells. Finally, our results appear generally applicable to other tissues, as nuclear translocation of Yki is detectable in other flattened epithelia such as the peripodial epithelium of the wing disc, where it promotes cell flattening.

Poster Number: P242
Tympanic membrane development: a tale of two parts
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Numerous diseases affect the tympanic membrane. Furthermore, as the gateway to the middle and inner ear, it is the most surgically manipulated structure in the treatment of ear disease. Despite this, our understanding of the tympanic membrane and how it forms lacks detail.

The mammalian tympanic membrane consists of the superior pars flaccida and the inferior pars tensa. Histological sections of the middle ear in both mouse and human embryonic samples show the pars flaccida has distinct morphological appearances and develops later than the pars tensa. Lineage tracing experiments using *sox17cre* and *wnt1cre* lines crossed with *R26-lacz* and *R26TdT* reporters reveal that the pars flaccida, unlike the pars tensa, does not have an endodermal layer. The Pars flaccida also demonstrates different epithelial marker expression to the pars tensa. These results have important implications for our understanding of diseases, such as cholesteatoma, that specifically affect certain parts of the tympanic membrane.

Poster Number: P243
Exploring the role of *Flk-1/Kdr* in mesodermal derivatives of the post-gastrulation mouse embryo
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FLK-1 is expressed first in the mesoderm and later in endothelial and hematopoietic cells. Germ-line *Flk-1* knock-outs result in embryonic lethality by embryonic day 9.0, mainly due to defects in vasculogenesis. However, a closer morphological examination of *Flk-1* mutants reveals defects in other previously disregarded mesodermal derivatives, such as the allantois and the developing heart. Since *Flk-1* is a key mesodermal gene that seems to be required for many aspects in tissue development, understanding how different lineages directly derived from the mesoderm are affected upon loss of *Flk-1* might shed light on molecular mechanisms driving edothelial/haematopoietic (or other lineages) potential in post-gastrulation embryos. We have undertaken a single-cell transcriptomic characterization of extra- and intraembryonic sub-dissected regions in *Flk-1* Knock-out and *Flk-1* Heterozygous 6 somite-pair embryos. With the generated data set, we investigated the consequences of loss of *Flk-1* in various mesodermal derivatives at the transcriptional and cellular levels.

Poster Number: P244

Concentration, DNA-binding kinetics and variability of Zelda underlie the timing of Zygotic Genome Activation in Drosophila

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During early embryogenesis, the zygotic genome becomes primed for zygotic transcription. In Drosophila, Zelda (Zld) has been identified as a major player in rendering the genome receptive to transcription. While present in the syncytium from the first nuclear division, activation of the genome doesn't occur until precisely 13 nuclear divisions later, indicating strict temporal control.

We have undertaken a quantitative approach to understand the kinetics of zygotic genome activation. Using Fluorescence Correlation Spectroscopy, we observed changes in the intra-nuclear concentration, distribution, DNA-binding kinetics and nucleus-to nucleus variability of Zld and have quantified its mobility before, during and after the timepoint of zygotic genome acitvation. We argue that the concentration of Zld determines its DNA-binding kinetics and therefore the temporal precision of the onset of zygotic gene expression. In ongoing experiments we are investigating the nature of Zld nuclear accumulations.

Our results underline the importance of Zld concentration, DNA-binding kinetics and cell/tissue varianbilities in instructing developmental fates.

Poster Number: P245

3D Analysis of Mouse Embryo by X-ray Computed Tomography

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X-ray Computed Tomography (CT) provides 3D imaging various types of samples. The state of the art of CT systems originally designed for industrial applications can contribute to our understanding on how the shape diversity observed among living organisms is defined and controlled during development and growth. CT has proven capability to explore embryonic formation in different developmental stages with high-resolution and in a non-destructive manner. The complexity of biological structures often requires a comprehensive approach to compare shapes, sizes and volumes of studied structures. Due to comparison of various mutant mouse models, data processing and quantification of morphological 3D changes can be challenging. In this work, we introduce industrial CT system as a new suitable tool for comparative developmental studies, embryo phenotyping, and morphology studies. This is demonstrated on selected structures and organs of mouse embryos by means of shape comparison, volume determination, thickness measurements, position/orientation analysis and 3D printing.

Poster Number: P246

Notch signalling regulates the emergence of thymic epithelial lineage required for T-cell tolerance induction

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T-cell development occurs in the thymus. Thymic epithelial cells (TEC), the key thymic stromal component, consist of two subtypes: cortical TEC (cTEC) and medullary TEC (mTEC). Whereas cTECs regulate T-cell commitment, proliferation and positive selection, mTECs mediate immune tolerance by deleting self-reactive T cells. cTECs and mTECs originate from bipotent TEC progenitors (TEPC) in development, but how TEPCs generate the two lineages remains poorly understood. Using genetic ablation and tissue culture, we established that Notch is required for mTEC development. This function is stage-specific, as early inhibition resulted in more severe mTEC hypoplasia. Moreover, fetal TECs retain immature markers in the Notch gain-of-function model, suggesting that Notch influences TEPC maturation. Transcriptomic and functional analysis further revealed interactions between Notch and FOXN1, a major regulator of TEC differentiation. This study identified a novel role of Notch in thymus organogenesis, and offered clues for improving *in vitro* differentiation of distinct TEC subtypes.

Poster Number: P247
Activity-dependent regulation of interneuron survival sculpts cortical networks
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An imbalance in the number or function of excitatory and inhibitory cortical neurons is a hallmark of neurodevelopmental disorders such as epilepsy, autism and schizophrenia. Despite being a common theme in these disorders, the mechanisms regulating the establishment of appropriate ratios for these neurons remain largely unknown. It has been described that inhibitory cells undergo programmed cell death in a cell autonomous manner in the developing mouse neocortex. Here we show that like their inhibitory counterparts, excitatory cells undergo programmed cell death during the first postnatal week of mouse development. Our results suggest that pyramidal cells dynamically adjust the number of inhibitory cells in nascent local cortical circuits through the regulation of PTEN levels in interneurons. Our findings reveal that early postnatal activity-dependent mechanisms establish the appropriate proportions of excitatory and inhibitory neurons in the cerebral cortex.

Poster Number: P248
Epithelial apical vertices are important for morphogenesis
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During animal development, many epithelial tissues extend in one orientation while narrowing in the orthogonal axis. This process is called convergence and extension. Cell rearrangement, which results from the remodelling of cell-cell contacts, is a key driving force in this process. In epithelia, cell-cell contacts are connected via vertices, where 3 or more cells meet. Whereas several recent studies have suggested that cell vertices are important sites for sensing and regulating tissue tension, it is unknown whether cell vertices play an active role in regulating cell rearrangement. Following up on our finding that the Immunoglobulin-superfamily protein Sidekick resides specifically at apical vertices (Lye et al. 2014,), we investigate the behaviour and role of vertices in epithelial morphogenesis in the gastrulating *Drosophila* embryo. Using automated cell tracking, quantitative analysis at the cellular and tissue scale and modelling, we reveal that apical vertices are important sites in regulating epithelial remodelling.

Poster Number: P249
Building and breaking epithelial integrity in the neural tube: an optogenetic approach
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My lab uses optogenetic and live confocal imaging within the zebrafish neural tube to test the role of cell polarity in building epithelial integrity during organ development and in breaking it during disease.

In combination with high resolution *in vivo* imaging, we use a new optogenetic approach to directly manipulate the polarity, signalling and division of single cells within the developing zebrafish brain. This allows us to explore how cell polarity and division are linked during development such that cells can divide without disrupting the strict organization of the tissue. We are also testing the role of polarity dysregulation in tissue disruption by optogenetically manipulating polarity-linked signalling pathways (such as the PI3K pathway) in the already established zebrafish neural tube epithelium. We hope to unravel parallel mechanisms of epithelial development and disease *in vivo*.

Exciting preliminary data suggests a link between apical protein localisation and cell division location and orientation.

Poster Number: P250
Crosstalk between Lgr5 positive epithelial cells and mesenchymal FGF10 is essential for CVP development
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Adult stem/progenitor cells in various organs including tongue papillae are reported Leucine-rich repeat-containing G protein-coupled receptor 5 (*Lgr5*) positive. Including adult taste stem/progenitor cells in circumvallate papillae (CVP) on posterior tongue, which are reported *Lgr5* positive. In this study, the *Lgr5* expression pattern during CVP development is confirmed. Since previous study has reported that mesenchymal FGF10 is essential for CVP development, and is necessary for the maintenance of epithelial *Lgr5* positive stem/progenitor cells in other organs. To confirm the interaction between *Lgr5* positive CVP epithelium and mesenchymal factor FGF10, 180 degree reverse recombination was performed after detaching tongue epithelium. Moreover, FGF10 protein soaked bead implantation was performed on 180 degree reverse recombination tongue for rescue study of CVP. This study may suggest that crosstalk between *Lgr5* positive epithelial cells and mesenchymal FGF10 would act pivotal roles in epithelial invagination of CVP formation during mouse tongue development.

Poster Number: P251
Nicotinamide adenine dinucleotide phosphate (NADPH) oxidases 1 (NOX1) and NOX4 expression during mouse lung and liver development
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Despite differences in the pathology, the role of nicotinamide adenine dinucleotide phosphate (NADPH) oxidases 1 (NOX1) and NOX4 during organ development is still not well elucidated. In this study, we examined their expressions in the developing mouse lung and liver. Immunofluorescence staining indicated that NOX1 and NOX4 proteins were highly expressed in early lung and liver development but were decreased at late gestation. Real time PCR analysis showed that *NOX1* in lung and *NOX4* in liver were gradually upregulated during development. Importantly, at E17.5, *NOX4* mRNA was expressed in the epithelium of the developing bronchus and bronchioles. These findings suggest a possible role of NOX4 in epithelium development of airway at E17.5 and could prevent from late pathological anomalies. Further experiments are necessary to elucidate functions of NOX1 and NOX4 at each stage of gestation together with pathophysiological evaluation.

Poster Number: P252
Neuromesodermal Progenitors are Conserved Source of Spinal Cord with Divergent Growth Dynamics
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Gastrulation is the process by which cells of the embryo become specified into distinct germ layers. Recently, retrospective clonal analysis studies in the mouse have demonstrated that germ layer specification continues throughout somitogenesis stages from a population of bipotent stem cells called neuromesodermal progenitors (NMps). Via a combination of genetic scarring and light-sheet imaging, we have traced spinal cord lineage of the zebrafish embryo. We find that the entire length of the spinal cord is generated from pool of NMps, but with vastly different population dynamics as those identified in the mouse. An initial population subdivides at early gastrula stages and is directly allocated neural and mesodermal of both the trunk and tail. A second population moves coherently into the tailbud where it undergoes delayed allocation to contribute neural and mesodermal compartment at late somitogenesis. Thus, NMps are a conserved population whose rates of differentiation and growth vary between species.

Poster Number: P253
Understanding lethality throughout development: the Sanger high throughput recessive lethality screen
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The Wellcome Trust Sanger Institute (WTSI) is a major contributor towards the worldwide effort to develop mouse models to understand human genetic disease. To date, 35% of over 1400 mouse knock-out lines studied within the WTSI primary phenotyping screen are classified as lethal or sub-viable at postnatal day 14 (P14). Here we present the results of the WTSI phenotypic effort to shed light on the developmental defects leading to embryonic and perinatal lethality. We systematically perform *in-vivo* and *ex-vivo* tests to phenotype the whole gestational period and the first week immediately after birth. Embryonic and placental samples are further investigated by several techniques such as 3D high resolution imaging, transcriptomic analysis and histopathology as part of the Deciphering Mechanism of Developmental Disorders (DMDD) program. Through these studies we determine whether lethality or reduced viability at P14 results from *in utero* morphological/functional defects or defects in parturition, breathing, feeding or homeostasis.

Poster Number: P254
High heterotypic interfacial tension is the motor for cell sorting at embryonic boundaries
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Sorting of different cell types into distinct groups separated by sharp delimitations, called embryonic boundaries, is fundamental to metazoan development. The principles underlying this phenomenon have remained highly controversial. Classical ‘differential adhesion’ and ‘differential tension’ hypotheses proposed that cell segregation was caused by global tissue differences in either cortical tension or adhesion. A fundamentally different mechanism is based on a local increase in cortical tension at the heterotypic contact between different cell types. We used the Xenopus gastrula to test directly side by side these different potential mechanisms. We demonstrate through direct experimental evidence and computer simulation that generation of high local tension at the heterotypic contact interface is the driving force for cell sorting, while tissue differences in cell-cell adhesion or cortical tension are incomparably less efficient. We propose a unifying model where this heterotypic tension is the key parameter for tissue separation, irrespective of the internal tissue properties.

Poster Number: P255
Understanding congenital disease through investigations of human embryonic and fetal development
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The Human Developmental Biology Resource is a unique resource funded by the MRC and Wellcome Trust. It provides human embryonic and fetal tissue for gene expression studies related to congenital disease, including both birth defects and inherited metabolic disorders. Use of the material should particularly illuminate developmental gene expression underlying aspects of functioning that characterise humans as opposed to lower animals. This research is essential if we are to introduce new methods for prevention of congenital defects and develop an improved understanding of “what makes us human”. The HDBR has ethics approval for the collection, storage and distribution of material between 4 and 21 weeks post conception. We will highlight data from recent projects that have used our resource to study gene expression in the developing human embryo and fetus.

Poster Number: P256
Analysis of abnormal embryo morphology using 3D imaging techniques
J Cleak[1], SJ Johnson[1], Z Szoke-Kovacs[1], N Horner[2], MLC Husbandry Team[1], S Wells[1], H Westerberg[2], L Teboul[1]

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As part of the International Mouse Phenotyping Consortium (IMPC) we have been running an embryonic phenotyping pipeline to characterise knock-out lines that are found to be embryonic lethal. The MRC Harwell team have now analysed over 500 mutant lines, uncovering a wealth of new information on gene function, both on previously studied genes and on genes without previous phenotyping data. Here, we present examples of extensive datasets, on one previously studied (*Pkd1*) and two novel (*Chic2, Tmem16b*) genes that are either lethal or sub-viable at the point of weaning. Micro-computed tomography (microCT) was used to produce 3-dimensional (3D) datasets of E18.5 embryos. We uncovered a variety of abnormal morphology affecting a range of structures, including the brain, cardiovascular, respiratory and renal systems. These 3D datasets offer a unique opportunity to comprehensively examine developmental defects and may indicate the cause of lethality. This data is then freely accessible through www.mousephenotype.org.

Poster Number: P257
Hepatic progenitor cell heterogeneity and their potential during liver differentiation
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A number of studies have observed heterogeneity in stem cell and progenitor cell populations *in vitro*, which was associated with diverse differentiation potential. However, heterogeneity of progenitor cells *in vivo* is less understood, including the vertebrate liver. We detected a heterogeneous Prospero-related homeobox 1 (Prox1) expression in hepatic progenitor cells using immunostainings in the zebrafish liver. In order to study heterogeneity of hepatic progenitor cells *in vivo*, I am creating an intramolecular tagged Prox1 transgenic zebrafish line. This provides a powerful tool for observing real-time Prox1 expression during development and growth. This approach will be applied to study the function of heterogeneity with respect to the potency of hepatic progenitor cells, which contribute to hepatocytes and biliary cells. The Prox1 reporter line can then be combined with lineage tracing tools in zebrafish. The value of this approach is to unravel the contribution of progenitors to the adult organ over time.

Poster Number: P258
Development of morphology annotation in the embryonic phenotyping pipeline used by the International Mouse Phenotyping Consortium
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Over the last five years MRC Harwell has produced and systematically phenotyped 500 out of the 5000 knock-out mouse lines annotated by the International Mouse Phenotyping Consortium (IMPC). Here we present the embryonic phenotyping pipeline. Gene expression is examined in E12.5 embryos for alleles containing *lacZ* reporter. Viability at various stages of gestation in lines that are lethal or sub-viable at weaning is investigated. For lethal lines, the oldest possible homozygous null embryos are harvested employing a triaging system. Their morphology is captured using either optical projection tomography (OPT) or micro-computed tomography (microCT), depending on embryonic stage. Recently, we have developed a manual annotation scheme to systematically document morphological defects observed in the images. In parallel, we have created software that automatically flags up regions of the embryo that differ from a WT average. Here we show these new tools and how we employ them in the identification of dysmorphologies.

Poster Number: P259
Novel insights into the regulation of dermal white adipose tissue: Defining dermal progenitor cell fate using a three-dimensional spheroid model
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During mouse skin development, the timing of commitment, degree of plasticity and signals that control the multiple fates of dermal progenitors remain poorly understood. To determine the molecular signals, which specifically influence lower dermal cells to follow adipogenic fate, we have established a 3D spheroid culture system from isolated embryonic dermis to model dermal white adipose tissue (DWAT) development. Interestingly, the adipogenic potential of 2D and 3D dermal cells differs *in-vitro*; E13.5 dermal cells established in 2D culture assume a fibroblastic morphology in comparison to adipogenic differentiation in 3D spheroid culture. This contrasting behaviour *in-vitro* poses the question as to what the default status of these cells is, and posits a key role for the overlying epidermis in establishing dermal fibroblast identity. By functionally modifying DWAT using small molecule modulators, we are currently examining how signalling pathways of interest control dermal cell fate decisions in the early embryo.

Poster Number: P260
Quantitative modelling and analysis of epithelial morphogenesis
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We are witnessing an avalanche of data on epithelial morphogenesis generated from molecular and live-imaging studies. This motivates mathematical modelling as an increasingly quantitative tool: mathematical models that are calibrated against experimental measurements and used to generate quantitative, testable predictions. To help facilitate this predict-test-refine-predict cycle, focusing on a widely used vertex model of epithelia, we reveal: how graph theoretic concepts may be used to reliably perform cell tracking for live-imaging data; how model parameter estimates and associated uncertainties can be quantified via different summary statistics from live-imaging data; and how quantitative model predictions may be influenced by parameter values and implementation details. Together, these contributions help enable the quantitative study of epithelia for a wide range of developmental applications.

Poster Number: P261
Hair follicle dermal condensation forms via Fgf20 primed cell cycle exit, cell motility, and aggregation
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Mesenchymal condensation is a common phenomenon during organ development. In the hair follicle, the dermal condensate (DC) is the precursor to the permanent, hair cycle regulating mesenchymal component of the hair follicle. The formation of the DC is dependent on epithelial Fibroblast Growth Factor 20 (Fgf20), as knock-out mice lack molecular and morphological attributes of DCs. However, the mechanisms driving mesenchymal condensation have remained uncharacterised. In this study, we use lineage tracing and whole-mount confocal microscopy to show that DCs are induced *de novo* and that cell cycle exit and cell shape change are early hallmarks of DC formation. We also demonstrate that DC forms via directed cell migration using live confocal microscopy. Further, our *in vivo* and *ex vivo* experiments indicate that Fgf20 induces dermal fibroblast migration, primes cell cycle exit and cell shape change, and that Fgf20 is necessary for the maintenance of the DC.

Poster Number: P262
Notch signalling: its implication in phenotypical heterogeneity of Holoprosencephaly
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The development of the brain is complex and requires tightly controlled spatial and temporal orchestration of numerous signalling pathways. In humans, Sonic Hedgehog (SHH) haploinsufficiency is the predominant cause of Holoprosencephaly (HPE), a structural brain malformation with phenotypical heterogeneity. In addition to SHH, 15 genes have been identified as having a role in the onset of HPE. All these HPE-associated genes, apart from DLL1, a ligand of the receptor NOTCH, have been shown to directly or indirectly affect SHH signalling during early brain development. The mechanism by which NOTCH dysfunction could cause HPE is still unexplained. Using chick and mouse models, we show that embryos lacking Notch activity exhibit a reduction of *Shh* signalling in the hypothalamus primordium. The resulting phenotype is reminiscent to a specific inactivation of *Shh* in this tissue. Our findings suggest that an interaction between the NOTCH and SHH pathways may underlie HPE cases.

Poster Number: P263
Modelling Kallmann Syndrome in the zebrafish: crucial roles for *Fgf* signalling and *anosmin* in olfactory development and GnRH neuron migration and evidence for a common signaling pathway.
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Kallmann Syndrome (KS) is characterised by absence of GnRH neurons in the hypothalamus, causing sterility, together with lack of the sense of smell, anosmia. Both defects have their origin in defective olfactory development: olfactory axons fail to extend from olfactory placode into the brain and GnRH neurons fail to migrate from placode to brain. KS can be sporadic or inherited. Familial disease is frequently due to mutations in F*GF8* or *FGFR1* or in *Anosmin*, encoding a secreted glycoprotein. Given the crucial role of *Anosmin*, it is remarkable that neither rats nor mice have *anosmin* orthologues, precluding their use in understanding key aspects of KS. We investigated *anosmin* and *Fgf8* function in zebrafish olfactory development and find both are crucial to axon pathfinding and GnRH neuron migration. Moreover, they function in development of other key axon pathways and we provide genetic evidence that they function in the same signalling pathway.

Poster Number: P264
Adprhl1 action in the developing vertebrate heart:- Comparison of *Adprhl1* knockout in the frog and mouse
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Adprhl1, a pseudoenzyme from the ADP-ribosylarginine hydrolase family, is essential for chamber outgrowth of the embryonic heart. We suspect Adprhl1 modifies actin filament dynamics and thus represents an excellent candidate to explore how cardiac myofibril assembly is initiated. Here, we use CRISPR-Cas9 gene editing to compare *adprhl1* knockout in *Xenopus* with a similar deletion in mouse. In *Xenopus laevis* embryos, one-cell injection of Cas9 protein and guide-RNAs targeting both homeologous alleles ensures the wildtype gene sequence is disrupted in all alleles of every daughter cell. The variability of subsequent DNA repairs has been mapped to the heart morphology of individual tadpoles, building a picture of mutations that cause null alleles. Targeting the same exons in mouse also produces an *Adprhl1*-null whose homozygous cardiac phenotype is presented. Finally we produce *Xenopus* pipelines for knockout and tagging of other Nkx2-5 target genes implicated in muscle assembly and chamber outgrowth phases of cardiogenesis.

Poster Number: P265
Conditional deletion of Wt1 in pleuroperitoneal folds leads to congenital diaphragmatic hernias
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Tissue sheets fusion is one of the fundamental processes during development. One example is the formation of diaphragm. Despite the high prevalence of congenital diaphragmatic hernia (CDH, 1 per 3000 live births), the exact mechanisms of how diaphragm is formed is not well understood. We have developed a mouse model of CDH, using the Prx1-Cre line to drive the conditional deletion of *Wt1* in mesenchymal cells in the diaphragm. ~70% of the $Prx1^{Cre/+}$;$Wt1^{loxP/loxP}$ embryos present with Bochdalek-type hernias. Connective tissue fibroblasts have been shown to guide the migration of myoblasts to the developing diaphragm. Here we showed the absence of connective tissue fibroblasts (Gata4+) and a delay of myoblasts migration in the mutant diaphragm where Wt1 is deleted. We are investigating the cellular and molecular mechanisms responsible for the defect in our model, in the hope that it will inform us more about the processes that lead to human CDH.

Poster Number: P266
Gestational exposure to dioxin as an environmental risk factor for neurodevelopmental disease
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3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is a persistent and toxic environmental pollutant, a ligand of the aryl hydrocarbon receptor (AhR). Gestational exposure to TCDD has been linked to changes in sexual behaviour, cognitive ability, anxiety, and traits linked to autism spectrum disorder (ASD) in humans. ASD-like behaviours have not been clearly demonstrated in a gestational TCDD exposure model, and the mechanism of action of TCDD on the developing brain is unknown. In this study, physiologically-relevant dioxin exposure was achieved by feeding C57BL/6J female mice a TCDD-spiked fish-based diet through gestation. The offspring were then tested with a battery of well-validated behavioural tests for ASD-like behaviours, which included tests for social and communication deficits, stereotyped behaviours, anxiety and memory. The effects of TCDD on dendritic structures in the hippocampus and cortex were studied at developmental time points. This study can further our understanding of how TCDD affects neurodevelopment and behaviour in a physiological model.

Poster Number: P267
Axial emergence through self-organization in Gastruloids, controlled aggregates of embryonic stem cells
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Emergence of a coordinate system, in a group of genetically equivalent cells, through asymmetries in gene expression and cell behavior, is a recurrent theme in morphogenesis. While molecular players are known, we do not understand how forces and geometry serve as sources of information for cells. Pre-existing spatial cues, species-specific geometry and extraembryonic signaling centers, confound studying these processes *in vivo*. Our work has shown that 3D aggregates of mouse embryonic stem cells – 'gastruloids'- can achieve 'symmetry-breaking' of body axes markers and axial organization within homogeneously distributed signals, thereby mimicking the morphogenetic events in mouse epiblasts. By combining experiments and modeling, we investigate the mechano-chemical feedbacks on cells that generate patterns scalable with aggregate size and guide the emergent cell behavior. To test the generality of such morphogenetic events, we use cell aggregates from zebrafish embryos and show that they can also develop a global coordinate system *de novo*.

Poster Number: P268

Spatially restricted regulation of cell competition by the cytokine Spätzle

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In growing tissues, cooperative behavior of cells is enforced by cell competition, wherein comparisons of fitness lead to selective elimination of suboptimal 'loser' cells. In *Drosophila* wing discs, this eliminaition is controlled by a genetic module consisting of the Toll ligand Spaetzle (Spz), several Toll related receptors, and NFkB factors. How signaling by this module is activated and restricted only to competing cells is unknown. Here, we demonstrate that elimination of 'loser' cells in Myc super-competition requires local synthesis and activation of Spz in the wing disc. We identify two SPs to mediate competitive signaling, and show that an increase in SP expression in 'winner' cells is required for Spz to kill 'loser' cells. Altogether, our results provide a model of signal initiation in Myc super-competition, and indicate that Spz-mediated competitive signaling is strictly confined to the imaginal disc, allowing errors in tissue fitness to be corrected without compromising organismal physiology.

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BSDB

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This year, is the **BSDB's 70th anniversary**, and this was clearly reflected at our **Spring Meeting**, 15-18 April 2018 in Warwick! Apart from an **outstanding speaker list**, and the award of most **BSDB medals & prizes** of 2018, we saw a very special event with many extras, as is well described here by **Dillan Saunders**. Dillan undertook his BSc Honours with Michael Akam studying centipedes, is currently performing his MSc in the lab of Megan Davey date-mapping the developing limb bud of chick with novel transgenic technologies. and will be returning to Cambridge later this year to begin The Wellcome Trust Developmental Biology PhD program. Dillan's contribution aligns with a **long-standing tradition of the BSDB to engage young members** (see our archive blog), and we strongly encourage PhD students and postdocs to make their voice heard by writing reports or articles for our website and newsletter.

BSDB 70th Anniversary Meeting Report

by Dillan Saunders

The British Society for Developmental Biology (BSDB) recently held its annual Spring Meeting at the University of Warwick. This was no ordinary meeting, though it is fair to say that BSDB meetings rarely are. This Spring Meeting celebrated the 70th anniversary of the BSDB and did so excellently, birthday cakes and all. With a retrospective look at the past of the society, and fantastic speakers showcasing present and ongoing work, the stage was set for a meeting that not only celebrated a strong history, but also looked forward, critically yet hopefully, to the future of Developmental Biology and of the BSDB itself.

The conference began with a **careers workshop** for students and post-docs (*see our blog post*). In keeping with the celebration of the BSDB's birthday, the focus of the workshop was on staying in academia. A variety of speakers and other group leaders fielded questions and shared details of the personal journeys to have brought them to their current positions. I had the opportunity to speak to **Henrik Semb** - whose example shows that not everyone follows a straight, let alone predictable, career trajectory. **Judith Kimble** shared her views on not seeing the lab as a place of work, and finally I got to hear **Ottoline Leyser**'s thoughts on work-life balance; a phrase which misleadingly implies that the two are opposed to one another. It would however be in our best interests, she explained, to see work and life as overlapping and complementary to one another.

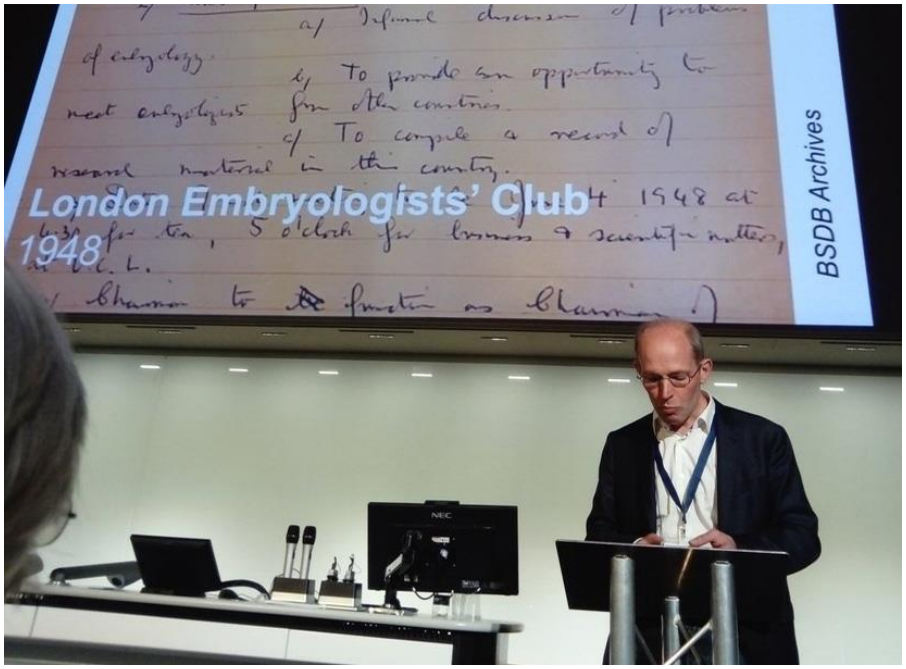
The career workshop

After the careers workshop came the first **plenary** talk, in which **Eric Wieschaus** explained his recent work on mesoderm invagination in *Drosophila* and how one transcriptional activation can lead to a sequence of events (*Weng and Wieschaus, 2017*). Thematically paired with this talk was **Maria Leptin**'s plenary lecture, in which she discussed the development of *in silico* models for actin dynamics in order to recapitulate mesoderm invagination (*Belmonte et al., 2017*).

Following a short break, **Emily Favuzzi** was presented with the **Beddington Medal** – awarded by the BSDB for the best PhD thesis in Developmental Biology of that year, for work on the transcriptional networks at play during interneuron development (*see our blog post*). She then gave a talk that illustrated how meticulous and comprehensive her work was (*Favuzzi et al., 2017*). This was followed up by a plenary talk from **Marianne Bronner** on the transcriptional networks of specific populations of neural crest cells, with attention to how her work with lampreys shows that the neural crest has acquired additional functions in the jawed vertebrates (*Green et al., 2017*). Unfazed by technical difficulties with the final slides of the presentation, Bronner took on the role of the lamprey and humorously indicated on herself the location of the neural crest cells.

Emilia receives the Beddington medal from Simon Bullock

The evening was capped off by three events that celebrated the **history**, and looked into the future, of the BSDB and Developmental Biology as a whole. First, came two talks from historians of science, **Nick Hopwood** and **Tim Horder**. Hopwood's talk detailed the story of the crystallization of modern Developmental Biology in the late '40s and '50s. He described how the London Embryologists Club began in 1948 and how it then broadened both its geographical location and the field that it represented to form the BSDB (*see also our archive blog*).



Nick Hopwood's lecture about DB's history

Off the back of the historians' view of the past, came a **panel discussion** of the future of the field. The panel was made up of **Ottoline Leyser**, **James Briscoe**, **Maria Leptin**, **Jonathan Slack**, **Judith Kimble** and **Patrick Lemaire**. They fielded several thought-provoking questions from the audience, which led to a lively discussion. As might be expected from a big anniversary meeting, there was much reminiscing on the early days of molecular Developmental Biology in the 1980s, often referred to as the 'Golden Age.' When asked what made this era such an exciting time for Developmental Biology, Jonathan Slack noted that it was a time when developmental biologists were becoming dissatisfied with the explanations of the previous heyday of embryology in the 1930s.

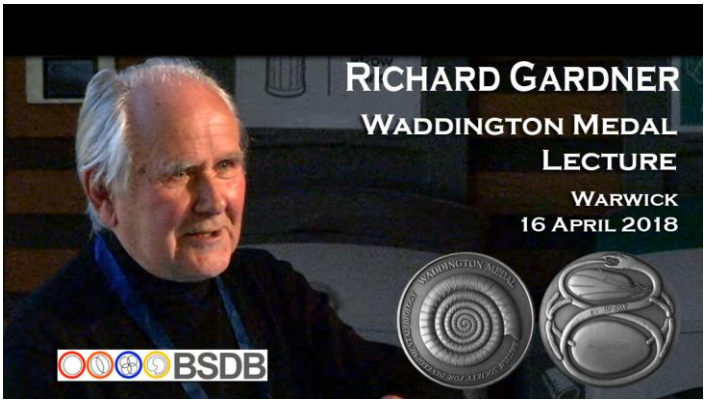
In the subsequent discussion, Ottoline Leyser pointed out that, what with the advent of new technologies and ideas, we are in fact in the midst of a golden age for Developmental Biology. Indeed, though there are still some who believe that certain areas of Developmental Biology hold no more secrets, recent years have shown new developments in, for example, the study of the anterior-posterior axis in *Drosophila* (*Clark and Akam, 2016*) and the *C. elegans* cell lineage (*Sammut et al., 2015*).

Other points of discussion included the importance of studying development within the context of time and the great potential of computational modelling. Discussed also were the logistics of maintaining an idea of the overall picture without becoming too focused on a single model system. The final event of the day was an informal round table discussion where the points raised previously, and many others, were discussed at length over much wine.

Monday began with a **plenary** talk from **Matthew Freeman**, amusingly titled 'Confessions of an ex-developmental biologist', in which he described his current focus on cell signalling and the pertinence of Cell Biology to the understanding of development (*e.g. Christova et al., 2013*). Following this, the two morning sessions covered 'TISSUE AND ORGAN DEVELOPMENT' and 'DEVELOPMENTAL GENE REGULATORY NETWORKS.' I listened to **James Briscoe**'s talk on the Sonic Hedgehog morphogen gradient in the neural tube and the interesting mathematical models that his lab has used to explore the time and precision of its patterning. **Virginia Papaioannou** then spoke about the role of Tbx6 in left-right axis establishment (*Concepcion et al., 2017*).

Also in this session were complementing talks from **Eileen Furlong** (*Mikhaylichenko et al., 2018*) and **Mike Levine** (*Lim et al., 2018*) on the relationships between enhancers and promoters and how chromatin architecture regulates gene expression. After a lunch poster session, the afternoon sessions began with talks on 'MECHANISMS OF GLOBAL GENE REGULATION' and 'CELL BIOLOGY AND DEVELOPMENT'. That afternoon, I caught a talk by **Robb Krumlauf**, in which he showed some fascinating lamprey experiments which supplied further detail on the ancient interactions between retinoic acid and *Hox* genes. Following this, **Caroline Telfer** demonstrated her impressive quantity of PhD work on the upstream regulation of the *GATA* genes, and then **Pavel Tomancak** showed a combination of beautiful live imaging and computational models for serosa closure in *Tribolium castaneum* embryos. The day's closing **plenary** lecture was given by **Janet Rossant**, which included her work on dramatically increasing CRISPR efficiency in early mouse blastocysts.

The highlight of this first evening was the announcement of the **Waddington Medal** and the Waddington Lecture. The most prestigious prize awarded by the BSDB, the Waddington Medal recognises an individual who has made major contributions to developmental biology in the UK. The recipient of the award is, by tradition, kept a secret until the president of the society awards the medal. Ottoline Leyser introduced the awardee of the medal, after a short bit of suspense and the interesting insight that the last three winners of the prize have been accomplished artists. The medal was awarded to **Richard Gardner** for his pioneering work on various aspects of early mouse development from clonal lineage analysis and transplantation to axis determination (*see our blog post*).



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In his subsequent lecture, Richard Gardner detailed some of the highlights of his impressive career, punctuated by humorous anecdotes and intriguing details. For instance, he commented on the four passions of Sydney Smith (*who taught Gardner at university*): Darwin, embryology, Ming dynasty porcelain, and wine (*most developmental biologists can relate to at least three*). Gardner also acknowledged his students, his mentor Robert Edwards, and collaborators such as Mary Lyon and Martin Johnson.

After the Waddington lecture, was the **student and post-doc social** in which we were split into teams to create a development-themed piece of art. An hour of glitter, glue, and coloured card later, the products of our endeavours included a model of Waddington's epigenetic landscape, an interactive and moving model of chick somite formation, and the winning entry, a performance piece showing the injection of labelled cells into a blastocyst.

The opening **plenary** lecture on Tuesday morning was given by **Sean Carroll**. In a similar vein to Matthew Freeman, he described how pursuing his boyhood passion for snakes led him away from developmental biology and to interesting work on the evolution of proteins in snake venom. I then attended the 'EVO-DEVO' session in the morning, which ran parallel to 'STEM CELLS AND REGENERATION'. In this session, I listened to many fascinating talks, which included **Patrick Lemaire**, on his computer models of ascidian cell fate determination, **Karen Sears** on the development of several unique aspects of bat morphology, and **Miltos Tsiantis** on the evolution of leaf form and the identification of a key regulator of leaf shape (*Vuolo et al., 2016*). Finishing off the session, **Peter Holland** covered his group's work on the ParaHox gene, *Pdx*, in a variety of different bilaterian species.

A second lunch poster session followed, and then the afternoon programming kicked into gear. These were talks grouped under the themes of 'POSITIONAL INFORMATION' and 'CELL FATE'. In the former, **Lee Niswander** gave a talk on neural tube closure defects (*Li et al., 2018*), and in the latter, **Olivier Pourquie** spoke about the importance of using cell culture and iPSCs, which his lab used to generate human pre-somitic mesoderm-like cells. In a talk that very much followed the themes of the conference, **James Sharpe** acknowledged the 50th anniversary of Lewis Wolpert's proposal of the French Flag Problem

and re-interpreted the potential solutions to the problem through his data indicating that digits are patterned by a Turing mechanism (*Green and Sharpe, 2015*).

The final order of business for the day was the BSDB's annual **general meeting**. This was an interesting insight into the inner workings of the society, which involved the election of new members to the committee and the presentation of committee officers' reports.

After the wrap up of the AGM was the **conference dinner and party**. This was a celebration worthy of marking 70 years of the BSDB - complete with balloons, good food, and plenty of wine. The dinner was topped off with cake, cut by four former presidents of the BSDB.

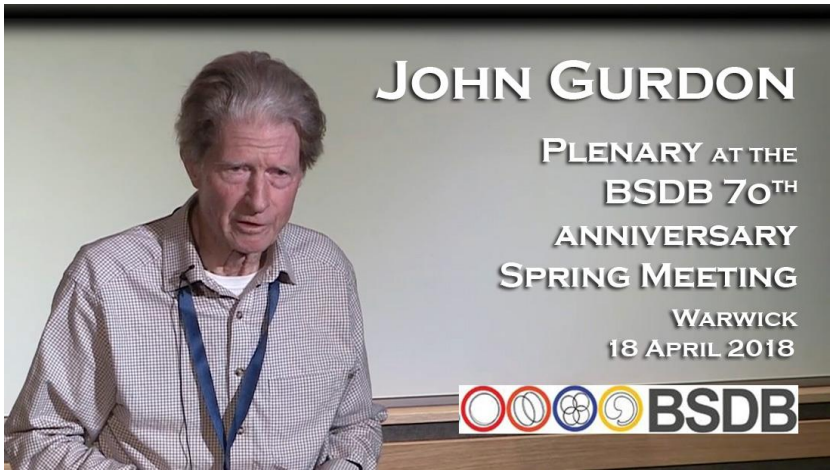
Also announced were the winners of the post-doc and PhD **poster prizes** (*see our blog post*), as well as the winners of the **advocacy writing competition**, which was initiated specifically for the 70th anniversary of the BSDB and saw submissions from students and post-docs on the history and future of the BSDB (*see our blog post*). Fuelled by the great atmosphere, and likely a bit of wine, the dancing began. It was a great experience to see everyone, at all career stages, let loose and enjoy themselves. Particularly popular were the **Developmental Biology-themed raps** (*to listen go to our blog post*), written and performed by Jerry aka **Gerald H Thomsen PhD**, and produced and mixed by **Philip Larsen**.. Overall, it was an excellent and celebratory evening.

Gerald Thomsen, Josh Brickman and Philip Larsen

The final morning of the meeting began with a **plenary** lecture from **Ottoline Leyser**. She spoke about her work with the plant hormone strigolactone, and its role in regulating the plasticity of branching, and the self-organising auxin network in plants (*Ligerot et al., 2017*).The enthralling lecture was enough to make anyone want to become a plant biologist. This was followed by two further plenary lectures from **Connie Eaves**, on the early haematopoietic cell lineage in humans (*Sawai et al., 2016*), and **Edith Heard**, on the role of X-chromosome chromatin architecture and its relationship to *Xist* and X-inactivation (*Galupa and Heard, 2018*). Then awarded the Cheryll Tickle Medal was awarded to **Christiana Ruhrberg** (*see our blog post*) by Cheryll Tickle herself. The Cheryll Tickle Medal is given to a mid-career, female scientist for her outstanding achievements in developmental biology. Christiana Ruhrberg then gave a great lecture on her scientific career so far.

www.youtube.com/watch?v=kr_dtuS6L9A

Of particular interest to me was how Ruhrberg neatly combined her early career work in neurogenesis and vasculogenesis to form the focus and direction of her group as a PI, working on the interplay between these two processes. Nicely linking in with the historical theme of the meeting, Ruhrberg noted that she was the first to have ever seen the current BSDB logo (*which shows the progression of embryonic development*), as the creator of the logo, Jeff Christiansen, was staying at her house when he designed it (*see our blog post*). The final lecture of the meeting was given by **John Gurdon**, on the stability and reversal of gene expression in development.



www.youtube.com/watch?v=cJgDCVrdfwA

This was my first BSDB meeting and it was overall an excellent experience. It showcased cutting-edge science and a great community, the strength of which was demonstrated by the creation of a scientific genealogy, which used pins and thread to plot mentor and mentee relationships as part of a huge interconnected network of developmental biologists.

Weaving pedigree networks: Eric Wieschaus, David Ish-Horowicz, Claudio Stern, Austin Smith

I would like to take this opportunity to thank the BSDB for the **conference grant** that enabled me to attend. The meeting gave me a new appreciation for the history of Developmental Biology and strengthened my excitement to be a part of its future. Here's to the next 70 years of the BSDB!

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At the 2018 Spring Meeting in Warwick, the PhD and PostDoc representatives organised a series of events for young researchers. These ranged from asking questions such as “What is the secret to success?” through to some crafty synthetic biology and ending with the award of the 2018 BSDB writing competition.

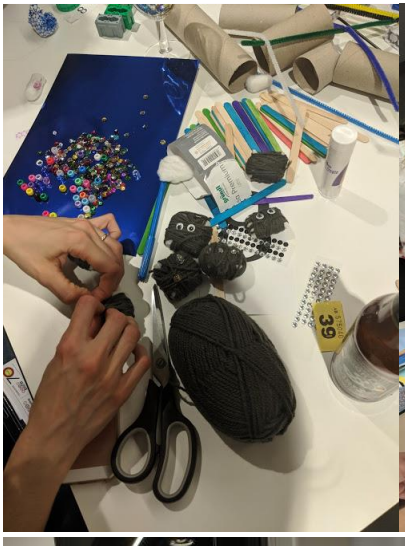
Career workshop

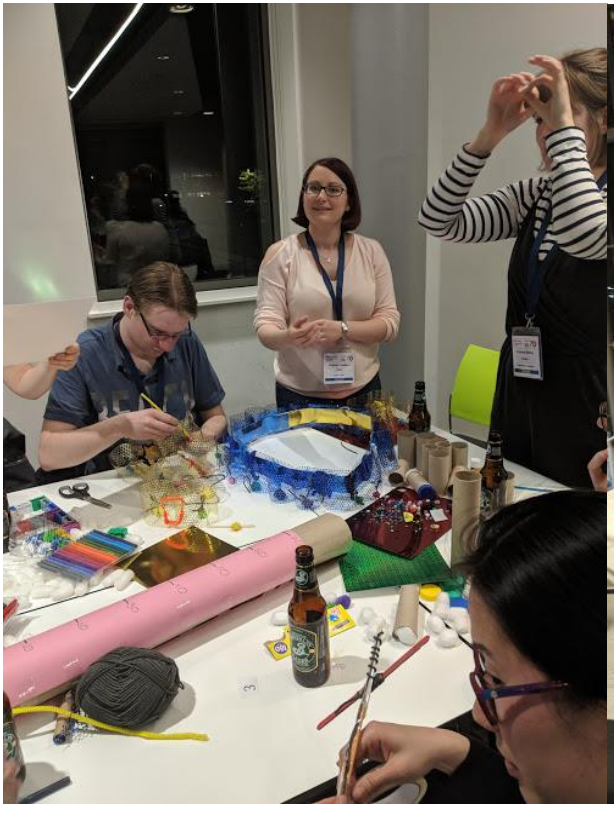
The career workshop kicked off the BSDB 70th birthday celebrations, with a topic focused on ‘building resilience and overcoming obstacles’. The idea was to utilise the knowledge and experience of the successful developmental biologists attending the meeting to give plenary and session talks. In total we had 18 tables, lead by Ottoline Leyser, Jordan Raff, Robb Krumlauf, Maria Leptin, Steve Wilson, Matthew Freeman, Fiona Watt, Magdalena Zernicka-Goetz, Jan Traas, Judith Kimble, Henrik Semb, Anne Ferguson-Smith, Patrick Lamaire, Jean Paul Vincent, Kate Storey, Austin Smith and Yohanns Belliache.

We wanted to have honest and open discussions about how to succeed in academia. ‘What is the secret to success, if there is any?!’. It is not very often you get to have opportunity to pick the brains of the leaders in your area of interests. This led to an afternoon of lively discussions.

Student/postdoc social

The format of the last couple of student/postdoc socials have been designed to get people to interact with people other than their lab mates! This year was no exception. This year’s activity was for randomly assigned teams to build models, within 1 hour, of any one of the following themes: fertilisation, plant development, somitogenesis, cell-fate determination and evo-devo.
We will let the pictures do the talking, but we were blown away by how amazing the models were and how much effort people put into making them. Megan Davey and Rita Sousa-Nunes judged the competition but had a hard time choosing winners since the models were excellent.





We are grateful to all the exhibitors who kindly donated prizes: Abcam, Class Learning, Proteintech, Philosophical Transactions B and Biographical Memoirs, The Company of Biologists, Stratech, 2BScientific and Indigo Scientific.

2018 BSDB Writing Competition

Finally, the student/postdoc events ended with the announcement of the 2018 Writing Competition. As part of the BSDB 70th anniversary celebrations, we initiated a writing competition where first prize was a trip to the 77th Annual Society of Developmental Biology meeting (Portland, Oregon, USA). Katherine Brown, Aidan Maartens, Ottoline Leyser and Jonathan Slack judged the competition, selecting Daniyal Jafree as the winner.

So this year, is the final year for us organising these events. It has been a blast. Thank you all for making it such a wonderful and memorable experience. Please don't forget to contact your future student (students@bsdb.org) or postdoc (postdocs@bsdb.org) reps for any comments or suggestions regarding the British developmental biology community.

See here for more pictures of the student/postdoc events.

Michelle and Alex