BSDB BSCB gs the geneticssociety

joint meeting including the **British Society for Cell Biology**
the **British Society for Developmental Biology**
and the **Genetics Society** to be held on
the **2nd-5th of April 2016** at the
University of Warwick with talks by

Bonnie Bassler
Marisa Bartolomei
David Baulcombe
Xiaowei Zhuang

Manuel Théry, John Briggs
Mathias Lutolf, Julie Ahringer
Didier Trono, Marika Charalambous
Jerne Ule, Stephen Goodwin, Arantza Barrios
David Traver, Sebastian Deindl, Dirk Schubeler
Thijn Brummelkamp, Marvin Tanenbaum
Vincent Colot, David Tollervey
Reiner Schulz, Marella de Brujin
Logan Kistler, Sam Reck-Peterson
Bruce Goode, Eamonn Mallon
Ulli Gruneberg, Rebecca Oakey
Nipam Patel, Linda Holland, Anna Akhmanova
Tarun Kapoor, Ralf Sommer, William Jeffery
Laure Bally Cuif, Joan Barau, Elizabeth Murchison
Angela Hay, Myriam Hemberger, Laura Johnston
Iain Cheeseman, Michael Goodisman, Axel Visel, Steve Goldman

the organisers are

Julie Welburn, Andrew Carter, Andy Oates
Henry Roehl, Rebecca Oakey, Marika Charalambous

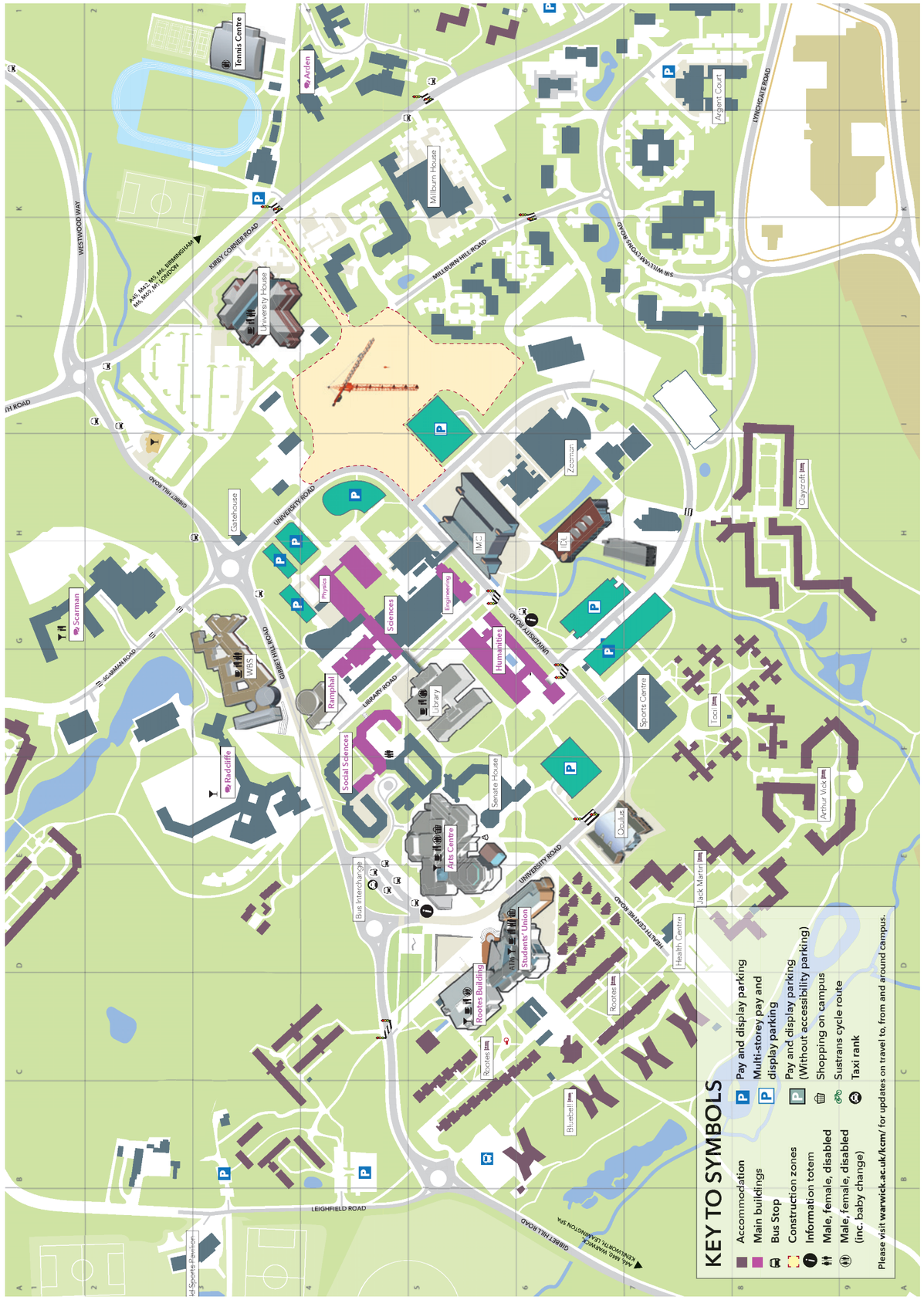
for more information and to register see

www.bscb-bsdb-gensoc-meetings.co.uk

The Company of Biologists

image courtesy of Susie Surfleet & Fiona Milne (University of Sheffield)

CAMPUS MAP



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ORGANISERS

Scientific Organising Committee – BSCB

Julie Welburn – Wellcome Trust Centre for Cell Biology, University of Edinburgh, Edinburgh
Andrew Carter – MRC Laboratory of Molecular Biology, Cambridge
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Josh Brickman – Danish Stem Cell Centre, University of Copenhagen, Copenhagen

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Hg3 Conferences
Events | Membership | Venue Finding

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DELEGATE INFORMATION

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General fax: +44 (0)24 7657 2661
Website: www.warwickconferences.com

Conference Registration
The Registration Desk is located in the Student Union Building on Sunday 2 April and in the Arts Centre Monday 3 – Wednesday 5 April.

The Registration Desk will be open at the following times:

Sunday 2 April	14:00 – 18:00 Student Union Building
Monday 3 April	07:30 – 20:00 Arts Centre
Tuesday 4 April	07:30 – 18:00 Arts Centre
Wednesday 5 April	08:00 – 12:00 Arts Centre

On registering, you will receive a name badge, conference programme and abstract book. Name badges must be worn for the duration of the meeting and are colour coordinated as below:

- Full residential delegates – Clear Badge Holder
- Non residential delegates – White Badge Holder
- Exhibitors – Red Badge Holder
- Conference organisers – Purple Badge Holder
- Speakers – Black Badge Holder

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 or key card, which gives access both to your room and the entry door to the residence. On the day of departure, keys 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 at the reception to gain access. See http://www2.warwick.ac.uk/services/sport/ 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 Mead Gallery, Arts Centre. 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 2 April – Dinner 18:00 - 19:00 – Rootes Restaurant, Rootes Building

Student and Post Doc Social – 21:00 Panorama Suite, Rootes Building
An entertaining social programme is being planned by the BSCB/BSDB/Genetics Society student representatives. In addition to the networking opportunities offered by the student's symposium, there will be a number of events specifically for students happening during the meeting schedule.

Monday 3 April – Dinner 19:00 – 20:00 – Rootes Restaurant, Rootes Building

Hooke Medal Talk 16:45 – 17:30
Waddington Medal Talk 20:00 – 21:00

Self service dinner will be served at 19:00 in the Rootes Restaurant for all residential delegates before the Waddington Medal Talk.

Monday 3 April – Drinks and Poster Session – 17:30 – 19:00 – Mead Gallery, Arts Centre
There will be a drinks and poster session on Monday which will provide the opportunity to meet with colleagues and enjoy a complimentary bottle of beer, glass of house wine or soft drink.

Tuesday 4 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.

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.

BSCB/BSDB/Genetics Society Spring Meeting – Scientific Programme 2017

Sunday 2 April 2017

13.00 - 15.00	Joint Officer's Meeting - National Grid Room, Arts Centre
14.00 – 18.00	Registration - Students Union Building
15.00 – 16.00	BSCB Committee Meeting - Ensemble Room, Arts Centre BSDB Committee Meeting - National Grid Room, Arts Centre Genetics Society Committee Meeting - Humanities 0.03, Humanities Building
16.00 – 18.00	Roundtable Careers Workshop - Studio, Arts Centre
18.00 – 19.00	**Dinner** - Rootes Restaurant, Rootes Building
19.00 – 20.00	**Plenary Session** - Main Lecture Theatre **PL01 Bonnie Bassler - Princeton University, Princeton, USA** Bacterial Quorum Sensing and its Control
20.00 - 21.00	**The Genetics Society Medal Lecture 2017** - Main Lecture Theatre Chair: Rebecca Oakey **PL02 Marisa Bartolomei - University of Pennsylvania Perelman School of Medicine, Philadelphia, USA** Epigenetic Regulation of Genomic Imprinting in Development and Disease
21.00 onwards	**Student and Post Doc Social/Drinks Reception** - Panorama Suite, Arts Centre

Monday 3 April 2017

07.30 – 20.00	Registration – Arts Centre		
07.30 - 09.00	**Breakfast – Rootes Restaurant, Rootes Building**		
Session 1 09.00 – 12.30	**Epigenetics** Main Lecture Theatre Chair: Anne Ferguson-Smith	**Neurons, Networks and Behaviour** Woods Scawen Lecture Theatre Chair: Bill Harris	**New Methods to Study Cell Biology** Cinema Chair: Alan Lowe
09.00 - 09.30	**S01 Julie Ahringer - University of Cambridge, Cambridge** Genome architecture and transcription regulation in C. elegans	**S05 Gregory Jefferis - MRC Laboratory of Molecular Biology, Cambridge** Development, Structure and Function of Neural Circuit Motifs	**S10 Manuel Thery - CEA Hospital Saint Louis, Paris** Microtubule rejuvenation
09.30 - 09.45	**O1 Miguel Branco - Blizard Institute, London** Regulation of LINE1 retrotransposons by 2-oxoglutarate-dependent dioxygenases	**O5 Annick Sawala - The Francis Crick Institute, London** The sex of specific neurons controls female body growth in Drosophila	**O7 Faraz Mardakheh - Barts Cancer Institute, London** Rapid profiling of interactome dynamics by analysis of protein-protein colocalisations on a global scale
09.45 - 10.15	**S02 Didier Trono - EPFL, Switzerland** Mobile elements, polydactyl proteins and the genesis of human-specific regulatory networks	**S06 Laure Bally Cuif - Institut Pasteur and CNRS, France** Spatio-temporal control of neural stem cell activity and pallium construction in the teleost zebrafish	**S11 John Briggs - MRC Laboratory of Molecular Biology, Cambridge** Determining structures of coated vesicles in vitro and in cells using cryo-electron tomography
10.15 - 10.30	**O2 Marika Charalambous - QMUL, London** Regulation of metabolism through imprinted genes	**S07 Stephen Goodwin - University of Oxford, Oxford** Neural circuitry coordinating male copulation	**S12 Mathias Lutolf - EPFL, Institute of Bioengineering, Switzerland** Bioengineered microenvironments to dissect stem cell self-organization
10.30 - 10.45	**O3 Antonius Plagge - University of Liverpool, Liverpool** Analysis of a knock-out mouse model for the microcephaly-associated Trappc9 gene and its epigenetic regulation by genomic imprinting		
10.45 – 11.15	**Refreshment Break and Exhibition Viewing Time** - Mead Gallery, Arts Centre		
11.15 - 11.45	**S03 Dirk Schubeler - Friedrich Miescher Institute for Biomedical Research, Switzerland** Reading and writing DNA methylation	**S08 Gilles Laurent - Max Planck Institute for Brain Research, Germany**	**S13 Sebastian Deindl - Uppsala University, Sweden** Structural Insights into the Autoinhibition of the Oncogenic Human Chromatin Remodeler Alc1
11.45 - 12.00	**O4 Katy McLaughlin - Institute of Genetics and Molecular Medicine, Edinburgh** Higher-order chromatin structure in the ground state of pluripotency	**O6 Sarah Foster - University of Cambridge, Cambridge** Chemical and mechanical signals interact to direct axon growth	**O8 Katja Kostelnik - QMUL, London** 'Car Sharing' – Intracellular Co-Trafficking of Junctional Adhesion Molecule C and its Neighbouring Proteins in Endothelial Cells

Monday 3 April 2017 *continued*

12.00 - 12.30	**S04 Vincent Colot - Institut de Biologie de l'Ecole Normale Supérieure, Paris** Transgenerational Epigenetics, transposable elements and heritable phenotypic variation	**S09 Arantza Barrios - UCL, London** Glia developmental plasticity couples behaviour to reproductive needs	**S14 Thijn Brummelkamp - NKI, Amsterdam** Haploid Genetics to study disease-related networks
12.30 – 14.00	**Lunch** - Mead Gallery, Arts Centre **Posters/Exhibition Viewing Time - Odd Poster Numbers** - Mead Gallery, Arts Centre		
Session 2 **14.00 – 15.30**	**Stem Cells in Vivo** Main Lecture Theatre Chair: Phil Jones	**Newly Tractable Systems** Wood Scawen Lecture Theatre Chair: Paul Hurd	**Nucleic Acids** Cinema Chair: Victoria Cowling
14.00 - 14.30	**S15 David Traver - UCSD, San Diego, USA** Ontogeny of hematopoietic stem cells	**S17 Reiner Schulz - King's College London, London** Exploring the epigenomic archive of environmental exposure preserved in the wood of forest trees	**S19 Marvin Tanenbaum - Hubrecht Institute, Netherlands** Dynamics of Translation of Single mRNA Molecules In Vivo
14.30 - 14.45	**O9 Nicolas Loyer - University of Dundee, Dundee** Drosophila neural stem cells are polarised by their daughter cells	**O11 Emily Hawkes - John Innes Centre, Norwich** Conserved long non-coding RNAs in the switch to flowering	**S20 David Tollervey - University of Edinburgh, Edinburgh** Nuclear RNA decay pathways aid rapid remodeling of gene expression in yeast
14.45 - 15.00	**S16 Marella de Brujin - University of Oxford, Oxford** Elucidating the birth of blood stem cells	**S18 Richard Buggs - Royal Botanical Gardens, Kew** Rising from the ashes: can genomic research help tree populations to recover from epidemics?	
15.00 - 15.15			**S21 Jerne Ule - The Francis Crick Institute, London** Exon Junction Complex inhibits recursive splicing of canonical exons
15.15 - 15.30	**O10 Andrew Renault - University of Nottingham, Nottingham** Quantifying the effective range and modelling in vivo signals regulating germ cell migration	**O12 Liisa Parts - University of Oxford, Oxford** Prevalence of agrochemical resistance-associated natural variation in wild populations of C. elegans	
15.30 – 16.00	**Refreshment Break and Exhibition Viewing Time** - Mead Gallery, Arts Centre		
16.00 – 16.45	**The Mendel Medal Lecture 2017** - Main Lecture Theatre Chair: Wendy Bickmore **PL03 David Baulcombe - Cambridge University, Cambridge** When genomes meet: RNA, epigenetics and the phenotypes of hybrid plants		
16.45 - 17.30	**Hooke Medal Lecture** - Main Lecture Theatre Chair: Anne Ridley **PL04 Ewa Paluch - UCL, London** Cell morphogenesis across scales, from molecular processes to cell-scale behaviours		
17.30 – 19.00	**Drinks Reception and Poster Viewing - Even Poster Numbers** - Mead Gallery, Arts Centre		
19.00 - 20.00	**Dinner** - Rootes Restaurant, Rootes Building		
20.00 – 21.00	**Waddington Medal Lecture** - Main Lecture Theatre		

Tuesday 4 April 2017

07.30 – 18.00	Registration – Arts Centre		
07.30 - 09.00	**Breakfast** - Rootes Restaurant, Rootes Building		
Session 3 **09.00 – 12.30**	**Evodevo** Main Lecture Theatre Chair: Michael Akam	**Cytoskeleton and Transport** Woods Scawen Lecture Theatre Chair: Simon Bullock	**Newly Tractable Systems** Cinema Chair: Paul Hurd
09.00 - 09.30	**S22 Angela Hay - Max Planck Institute for Plant Breeding Research, Germany** Explosive seed dispersal	**S27 Bruce Goode - Brandeis University, USA** Mechanisms of microtubule-actin coordination: a journey from yeast to mammals	**S31 Eamonn Mallon - University of Leicester, Leicester** The power behind the throne: epigenetics in social insects
09.30 - 09.45	**S23 Nipam Patel - UC Berkeley, USA** Germline regeneration in the crustacean, Parhyale hawaiensis	**O15 M McClintock - MRC Laboratory of Molecular Biology, Cambridge** Localising mRNA drives assembly of in vitro reconstituted mRNPs and stimulates their transport through activation of cytoplasmic dynein	**O19 Anna Piliszek - Institute of Genetics and Animal Breeding PAS, Poland** Primitive endoderm and epiblast specification during preimplantation development of rabbit embryos
09.45 - 10.00		**S28 Sam Reck-Peterson - University of California San Diego, USA** Regulation of human cytoplasmic dynein revealed through a proteomics approach	**S32 Mike Goodisman - School of Biological Sciences, Atlanta, USA** DNA Methylation in Social Insects
10.00 - 10.15	**S24 Linda Holland - University of California San Diego, USA** Hybrids Between the Two Most Phylogenetically Distant Genera of Cephalochordates Give Insights into the Evolution of Pharyngeal Development		
10.15 - 10.30		**O16 Francisca Nunes de Almeida - UCL, London** Cdc42 controls epithelial polarity by coordinating cortical polarization and plasma membrane specialization through Par6	**O20 Bryony Leeke - The Francis Crick Institute, London** Using metatherians to elucidate the evolution of mammalian epigenetic pathways
10.30 – 11.00	**Refreshment Break and Exhibition Viewing Time** - Mead Gallery, Arts Centre		
			Mechanisms in Gene Expression Cinema Chair: Irina Stancheva
11.00 - 11.30	**S25 Ralf Sommer - Max Planck Institute for Developmental Biology, Germany** The mechanisms of developmental plasticity: from switch genes and epigenetics to the interplay of organisms and their environment	**S29 Anna Akhmanova - Utrecht University, Netherlands** Regulation of microtubule minus-end dynamics at spindle poles by microcephaly-related proteins ASPM and katanin	**S33 Axel Visel - Lawrence Berkeley National Lab, California, USA** Distant-Acting Enhancers in Development, Disease, and Evolution
11.30 - 11.45	**O13 Matthew Benton - University of Cologne, Cologne** The shortest germ: Evolution of an	**O17 Alistair Hume - University of Nottingham, Nottingham** Rab27a co-ordinates actin-dependent long-	**O21 Emma Farley - UCSD, La Jolla, USA** Regulatory principles governing enhancer function

Tuesday 4 April 2017 *continued*

	extreme short-germ mode of segmentation within the beetles	range organelle transport by integrating the activity of motors and track assembly proteins	
11.45 - 12.00	**S26 William Jeffrey - University of Maryland, College Park Maryland, USA** From Genotype to Phenotype: Evolution and Development of Cavefish Eye Loss	**S30 Tarun Kapoor - The Rockefeller University, New York, USA** Examining how nanometer-sized proteins assemble dynamic micron-sized structures needed for successful cell division	**O22 Rebecca Oakey - King's College London, London** Transcription of intragenic CpG islands and their associated epigenetic marks as regulators of tissue- and developmental-stage specific transcription of related host genes
12.00 - 12.15			**O23 Maria Gomez Lamarca - University of Cambridge, Cambridge** CSL DNA-binding dynamics are a major point of regulation in determining the functional consequences of Notch activation
12.15 - 12.30	**O14 Neal Anthwal - King's College London, London** Break down of Meckel's cartilage provides clues to the evolution of mammals	**O18 Anthony Roberts - Birkbeck College, London** Switching On and Off the Motor Activity of Intraflagellar Transport Dynein	**O24 Evi Vlassaks - University of Manchester, Manchester** Exploiting Notch regulation to probe alternative mechanisms of TSC signaling
12.30 – 14.30	**Lunch** - Mead Gallery, Arts Centre **Poster/Exhibition Viewing Time** – Mead Gallery, Arts Centre		
14.30 – 15.30	BSDB AGM - Main Lecture Theatre	Genetics Society AGM - Cinema	BSCB AGM - Woods Scawen Lecture Theatre
15.30 – 17.00	**PhD/Postdoc Symposium** - Main Lecture Theatre		
15.30 - 15.45	**O25 Gautam Dey - MRC Lab for Molecular Cell Biology, London** Binary fission: from archaea to unicellular eukaryotes		
15.45 - 16.00	**O26 Alice Sherrard - Cellular and Molecular Medicine, Bristol** Imaging chromatin dynamics reveals a novel mechanism for nuclear organisation after cell division		
16.00 - 16.05	**FT01 M Javed - University of Veterinary and Animal Sciences, Pakistan** Genomic Relation of Human Aggression Behavior in Convicted Offenders for Physical Assault and Terrorism		
16.05 - 16.10	**FT02 Priscila Ramos-Ibeas - The University of Nottingham, Nottingham** Capturing emerging pluripotency in the pig early embryo by modulation of WNT and ERK signalling pathways		
16.10 - 16.15	**FT03 Edward Tunnacliffe - UCL, London** Gene family expansion allows diversification of transcriptional bursting dynamics		
16.15 - 16.20	**FT04 Valerie Bentivegna - University of Dundee, Dundee** The biomechanics of cells and the 3D structures they form: novel tools for mechanobiology		
16.20 - 16.25	**FT05 Surangi Perera - University of Cambridge, Cambridge** The Development of Olfactory Ensheathing Cells from the Neural Crest		
16.25 - 16.40	**O27 A Pardal - University of Warwick, Coventry** Chromatin-remodelling ATPase central subunits and plant defence		
16.40 - 16.55	**O28 Michelle Ware - University of Cambridge, Cambridge** Circadian-related gene expression in the suprachiasmatic nucleus of an R6/2 mouse model of Huntington's disease in response to a light pulse		

Tuesday 4 April 2017 *continued*

17.00 - 17.15	**Refreshment Break**
17.15 - 17.45	**Beddington Medal Lecture** - Main Lecture Theatre **PL05 Erik Clark** - University of Cambridge, Cambridge The evolution and development of Drosophila segment patterning
17.45 - 18.15	**Women in Cell Biology Medal Lecture** - Main Lecture Theatre Chair: Julie Welburn **PL06 Victoria Sanz Moreno** - King's College London, London Connecting actomyosin dynamics to transcriptional responses for efficient cancer cell migration and invasion
18.15 - 19.00	**Cheryll Tickle Medal Lecture** - Main Lecture Theatre **PL07 Jenny Nichols** - University of Cambridge, Cambridge
20.00 onwards	**Conference Dinner** – Panorama Suite, Rootes Building

Wednesday 5 April 2017

08.00 – 12.00	Registration – Arts Centre		
07.30 - 09.00	**Breakfast** - Rootes Restaurant, Rootes Building		
Session 4 **09.30 – 11.00**	**Mechanisms in Gene Expression** Main Lecture Theatre Chair: Irina Stancheva	**Cell Competition** Woods Scawen Lecture Theatre Chair: Eugenia Piddini	**Cell Division and Genome Stability** Cinema Chair: Jordan Raff
09.30 - 10.00	**S34 Joan Barau - Institut Curie, Paris** The novel de novo DNA methyltransferase DNMT3C protects male fertility against transposon activity	**S36 Elizabeth Murchison - University of Cambridge, Cambridge** Two transmissible cancers in Tasmanian devils	**S38 Iain Cheeseman - Whitehead Institute and Department of Biology, Cambridge, USA** Generating a dynamic kinetochore-microtubule interface
10.00 - 10.15	**O29 Minghao Chia - The Francis Crick Institute, London** A long undecodable transcript isoform mediates transcriptional repression of the NDC80 gene during early meiosis in budding yeast	**O31 C Hogan - Cardiff University, Cardiff** Differential EphA2 drives segregation and extrusion of Ras-transformed epithelial cells from normal tissues	**O33 Alexis Barr - Institute of Cancer Research, London** DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression
10.15 - 10.45	**S35 Myriam Hemberger - Babraham Institute, Cambridge** The critical role of the placenta for normal development	**S37 Laura Johnston - Columbia University Medical Center, New York, USA** Cell competition promotes bilateral symmetry through a Dilp8/Lgr3-dependent mechanism	**S39 Uli Gruneberg - University of Oxford, Oxford** Regulation of the spindle assembly checkpoint by mitotic phosphatases
10.45 - 11.00	**O30 A Zaucker - University of Warwick, Coventry** Coordinate Regulation of Development by a Shared RNA Element	**O32 Marcelo Boareto - ETH Zurich, Basel** Interplay between Notch signaling and ID proteins during adult and embryonic neurogenesis	**O34 Sarah McClelland - QMUL, London** Biased Mis-segregation of Human Chromosomes
11.00 – 11.30	**Refreshment Break** - Mead Gallery, Arts Centre		
11.30 – 12.30	**Plenary Session** - Main Lecture Theatre Chair: Andrew Carter **PL08 Xiaowei Zhuang** - Harvard University, Zhuang Lab, Cambridge, USA Illuminating biology at the nanoscale and systems scale using single-molecule and super-resolution imaging		
12.30 onwards	**Take away lunch and delegates depart**		

OTHER PROGRAMME EVENTS

Sunday 2 April – 16:00–18:00
Careers Workshop - Studio, Arts Centre

The careers workshop will consist of roundtable discussions with table leaders from academia and industry.

The confirmed table leaders can be found below:

- Aidan Maartens – The Node manager
- Ben Steventon – Henry Dale Fellow, Department of Genetics, University of Cambridge
- Georgina Mackenzie – Science Portfolio Adviser in the Neuroscience and Mental Health team, Wellcome Trust
- Ann Le Good – Senior editor, Nature Communications
- Mark Abthorpe – Patient Attorney, Carpmaels & Ransford
- Alicia Greated – Director of Research and Enterprise, Heriot-Watt University
- Dr Joanna Huddleston – Dept. of Business Innovation and Skills, fast track civil service
- Dr Kathryn Woodfine – Field Applications Specialist, Agilent Technologies
- Dr Victoria Sanz-Moreno – Team Leader (Women in Science), King's College London
- Hayley McCulloch – Science Teacher, Chesterton Community College

For further information on the table leaders please refer to the Careers Workshop Biography section.

SPONSORS AND EXHIBITORS

The Societies would like to thank the following organisations for their generous support of the Spring Conference 2017

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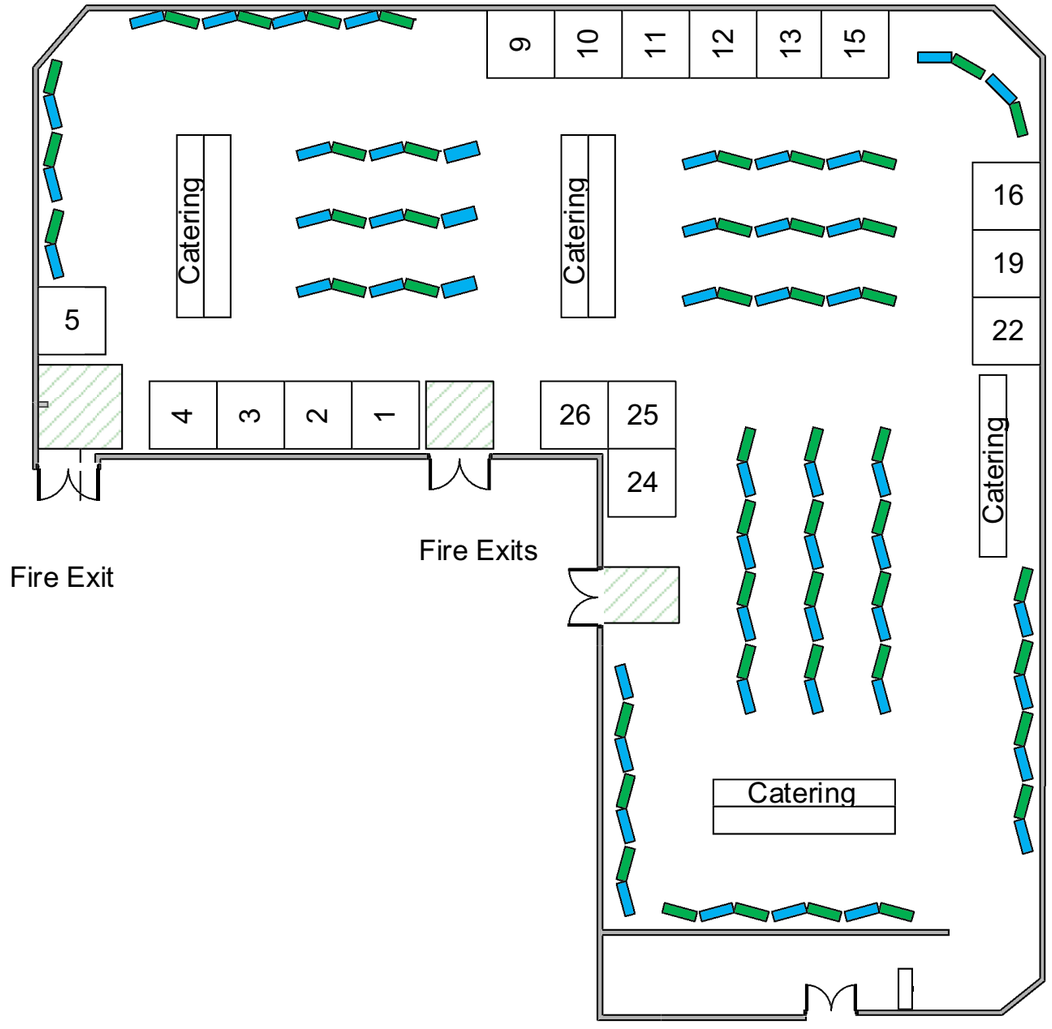

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Stand 4
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Stand 5
Stratech Scientific Ltd

Stand 9
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Stand 10
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EXHIBITOR INFORMATION

Stands 1 & 2

The Company of Biologists
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Website: http://www.biologists.com

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Stand 3

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Website: www.enzolifesciences.com

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Stand 4

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Stand 9

DMDD (Deciphering the Mechanisms of Developmental Disorders)
The Francis Crick Institute
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Telephone: 0203 7962951
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

eMouseAtlas
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IGMM
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Telephone: 0131 651 8549
Website: www.emouseatlas.org

eMouseAtlas (www.emouseatlas.org) is a web-based resource enabling visualisation of mouse embryo development. Using state-of-the-art web technology we provide full 3D embryo models with anatomy, cellular-resolution histology annotation, and the EMAGE database of spatially mapped gene and enhancer expression patterns.

Stand 11

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Stand 11

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Website: www.bitplane.com

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 12

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Stand 13

Cell Signalling Technology
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Contact Name: Davin Miller
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Website: www.cellsignal.com

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LI-COR Biosciences
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Website: www.vectorlabs.com

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OVERVIEW OF SHORT TALK 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 2 April, 2017
Plenary Session
Main Lecture Theatre 19:00 – 20:00

PL01 19:00 – 20:00
Bacterial Quorum Sensing and its Control
B L Bassler

Sunday 2 April, 2017
The Genetics Society Medal Lecture 2017
Main Lecture Theatre 20:00 – 21:00

PL02 20:00 – 21:00
Epigenetic Regulation of Genomic Imprinting in Development and Disease
M S Bartolomei

Monday 3 April, 2017
Session 1 Epigenetics
Main Lecture Theatre 09:00 – 12:30

S01 09:00 – 09:30
Genome architecture and transcription regulation in *C. elegans*
J Ahringer

O1 09:30 – 09:45
Poster Number: P059
Regulation of LINE1 retrotransposons by 2-oxoglutarate-dependent dioxygenases
L de la Rica, K C Cheng, O Deniz, **M R Branco**

S02 09:45 – 10:15
Mobile elements, polydactyl proteins and the genesis of human-specific regulatory networks
D Trono

O2 10:15 – 10:30
Regulation of metabolism through imprinted genes
M Charalambous

O3 10:30 – 10:45
Poster Number: P061
Analysis of a knock-out mouse model for the microcephaly-associated *Trappc9* gene and its epigenetic regulation by genomic imprinting
M Pulix, T Leather, K Ingram, L Livoti, P Arnaud, H Poptani, **A Plagge**

S03 11:15 – 11:45
Reading and writing DNA methylation
D Schubeler

O4 11:45 – 12:00
Poster Number: P054
Higher-order chromatin structure in the ground state of pluripotency
K A McLaughlin, I M Fliamer, H K Mjoseng, R Shukla, J P Thomson, W A Bickmore, R R Meehan

S04 12:00 – 12:30
Transgenerational Epigenetics, transposable elements and heritable phenotypic variation
V Colot

Monday 3 April, 2017
Session 1 Neurons, Networks and Behaviour
Woods Scawen Lecture Theatre 09:00 – 12:30

S05 09:00 – 09:30
Development, Structure and Function of Neural Circuit Motifs
G Jefferis

O5 09:30 – 09:45
Poster Number: P117
The sex of specific neurons controls female body growth in *Drosophila*
A Sawala, A P Gould

S06 09:45 – 10:15
Spatio-temporal control of neural stem cell activity and pallium construction in the teleost zebrafish
I Foucher, G Furlan, V Cuccioli, N Vuillemin, E Beaurepaire, C Houart, **L Bally-Cuif**

S07 10:15 – 10:45
Neural circuitry coordinating male copulation
H J Pavlou, A C Lin, M C Neville, T Nojima, F Diao, B E Chen, B H White, **S F Goodwin**

S08 11:15 – 11:45
G Laurent

O6 11:45 – 12:00
Poster Number: P110
Chemical and mechanical signals interact to direct axon growth
S K Foster, K Franze

S09 12:00 – 12:30
Glia developmental plasticity couples behaviour to reproductive needs
M Sammut, S J Cook, R C Bonnington, B Kim, L Molina, D H Hall, S W Emmons, R J Poole, **A Barrios**

Monday 3 April, 2017
Session 1 New Methods to Study Cell Biology
Cinema 09:00 – 12:30

S10 09:00 – 09:30
Microtubule rejuvenation
L Schaedel, C Aumeier, J Gaillard, **M Théry**, K Karin John

O7 09:30 – 09:45
Poster Number: P127
Rapid profiling of interactome dynamics by analysis of protein-protein colocalisations on a global scale
F Mardakheh

S11 09:45 – 10:15
Determining structures of coated vesicles in vitro and in cells using cryo-electron tomography
J A G Briggs

S12 10:15 – 10:45
Bioengineered microenvironments to dissect stem cell self-organization
M P Lutolf

S13 11:15 – 11:45
Structural Insights into the Autoinhibition of the Oncogenic Human Chromatin Remodeler Alc1
L Lehmann, S Aibara, E Marklund, A Leitner, **S Deindl**

O8 11:45 – 12:00
Poster Number: P130
'Car Sharing' – Intracellular Co-Trafficking of Junctional Adhesion Molecule C and its Neighbouring Proteins in Endothelial Cells
K B Kostelnik, V Rajeeve, I J White, P R Cutillas, T Nightingale

S14 12:00 – 12:30
Haploid Genetics to study disease-related networks
T Brummelkamp

Monday 3 April, 2017
Session 2 Stem Cells in Vivo
Main Lecture Theatre 14:00 – 15:30

S15 14:00 – 14:30
Ontogeny of hematopoietic stem cells
D Traver

O9 14:30 – 14:45
Poster Number: P159
Drosophila neural stem cells are polarised by their daughter cells
N Loyer, J Januschke

S16 14:45 – 15:15
Elucidating the birth of blood stem cells
M de Bruijn

O10 15:15 – 15:30
Poster Number: P165
Quantifying the effective range and modelling in vivo signals regulating germ cell migration
K Kenwrick, M R Owen, **A D Renault**

Monday 3 April, 2017
Session 2 Newly Tractable Systems
Woods Scawen Lecture Theatre 14:00 – 15:30

S17 14:00 – 14:30
Exploring the epigenomic archive of environmental exposure preserved in the wood of forest trees
F Rossi, **R Schulz**

O11 14:30 – 14:45
Poster Number: P138
Conserved long non-coding RNAs in the switch to flowering
E Hawkes, S Hennelly, K Sanbonmatsu, C Dean, J Irwin

S18 14:45 – 15:15
Rising from the ashes: can genomic research help tree populations to recover from epidemics?
R J A Buggs

O12 15:15 – 15:30
Poster Number: P139
Prevalence of agrochemical resistance-associated natural variation in wild populations of *C. elegans*
L Parts, A Flemming, A Woollard

Monday 3 April, 2017
Session 2 Nucleic Acids
Cinema 14:00 – 15:30

S19 14:00 – 14:30
Dynamics of Translation of Single mRNA Molecules In Vivo
T A Hoek, X Yan, D Khuperkar, S A Ruijtenberg, R D Vale, **M E Tanenbaum**

S20 14:30 – 15:00
Nuclear RNA decay pathways aid rapid remodeling of gene expression in yeast
S Bresson, A Tuck, **D Tollervey**

S21 15:00 – 15:30
Exon Junction Complex inhibits recursive splicing of canonical exons
L Blazquez, W Emmett, C Sibley, **J Ule**

Monday 3 April, 2017
The Mendel Medal Lecture 2017
Main Lecture Theatre 16:00 – 16:45

PL03 16:00 – 16:45
When genomes meet: RNA, epigenetics and the phenotypes of hybrid plants
D Baulcombe

Monday 3 April, 2017
Hooke Medal Lecture
Main Lecture Theatre 16:45 – 17:30

PL04 16:45 – 17:30
Cell morphogenesis across scales, from molecular processes to cell-scale behaviours
E K Paluch

Tuesday 4 April, 2017
Session 3 Evodevo
Main Lecture Theatre 09:00 – 12:30

S22 09:00 – 09:30
Explosive seed dispersal
A Hay

S23 09:30 – 10:00
Germline regeneration in the crustacean, *Parhyale hawaiensis*
M S Modrell, C Winchell, A Price, A Kaczmarczyk, **N H Patel**

S24 10:00 – 10:30
Hybrids Between the Two Most Phylogenetically Distant Genera of Cephalochordates Give Insights into the Evolution of Pharyngeal Development
L Z Holland, H Ono

S25 11:00 – 11:30
The mechanisms of developmental plasticity: from switch genes and epigenetics to the interplay of organisms and their environment
R J Sommer

O13 11:30 – 11:45
Poster Number: P075
The shortest germ: Evolution of an extreme short-germ mode of segmentation within the beetles
M A Benton, S Roth

S26 11:45 – 12:15
From Genotype to Phenotype: Evolution and Development of Cavefish Eye Loss
W R Jeffery

O14 12:15 – 12:30
Poster Number: P067
Break down of Meckel's cartilage provides clues to the evolution of mammals
N Anthwal, D J Urban, Z X Luo, K Sears, A S Tucker

Tuesday 4 April, 2017
Session 3 Cytoskeleton and Transport
Woods Scawen Lecture Theatre 09:00 – 12:30

S27 09:00 – 09:30
Mechanisms of microtubule-actin coordination: a journey from yeast to mammals
J Henty-Ridilla, J A Eskin, A Rankova, K Kenny, **B L Goode**

O15 09:30 – 09:45
Poster Number: P046
Localising mRNA drives assembly of *in vitro* reconstituted mRNPs and stimulates their transport through activation of cytoplasmic dynein
M A McClintock, C I Dix, K Zhang, H T Hoang, A P Carter, S L Bullock

S28 09:45 – 10:15
Regulation of human cytoplasmic dynein revealed through a proteomics approach
W B Redwine, M E DeSantis, I Hollyer, Z M Htet, P T Tran, S K Swanson, L Florens, M P Washburn, **S L Reck-Peterson**

O16 10:15 – 10:30
Poster Number: P044
Cdc42 controls epithelial polarity by coordinating cortical polarization and plasma membrane specialization through Par6
F Nunes de Almeida, R F Walther, E Vlassaks, F Pichaud

S29 11:00 – 11:30
Regulation of microtubule minus-end dynamics at spindle poles by microcephaly-related proteins ASPM and katanin
K Jiang, L Rezabkova, S Hua, Q Liu, G Capitani, R A Kammerer, M O Steinmetz, **A Akhmanova**

O17 11:30 – 11:45
Poster Number: P048
Rab27a co-ordinates actin-dependent long-range organelle transport by integrating the activity of motors and track assembly proteins
A N Hume, C L Robinson, D A Briggs, A Stainthorp, E V Sviderskaya, E Kerkhoff, T Welz, L Montoliu

S30 11:45 – 12:15
Examining how nanometer-sized proteins assemble dynamic micron-sized structures needed for successful cell division
T M Kapoor

O18 12:15 – 12:30
Poster Number: P051
Switching On and Off the Motor Activity of Intraflagellar Transport Dynein
K Toropova, M Mladenov, **A J Roberts**

Tuesday 4 April, 2017
Session 3 Newly Tractable Systems
Cinema 09:00 – 10:30

S31 09:00 – 09:30
The power behind the throne: epigenetics in social insects
E B Mallon

O19 09:30 – 09:45
Poster Number: P143
Primitive endoderm and epiblast specification during preimplantation development of rabbit embryos
A Piliszek, Z Madeja, P Pawlak, A C Konarska Diaz, B Plusa

S32 09:45 – 10:15
DNA Methylation in Social Insects
M A D Goodisman

O20 10:15 – 10:30
Poster Number: P184
Using metatherians to elucidate the evolution of mammalian epigenetic pathways
B Leeke, F Decarpentrie, S K Mahadevaiah, J Zohren, S Wood, S Horswell, M N Sangrithi, J M A Turner

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Tuesday 4 April, 2017
Mechanisms in Gene Expression
Cinema 11:00 – 12:30

S33 11:00 – 11:30
Distant-Acting Enhancers in Development, Disease, and Evolution
A Visel

O21 11:30 – 11:45
Poster Number: P100
Regulatory principles governing enhancer function
K M Olson, F Lim, C DeBoever, K M Frazer, **E K Farley**

O22 11:45 – 12:00
Transcription of intragenic CpG islands and their associated epigenetic marks as regulators of tissue- and developmental-stage specific transcription of related host genes
S Amante, M Cowley, N Barkas, S Contreras, R Schulz, **R J Oakey**

O23 12:00 – 12:15
Poster Number: P088
CSL DNA-binding dynamics are a major point of regulation in determining the functional consequences of Notch activation
M J Gomez Lamarca, J Falo Sanjuan, R Stojnic, S Abdul-Rehman, L Muresan, G Cerda-Moya, M Jones, K O'Holleran, R Kovall, S J Bray

O24 12:15 – 12:30
Poster Number: P089
Exploiting Notch regulation to probe alternative mechanisms of TSC signaling
E Vlassaks, S Woodcock, H Shimizu, M Baron

Tuesday 4 April, 2017
PhD/Postdoc Symposium
Main Lecture Theatre 15:30 – 17:00

O25 15:30 – 15:45
Poster Number: P003
Binary fission: from archaea to unicellular eukaryotes
G Dey, G Risa, S Culley, R Henriques, R Desai, B Baum

O26 15:45 – 16:00
Poster Number: P007
Imaging chromatin dynamics reveals a novel mechanism for nuclear organisation after cell division
A S Sherrard, A K Kaidi

FT01 16:00 – 16:05
Poster Number: P101
Genomic Relation of Human Aggression Behavior in Convicted Offenders for Physical Assault and Terrorism
M Javed, A Nadeem, M E Babar, W Shehzad, T Hussain, N Mukhtar, T Yaqub

FT02 16:05 – 16:10
Poster Number: P156
Capturing emerging pluripotency in the pig early embryo by modulation of WNT and ERK signalling pathways
P Ramos-Ibeas, S Withey, D Klisch, J Nichols, R Alberio

FT03 16:10 – 16:15
Poster Number: P097
Gene family expansion allows diversification of transcriptional bursting dynamics
E Tunnacliffe, A M Corrigan, J R Chubb

FT04 16:15 – 16:20
Poster Number: P131
The biomechanics of cells and the 3D structures they form: novel tools for mechanobiology
V Bentivegna, F Stewart, S Cochran, I Näthke

FT05 16:20 – 16:25
Poster Number: P78
The Development of Olfactory Ensheathing Cells from the Neural Crest
S N Perera, R Williams, D Buehler, T Sauka-Spengler, M Southard-Smith, C V H Baker

O27 16:25 – 16:40
Poster Number: P060
Chromatin-remodelling ATPase central subunits and plant defence
A J Pardal, Dr Ntoukakis

O28 16:40 – 16:55
Poster Number: P106
Circadian-related gene expression in the suprachiasmatic nucleus of an R6/2 mouse model of Huntington's disease in response to a light pulse
M Ware, K Ouk, A J Morton

Tuesday 4 April, 2017
Beddington Medal Lecture
Main Lecture Theatre 17:15 – 17:45

PL05 17:15 – 17:45
The evolution and development of Drosophila segment patterning
E Clark, A D Peel, M E Akam

Tuesday 4 April, 2017
Women in Cell Biology Medal Lecture
Main Lecture Theatre 17:45 – 18:15

PL06 17:45 – 18:15
Connecting actomyosin dynamics to transcriptional responses for efficient cancer cell migration and invasion
V Sanz-Moreno

Tuesday 4 April, 2017
Cheryll Tickle Medal Lecture
Main Lecture Theatre 18:15 – 19:00

PL07 18:15 – 19:00
J Nichols

Wednesday 5 April, 2017
Session 4 Mechanisms in Gene Expression
Main Lecture Theatre 09:30 – 11:00

S34 09:30 – 10:00
The novel *de novo* DNA methyltransferase DNMT3C protects male fertility against transposon activity
J Barau, A Teissandier, N Zamudio, S Roy, V Nalesso, Y Hérault, F Guillou, D Bourc'his

O29 10:00 – 10:15
Poster Number: P085
A long undecodable transcript isoform mediates transcriptional repression of the *NDC80* gene during early meiosis in budding yeast
M Chia, A Tresenrider, J Chen, G Spedale, E Ünal, F J van Werven

S35 10:15 – 10:45
The critical role of the placenta for normal development
M Hemberger

O30 10:45 – 11:00
Poster Number: P091
Coordinate Regulation of Development by a Shared RNA Element
A Zaucker, A Nagorska, Y Wang, S Huang, L Cooper, P Kumari, N Hecker, J Brosens, J Gorodkin, K Sampath

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Wednesday 5 April, 2017
Session 4 Cell Competition
Woods Scawen Lecture Theatre 09:30 – 11:00

S36 09:30 – 10:00
Two transmissible cancers in Tasmanian devils
E P Murchison

O31 10:00 – 10:15
Poster Number: P001
Differential EphA2 drives segregation and extrusion of Ras-transformed epithelial cells from normal tissues
S Porazinski, J de Navascues, Y Yako, W Hill, M Jones, R Maddison, Y Fujita, **C Hogan**

S37 10:15 – 10:45
Cell competition promotes bilateral symmetry through a Dilp8/Lgr3-dependent mechanism
A Kodra, C Bergantinos, K Kanakousaki, J Colombani, D Andersen, P Leopold, **L A Johnston**

O32 10:45 – 11:00
Poster Number: P112
Interplay between Notch signaling and ID proteins during adult and embryonic neurogenesis
M Boareto, D Iber, V Taylor

Wednesday 5 April, 2017
Session 4 Cell Division and Genome Stability
Cinema 09:30 – 11:00

S38 09:30 – 10:00
Generating a dynamic kinetochore-microtubule interface
I M Cheeseman

O33 10:00 – 10:15
Poster Number: P009
DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression
A R Barr, S Cooper, F S Heldt, F Butera, H Stay, J Mansfeld, B Novak, C Bakal

S39 10:15 – 10:45
Regulation of the spindle assembly checkpoint by mitotic phosphatases
U Gruneberg, D Hayward, J Bancroft

O34 10:45 – 11:00
Poster Number: P016
Biased Mis-segregation of Human Chromosomes
J T Worrall, T van Lingen, **S E McClelland**

Wednesday 5 April, 2017
Plenary Session
Main Lecture Theatre 11:30 – 12:30

PL08 11:30 – 12:30
Illuminating biology at the nanoscale and systems scale using single-molecule and super-resolution imaging
X Zhuang

OVERVIEW OF ABSTRACTS SELECTED FOR POSTERS

Cell competition

Poster Number: P1
Differential EphA2 drives segregation and extrusion of Ras-transformed epithelial cells from normal tissues
S Porazinski, J de Navascues, Y Yako, W Hill, M Jones, R Maddison, Y Fujita, **C Hogan**

Poster Number: P2
Transcriptional factors of trophectoderm (TE) and inner cell mass (ICM) in rabbit embryos obtained in vivo, compared with mice model
K Barłowska, Z Madeja, P Pawlak, A Piliszek

Cell division and genome stability

Poster Number: P3
Binary fission: from archaea to unicellular eukaryotes
G Dey, G Risa, S Culley, R Henriques, R Desai, B Baum

Poster Number: P4
Mitotic centrosome assembly in flies requires conserved domains in Cnn that assemble into micron-scale structures
Z Feng, **A Caballe**, A Wainman, S Johnson, A F M Haensele, M A Cottee, P T Conduit, S M Lea, J W Raff

Poster Number: P5
Adhesion, not cortical tension, is vital for successful cytokinesis in RPE-1 cells
C L Dix, H K Matthews, L Wolf, S McLaren, B Baum

Poster Number: P6
Dynamic tracking of centriole elongation reveals key aspects of how centrioles grow in Drosophila embryos
M G Aydogan, A Wainman, **S Saurya**, T L Steinacker, Z A Novak, J Baumbach, N Muschalik, J W Raff

Poster Number: P7
Imaging chromatin dynamics reveals a novel mechanism for nuclear organisation after cell division
A S Sherrard, A K Kaidi

Poster Number: P8
Integrin beta 3 regulates cellular senescence by activating the TGFβ pathway
V Rapisarda, M Borghesan, **A O'Loghlen**

Poster Number: P9
DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression
A R Barr, S Cooper, F S Heldt, F Butera, H Stay, J Mansfeld, B Novak, C Bakal

Poster Number: P10
Stomatin: a plasma membrane protein involved in late stages of cytokinesis
F Dona, S J Terry, U Eggert

Poster Number: P11
Untangling Polo kinase recruitment during centrosome maturation
I Alvarez Rodrigo, L Gartenmann, J W Raff

Poster Number: P12
Cell cycle regulation of Trunk Neural Crest migration
Z Alhashem, C Linker

Poster Number: P13
A robust DNA damage response to ionizing radiation ensures genome stability in planarian stem cells
S Sahu, P Abnave, N Kosaka, A Dattani, J Thompson, M Hill, A A Aboobaker

Poster Number: P14
Tip60 histone acetyltransferase targeted small molecule inhibitor (TH1834) induces genomic instability and apoptosis in breast cancer but not normal cells
A McGuire, A Shalaby, O Kalinina, E Holian, M Webber, M Scobie, L Eriksson, E Bourke, M J Kerin, **J A L Brown**

Poster Number: P15
Parallel deubiquitylase family screens identify OTUD6B and JOSD2 as regulators of KIFC1/HSET expression and centrosome clustering in breast cancer cells
A B Fielding, D Sabat-Pospiech, I A Prior, J M Coulson

Poster Number: P16
Biased Mis-segregation of Human Chromosomes
J T Worrall, T van Lingen, **S E McClelland**

Poster Number: P17
Cell size regulation in Drosophila sensory organ precursor asymmetric cell divisions
N Ramkumar, N Rodrigues, B Baum

Poster Number: P18
A new tool for identifying substrates of Aurora kinases
J Deretic, A R Kerr, T Ly, J P Welburn

Cytoskeleton and transport

Poster Number: P19
A link between planar polarity and staircase-like bundle architecture in hair cells
A Tadenev, N Devanney, M Cayouette, **B Tarchini**

Poster Number: P20
Regulation of microtubule function in endothelial cells
K Naylor, A Lampropoulou, J Brash, C Raimondi, C Ruhrberg

Poster Number: P21
Cooling evokes spatial and functional rescue of vascular alpha 2C-Adrenoceptors: Role of ROS, Rho and filamin
K Issa, M Fardoun, **A Eid**

Poster Number: P22
Paracrine-mediated invasion induced by centrosome amplification
T Arnandis, V Rajeeve, C H Brennan, P R Cutillas, S A Godinho

Poster Number: P23
Ciliopathy protein TMEM67 regulates laminin-dependent cell migration via formation of the perinuclear actin cap
A Toynbee, A Barker, K Curry, B Meadows, H Dawe

Poster Number: P24
The Exocyst component EXOC4 is required to position the centrosome during primary cilium biogenesis
L Adams, C Horton, I Jourdain, H Dawe

Poster Number: P25
Investigating biomechanical forces in zebrafish brain morphogenesis
C L Bromley, C Schwayer, D J Kelly, C P Heisenberg, D M Owen, J Clarke

Poster Number: P26
How human cytoplasmic dynein-1 can be auto-inhibited and activated
H E Foster, K Zhang, A P Carter

Poster Number: P27
A change in the polarity of a contractile actomyosin network underlies behaviourial change during Drosophila morphogenesis
P Pulido Companys, M Bischoff

Poster Number: P28
A Novel GTPase System Regulates β-Catenin Nuclear Transport in Development and Disease
J N Griffin, F del Viso, A R Duncan, A Robson, S Kulkarni, K J Liu, M K Khokha

Poster Number: P29
Centrosome amplification drives nuclear deformability and translocation during 3-D cell migration
P M Monteiro, S A Godinho

Poster Number: P30
Fission Yeast Sec3 Bridges the Exocyst Complex to Exo- and Endocytosis
C G Horton, L Adams, I Jourdain

Poster Number: P31
Subcellular dynamics and genetic regulation of dense core granule compartment formation and maturation using live-cell imaging of Drosophila secondary cells
B Kroeger, F Castellanos, M Wainwright, S Redhai, D Goberdhan, **C Wilson**

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‘Exosome signatures’ as biomarkers for centrosome-targeted therapy in pancreatic ductal adenocarcinoma (PDAC)
S D Adams, T Arnandis, P Monteiro, H M Kocher, S A Godinho

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The role of actomyosin in the transition from migratory to constrictive cell behaviour during Drosophila abdominal morphogenesis
A Norris, M Bischoff

Poster Number: P34
Regulation of E-cadherin endocytosis downstream of p120 catenin
J Greig, N Bulgakova

Poster Number: P35
The molecular basis determining organ accessibility: systemic versus local growth factors
K S Stapornwongkul, J P Vincent

Poster Number: P36
Molecular mechanisms regulating human CENP-E and chromosome movement in mitosis
T Legal, J Welburn

Poster Number: P37
Orchestrated patterning of a group of cells: the fly ommatidium as a case study
L Blackie, M Tozluoglu, S Banerjee, Y Mao, F Pichaud

Poster Number: P38
The family specific α4 helix of the kinesin-13, MCAK, is critical to microtubule end recognition
J T Patel, H R Belsham, A J Rathbone, B Wickstead, C Gell, **C T Friel**

Poster Number: P39
Four-stranded mini microtubules formed by Prosthecobacter BtubAB show dynamic instability
X Deng, G Fink, T A M Bharat, S He, D Kureisaite-Ciziene, J Löwe

Poster Number: P40
An actomyosin ring allows for differential release of pro-inflammatory and pro-haemostatic molecules from endothelial cells
C L Robinson, J J McCormack, W Grimes, I J White, L P Cramer, D F Cutler, T D Nightingale

Poster Number: P41
Radixin Mediates E-cadherin Localisation and Acinar-like Morphogenesis of Prostate Cancer Spheroids
J Clucas, P Riou, F Miralles, P Parker, **F Valderrama**

Poster Number: P42
Characterising intracellular trafficking and ubiquitylation of Junctional Adhesion Molecule C (JAM-C)
A R Barker, I J White, M Aurrand-Lions, S Nourshargh, T Nightingale

Poster Number: P43
Mutational analysis of the regulation of Notch receptor trafficking and signalling in Drosophila melanogaster
Z Huang, H Shimizu, M Baron

Poster Number: P44
Cdc42 controls epithelial polarity by coordinating cortical polarization and plasma membrane specialization through Par6
F Nunes de Almeida, R F Walther, E Vlassaks, F Pichaud

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Localising mRNA drives assembly of in vitro reconstituted mRNPs and stimulates their transport through activation of cytoplasmic dynein
M A McClintock, C I Dix, K Zhang, H T Hoang, A P Carter, S L Bullock

Poster Number: P47
Assembly Mechanisms of Dynein Motors
G Mali, M Keighren, A von Kriegsheim, A Jarman, P Mill

Poster Number: P48
Rab27a co-ordinates actin-dependent long-range organelle transport by integrating the activity of motors and track assembly proteins
A N Hume, C L Robinson, D A Briggs, A Stainthorp, E V Sviderskaya, E Kerkhoff, T Welz, L Montoliu

Poster Number: P49
Dual nucleotide recognition underlies tip-binding specificity of mammalian EB proteins
D Roth, B P Fitton, **A Straube**

Poster Number: P50
Location, location, location: PKD2 in the cilium prevents renal cyst formation
R V Walker, J L Keynton, D T Grimes, M Knight, D P Norris

Poster Number: P51
Switching On and Off the Motor Activity of Intraflagellar Transport Dynein
K Toropova, M Mladenov, **A J Roberts**

Poster Number: P52
Unravelling the roles of kinesin-1 during neuronal growth and maintenance
Y T Liew, A Prokop

Poster Number: P175
GSK3 roles during murine neural crest cell migration
A Lopez Muñoz, S Gonzalez Malagon, K Liu

Epigenetics

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Investigating the role of lysine acetyltransferase cbp-1 in regulating the lifespan of Caenorhabditis elegans
A R Guillermo, K Chocian, A Woollard

Poster Number: P54
Higher-order chromatin structure in the ground state of pluripotency
K A McLaughlin, I M Fliamer, H K Mjoseng, R Shukla, J P Thomson, W A Bickmore, R R Meehan

Poster Number: P55
The role of chromatin helicase homolog Lsh in de novo DNA methylation during mouse embryonic development
A C Revuelta, H K Mjoseng, L Duthie, J C Wills, A J Finch, D S Dunican, R R Meehan

Poster Number: P56
R-loop, regulator of gene expression by epigenetic modification
Y C Chen

Poster Number: P57
O-GlcNAcylation of Host Cell Factor is essential for Drosophila development
D Mariyappa, A T Ferenbach, D M F van Aalten

Poster Number: P58
Depletion of DNMT1 in differentiated human cells highlights key classes of dependent genes
K M O'Neill, **R E Irwin**, S J Mackin, J Loughery, D McArt, C P Walsh, A Thakur, S J Thursby, C Bertens, L Masala

Poster Number: P59
Regulation of LINE1 retrotransposons by 2-oxoglutarate-dependent dioxygenases
L de la Rica, K C Cheng, O Deniz, **M R Branco**

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Chromatin-remodelling ATPase central subunits and plant defence
A J Pardal, Dr Ntoukakis

Poster Number: P61
Analysis of a knock-out mouse model for the microcephaly-associated Trappc9 gene and its epigenetic regulation by genomic imprinting
M Pulix, T Leather, K Ingram, L Livoti, P Arnaud, H Poptani, **A Plagge**

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Identification of long non-coding RNAs in planarian pluripotent stem cells – a combined transcriptomic and epigenetic approach
D Sridhar, D Kao, Y Mihaylova, A Aboobaker

Poster Number: P176
Parp1 is required for imprint methylation maintenance
R Strogantsev, C Senner, M Hemberger

Evodevo

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Endoderm on the face: Pre-oral expansion of the primitive gut in non-teleost fishes and its evolutionary implications
M Minarik, B D Metscher, J Stundl, P Fabian, L Arias-Rodriguez, M Psenicka, R Cerny

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Conditional deletion of WT1 using Prx1-Cre causes congenital diaphragmatic hernia in mice
L Cleal, N Hastie, Y Y Chau

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Regulatory mechanism of Tbx5 in the forelimb and its adaptation in flightless birds
S Nishimoto, M P O Logan

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Staging mouse embryos harvested on embryonic day 14 (E14.5)
S H Geyer, R Wilson, F Prin, D Szumska, R Ramirez-Solis, C Tudor, J White, **J Lane**, T J Mohun, W J Weninger

Poster Number: P67
Break down of Meckel's cartilage provides clues to the evolution of mammals
N Anthwal, D J Urban, Z X Luo, K Sears, A S Tucker

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Axial skeletal development in the skate, Leucoraja erinacea
K E Criswell, M I Coates, J A Gillis

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Establishing the mechanism of the calcium wave at Drosophila egg activation
A H York-Andersen, A Berry, R Turnbull, T T Weil

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The role of hairy in the genetic regulatory network for posterior segment addition in the spider Parasteatoda tepidariorum
C Bonatto Paese, A S Schoenauer, A P M McGregor

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Analysis of the expression and function of Wnt10 in Drosophila melanogaster
M Holzem, **L Bideau**, A P McGregor

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Investigating the role of gene duplication and divergence during the evolution of spiders and other arachnids
L M Baudouin Gonzalez, D J Leite, P P Sharma, A P McGregor

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The shortest germ: Evolution of an extreme short-germ mode of segmentation within the beetles
M A Benton, S Roth

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Investigating gene regulatory network architecture and evolution in different developmental contexts
A D Buffry, S Kittelmann, G Haines-Woodhouse, I Almudi, S Arif, N Posnien, J L Gómez-Skarmeta, A P McGregor

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Telling good segmentation from bad
R Narayanan, I Lengyel, G Valentin, L Lleras Forero, S Schulte-Merker, L G Morelli, A C Oates

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Mechanisms in gene expression

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Developmental genes and impacts on human diseases
M Abu-Elmagd, P Pushparaj, M Al-Qahtani

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Highly variable penetrance of abnormal phenotypes in embryonic lethal knockout mice
T Mohun, R Wilson, S H Geyer, L Reissig, J Rose, D Szumska, E Hardman, F Prin, C McGuire, R Ramirez-Solis, J White, A Galli, C Tudor, E Tuck, C Icoresi Mazzeo, J C Smith, E Robertson, D J Adams, W J Weninger

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The Development of Olfactory Ensheathing Cells from the Neural Crest
S N Perera, R Williams, D Buehler, T Sauka-Spengler, M Southard-Smith, C V H Baker

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Seperable control of growth and patterning by Dpp in Drosophila wing precursors
R Ziukaite, C Alexandre, P Sanchez Bosch, J P Vincent, K Basler

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The regulation of embryonic stem cell differentiation by Nrf2
W Wongpaiboonwattana, M Stavridis, A Dinkova-Kostova

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The effects of exogenous expression of MyoD fusion proteins on the myogenic regulatory factors (MRFs) in fibroblasts – development of a tool to identify MRF target genes in somites of chicken embryo
A Harasani, R Stöger, T Parr, D Sweetman

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Role of the transcription factor Odd-skipped in neural arbour formation in Drosophila
K Yeoh, **C Larsen**

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Interpreting Neonatal Lethal Phenotypes in Mouse Mutants: A New Screen to Gain Insights into Gene Function and Human Diseases
E Siragher, A Green, R McLaren, C Mazzeo, M Dabrowska, E Tuck, C Tudor, E Ryder, T Mohun, A Galli

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Gremlin, gradients and ectoderm patterning
J Pegge, A J Tatsinkam, C C Rider, E Bell

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A long undecodable transcript isoform mediates transcriptional repression of the NDC80 gene during early meiosis in budding yeast
M Chia, A Tresenrider, J Chen, G Spedale, E Ünal, F J van Werven

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SEMA3E and SEMA3C Cooperate to establish vascular boundaries
A G Navarro-Aragall, A Plein, L Denti, S Chauvet, P Scambler, C Ruhrberg

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Mechanism of expression regulation by STR (microsatellite)
N Tang, S L Ma, H Y Chen

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CSL DNA-binding dynamics are a major point of regulation in determining the functional consequences of Notch activation
M J Gomez Lamarca, J Falo Sanjuan, R Stojnic, S Abdul-Rehman, L Muresan, G Cerda-Moya, M Jones, K O'Holleran, R Kovall, S J Bray

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Exploiting Notch regulation to probe alternative mechanisms of TSC signaling
E Vlassaks, S Woodcock, H Shimizu, M Baron

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The Gene Expression Database (GXD): an integrated resource for gene expression information for the developing mouse
T F Hayamizu, J H Finger, I J McCright, C M Smith, J Xu, J A Kadin, J E Richardson, M Ringwald

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A Zaucker, A Nagorska, Y Wang, S Huang, L Cooper, P Kumari, N Hecker, J Brosens, J Gorodkin, K Sampath

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Molecular logic behind Satellite cells specification in Drosophila
H Boukhatmi, S J Bray

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Cell identity switching in zebrafish hindbrain segmentation
M Addison, D Wilkinson

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E Burton, B H Jennings

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Exploring the connection between Oct4 and adhesion molecules in the pluripotent state
E Morganti, H Peradziryi, M Lowndes, J Brickman

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Gene family expansion allows diversification of transcriptional bursting dynamics
E Tunnacliffe, A M Corrigan, J R Chubb

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m6A potentiates Sxl alternative pre-mRNA splicing for robust Drosophila sex determination
M Soller, Z Bodi, E Sanchez-Moran, N Mongan, N Archer, R Fray, I Haussmann

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Regulatory principles governing enhancer function
K M Olson, F Lim, C DeBoever, K M Frazer, **E K Farley**

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Z Q Chen, N Daudet

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Establishing the chick as a model for anterior segment development
V Trejo, J Rainger

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Notch and Lmx1a: An antagonistic partnership during formation of inner ear sensory patches
Z F Mann, M Zak, V Plagnol, N Daudet

Neurons, networks and behaviour

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M Javed, A Nadeem, M E Babar, W Shehzad, T Hussain, N Mukhtar, T Yaqub

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Identifying additional protein interactors of members of the Sm protein family and the implications in Spinal Muscular Atrophy pathogenesis
L W Thompson, J E Sleeman

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Control of Cell-Cell interactions in Forebrain Morphogenesis
F A Giger, C Houart

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Microautophagy-mediated degradation of Arouser regulates lipid metabolism and feeding behaviour in Drosophila
A C Jacomin, Z Hussain, A Varga, A Jain, M Eddison, K G Moffat, T Johansen, G Juhasz, I P Nezis

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Splicing factor proline-glutamine rich (SFPQ) in motor axon development and neurodegeneration
R Taylor, T Fielding, P Gordon, C Houart

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Circadian-related gene expression in the suprachiasmatic nucleus of an R6/2 mouse model of Huntington's disease in response to a light pulse
M Ware, K Ouk, A J Morton

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Automated animal tracking and quantitative analysis of C. elegans social behaviour
S S Ding, L J Schumacher, A E Javer, R G Endres, A E X Brown

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The role of the splicing factor SFPQ in motor neuron development and degenerative disease
P M Gordon, T Fielding, S Jinu-Thomas, C Houart

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formin-like regulates terminal branching in multidendritic neurons
K Massey, C Mencarelli, T Kroecher, F Pichaud

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Chemical and mechanical signals interact to direct axon growth
S K Foster, K Franze

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Piezo Proteins in Axon Growth and Pathfinding
E K Pillai, K Franze

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Interplay between Notch signaling and ID proteins during adult and embryonic neurogenesis
M Boareto, D Iber, V Taylor

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Four-dimensional dense reconstruction of retinogenesis in zebrafish
A Azizi, Y Wan, P J Keller, W A Harris

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Neurotransmitter specification in the ventral nerve cord of Drosophila melanogaster
E E Higginbotham, H Ironfield, H Lacin, J W Truman, M Landgraf

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Studying the role of Bod1 in the development and function of iPS derived neuronal tissue
I M Porter, M Porter, L Davidson, J R Swedlow

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Optogenetic activation of mechanical forces to control neuronal polarisation
A Dimitracopoulos, R Shahapure, K Franze

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The sex of specific neurons controls female body growth in Drosophila
A Sawala, A P Gould

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Characterizing the role of foxm1 during tail regeneration in Xenopus tropicalis
D Pelzer, K Dorey

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Transcriptional regulator Nolz1 is required for establishment of dopaminergic circuitry during embryonic development
C Soleilhavoup, K Patrick, E Boobalan, P Garcao, B Brooks, L Panman

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Developing new Drosophila models to understand Dystonia pathogenesis
M Pöttler, B Hassan, P Callaerts, R Goodchild

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4D lineage based temperature sensitive embryonic lethal screen to identify regulators of left-right asymmetric neurogenesis
T W Mullan, R F Wademan, T J Felton, O Kasem, R Schnabel, R J Poole

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Sexy learning in C. elegans
L Molina-Garcia, L Lin, R J Poole, A Barrios

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A direct glia-to-neuron cell fate switch in the C. elegans male
R C Bonnington, M Sammut, L Molina Garcia, K Khambhaita, D J Elliott, B Kim, S J Cook, D H Hall, S W Emmons, A Barrios, R J Poole

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M Sammut, K Khambaita, R Bonnington, D Elliott, A Barrios, R J Poole

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T Felton, T Mullen, J Tam, J Yeung, O Kasem, A Aldabergenova, R Scnabel, R J Poole

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Role of Fgf signalling in positioning neurogenic regions in the early embryonic vertebrate brain
C Smith, E Trebert, M Pradoz Uhle, **F R Schubert**

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The role of NFκB in early neural specification of human embryonic stem (hES) cells
L M FitzPatrick, K E Hawkins, J M K M Delhove, E Fernandez, C Soldati, A Nohturfft, S N Waddington, J P Bolanos, D L Medina, T R McKay

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New methods to study cell biology

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Rapid profiling of interactome dynamics by analysis of protein-protein colocalisations on a global scale
F Mardakheh

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Invadolysin: A novel secreted metalloprotease is enriched in the extracellular vesicle fraction of human plasma
K Abhinav, M M Heck

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Functional characterisation of metachronous cell state transitions
C Mulas, A Hodgson, T Kohler, C Agley, J Nichols, K Chalut, A G Smith

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‘Car Sharing’ – Intracellular Co-Trafficking of Junctional Adhesion Molecule C and its Neighbouring Proteins in Endothelial Cells
K B Kostelnik, V Rajeeve, I J White, P R Cutillas, T Nightingale

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The biomechanics of cells and the 3D structures they form: novel tools for mechanobiology
V Bentivegna, F Stewart, S Cochran, I Näthke

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The versatile application of cultured insect cells in cell biology research and Higher Education cell biology teaching
M Figgitt

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Understanding the phenotypic and pathological outcomes of Notch mutations
G Monticone, E Foteinou, H Shimizu, M Wilkin, M Baron

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Biomimetic hydrogels to steer stem cell fate choices
K Chalut, C Agley, M Segel, R Franklin, J Silva

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Putative interactors of a rhomboid protease
K N Ikeda, M Freeman

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Mechanisms of skull expansion
J M Tabler, J Hibbard, J B Wallingford

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Early Detection of Ovarian Cancer (BARCA 1 & BARCA 2 Mutation) risk prediction for Bangladesh
M D Islam

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Conserved long non-coding RNAs in the switch to flowering
E Hawkes, S Hennelly, K Sanbonmatsu, C Dean, J Irwin

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Prevalence of agrochemical resistance-associated natural variation in wild populations of C. elegans
L Parts, A Flemming, A Woollard

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DNA extraction from oak heartwood: motivation and challenges
F Rossi, R Schulz

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Gastruloids develop the three body axes in the absence of extraembryonic tissues and spatially localised signalling
D A Turner, L Alonso-Crisostomo, M Girgin, P Baillie-Johnson, C R Glodowski, P C Hayward, J Collignon, C Gustavsen, P Serup, B Steventon, M Lutolf, A Martinez Arias

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High-throughput discovery of novel developmental phenotypes
J Cleak, S Johnson, Z Szoke-Kovacs, N Horner, J Brown, S Wells, H Westerberg, **L Teboul**

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Primitive endoderm and epiblast specification during preimplantation development of rabbit embryos
A Piliszek, Z Madeja, P Pawlak, A C Konarska Diaz, B Plusa

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Using metatherians to elucidate the evolution of mammalian epigenetic pathways
B Leeke, F Decarpentrie, S K Mahadevaiah, J Zohren, S Wood, S Horswell, M N Sangrithi, J M A Turner

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Investigating diet-induced renal lipotoxicity using Drosophila models
A Lubojemska, M I Stefana, A P Gould

Stem cells in vivo

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Is there a role for Neuronal Cell Adhesion Molecule in the hypothalamus?
A W Moore, A J Furley, M Placzek

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Conserved principles of primordial germ cell (PGC) specification and development between the human and pig highlight the porcine as a reliable and accessible model for investigation
S Withey, H Zhang, W W C Tang, N Irie, D Klisch, C Allegrucci, M A Surani, R Alberio

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The abrogation of condensin function provides independent evidence for defining the self-renewing population of pluripotent stem cells
A G Lai, N Kosaka, P Abnave, S Sahu, A A Aboobaker

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A genome-wide approach to characterize spatial pattering of neurogenesis in the zebrafish hindbrain
M Tambalo, R Mitter, A Stewart, D N Wilkinson

Poster Number: P148
Esrrb complementation rescues development of Nanog-null germ cells
H G Leitch, M Zhang, W W C Tang, N Festuccia, E Hall-Ponsele, J Nichols, M A Surani, A Smith, I Chambers

Poster Number: P149
Uncovering a central role for Id4 in the regulation of adult hippocampal neural stem cell quiescence
I M Blomfield, N Urbán, F Guillemot

Poster Number: P150
The blueprint of primate preimplantation development
T E Boroviak, G G Stirparo, S Dietmann, I Herraez, H Mohammed, W Reik, A G Smith, E Sasaki, J Nichols, P Bertone

Poster Number: P151
The Role of SUMOylation of Sox2 in the Regulation of Neural Stem Cells Proliferation and Multipotency
E Marelli, P J Scotting

Poster Number: P152
Transmembrane protein 33 (tmem33) is essential for VEGF-mediated calcium signalling during angiogenesis in zebrafish embryos
A M Savage, H R Kim, E Markham, E Honore, F J M van Eeden, T J A Chico, R N Wilkinson

Poster Number: P153
foxc1a and foxc1b exhibit distinct compensatory requirements during brain and trunk angiogenesis and haematopoietic stem cell formation in zebrafish
Z Jiang, T Evans, M Loose, T J A Chico, R N Wilkinson

Poster Number: P154
Early-life remodelling of the gut microbiome promotes intestinal homeostasis and longevity in Drosophila
F Obata, C Fons, A P Gould

Poster Number: P155
Decoding the molecular identity of neural stem cell types: a single-cell transcriptomic approach
J Gil-Ranedo, T Bossing, C S Barros

Poster Number: P156
Capturing emerging pluripotency in the pig early embryo by modulation of WNT and ERK signalling pathways
P Ramos-Ibeas, S Withey, D Klisch, J Nichols, R Alberio

Poster Number: P157
dMob4 is required for mitotic reactivation of Drosophila neural stem cells
E Gonzaga, T Bossing, C Barros

Poster Number: P158
Tfec controls cytokine expression in the haematopoietic stem cell vascular niche and expands haematopoietic stem cells
C B Mahony, C Pasche, T Matthes, J Y Bertrand

Poster Number: P159
Drosophila neural stem cells are polarised by their daughter cells
N Loyer, J Januschke

Poster Number: P160
A single-cell screening approach to brain tumour initiation
L Rodriguez-Diaz, J Gil-Ranedo, K Jaworek, J Marques, E Costa, T Bossing, C S Barros

Poster Number: P161
Hormonal regulation of neural stem cell proliferation in Drosophila
C O Fons, R Sous-Nunes, L Y Cheng, A P Gould

Poster Number: P162
Disticnt roles of two pax7 stem cell populations in larval zebrafish muscle repair
T Pipalia, J Koth, S Roy, C Hammond, K Kawakami, S Hughes

Poster Number: P163
A novel and unusually dynamic progenitor cell population integrates the transition zone between pseudostratified and squamous epithelium
F Campo-Paysaa, J D Clarke, R J T Wingate

Poster Number: P164
KLF4 supports establishment of pluripotency in vivo by controlling levels of endoderm specific GATA6 transcription factor
A Al-Anbaki, **B Plusa**

Poster Number: P165
Quantifying the effective range and modelling in vivo signals regulating germ cell migration
K Kenwrick, M R Owen, **A D Renault**

Poster Number: P166
The role of Deltex modulation of Notch signalling in regulating homoeostasis of the Drosophila midgut
J B Fuelle, S Hosseini Alghaderi, M Wilkin, M Baron

Poster Number: P167
Modulation of gata2a levels through an endothelial enhanceris required for generation of definitive haematopoietic stem cells
T Dobrzycki, M Krecsmarik, R Rispoli, R Patient, **R Monteiro**

Poster Number: P168
Investigating the role of the ARF GTPase arf-3 in regulating seam cell development and secretion
A Walker, A Woollard

Poster Number: P169
Probing the skeletal stem cell niche through functional investigation of Prx1 expressing cells
S V Pretorius

Poster Number: P170
Studying consequences of vascular dementia CADASIL Notch3 mutations in cell culture and iPS derived in vitro differentiated tissue models
S S Hosseini Alghaderi, W Zhang, M Baron, T Wang

Poster Number: P171
Asymmetric localization of Miranda in Drosophila neuroblasts involves the cognate mRNA independent of local translation
A Ramat, J Januschke

Poster Number: P172
Using C. elegans stem-like epithelial development to study mechanisms of biological robustness
S P R Gilbert, D Katsanos, S Koneru, I Razzaq, R Ghose, M Barkoulas

Poster Number: P173
Protection of embryonic muscle stem cells in vivo
S Dietrich, F Berti, M Kováč, **H Daventry**, M Guille, F Schubert

Poster Number: P183
Single cell expression profiling of neural crest-derived cells identifies partially-restricted intermediate pigment progenitor cell
T Subkhankulova, M Nikaido, G Aquino, H Schwetlick, T Sauker-Spengler, A Rocco, **R N Kelsh**

Poster Number: P185
CXCR4 and c-Kit signalling are required for directed migration of chicken primordial germ cells through the chick embryonic vascular system
A Idoko-Akoh, H Sang, M McGrew

SHORT TALKS AND SPEAKER ABSTRACTS

Date: Sunday 2 April, 2017
Session: Plenary Session
Time: 19:00 – 20:00
Venue: Main Lecture Theatre

PL01 19:00 – 20:00
Bacterial Quorum Sensing and its Control
B L Bassler[1,2]

[1]Molecular Biology, Princeton University, Princeton, USA; [2]Howard Hughes Medical Institute, Princeton, USA

Bacteria communicate with one another via the production and detection of secreted signal molecules called autoinducers. This cell-to-cell communication process, called “Quorum Sensing”, allows bacteria to synchronize behavior on a population-wide scale. Behaviors controlled by quorum sensing are usually ones that are unproductive when undertaken by an individual bacterium acting alone but become effective when undertaken in unison by the group. We developed small molecule quorum-sensing agonists and antagonists to discover the principles underlying the exquisite selectivity quorum-sensing regulatory proteins have for their partner interacting molecules. Beyond learning about fundamental principles underlying quorum sensing, another use for our synthetic molecules is to control quorum sensing on demand. Our most potent quorum sensing modulators protect animals from quorum-sensing-mediated killing by pathogenic bacteria and the compounds prevent biofilm formation. These results validate the notion that targeting quorum sensing has potential for antimicrobial drug development.

Date: Sunday 2 April, 2017
Session: The Genetics Society Medal Lecture 2017
Time: 20:00 – 21:00
Venue: Main Lecture Theatre

PL02 20:00 – 21:00
Epigenetic Regulation of Genomic Imprinting in Development and Disease
M S Bartolomei

Cell and Developmental Biology, University of Pennsylvania Perelman School of Medicine, Philadelphia, USA

Imprinted genes are expressed from a single parental allele and most reside in clusters that are located throughout the mammalian genome. The clusters typically contain an imprinting control region (ICR), which harbors allele-specific methylation and governs imprinting. Although most imprinted clusters use lncRNAs to regulate imprinted gene expression, a few are regulated by CTCF. One such cluster harbors the *H19* and *Igf2* imprinted genes, and is controlled by an ICR that contains multiple CTCF binding sites. Gain of maternal methylation and loss of paternal hypermethylation of the *H19*/*IGF2* ICR are associated with the human growth disorders Beckwith-Wiedemann Syndrome and Silver-Russell Syndrome, respectively. Using gene targeting and genome editing, we have generated cell lines and mice to study imprinting mechanisms and model the epigenetic mutations in human syndromes. We have also developed SNP-FISH to study the dynamics of allele-specific gene expression at the single cell level.

Date: Monday 3 April, 2017
Session: Epigenetics
Time: 09:00 – 12:30
Venue: Main Lecture Theatre

S01 09:00 – 09:30
Genome architecture and transcription regulation in *C. elegans*
J Ahringer

The Gurdon Institute, University of Cambridge, Cambridge, UK

All nuclear events take place in the context of chromatin, the organization of genomic DNA with histones and hundreds of associated proteins and RNAs. Regulating the composition and structure of chromatin controls transcription and other nuclear processes, and is important for cell fate decisions, the expression of cell identity, the maintenance of pluripotency, and the transformation to cancer. We use *C. elegans* to study chromatin regulation in gene expression and genome organization in a whole organismal context, because it has a complement of core chromatin factors very similar to that of humans, a small well-annotated genome (30x smaller than human), RNAi for loss of function studies, and well-characterised cell fates. I will discuss our work on the properties and activities of promoters and enhancers, the regulation and function of chromatin domains, and interactions between regulatory elements.

O1 09:30 – 09:45
Poster Number: P059
Regulation of LINE1 retrotransposons by 2-oxoglutarate-dependent dioxygenases
L de la Rica, K C Cheng, O Deniz, **M R Branco**

Blizard Institute, QMUL, London, UK

Expression of retrotransposons such as LINE1 elements is kept under tight control via epigenetic mechanisms such as DNA methylation. Yet in tissues such as the brain and embryonic stem cells (ESCs), LINE1s undergo a loss of DNA methylation and increase in expression. TET enzymes, which can mediate DNA demethylation, are highly expressed in these tissues, suggesting a possible involvement of TETs in LINE1 activation. We found that TETs target evolutionarily young LINE1 elements in ESCs and drive LINE1 demethylation. Surprisingly, LINE1s are kept repressed through additional TET-dependent activities. On the other hand, addition of ascorbate and alpha-ketoglutarate, two key co-factors of 2-oxoglutarate-dependent dioxygenases such as TETs, drives LINE1 activation in ESCs. We found that ascorbate-mediated activation of LINE1s is independent of TET activity, suggesting the involvement of other 2-oxoglutarate-dependent dioxygenases. Our data raise the possibility that retrotransposition can be modulated by nutritional and metabolic inputs via epigenetic mechanisms.

S02 09:45 – 10:15
Mobile elements, polydactyl proteins and the genesis of human-specific regulatory networks
D Trono

School of Life Sciences, EPFL, Lausanne, Switzerland

Transposable elements (TEs) likely account for at least two-thirds of the human genome, and are subjected to epigenetic control mechanisms from the earliest stages of embryonic development. An important component of this process is the sequence-specific recognition of TEs by KRAB-containing zinc finger proteins (KZFPs), a large family of transcription factors that act by recruiting inducers of heterochromatin formation and DNA methylation. It is generally held that TEs then become permanently silenced, and that the evolutionary selection of KZFPs and other TE controllers is the result of a simple evolutionary arms race between the host and these genetics invaders. I will discuss recent evidence that invalidates this dual assumption, and instead suggests that KZFPs are the instruments of a massive enterprise of TE domestication, whereby transposon-based regulatory sequences and their cellular ligands establish species-specific transcription regulation networks that influence multiple aspects of human biology.

O2 10:15 – 10:30
Poster Number: P185
Regulation of metabolism through imprinted genes
M Charalambous

QMUL, London

The process of genomic imprinting epigenetically regulates the dosage of a class of genes known for their actions in developmental growth pathways. Moreover, it is increasing clear that imprinted gene dosage misregulation - in both humans and in animal models – has consequences for lifetime metabolic health. It is

currently unclear why imprinted gene disruption causes metabolic disease in adulthood. One possibility is that imprinted genes act in developmental pathways to define the future body plan and mediate set points of central energy homeostasis. Another explanation is that the products are continuously required in metabolic tissues to maintain their functions.
The product of the imprinted delta-like homologue 1 gene, DLK1, is an endocrine signalling molecule that reaches a high concentration in the maternal circulation during late pregnancy. We found that the conceptus is the source of maternal circulating DLK1 during pregnancy and can be used to predict pregnancy outcome in humans. In the absence of conceptus-derived DLK1, maternal plasma cholesterol is elevated and fasted ketone levels are reduced. Furthermore, lack of DLK1 during the mother's development additionally impairs her ability to respond to the metabolic demands of pregnancy. Our previous studies with genetically-modified mice showed that DLK1 shifts nutrient metabolism towards fatty acid oxidation, in part through modulation of the growth hormone axis. By modulating gene dosage we demonstrated that DLK1 levels modulate the size of the pituitary gland during development, and may act to maintain hormonal homeostasis throughout life.

O3 10:30 – 10:45
Poster Number: P061
Analysis of a knock-out mouse model for the microcephaly-associated *Trappc9* gene and its epigenetic regulation by genomic imprinting
M Pulix[1], T Leather[2], K Ingram[1], L Livoti[1], P Arnaud[3], H Poptani[2], **A Plagge**[1]

[1]Cellular and Molecular Physiology, University of Liverpool, Liverpool, UK; [2]Centre for Preclinical Imaging, University of Liverpool, Liverpool, UK; [3]Genetique, Reproduction and Developpment, Universite Clermont Auvergne, Clermont-Ferrand, France

Homozygous mutations of *TRAPPC9* cause microcephaly, intellectual disability, white matter hypoplasia and developmental delays in human. *Trappc9* forms part of the trafficking protein particle II complex, which mediates vesicle transport at the ER/Golgi. It also interacts with the dynactin/dynein motor complex involved in retrograde transport and signalling along microtubuli. The *Trappc9* gene is located within the *Peg13*/*Kcnk9* cluster of imprinted genes on mouse chromosome 15 / human chromosome 8. In a first *Trappc9* knock-out (KO) mouse model we found brain weights and volumes (via MRI) to be reduced by 10% at 3-months of age. *Trappc9* is expressed in neurons and neural progenitor cells (NPCs), and Sox2-positive NPCs are reduced by 15% in the hippocampal dentate gyrus. Female KOs show a 20% increase in body weight. Pyrosequencing of brain cDNA SNPs show imprinted expression of *Trappc9* preferentially (70%) from the maternal allele, which is not associated with promoter DNA methylation.

S03 11:15 – 11:45
Reading and writing DNA methylation
D Schubeler

Epigenetics, FMI, Basel, Switzerland

How is DNA methylation involved in gene regulation? We are using mammalian stem cell models to monitor the epigenome and its dynamics in an unbiased way and to identify its dependency on DNA sequence. Our goal is to generate regulatory, which we test in cellular models by genetic perturbation and genome editing approaches. To create functional genomic binding maps we use a biotin tagging approach to map readers (Baubec et al., Cell 2013) and writers of DNA methylation (Baubec et al. Nature 2015). We further

identified NRF1 as a TF that occupies many additional sites in the unmethylated genome amd which depends on other factors to induce local hypomethylation (Domcke, Bardet et al., Nature 2015). These results highlight the interplay between the machineries that set and read DNA methylation and illustrate how transcription factors cause local sites of reduced methylation other factors require this local hypomethylation for binding.

O4 11:45 – 12:00
Poster Number: P054
Higher-order chromatin structure in the ground state of pluripotency
K A McLaughlin, I M Fliamer, H K Mjoseng, R Shukla, J P Thomson, W A Bickmore, R R Meehan

MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, Edinburgh, UK

Mouse embryonic stem cells (mESCs) are an excellent model for studying epigenetics and chromatin structure. Recently refined culturing conditions (2i) can harness mESCs in a pluripotent ‘ground state’. This growth environment generates a naïve and homogenous cell population, in contrast to heterogeneous and metastable serum-cultured cells. Epigenetically, 2i culture promotes global hypomethylation and redistribution of polycomb marks. We investigated the effects of this altered epigenetic landscape on chromatin structure. We used a targeted, single-locus approach (FISH) and a genome-wide approach (HiC) to analyse differences in chromatin structure between conventionally serum-cultured and ground state mESCs. We find that chromatin structure is globally altered in mESCs in 2i. Mechanistically, we suggest that the epigenetic changes – not the pluripotency status of the cell population - are responsible for driving these structural changes.

S04 12:00 – 12:30
Transgenerational Epigenetics, transposable elements and heritable phenotypic variation
V Colot

Institut de Biologie de l'Ecole Normale Superieure (IBENS), CNRS-INSERM-ENS, Paris, France

Transgenerational epigenetics is defined in opposition to developmental epigenetics and implies an absence of resetting of epigenetic states between generations. Transgenerational epigenetics is best documented in plants where, as in mammals, it entails heritable changes of DNA methylation over repeat sequences, notably transposable elements and their relics. We have created a large population of near-isogenic, epigenetic Recombinant Inbred Lines (epiRILs) in Arabidopsis and this population has enabled us to reveal a substantial potential for heritable epigenetic variation with phenotypic consequences at the whole genome level. We have also shown that the transgenerational stability of epigenetic changes differs greatly among repeat sequences and we have identified several of the factors involved. However, it is still not known how much of this potential for transgenerational epigenetics actually occurs in nature and what its contribution to the generation of heritable phenotypic variation might be. I will present our efforts towards answering these questions.

Date: Monday 3 April, 2017
Session: Neurons, Networks and Behaviour
Time: 09:00 – 12:30
Venue: Woods Scawen Lecture Theatre

S05 09:00 – 09:30
Development, Structure and Function of Neural Circuit Motifs
G Jefferis

Division of Neurobiology, MRC Laboratory of Molecular Biology, Cambridge, UK

I will show examples of how we are using the Drosophila nervous system to explore the genetic basis and organisational logic of elementary circuit motifs in the brain. This will cover circuitry associated with both instinctive, sexually dimorphic behaviours and the interaction of learned and unlearned behaviours. I will showcase work that combines high resolution anatomy (including whole brain electron microscopy connectomics), physiology and developmental analysis to reach an integrated understanding of circuit logic.

O5 09:30 – 09:45
Poster Number: P117
The sex of specific neurons controls female body growth in *Drosophila*
A Sawala, A P Gould

Physiology and Metabolism Group, The Francis Crick Institute, London, UK

Sexual size dimorphism is widespread throughout the animal kingdom but its underlying mechanisms are not well characterised. Here, we use tissue-specific genetics in the fruit fly *Drosophila* to investigate how this type of size dimorphism is established. We find that the larger female body size in this species is established very early in larval development via an increase in the mass-specific growth rate. We demonstrate that the female sex determination gene, *Sex-lethal* (*Sxl*), functions in the nervous system as part of a relay that increases growth remotely in peripheral larval tissues. Surprisingly, neuronal Sxl is both necessary and sufficient to increase larval body size in females. Sxl acts specifically in peptidergic and GABAergic neuronal subsets to regulate female growth, and this is selective for larval not imaginal tissue types. We conclude that sex-specific growth patterns in insects, as in mammals, are specified via both tissue-autonomous and non-autonomous mechanisms.

S06 09:45 – 10:15
Spatio-temporal control of neural stem cell activity and pallium construction in the teleost zebrafish
I Foucher[1], G Furlan[1,2], V Cuccioli[1], N Vuillemin[3], E Beaurepaire[3], C Houart[4], **L Bally-Cuif**[1]

[1]Department of Developmental and Stem Cell Biology, Institut Pasteur and CNRS UMR3738, Paris, France; [2]Centre de Recherche en Cancerologie de Lyon, INSERM U1052-CNRS UMR5286, Lyon, France; [3]Laboratory for Optics and Biosciences, Ecole Polytechnique, CNRS UMR 7645 and INSERM U1182, Palaiseau, France; [4]Medical Research Council Centre for Developmental Neurobiology, King’s College London, London, UK

The adult teleost brain harbors multiple neural stem cell (NSC) niches, engaged in constitutive neurogenesis. In the dorsal telencephalon (pallium), life-long neurogenesis is driven by radial glia NSCs. We are using this

model to understand how the pallial macroarchitecture is built from NSCs over time, in zebrafish compared to other vertebrates. To gain insight into this question, we developed genetic tools to birthdate the generation of pallial neurons from NSCs and generate a 4-dimensional (3D + time) map of pallium construction in the adult zebrafish. These data, together with Cre-lox-mediated tracing including brainbow clones, highlight a simple mode of pallium construction primarily driven by the spatio-temporal control of NSC activity and sharing distinct traits with pallium genesis in mammals and non-mammalian amniotes such as birds or reptiles. We propose that zebrafish pallium formation may recapitulate a basal scheme from which vertebrate pallial architectures were elaborated.

S07 10:15 – 10:45
Neural circuitry coordinating male copulation
H J Pavlou[1], A C Lin[1], M C Neville[1], T Nojima[1], F Diao[2], B E Chen[3], B H White[2], **S F Goodwin**[1]

[1]Centre for Neural Circuits and Behaviour, University of Oxford, Oxford, UK; [2]Laboratory of Molecular Biology, National Institute of Mental Health, Bethesda, USA; [3]Departments of Medicine and Neurology and Neurosurgery, McGill University, Montreal, Canada

Copulation is the goal of the courtship process, crucial to reproductive success and evolutionary fitness. Identifying the circuitry underlying copulation is a necessary step towards understanding universal principles of circuit operation, and how circuit elements are recruited into the production of ordered action sequences. Here, we identify key sex-specific neurons that mediate copulation in *Drosophila*, and define a sexually dimorphic motor circuit in the male abdominal ganglion that mediates the action sequence of initiating and terminating copulation. This sexually dimorphic circuit composed of three neuronal classes – motor neurons, interneurons and mechanosensory neurons – controls the mechanics of copulation. By correlating the connectivity, function and activity of these neurons we have determined the logic for how this circuitry is coordinated to generate this male-specific behavior, and sets the stage for a circuit-level dissection of active sensing and modulation of copulatory behavior.

S08 11:15 - 11:45
G Laurent

O6 11:45 – 12:00
Poster Number: P110
Chemical and mechanical signals interact to direct axon growth
S K Foster, K Franze

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

During brain development, growing neurons navigate through a highly complex environment as they extend towards their synaptic targets. Studies of axon pathfinding have focused primarily on chemical guidance, but neurons also sense and respond to mechanical properties of their environment such as the local tissue stiffness, and such mechanical signals strongly influence axon growth and guidance. Growing neurons must integrate these diverse signals present in their environment. We find that substrate stiffness modulates the response of *Xenopus laevis* CNS neurons to the repulsive guidance signal semaphorin3A (Sema3A), with softer substrates attenuating the Sema3A response. Cyclic GMP – a critical regulator of chemical guidance cue signalling – is elevated on soft substrates, and pharmacological studies indicate that cGMP plays a role in the stiffness-dependent modulation of the Sema3A response.

S09 12:00 – 12:30
Glia developmental plasticity couples behaviour to reproductive needs
M Sammut[1], S J Cook[2], R C Bonnington[1], B Kim[3], L Molina[1], D H Hall[2], S W Emmons[2], R J Poole[1], **A Barrios**[1]

[1]Cell and Developmental Biology, University College London, London, UK; [2]Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, NY, US; [3]Molecular Genetics, Albert Einstein College of Medicine, NY, US

During sexual maturation, the nervous system undergoes sexually dimorphic changes that couple behaviour to reproduction. What are the mechanisms underlying sex-specific remodeling of behaviour? We have discovered two new classes of male-specific neurons in *C. elegans* that arise during sexual maturation from differentiated glial cells that are present in both sexes. One class, termed MCMs, is specifically required for male-specific associative learning. The MCM interneurons modulate sensory processing so that rewarding sexual experiences can override aversive experiences, thus influencing behaviour according to the new reproductive needs of the adult male. The other class, termed PHD, arises from a direct glia-to-neuron cell-fate switch during which, functional glial cells in the male tail undergo dramatic morphological and molecular changes to become cholinergic sensory neurons. PHD neurons are then incorporated into the male's sensory-motor mating circuit. Through cell ablation and functional imaging of neuronal activity, we are currently elucidating their role in behaviour.

Date: Monday 3 April, 2017
Session: New Methods to Study Cell Biology
Time: 09:00 – 12:30
Venue: Cinema

S10 09:00 – 09:30
Microtubule rejuvenation
L Schaedel[1], C Aumeier[1], J Gaillard[1], **M Théry**[1], K Karin John[2]

[1]Biotechnology Institute of Grenolbe, CEA, Grenoble, France; [2]University Grenoble Alpes, CNRS, Grenoble, France

Microtubules grow and shrink by tubulin dimer addition and removal from their ends. We recently found that dimers can also be exchanged along the microtubule lattice. Microtubules that were submitted to mechanical stress could self-repair by incorporation of free dimers in the damaged regions. Here we will present new data about free dimers exchange along the lattice of microtubules that were not submitted to mechanical stress.

O7 09:30 – 09:45
Poster Number: P127
Rapid profiling of interactome dynamics by analysis of protein-protein colocalisations on a global scale
F Mardakheh

Molecular Oncology, Barts Cancer Institute, London, UK

Localisation and protein function are intimately linked in eukaryotes, as proteins are localised to specific compartments where they come into proximity of other functionally relevant proteins. Significant co-localisation of two proteins can therefore be indicative of their functional association. We here present COLA, a proteomics based method coupled with a bioinformatics framework to detect protein-protein co-localisations on a global scale. COLA reveals functional interactions by matching proteins with significant similarity in their subcellular localisation signatures. The rapid nature of COLA allows mapping of interactome dynamics across different conditions or treatments with high precision.

S11 09:45 – 10:15
Determining structures of coated vesicles in vitro and in cells using cryo-electron tomography
J A G Briggs[1,2]

[1]Structural and Computational Biology Unit, EMBL, Heidelberg, Germay
[2]Structural Studies Division, MRC-LMB, Cambridge, UK

We are investigating the principles of coated trafficking vesicle assembly by determining the structures of coats in their assembled form. By combining cryo-electron tomography with computational image processing, we can visualize the structures of coats assembled on membranes in in vitro budding reactions with sufficient resolution to resolve individual alpha-helices in the component proteins. The same methods can be used to determine the structures of assembled coats directly within cells, validating and extending in vitro observations. I will discuss the potential of the technology, and present our most recent data on the structures of assembled coats and regulatory proteins in vitro and in vivo.

S12 10:15 – 10:45
Bioengineered microenvironments to dissect stem cell self-organization
M P Lutolf

Institute of Bioengineering, EPFL, Lausanne, Switzerland

The earliest steps of development are characterized by cellular reorganization and differentiation within a 3D microenvironment. This 3D context allows for a complex interplay between biochemical and mechanical signals, and governs important cellular rearrangements leading to morphogenesis. In vitro approaches have attempted to recapitulate key features of these processes, and it has become possible to generate an increasing variety of self-organizing tissue constructs termed ‘organoids’. While important aspects of the 3D in vivo organization have been recreated using organoids, such studies have been exclusively performed in ill-defined matrices whose properties cannot be controlled. As such, the uncharacterized interactions between cells and this extracellular matrix have proven to be a major challenge to understanding the underlying regulatory mechanisms governing morphogenesis. In this talk, I will highlight our recent efforts to employ tunable synthetic hydrogels to disentangle the contributions of biochemical and mechanical effectors in specifying stem cell fate and self-organization.

S13 11:15 – 11:45
Structural Insights into the Autoinhibition of the Oncogenic Human Chromatin Remodeler Alc1
L Lehmann[1], S Aibara[2], E Marklund[1], A Leitner[3], **S Deindl**[1]

[1]Department of Cell and Molecular Biology, Science for Life Laboratory, Uppsala University, Uppsala, Sweden; [2]Department of Biochemistry and Biophysics, Science for Life Laboratory and Stockholm University, 10691 Stockholm and 17121 Solna, Sweden; [3]Department of Biology, Institute of Molecular Systems Biology, Swiss Federal Institute of Technology, 8093 Zürich, Switzerland

Human Alc1 is an oncogene-encoded Snf2-family chromatin-remodeling enzyme (remodeler). Alc1 is unique among remodelers in that it possesses a macro domain capable of binding poly(ADP-ribose) (PAR). Engagement of the macro domain with PARylated Parp1 activates Alc1, but the underlying mechanism remains unclear. Here, we observe that deletion of the macro domain/linker of Alc1 abolishes its dependence on PAR-mediated activation. Using an integrative structural biology approach, we model the solution structure of Alc1 and find that its two ATPase lobes are splayed apart such that they are unlikely to support catalysis. Our data are consistent with a mechanism where the ATPase of Alc1 is autoinhibited by its macro domain/linker. Engagement of the macro domain with PARylated Parp1 likely releases this autoinhibited conformation and activates Alc1 upon recruitment to PARylated sites of DNA damage.

O8 11:45 – 12:00
Poster Number: P130
'Car Sharing' – Intracellular Co-Trafficking of Junctional Adhesion Molecule C and its Neighbouring Proteins in Endothelial Cells
K B Kostelnik[1], V Rajeeve[2], I J White[3], P R Cutillas[2], T Nightingale[1]

[1]William Harvey Research Institute, Barts and The London School of Medicine, Queen Mary University of London, London, UK; [2]Cell Signalling and Proteomics Group, Barts Cancer Institute, Queen Mary University of London, London, UK; [3]MRC Laboratory for Molecular Cell Biology, University College London, London, UK

Interendothelial junctions are dynamic structures consisting of junctional proteins imperative to vascular permeability, leukocyte extravasation and angiogenesis. The junctional adhesion molecule C (JAM-C) is pivotal during junctional remodelling and faulty expression/function has been associated with multiple inflammatory diseases including atherosclerosis and heart disease. Following an inflammatory stimulus dynamic changes of JAM-C levels can be observed at endothelial junctions and in intracellular vesicular pools. This might serve to regulate JAM-C functions, however, little is known regarding JAM-C internalisation and redistribution. To gain deeper insight into its intracellular trafficking we generated a JAM-C-horseradish peroxidase fusion protein and identified neighbouring proteins of JAM-C using a novel biotinylation-based pull-down and mass spectrometry approach. By mapping the proteomic inventory surrounding vesicular as well as surface JAM-C we distinguished co-trafficked from non-co-trafficked proteins. We can now identify key players involved in dynamic trafficking of JAM-C and support further elucidation of its function at interendothelial junctions.

S14 12:00 – 12:30
Haploid Genetics to study disease-related networks
T Brummelkamp

Netherlands Cancer Institute, NKI, Amsterdam,Netherlands

Basic research carried out over the last thirty years in the field of molecular biology has revolutionized our understanding of cell biology. However, that even with today's knowledge it remains largely impossible to predict key players in networks related to human disease. Therefore, our goal is to advance genetics in human cells in order to obtain accurate and complete overviews of genes that play a role in phenotypes of interest and to map genetic networks that enhance or suppress disease-related cellular states. Using random mutagenesis in haploid human cells we apply a sensitive approach to directly couple genomic mutations to protein measurements in individual cells. This scalable, sequencing-based procedure elucidates the genetic landscapes that control protein states, identifying genes that cause very narrow phenotypic effects and genes that lead to broad phenotypic consequences.

Date: Monday 3 April, 2017
Session: Stem Cells in Vivo
Time: 14:00 – 15:30
Venue: Main Lecture Theatre

S15 14:00 – 14:30
Ontogeny of hematopoietic stem cells
D Traver

Cell and Developmental Biology, UCSD, La Jolla, USA

Hematopoietic stem cells (HSCs) underlie the continued production of blood and immune cell lineages for the lifetime of an organism. In all vertebrate embryos examined, HSCs arise from the unique transdifferentiation of hemogenic endothelium comprising the floor of the dorsal aorta during a brief developmental window. To date, this process has not been replicated *in vitro* from pluripotent precursors, partly because the full complement of required signaling inputs remains to be determined. Our current efforts are aimed at elucidating the molecular cues required to specify HSCs through aortic endothelial intermediates. Many signaling pathways are known to regulate HSC emergence, including those triggered by presentation of Notch, BMP, FGF, and Wnt ligands, but their epistatic relationships and how each is integrated into HSC precursors remain poorly understood. How these and other signaling inputs are integrated to generate HSC fate will be discussed.

O9 14:30 – 14:45
Poster Number: P159
Drosophila neural stem cells are polarised by their daughter cells
N Loyer, J Januschke

School of Life Sciences, University of Dundee, Dundee, UK

Drosophila neural stem cells (neuroblasts) divide asymmetrically to both self-renew and generate Ganglion Mother Cells (GMCs) daughter cells. A noticeable feature of larval neuroblasts is the fact that their division orientation is maintained from one cell cycle to the next, even when isolated from their niche in neuroblast/GMCs clusters. This relies on an apical microtubule network acting as an intrinsic polarising cue which disruption, however, only partially affects division orientation maintenance. Here, we used live imaging of cultured *Drosophila* larval brains, genetics and laser ablation to demonstrate that the GMC acts as an additional – this time external – polarity cue also participating to neuroblasts division axis maintenance. We further investigated the role of the midbody, a structure forming at the neuroblast/GMC interface following cytokinesis, which likely participates to this mechanism and allows neuroblasts to distinguish their latest daughter cells from the previous ones.

S16 14:45 – 15:15
Elucidating the birth of blood stem cells
M de Bruijn

MRC Molecular Haematology Unit, WIMM, Radcliffe0 Department of Medicine, University of Oxford, Oxford, UK

The current interest in stem cell-based therapies has emphasized the importance of understanding how tissue specific stem cells are born in embryonic development. In vertebrate embryos, blood stem cells are generated from a subset of the aortic endothelium, the hemogenic endothelium, via a process called endothelial-to-hematopoietic transition (EHT). Studies aimed at obtaining a mechanistic insight into EHT have been hampered by a lack of markers that allowed for the identification and isolation of hemogenic endothelium. In our ongoing work we have identified cell type and developmental stage specific enhancers of Runx1, a critical regulator of EHT, and generated transgenic enhancer-reporter mouse models to isolate hemogenic endothelium. Functional and expression analysis of hemogenic endothelium established that these cells undergo hematopoietic specification early in development when still part of the endothelial cell layer and identified new candidate players and pathways involved in the birth of blood stem cells.

O10 15:15 – 15:30
Poster Number: P165
Quantifying the effective range and modelling *in vivo* signals regulating germ cell migration
K Kenwrick[1], M R Owen[2], **A D Renault**[1]

[1]School of Life Sciences, University of Nottingham, Nottingham, UK; [2]School of Mathematical Sciences, University of Nottingham, Nottingham, UK

To understand the effects of extracellular signalling molecules it is important to have quantitative information about their range of influence *in vivo*. In *Drosophila*, embryonic germ cell migration requires spatial information provided by diffusible signals dependent on two pathways: Wunen and HMG-CoA reductase (HMGCR). Wunen expression effectively repels germ cells whilst HMGCR expression attracts. To explore the nature of the HMGCR-dependent signal and we ectopically expressed HMGCR-GFP in wild type embryos and also those otherwise null for HMGCR or Wunen. Using germ cell positioning relative to the ectopic domains in fixed tissue, and trajectories of migration from live light sheet microscopy we have determined that the HMGCR dependent signal operates over a long range *in vivo* and acts competitively with that provided by Wunen. These characteristics are feeding into mathematical models that we are developing to infer the chemotactic gradients and explain the behaviour of the germ cells.

Date: Monday 3 April, 2017
Session: Newly Tractable Systems
Time: 14:00 – 15:30
Venue: Woods Scawen Lecture Theatre

S17 14:00 – 14:30
Exploring the epigenomic archive of environmental exposure preserved in the wood of forest trees
F Rossi, **R Schulz**

Medical and Molecular Genetics, King's Collge London, London, UK

Trees are exposed to large variations in environmental conditions. Yet, they are long-lived, demonstrating a large capacity to sense and adapt to their environment. These adaptations include changes to wood anatomy, most apparent as ring formation due to seasonal climate variation. Macroscopic features of growth rings are long established biomarkers of past growth conditions. Wood, while a terminal tissue, also retains small, recoverable amounts of DNA that may represent an analogous, centuries-spanning epigenetic record of past growth conditions. We have generated a collection of wood samples of veteran oak trees, each covering the period from AD ~1776 to the present. We aim to generate time series of genome-wide DNA methylation profiles to determine whether they contain traces of past growth conditions, especially traces of 1816, the “year without summer”. However, low DNA yield, high polyphenol content and DNA damage pose significant challenges that we are currently addressing.

O11 14:30 – 14:45
Poster Number: P138
Conserved long non-coding RNAs in the switch to flowering
E Hawkes[1], S Hennelly[2], K Sanbonmatsu[2], C Dean[1], J Irwin[1]

[1]John Innes Centre, Norwich Research Park, Norwich, UK; [2]Los Alamos National Laboratory, Los Alamos, New Mexico, USA

Since their discovery, long non-coding RNAs (lncRNAs) have in turn been described as essential genomic regulators or as transcriptional noise. We are interested in the functional significance of a group of lncRNAs (*COOLAIR*) that are transcribed in the antisense direction at an important *Arabidopsis thaliana* floral repressor gene, *FLC*. Previous work has revealed a role for *COOLAIR* antisense RNAs in regulation of *FLC* sense expression levels and, consequently, flowering time. We found *COOLAIR* secondary structure and transcription, but not primary nucleotide sequence, to be conserved across multiple flowering plants, supporting a regulatory role. Natural variation across and within species creates subtle changes in *COOLAIR* secondary structure and transcript architecture that may modulate its activity. We propose an evolutionarily conserved lncRNA that is neither essential regulator nor transcriptional noise, but rather fine-tunes the switch to flowering.

S18 14:45 – 15:15
Rising from the ashes: can genomic research help tree populations to recover from epidemics?
R J A Buggs[1,2]

[1]Natural Capital and Plant Health, Royal Botanic Gardens Kew, Richmond, UK; [2]School of Biological and Chemical Sciences, Queen Mary University of London, London, UK

Ongoing human dispersal of pests and pathogens around the globe is causing widespread devastation of plant populations. We have a track record of mitigating these threats for crops by breeding or pesticide development. For native tree populations, we have no such track record. We cannot apply pesticides to vast acreages of native woodland, and breeding trees with generation times measured in decades is a very long term undertaking. Our best prospects may be in accelerating breeding using genomic knowledge. Genomic prediction, already used successfully in annual crops, has even greater potential to reduce generation times of breeding programmes for trees. I will review the case study of ash trees, which are currently threatened by both ash dieback and the emerald ash borer, and the potential for current genomic research, some of which I am leading, to generate to viable solutions.

O12 15:15 – 15:30
Poster Number: P139
Prevalence of agrochemical resistance-associated natural variation in wild populations of *C. elegans*
L Parts[1], A Flemming[2], A Woollard[1]

[1]Department of Biochemistry, University of Oxford, Oxford, UK; [2]Jealott's Hill International Research Centre, Syngenta Ltd., Bracknell, UK

Resistance to pesticides is a growing global food security problem and an emerging issue for the agrochemical sector, yet little is known about the prevalence, molecular mechanism and evolutionary biology of resistance. Using *Caenorhabditis elegans* as a model organism and utilising the existing bank of over 200 wild isolates, we have assessed natural variation in pesticide resistance, an idea supported by a previous report linking natural variation in the Hawaiian strain CB4856 to resistance to a commonly used anthelmintic (PMID:22301316). We looked at the development of 25 *C. elegans* wild isolates upon exposure to 21 different pesticides and demonstrated both increased sensitivity as well as increased resistance to particular chemicals in different wild strains. We plan to identify the genetic basis of particular variation in resistance as well as to model the emergence of agrochemical resistance in an experimental evolution approach.

Date: Monday 3 April, 2017
Session: Nucleic Acids
Time: 14:00 – 15:30
Venue: Cinema

S19 14:00 – 14:30
Dynamics of Translation of Single mRNA Molecules In Vivo
T A Hoek[1], X Yan[2], D Khuperkar[1], S A Ruijtenberg[1], R D Vale[2], **M E Tanenbaum**[1]

[1]Hubrecht Institute, Hubrecht Institute, Utrecht, The Netherlands; [2]Department of Cell and Mol Pharmacology, UCSF, San Francisco, USA

Regulation of mRNA translation, the process by which ribosomes decode mRNAs into polypeptides, is used to tune cellular protein levels. Methods for observing the complete process of translation from single mRNAs in vivo have been unavailable. We have developed a method for long-term (>1 hr) imaging of single mRNAs undergoing hundreds of rounds of translation in live cells, enabling quantitative measurements of ribosome initiation, elongation and stalling. This approach reveals a surprising heterogeneity in the translation of individual mRNAs within the same cell, including rapid and reversible transitions between a translating and non-translating state, and substantial heterogeneity in ribosome pausing at regulatory pause sites. The ability to observe translation of single mRNA molecules in live cells for long periods of time provides a powerful approach to study translation regulation.

S20 14:30 – 15:00
Nuclear RNA decay pathways aid rapid remodeling of gene expression in yeast
S Bresson[1], A Tuck[2], **D Tollervey**[1]

[1]Wellcome Trust Centre for Cell Biology, University of Edinburgh, Edinburgh, Scotland
[2]Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

In yeast, the nuclear RNA surveillance system is active on all pre-mRNA transcripts and modulated by nutrient availability. To test the role of nuclear surveillance in reprogramming gene expression, we identified transcriptome-wide binding sites for RNAPII and the exosome cofactors Mtr4 (TRAMP complex) and Nab3 (NNS complex) by UV-crosslinking immediately following glucose withdrawal (0, 4, 8min). In glucose, Nab3 and Mtr4 were mainly bound at promoter-proximal sites on mRNAs, reflecting early transcription termination. Following glucose withdrawal, many growth-related mRNAs showed reduced transcription but increased Nab3 binding, accompanied by downstream recruitment of Mtr4 and oligo(A) tailing. We conclude that transcription termination is followed by TRAMP-mediated RNA decay. Upregulated transcripts evaded surveillance factor binding following glucose withdrawal. A subset of upregulated genes use alternative transcription starts to bypass the synthesis of non-coding RNAs that include strong NNS binding sites. Nuclear surveillance pathways therefore regulate both positive and negative responses to glucose availability.

S21 15:00 – 15:30
Exon Junction Complex inhibits recursive splicing of canonical exons
L Blazquez[1,2], W Emmett[1,2], C Sibley[1,2], **J Ule**[1,2]

[1]The Francis Crick Institute, London, UK; [2]Department of Molecular Neuroscience, UCL Institute of Neurology, London, UK

We recently identified recursive splicing (RS) in human introns, which requires exon definition via a cryptic 'RS-exon' that is located downstream of the recursive splice site. We now find that approximately 4% of human exons are canonical RS-exons, which can be regulated by the exon-junction complex (EJC). Deposition of EJC structurally blocks recursive splicing, ensuring high inclusion of the canonical RS-exons. This mechanism is conserved in mice but not in Drosophila, where EJC is not deposited in a splicing-dependent manner. Interestingly, canonical RS-exons are rare in Drosophila and tend to be lowly included, indicating that EJC is not capable of repressing recursive splicing in Drosophila. The repressive function of EJC is associated with microcephaly in mouse and craniofacial disorders in human. In summary, repression of recursive splicing by EJC is a new mechanism for alternative splicing that was gained in vertebrates, thus ensuring high inclusion of canonical RS-exons.

Date: Monday 3 April, 2017
Session: The Mendel Medal Lecture 2017
Time: 16:00 – 16:45
Venue: Main Lecture Theatre

PL03 16:00 – 16:45
When genomes meet: RNA, epigenetics and the phenotypes of hybrid plants
D Baulcombe

Plant Sciences, Cambridge University, Cambridge, UK

Eukaryotes contain small regulatory RNAs that are negative regulators of gene expression acting at the level of messenger RNA turnover or translation. Others participate in more complex epigenetic systems affecting chromatin or they act as part of an RNA signal that moves between cells. In plants the posttranscriptional mechanism is involved in defense against RNA viruses. The chromatin effects play a role in defense against DNA viruses and transposable elements and it is associated with the establishment of heritable epigenetic marks. There are secondary effects of the epigenetic marks that may influence the expression of adjacent genes in the sense of McClintocks "controlling elements". In most instances the effect is gene silencing and in some instances the effect may influence the biology of the affected plant. I will describe how RNA silencing may be particularly important following wide cross hybridisation and how it may influence hybrid vigour and transgressive segregation.

Date: Monday 3 April, 2017
Session: Hooke Medal Lecture
Time: 16:45 – 17:30
Venue: Main Lecture Theatre

PL04 16:45 – 17:30
Cell morphogenesis across scales, from molecular processes to cell-scale behaviours
E K Paluch

MRC LMCB, University College London, London, UK

A precise control of cell shape is key to cell physiology. Cell morphology is controlled by mechanical forces acting on the cell surface, to understand cell shape we must thus understand how cells control the mechanical properties of their surface. In animal cells, shape is primarily determined by the cellular cortex, a thin network of actin filaments and myosin motors bound to the plasma membrane. We investigate how cell surface mechanics arise from the microscopic organisation of the cortical network, and how changes in these properties drive cell deformation. We have developed methods to investigate the nanoscale architecture of the cortex and are exploring how the organisation of actin filaments and the spatial distribution of motor proteins in the cortex control network mechanics. Using a combination of cell biology experiments, quantitative imaging and theoretical modelling, we aim to understand cell surface tension generation and the control of cell shape across scales.

Date: Tuesday 4 April, 2017
Session: Evodevo
Time: 09:00 – 12:30
Venue: Main Lecture Theatre

S22 09:00 – 09:30
Explosive seed dispersal
A Hay

Comparative Development and Genetics, Max Planck Institute for Plant Breeding Research, Koln, Germany

How mechanical and biological processes are integrated across different scales to create complex traits is largely unknown. In this work, we combine biological, mathematical, and computational approaches to understand the mechanical basis for explosive seed dispersal – a key life history trait underpinning invasive behavior in the common weed *Cardamine hirsuta*. We have exploited the experimental tractability of *C. hirsuta* – a close relative of the model organism *Arabidopsis thaliana* – to understand the mechanism of explosive pod shatter and provide insights into the origin of this striking trait.

S23 09:30 – 10:00
Germline regeneration in the crustacean, *Parhyale hawaiensis*
M S Modrell, C Winchell, A Price, A Kaczmarczyk, **N H Patel**

Molecular Cell Biology, UC Berkeley, Berkeley, USA

The amphipod crustacean, *Parhyale hawaiensis*, derives its primordial germ cells from a single precursor cell (“g” cell) at the eight-cell stage, and the unique fate of this cell appears to be established via the unequal segregation of maternal cytoplasmic components. If this “g” cell is ablated, the animal hatches without a detectable germline as assayed by morphology and the expression of Vasa and Piwi. Remarkably, however, these animals are fertile as adults, and in these ablated animals germline cells reappear about halfway through juvenile development. We have used somatic transgenesis to determine the source of this replacement germline and find that it derives from mesoderm. We suggest that *Parhyale* possesses both a maternal mechanism involving cytoplasmic localization to specify germline in the embryo, as well as a later inductive mechanism that can act as a backup system.

S24 10:00 – 10:30
Hybrids Between the Two Most Phylogenetically Distant Genera of Cephalochordates Give Insights into the Evolution of Pharyngeal Development
L Z Holland, H Ono

Scripps Institution of Oceanography, University of California San Diego, La Jolla, USA

In the cephalochordate *Branchiostoma*, larval gill slits are on the right and mouth on the left. At metamorphosis, the mouth moves anteriorly, a second row of gill slits appears on the right, the first row moves left and gill bars divide each slit. Pharyngeal development in *Asymmetron*, which split from *Branchiostoma* ~150 mya, is similar, but gill slits are ventral. The emerging picture involves first specifying the territory for larval gill slits, then positioning them and dividing the territory into gill slit primordia. Surprisingly, the two genera hybridize. Both crosses (*Branchiostoma* female x *Asymmetron* male and vice versa) give larvae with gill

slits in intermediate positions. Some hybrids metamorphose, albeit with an abnormal pharynx. How does pharyngeal patterning differ between purebreds and hybrids? Is the mechanism patterning the second row of gill slits conserved with that for the first? Why is the second row of gill slits in hybrids abnormal?

S25 11:00 – 11:30
The mechanisms of developmental plasticity: from switch genes and epigenetics to the interplay of organisms and their environment
R J Sommer

Department for Integrative Evolutionary Biology, Max Planck Institute for Developmental Biology, Tuebingen, Germany

Developmental plasticity is increasingly recognized as primary mechanism for the emergence of novelty. However, molecular mechanisms underlying this phenomenon remain elusive. The nematode *Pristionchus pacificus* exhibits developmental plasticity for its mouth-form and feeding strategies. Individuals develop one of two alternative mouth-forms, a predatory eurystomatous (Eu, wide-mouthed) or a bacteriovorous stenostomatous (St, narrow-mouthed) form. Using genetic screens we have identified developmental switch genes that regulated plasticity. *eud-1* mutants are all-St, whereas mutants in the downstream nuclear-hormone-receptor *nhr-40* are all-Eu. More recent work indicates that *eud-1* expression is under epigenetic control involving the histone acetyltransferase *lsy-12*, which acts through an antisense RNA at the *eud-1* locus itself and up-regulates *eud-1* expression. Here we present our most recent molecular findings on i) the molecular mechanisms underlying plasticity, ii) the interaction of this regulatory network with the environment and iii) first insight into the involvement of small RNAs and Argonaute proteins.

O13 11:30 – 11:45
Poster Number: P075
The shortest germ: Evolution of an extreme short-germ mode of segmentation within the beetles
M A Benton, S Roth

Department for Developmental Biology, University of Cologne, Cologne, Germany

A segmented body plan is one of the key traits underlying the immense evolutionary success of insects. However, the manner in which segments are generated embryonically varies greatly between species. The best studied mode of segmentation (“long-germ”) is seen in flies like Drosophila melanogaster, where all segments are specified near simultaneously at the blastoderm stage. However, most insects only generate some segments at the blastoderm stage, while the rest are generated sequentially during posterior elongation of the embryo (“short-/intermediate-germ”). The long-germ mode has seemingly evolved several times from the ancestral short-germ mode, but the opposite has never been described. I will present my results from the previously uncharacterised beetle Atrachya menetriesi, which I have found to display the most extreme-short-germ mode ever described. This finding is remarkable because, based on current data, Atrachya seems to represent an actual example of the “re-evolution” of the short-germ mode from a long-/intermediate-germ ancestor.

S26 11:45 – 12:15
From Genotype to Phenotype: Evolution and Development of Cavefish Eye Loss
W R Jeffery

Biology, University of Maryland, College Park, USA

The teleost *Astyanax mexicanus* has eyed surface-dwelling (SF) and eyeless cave-dwelling (CF) morphs. CF embryos initiate but later arrest eye development. Multiple genes and QTL control the eyeless phenotype. A QTL on chromosome 21 contains the mutated *cbsa* gene encoding cystathionine ßsynthase, which converts homocysteine to cystathionine. Accordingly, homocysteine levels are increased during CF eye development. The known role of homocysteine in human cardiovascular disease prompted investigation of its effects on CF vascular development. Angiography revealed major leakages in CF eye vasculature frequently leading to hemorrhages. The hemorrhages are reversed within a few days, leaked blood cells are removed from the optic area by macrophages, and the afflicted CF larvae develop into normal adults. Knockdown of cbsa in SF induced optic vascular leakage and hemorrhages. The CF eyeless phenotype may have evolved by cbsa/homocysteine mediated effects on the optic vasculature, imposing anoxia and trophic deprivation on the developing eye.

O14 12:15 – 12:30
Poster Number: P067
Break down of Meckel’s cartilage provides clues to the evolution of mammals
N Anthwal[1], D J Urban[2], Z X Luo[3], K Sears[2], A S Tucker[1]

[1]Craniofacial Development and Stem Cell Biology, King’s College London, London, UK; [2]School of Integrative Biology, University of Illinois, Urbana, USA; [3]Organismal Biology, University of Chicago, Chicago, USA

The separation of the middle ear ossicles from the mandible by the breakdown of the Meckel’s cartilage is a key anatomical change during the evolution of mammals. Fossilised pre-mammalian synapsids posses a persistent ossified Meckel’s cartilage. These fossils are believed to be transitory forms, since only non-mammalian extant gnathostomes maintain Meckel’s cartilage to adulthood. We present biological mechanisms underlying the breakdown of Meckel’s cartilage, including the recruitment of chondroclast cells . Genetic or drug induced perturbations of clast cells in mice and opossums results in the persistence Meckel’s cartilage. Furthermore, we demonstrate that the Meckel’s undergoes ossification in mutant mice, in doing so phenocopying the Mesozoic pre-mammalian synapsids.

Date: Tuesday 4 April, 2017
Session: Cytoskeleton and Transport
Time: 09:00 – 12:30
Venue: Woods Scawen Lecture Theatre

S27 09:00 – 09:30
Mechanisms of microtubule-actin coordination: a journey from yeast to mammals
J Henty-Ridilla, J A Eskin, A Rankova, K Kenny, **B L Goode**

Biology Department, Brandeis University, Waltham, USA

Tight coordination between the microtubule (MT) and actin cytoskeletons is critical for cell migration, axonal pathfinding, and many other processes; however, the mechanisms underlying MT-actin crosstalk have remained elusive. This talk will show how our work on formin regulation in yeast led to the discovery of new roles for human CLIP-170 in MT-actin crosstalk. Using in vitro single-molecule imaging, we directly visualize CLIP-170 and formin Dia1 forming a barbed-end tracking complex that produces the fastest rates of actin filament elongation ever recorded. Further, we use an in vitro MT-actin co-reconstitution system to show that CLIP-170, Dia1, and EB1 work in concert to trigger the polymerization of actin filaments from MT ends. Using a specific allele of CLIP-170, we demonstrate that these activities are required for proper dendritic elaboration in primary neurons. Thus, our work offers the first mechanism to explain how dynamic MT plus ends spatially regulate actin assembly.

O15 09:30 – 09:45
Poster Number: P046
Localising mRNA drives assembly of *in vitro* reconstituted mRNPs and stimulates their transport through activation of cytoplasmic dynein
M A McClintock[1], C I Dix[1], K Zhang[2], H T Hoang[1], A P Carter[2], S L Bullock[1]

[1]Division of Cell Biology, MRC Laboratory of Molecular Biology, Cambridge, UK; [2]Division of Structural Studies, MRC Laboratory of Molecular Biology, Cambridge, UK

Cytoplasmic dynein-1 is a versatile microtubule-based motor that mediates the majority of minus end-directed processes in the cell. The diversity of these processes demands strict spatial, temporal and compositional regulation of dynein motility, though little is understood about how this is achieved. To investigate the regulation of dynein-cargo complexes, we have reconstituted a minimal transport competent mRNP *in vitro* and analysed its behaviour by single-molecule microscopy. Our results show that the RNA-binding protein Egalitarian, the adaptor BicD, and the dynactin complex are sufficient for robust dynein-dependent mRNA transport. Remarkably, the presence of mRNA is essential for robust activation of long distance dynein motion by Egalitarian and BicD. Our findings suggest that cargo association with adaptor proteins is a key step in the activation of dynein motility in cells. We are currently investigating how RNA activates motility and will present our latest findings at the meeting.

S28 09:45 – 10:15
Regulation of human cytoplasmic dynein revealed through a proteomics approach
W B Redwine[3], M E DeSantis[1], I Hollyer[5], Z M Htet[1], P T Tran[1], S K Swanson[4], L Florens[4], M P Washburn[4], **S L Reck-Peterson**[1,2,3]

[1]Cellular and Molecular Medicine, University of California San Diego, La Jolla, USA; 2Biology, University of California San Diego, La Jolla, USA; [3]Cell Biology, Harvard Medical School, Boston, USA; [4]Stowers Institute for Medical Research, Kansas City, USA; [5]Feinberg School of Medicine, Northwestern University, Chicago, USA

In human cells, cytoplasmic dynein-1 is essential for long-distance transport of multiple types of cargos, including organelles, RNAs, protein complexes, and viruses, towards microtubule minus ends. To understand how a single motor can achieve cargo specificity, we identified the human dynein proteome by attaching a promiscuous biotin ligase (“BioID”) to seven distinct components of the dynein machinery. This method reported spatial information about the large moving cytosolic dynein complex in living cells. To achieve maximal motile activity, human dynein requires “activators”, of which only a few have been described. Here we developed methods to identify activators, including two novel ones, ninein and ninein-like. Thus, dynein appears to have far fewer activators than cargos. Indeed, our analysis of the proteome of six dynein activators, suggests that dynein cargo specificity is controlled in a tiered fashion in which activators constitute the first, but not exclusive layer of regulation.

O16 10:15 – 10:30
Poster Number: P044
Cdc42 controls epithelial polarity by coordinating cortical polarization and plasma membrane specialization through Par6
F Nunes de Almeida, R F Walther, E Vlassaks, F Pichaud

MRC LMCB, University College London, London, UK

How cortical polarity arises and translates into plasma membrane specialization during epithelial morphogenesis is not fully understood. To study this question, we used the cellularizing embryo and fly photoreceptor to show that partitioning of the cortex into a sub-apical domain and apical junctional belt (*Zonula Adherens, ZA*) relies on two convergent pathways, connected through Par6. Cortical polarity arises through Par6-aPKC segregating away from Bazooka (Baz), a molecular sorting mechanism that we show is controlled by the small GTPase Cdc42. Moreover, we find that Par6 binds to Exo84 to promote exocyst-dependent delivery of Crumbs, which enables sub-apical membrane and ZA morphogenesis. We conclude that polarization of the apical cortex is an emergent property of the Cdc42-Par6-aPKC-Baz biochemical module, with Cdc42 regulating the apical localization of Par6-aPKC. Translating cortical polarity into membrane specialization relies on a delivery-based positive feedback loop, which also acts as a cortical asymmetry amplifier through Crumbs.

S29 11:00 – 11:30
Regulation of microtubule minus-end dynamics at spindle poles by microcephaly-related proteins ASPM and katanin
K Jiang[1], L Rezabkova[2], S Hua[1], Q Liu[1], G Capitani[2], R A Kammerer[2], M O Steinmetz[2], **A Akhmanova**[1]

[1]Cell Biology, Utrecht University, Utrecht, The Netherlands; [2]Laboratory of Biomolecular Research, Paul Scherrer Institut, Villigen PSI, Switzerland

Microcephaly is a neurodevelopmental disorder characterized by small head and brain, and intellectual disability. ASPM (abnormal spindle-like microcephaly-associated) is the most common gene mutated in microcephaly patients, but the molecular mechanisms underlying ASPM activity are poorly understood. We found that ASPM forms a physiological complex with the microtubule-severing protein katanin, which is also known to be mutated in microcephaly patients. ASPM and katanin localize to spindle poles in a mutually dependent manner and regulate spindle flux and spindle positioning. In vitro reconstitution experiments demonstrated that ASPM autonomously tracks growing microtubule minus ends and inhibits their growth, while katanin decorates and bends both ends of dynamic microtubules and enhances the minus-end blocking activity of ASPM. ASPM also binds along microtubules and recruits katanin, promoting efficient katanin-mediated severing of dynamic microtubules. We propose that ASPM-katanin complex controls microtubule disassembly at spindle poles, and that misregulation of this process can lead to microcephaly.

O17 11:30 – 11:45
Poster Number: P048
Rab27a co-ordinates actin-dependent long-range organelle transport by integrating the activity of motors and track assembly proteins
A N Hume[1], C L Robinson[1], D A Briggs[1], A Stainthorp[1], E V Sviderskaya[2], E Kerkhoff[3], T Welz[3], L Montoliu[4]

[1]School of Life Sciences, University of Nottingham, Nottingham, UK; [2]Division of Biomedical Sciences, St. George's, University of London, London, UK; [3]Department of Neurology, University Hospital Regensburg, Regensburg, Germany; [4]Molecular and Cellular Biology, 3Centro Nacional de Biotecnologia (CNB-CSIC), Madrid, Spain

Cell biologists generally consider that microtubules and actin play complementary roles in long- and short-distance transport in animal cells. On the contrary, using melanosomes of melanocytes as a model, we recently discovered that motor myosin-Va, works with dynamic actin tracks, to drive long-range transport in microtubule depleted cells. This suggests that in animals, as in yeast and plants, myosin/actin can drive long-range transport. Here we show that the actin assembly activity of spire and formin (Fmn-1) proteins is required for myosin-Va-dependent transport. Moreover we show that, in addition to recruiting myosin-Va, Rab27a recruits spire/Fmn-1 to melanosomes, thereby integrating motor and track assembly activity at the organelle membrane. Based on this we suggest a model in which organelles and force generators (motors and track assemblers) are linked forming a cell-wide network that allows the collective activity of the force generators to rapidly disperse the population of organelles long-distance throughout the cytoplasm.

S30 11:45 – 12:15
Examining how nanometer-sized proteins assemble dynamic micron-sized structures needed for successful cell division
T M Kapoor

Selma and Lawrence Ruben Laboratory of Chemistry and Cell Biology, The Rockefeller University, New York, USA

We study basic mechanisms underlying cell division with the long-term goal to develop new and effective therapies. We combine synthetic chemistry, the discovery and use of chemical probes, biochemistry and quantitative cell biology to answer long-standing questions relating to cell division. I will highlight our recent efforts to reconstitute a 'minimal' cell division apparatus with purified proteins. These studies, combined with high-resolution live cell imaging, are providing insight into how essential proteins can be regulated by microtubule or overlap lengths, simple geometric features that can be ~1000-fold larger than the proteins. The principles of dynamic self-assembly that we uncover by studying the microtubule-based structures needed for error-free cell division are likely to be general and can help explain the assembly of other complex cellular architectures, such as those needed for directional transport in neurons.

O18 12:15 – 12:30
Poster Number: P051
Switching On and Off the Motor Activity of Intraflagellar Transport Dynein
K Toropova, M Mladenov, **A J Roberts**

Institute of Structural and Molecular Biology, Birkbeck, London, UK

Cilia are multi-functional organelles that are constructed using intraflagellar transport (IFT) of cargo to and from their tip. It is widely held that the retrograde IFT motor, dynein-2, must be controlled in order to reach the ciliary tip and then unleashed to power the return journey. However, the mechanism is unknown. Here, we systematically define the mechanochemistry of human dynein-2 motors as monomers, dimers, and multi-motor assemblies with kinesin-II. Combining these data with insights from single-particle electron microscopy, we discover that dynein-2 dimers are intrinsically autoinhibited. Inhibition is mediated by trapping dynein-2's mechanical "linker" and "stalk" domains within a novel motor-motor interface. We find that linker-mediated inhibition enables efficient transport of dynein-2 by kinesin-II *in vitro*. These results suggest a conserved mechanism for auto-regulation among dimeric dyneins, which is exploited as a switch for dynein-2's recycling activity during IFT.

Date: Tuesday 4 April, 2017
Session: Newly Tractable Systems
Time: 09:00 - 10:30
Venue: Cinema

S31 09:00 – 09:30
The power behind the throne: epigenetics in social insects
E B Mallon

Department of Genetics, University of Leicester, Leicester, UK

Hymenopteran insects (ants, bees and wasps) are important emerging models for epigenetics. This is due to theoretical predictions for a role for genomic imprinting in their social organisation (e.g. worker reproduction) and on data showing a fundamental role for methylation in their biology. All social insect genome projects have thus far found methylation and there is evidence for it in non-sequenced species as well. It is often stated that the identification of genomic imprintng, a key function of methylation in other species, should be a priority.
I will discuss our work looking a the role of methylation in bumblebee social organisation. I will also discuss work trying to identify genomic imprinting in bumblebees. Finally I will touch on some work showing an epigenetic response to neonicotinoids, an insecticide thought to be important for pollinators' decline.

O19 09:30 – 09:45
Poster Number: P143
Primitive endoderm and epiblast specification during preimplantation development of rabbit embryos
A Piliszek[1], Z Madeja[2], P Pawlak[2], A C Konarska Diaz[1], B Plusa[3]

[1]Department of Experimental Embryology, Institute of Genetics and Animal Breeding PAS, Jastrzebiec, Poland; [2]Department of Genetics and Animal Breeding, Poznan University of Life Sciences, Poznan, Poland; [3]Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Preimplanation development of mammalian embryos comprises two consecutive cell fate decisions, and their proper execution is necessary for the formation of three cell lineages: pluripotent epiblast (EPI), and extraembryonic primitive endoderm (PrE) and trophectoderm. Here we present stage-by-stage analysis of the formation of EPI and PrE during rabbit preimplantation development. Our data suggest that reciprocal repression of GATA6 and NANOG might not be essential for initiation of PrE versus EPI specification in the rabbit, and that FGF/ERK inhibition is not sufficient to sustain naive pluripotency in the rabbit epiblast. Consistent with that observation, we show that FGF/ERK inhibition (2i/3i treatment), although proven successful in the murine ES cell derivation, does not support derivation of pluripotent ES cell lines in the rabbit. These results suggest differences in PrE versus EPI specification and in mechanisms regulating pluripotency between different mammals.

S32 09:45 – 10:15
DNA Methylation in Social Insects
M A D Goodisman

Biological Sciences, Georgia Tech, Atlanta, USA

The evolution of sociality represented one of the major transition points in biological history. Social insects, which are the most successful social animals, succeed because of the remarkable caste system displayed by colony members. The developmental plasticity leading to castes relies fundamentally on epigenetic information. DNA methylation is one of the most widespread epigenetic marks and has been linked to developmental plasticity in insects. This research applies an evolutionary framework to studying epigenetics. Analyses suggest that DNA methylation is generally conserved in insects with functional methylation systems. DNA methylation is targeted to ubiquitously transcribed genes. Different insects show surprising variation in levels of DNA methylation. The distribution of DNA methylation in social insect genomes has also been linked to histone modifications and alternative splicing. Overall, this research reveals evolutionary conservation and variability of DNA methylation in insects and provides insight into the function of DNA methylation across eukaryotic systems.

O20 10:15 – 10:30
Poster Number: P184
Using metatherians to elucidate the evolution of mammalian epigenetic pathways
B Leeke, F Decarpentrie, S K Mahadevaiah, J Zohren, S Wood, S Horswell, M N Sangrithi, J M A Turner
The Francis Crick Institute, London, UK

Metatherians diverged from eutherian mammals 160-180Mya, and are an excellent model system for researching mammalian evolution. We have recently used the metatherian Monodelphis domestica, to understand the evolution of mammalian epigenetic pathways. We focus on X-chromosome inactivation (XCI), the silencing of one X chromosome that ensures an equal dosage of X-gene products between females (XX) and males (XY). Eutherian XCI is mediated by the non-coding RNA Xist, and maintenance of XCI relies on epigenetic marks on the inactive X (Xi), particularly hypermethylation of CpG islands. Metatherians have no Xist gene, and examination of specific Xi-genes suggests that they do not exhibit CGI hypermethylation. We will describe our ongoing characterisation of a potential metatherian Xist equivalent, Rsx, and the application of methylation sequencing to generate genome-scale methylation maps in this species. Our findings suggest both shared and distinct epigenetic mechanisms driving the silencing of the X chromosome between metatherians and eutherians.

Date: Tuesday 4 April, 2017
Session: Mechanisms in Gene Expression
Time: 11:00 – 12:30
Venue: Cinema

S33 11:00 – 11:30
Distant-Acting Enhancers in Development, Disease, and Evolution
A Visel

[1]Functional Genomics Department, Lawrence Berkeley National Laboratory, Berkeley, USA; [2]Joint Genome Institute, Walnut Creek, USA; [3]School of Natural Sciences, University of California, Merced, USA

The human genome harbors tens of thousands of distant-acting gene regulatory sequences that play important roles in the development and function of the human body. Multiple converging lines of evidence from experimental and human genetic studies indicate that both common and rare sequence variants involving enhancers play major roles in Mendelian and complex human disease phenotypes. However, the underlying molecular mechanisms are difficult to study due to our limited understanding of the *in vivo* functions of enhancers. We use a combination of sequence-based molecular approaches (ChIP-seq), large-scale transgenic mouse studies (http://enhancer.lbl.gov), and CRISPR genome editing in the mouse model to study the *in vivo* function of enhancers in developmental, evolutionary, and disease-related processes. Using examples from our ongoing work, I will illustrate how these studies provide insight into the function and evolution of distant-acting regulatory sequences and offer a starting point for understanding their role in human disease.

O21 11:30 – 11:45
Poster Number: P100
Regulatory principles governing enhancer function
K M Olson[1,2], F Lim[1,2], C DeBoever[3], K M Frazer[3], **E K Farley**[1,2]

[1]Department of Medicine, UCSD, La Jolla, USA; [2]Division of Biological Sciences, UCSD, La Jolla, USA; [3]Department of Pediatrics, UCSD, La Jolla, USA

Enhancers are genomic elements that encode the instructions for when and where genes are expressed during development and homeostasis. The majority of mutations leading to disease are thought to reside within enhancers. However, we do not understand which changes in enhancer sequence are inert sequence variations between individuals and which mutations impact gene regulation and cell identity. These fundamental questions remain unsolved because we cannot relate enhancer sequence to gene expression patterns and phenotype. To address this problem, we developed high-throughput assays to test millions of enhancer variants for function in millions of embryos. The model organism that enables such in-depth functional approaches is the marine chordate *Ciona intestinalis*. I will discuss our recent experiments using this approach to identify organizational constraints and other regulatory principles governing enhancer function. I will also discuss how we are using these principles to pinpoint mutations associated with disease.

O22 11:45 – 12:00
Poster Number: P099
Transcription of intragenic CpG islands and their associated epigenetic marks as regulators of tissue- and developmental-stage specific transcription of related host genes
S Amante, M Cowley, N Barkas, S Contreras, R Schulz, **R J Oakey**

Medical and Molecular Genetics, King's College London, London, UK

CpG islands (CGIs) are associated with transcription start sites of genes, they are rich in CpGs and frequently un-methylated. Their definition derives from bioinformatics-based criteria; however, empirical methods have identified previously unannotated CGIs in intragenic locations of many vertebrate genes. RNA processing involves multiple steps that provide opportunities for regulating gene expression, for

instance by changing the abundance of transcripts or generating isoforms. Accumulating data reveal that epigenetic modifications at intragenic CGIs (iCGIs) influence isoforms through polyadenylation site choice. In seeking to investigate the role(s) of iCGIs and alternative polyadenylation site usage in generating tissue-specific transcripts, we used genome-wide-analyses to assess transcriptional activity upstream, spanning, and at iCGIs. We report that iCGIs influence gene transcription and polyadenylation site choice in a tissue-specific way at 1427 discrete loci and correlate this with DNA methylation state and histone modifications at these iCGIs between tissues.

O23 12:00 – 12:15
Poster Number: P088
CSL DNA-binding dynamics are a major point of regulation in determining the functional consequences of Notch activation
M J Gomez Lamarca[1], J Falo Sanjuan[1], R Stojnic[1], S Abdul-Rehman[2], L Muresan[2], G Cerda-Moya[1], M Jones[1], K O'Holleran[2], R Kovall[3], S J Bray[1]

[1]Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK; [2]Cambridge Advance Imaging Centre, University of Cambridge, Cambridge, UK; [3]College of Medicine, University of Cincinnati, Cincinnati, USA

Notch pathway is a major signalling pathway involved in development. Upon activation, Notch, the transmembrane receptor, undergoes two cleavages, releasing its intracellular domain (NICD). NICD forms a complex with a DNA-binding transcription factor, CSL, and the co-activator Mastermind to stimulate transcription. Chromatin immunoprecitation studies of CSL binding, indicates that Notch activation is accompanied by changes in the genomic occupancy of CSL, suggesting that NICD stimulates CSL movement and/or binding kinetics. To investigate this, we studied CSL nuclear dynamics using live imaging techniques, including Fluorescence Recovery After Photobleaching and Single Molecule Tracking. Our results revealed that in Notch-OFF cells, only a small fraction of CSL molecules are bound to DNA at anytime, and their binding is highly dynamic. In Notch-ON cells, CSL becomes highly enriched at target loci. Two different mechanisms operate: Notch induced “assisted loading” increases the number of CSL complexes recruited, and Mastermind functionality favours an increased dwell time.

O24 12:15 – 12:30
Poster Number: P089
Exploiting Notch regulation to probe alternative mechanisms of TSC signaling
E Vlassaks, S Woodcock, H Shimizu, M Baron

Faculty of Life Sciences, University of Manchester, Manchester, UK

Tuberous sclerosis is caused by mutations in Tuberous Sclerosis Complex (TSC)-1 and TSC-2 genes, and manifests in hamartomas throughout the body. The TSC proteins form a complex that is involved in the control of cell growth and division by repressing the Rheb GTPase and thus controlling mTOR signaling on the surface of lysosomes. Inhibiting mTOR has demonstrated clinical efficacy in treating TSC-associated tumors, however, responses are usually only partial and regrowth occurs after drug withdrawal. Work in *Drosophila* suggests that the partial success is due to the fact that Rheb also targets Tor-independent mechanisms. Following a genome-wide RNAi screen in *Drosophila*, we found that TSC knockdown specifically downregulates a form of ligand-independent Notch signaling. Moreover, we observed that this is independent of Tor, but dependent of Rheb. We are now exploiting the mechanistic links between TSC/Rheb and Notch, which can provide new opportunities in the search for better drug targets.

Date: Tuesday 4 April, 2017
Session: PhD/Postdoc Symposium
Time: 15:30 – 17:00
Venue: Main Lecture Theatre

O25 15:30 – 15:45
Poster Number: P003
Binary fission: from archaea to unicellular eukaryotes
G Dey[1], G Risa[1], S Culley[1], R Henriques[1], R Desai[2], B Baum[1]

[1]MRC Lab for Molecular Cell Biology, University College London, London, UK; [2]Biological Making Lab, The Francis Crick Institute, London, UK

Eukaryotes evolved from a genomic merger between an archaeal host and a bacterial endosymbiont. Since the first eukaryote was therefore topologically linked to its putative archaeal ancestor by an unbroken sequence of cell divisions, understanding division mechanisms that survived the transition from archaea to eukaryotes could shed new light on the origins of the eukaryotic cell cycle. The thermophilic model archaeon *Sulfolobus* uses homologs of eukaryotic proteins to regulate a phasic eukaryote-like division cycle. We are leveraging novel super-resolution imaging approaches and microfluidics to better understand the role of ESCRTIII homologs in *Sulfolobus* binary fission. In parallel, we are investigating the dynamics of, and a possible role for ESCRTIII in, nuclear division ('closed mitosis') in fission yeast. I will present our latest experimental results, hoping in the future to probe 'inside-out' models for eukaryogenesis that envisage the eukaryotic nucleus as the topological equivalent of an archaeal cell.

O26 15:45 – 16:00
Poster Number: P007
Imaging chromatin dynamics reveals a novel mechanism for nuclear organisation after cell division
A S Sherrard, A K Kaidi

Cellular and Molecular Medicine, University of Bristol, Bristol, UK

Re-establishment of nuclear structure and chromatin organisation after cell division is integral for genome regulation and cell function. However, the mechanisms underlying this process remain incompletely understood. Given the dramatic re-organisation of the nucleus during and after mitosis, we hypothesised that nuclear organisation after mitosis may be driven by filamentous structures such as polymerised actin (F-actin). Accordingly, we discovered a transient and pronounced assembly of F-actin in the nuclei of daughter cells upon exiting mitosis. By developing a quantitative method for imaging chromatin dynamics in intact cell using florescent lifetime imaging microscopy (FLIM), we identified a key role for this F-actin in chromatin de-condensation after mitosis. A combination of quantitative biochemical and cell imaging assays revealed that interference with this nuclear F-actin assembly impairs the re-establishment of nuclear structure and chromatin organisation post mitosis, and influences transcription and replication in the daughter cells.

FT01 16:00 – 16:05
Poster Number: P101
Genomic Relation of Human Aggression Behavior in Convicted Offenders for Physical Assault and Terrorism
M Javed[1], A Nadeem[1], M E Babar[2], W Shehzad[1], T Hussain[2], N Mukhtar[3], T Yaqub[3]

[1]Institute of Biochemisty and Biotechnology, University of Veterinary and Animal Sciences, Lahore, Pakistan; [2]Department of Molecular Biology, Virtual University, Lahore, Pakistan; [3]Department of Microbiology, University of Veterinary and Animal Sciences, Lahore, Pakistan

Genomic association of human negatively driven behavior lies under the control of Serotonergic system derived by *MAOA* gene responsible for criminal violence and aggression. In this context, following study was planned to evaluate the genetic variants in MAOA gene associated with the violence in convicted offenders of Physical assault and terrorism from Central Jail in Lahore, Pakistan. Blood/Saliva /Buccal swabs samples were collected from Jail of Punjab, Pakistan and organic method of DNA extraction was used. Exonic regions of the gene were amplified and sequences. Analysis of region indicated two polymorphisms. The exon 13 having heterozygous SNP, AT instead of TT. This SNP was found strongly associated with level of aggression score calculated on a specially designed proforma. These SNPs can be potential markers for detecting the level of eggression and to design a national stretegic plan for controlling the risk factors behind this raising concern regarding aggression.

FT02 16:05 – 16:10
Poster Number: P156
Capturing emerging pluripotency in the pig early embryo by modulation of WNT and ERK signalling pathways
P Ramos-Ibeas[1], S Withey[1], D Klisch[1], J Nichols[2], R Alberio[1]

[1]School of Biosciences, The University of Nottingham, Nottingham, UK; [2]Wellcome Trust-Medical Research Council Stem Cell Institute, University of Cambridge, Cambridge, UK

Despite multiple attempts, germline competent pig ESCs have not yet been established. Here we set out to elucidate how pluripotency emerges during pig embryo development and investigated how WNT and ERK (PD0325901) modulation can promote NANOG expression in the epiblast and support the establishment of pESC. t2iGö inhibition during the morula to blastocyst transition prevented hypoblast segregation, resulting in ICM enriched for NANOG+ cells and devoid of SOX17+ cells. WNT inhibition alone did not affect SOX17 expression in the ICM, whereas in combination with PD resulted in no SOX17 expression. Pig ESC derivations using t2iLGö and WNTi + PD were unsuccessful, however cell lines could be established when cultured with WNTi + FGF with or without Activin A (7 passages). These experiments demonstrate contrasting roles of ERK and WNT signalling during the formation of the ICM and in self-renewing pig ESC cultures.

FT03 16:10 – 16:15
Poster Number: P097
Gene family expansion allows diversification of transcriptional bursting dynamics
E Tunnacliffe, A M Corrigan, J R Chubb

MRC-LMCB, UCL, London, UK

During the evolution of gene families, diversification often follows gene duplication which can result in the generation of novel protein functions. However, in some instances, notably histones, gene families can expand while preserving protein sequence. Why would a cell need to maintain multiple copies of the same

gene? Here we have addressed this question for an actin gene family containing 17 genes encoding an identical protein. We show that family members display different transcriptional dynamics with strong 'bursty' behaviours contrasted by more stable transcriptional activity. These differences in transcription dynamics could play a functional role with constitutive protein production supplemented by more transient responses to environmental stimuli enabling precise regulation within a highly compact genome. We are now investigating the downstream effects of these differential dynamics at both the mRNA and protein level as well as probing the genetic determinants by promoter switching.

FT04 16:15 – 16:20
Poster Number: P131
The biomechanics of cells and the 3D structures they form: novel tools for mechanobiology
V Bentivegna[1], F Stewart[1], S Cochran[2], I Näthke[1]

[1]Cell and Developmental Biology, School of Life Sciences, University of Dundee, Dundee, UK; [2]School of Engineering, University of Glasgow, Glasgow, UK

During development and disease progression, cells undergo mechanical changes and respond differently to physical cues. Understanding these changes requires novel tools to measure mechanical properties of 3D tissues. Furthermore, related computational techniques are needed to show how properties of individual cells generate the mechanical properties of 3D structures they form. We used atomic force microscopy (AFM) to compare the mechanical properties of cells in 2D monolayers and in 3D cysts. However, AFM requires contact with the sample, making measurements in cysts difficult and unreliable. Microultrasound is an alternative approach that does not require contact. Preliminary results show that microultrasound can measure size and mechanical properties of living 3D structures. We are currently using markers for mechanical stress to determine the effect of compression created by ultrasound radiation pressure. Eventually, this approach could permit measurement of mechanical properties of tissue *in situ* to reveal how mechanics influences tissue behaviour.

FT05 16:20 – 16:25
Poster Number: P78
The Development of Olfactory Ensheathing Cells from the Neural Crest
S N Perera[1], R Williams[2], D Buehler[3], T Sauka-Spengler[2], M Southard-Smith[3], C V H Baker[1]

[1]Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK; [2]Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, UK; [3]Division of Genetic Medicine, Vanderbilt University Medical Center, Nashville, USA

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 the molecular mechanisms underlying neural crest differentiation into OECs, as opposed to Schwann cells, which are less effective in spinal cord repair. To achieve this, I am taking 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 should identify candidate genes that may be important specifically for OEC differentiation and that distinguish different OEC subpopulations.

O27 16:25 – 16:40
Poster Number: P060
Chromatin-remodelling ATPase central subunits and plant defence
A J Pardal, Dr Ntoukakis

School of Life Sciences, University of Warwick, Coventry, West Midlands

Plants can detect pathogen microorganisms and build up defences accordingly. In order to survive and guarantee the provision of seeds for the next generation, the limited plant resources need to be finely tuned in the trade-off between growth and defence upon pathogen perception. Gene reprogramming is therefore a major component of the innate plant defence. Chromatin remodelling complexes have been pinpointed as regulators of immunity. Here we report a susceptibility screening, using the *Arabidopsis – Pseudomonas siryngae* pathosystem, for chromatin remodelling ATPases as novel regulators of plant immunity. We characterise the biological function and we are interested in describing its molecular mechanism of action. Our preliminary data highlights chromatin remodelling as a target for gene silencing via a negative feed-back loop mechanism, allowing the plant to recover pre-defensive genetic program in order to re-gain successful growth and reproduction.

O28 16:40 – 16:55
Poster Number: P106
Circadian-related gene expression in the suprachiasmatic nucleus of an R6/2 mouse model of Huntington's disease in response to a light pulse
M Ware, K Ouk, A J Morton

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

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.

Date: Tuesday 4 April, 2017
Session: Beddington Medal Lecture
Time: 17:15 – 17:45
Venue: Main Lecture Theatre

PL05 17:15 – 17:45
The evolution and development of Drosophila segment patterning
E Clark[1], A D Peel[2], M E Akam[1]

[1]Department of Zoology, University of Cambridge, Cambridge, UK; [2]School of Biology, University of Leeds, Leeds, UK

The Drosophila “segmentation cascade” is a paradigm for developmental pattern formation and has been studied for decades. However, two key aspects of Drosophila segmentation are still not well understood. First, the more complex later stages of patterning, involving the so-called “pair-rule” genes, are not understood at the systems level. Second, the relationship between the simultaneous, “long-germ” mode of patterning seen in Drosophila, and the sequential, “short-germ” mode of patterning seen in most other arthropods remains mysterious. I have been using a combination of models and experiments to unravel the first problem, revealing a previously unrecognised role for temporal information in spatially patterning the Drosophila embryo. Unexpectedly, these findings also shed light on the second problem, as they suggest a simple evolutionary mechanism by which to transition between simultaneous and sequential modes of segmentation.

Date: Tuesday 4 April, 2017
Session: Women in Cell Biology Medal Lecture
Time: 17:45 – 18:15
Venue: Main Lecture Theatre

PL06 17:45 – 18:15
Connecting actomyosin dynamics to transcriptional responses for efficient cancer cell migration and invasion
V Sanz-Moreno

Randall Division of Cell and Molecular Biophysics, King’s College London, London, UK

Rho GTPases are molecular switches that control the cytoskeleton. Deregulation of Rho GTPases can result in aberrant function and disease, including cancer. The spreading of cancer cells from one part of the body to another, called metastasis, is one of the biggest causes of cancer death. To metastasise, tumor cells must move through tissues and cross tissue boundaries, which requires cell motility, remodelling of cell-cell contacts and interactions with the extracellular matrix. Rho GTPases control actomyosin contractility, adhesive forces and matrix degradation, all necessary for cells to migrate and disseminate efficiently. We have used a combination of “OMICs”, state of the art microscopy in 3D matrices, molecular biology and animal models to understand how actomyosin perpetuates invasive behaviours in human tumours via strong cross-talks with pro-tumorigenic and pro-metastatic transcriptional programs.

Date: Tuesday 4 April, 2017
Session: Cheryll Tickle Medal Lecture
Time: 18:15 – 19:00
Venue: Main Lecture Theatre

PL07 18:15 – 19:00
J Nichols

Date: Wednesday 5 April, 2017
Session: Mechanisms in Gene Expression
Time: 09:30 – 11:00
Venue: Main Lecture Theatre

S34 09:30 – 10:00
The novel de novo DNA methyltransferase DNMT3C protects male fertility against transposon activity
J Barau[1], A Teissandier[1], N Zamudio[1], S Roy[2], V Nalesso[3], Y Hérault[3], F Guillou[2], D Bourc'his[1]

[1]Genetics and Developmental Biology, Institut Curie, Paris, France; [2]Physiologie de la Reproduction et des Comportements, INRA, Nouzilly, France; [3]Translational Medicine and Neurogenetics, IGBMC, Illkirch, France

DNA methylation-based epigenetic repression of transposons is of paramount importance for mouse spermatogenesis. However, the *de novo* methyltransferase responsible for this process is still uncertain. Single inactivation of the currently known enzymes, DNMT3A and DNMT3B, do not show germline methylation defects at transposons. We have now identified DNMT3C, a novel *de novo* cytosine methyltransferase enzyme that is absolutely required for the establishment of the epigenetic silencing of transposons in the male germline. DNMT3C mutant males are infertile in the context of a massive transposon reactivation and interruption of spermatogenesis at meiosis. We show that DNMT3C is highly specialized in *de novo* methylation of retrotransposon promoters, likely being the downstream enzyme of piRNA-directed DNA methylation. The discovery of DNMT3C challenges our current views on the evolution of DNA methyltransferases, the biochemistry of *de novo* methylation in the male germline, and the epigenetic control of reproduction in mammals, including that of humans.

O29 10:00 – 10:15
Poster Number: P085
A long undecodable transcript isoform mediates transcriptional repression of the *NDC80* gene during early meiosis in budding yeast
M Chia[1], A Tresenrider[2], J Chen[2], G Spedale[1], E Ünal[2], F J van Werven[1]

[1]Cell Fate and Gene Regulation Lab, The Francis Crick Institute, London, UK; [2]Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA

To ensure faithful chromosome segregation during budding yeast meiosis, expression levels of the outer kinetochore protein *Ndc80* are tightly controlled. During early meiosis, transcription of a long undecodable transcript isoform ($NDC80^{luti}$) represses expression of the canonical NDC80 protein coding isoform ($NDC80^{ORF}$) in cis. $NDC80^{luti}$ transcription establishes a repressive chromatin state at the 5' end of *NDC80* and repression depends on the Set2/Rpd3S and the Set3C pathways. Furthermore, multiple upstream open reading frames in $NDC80^{luti}$ prevent its translation into Ndc80. This repression mechanism is highly dynamic because $NDC80^{luti}$ transcription is quickly switched off and $NDC80^{ORF}$ is rapidly de-repressed when cells are returned to the mitotic cell cycle. In conclusion, repression of $NDC80^{ORF}$ by a long isoform is mediated through a combination of transcriptional interference, repressive chromatin, and translational control. We propose that this could be a generic mechanism for temporal transcriptional repression in cell fate-regulatory programs.

S35 10:15 – 10:45
The critical role of the placenta for normal development
M Hemberger

Epigenetics Programme, The Babraham Institute, Cambridge, UK

A functional placenta is key to reproductive success, yet this organ is still often overlooked as the potential origin of developmental failure. In a placental phenotyping screen carried out as part of the Deciphering the Mechanisms of Developmental Disorders (DMDD) consortium, we find that two-thirds of embryonic lethal gene mutations exhibit placental defects, a number far higher than appreciated to date. Our further efforts focus on elucidating the epigenetic and transcriptional regulation of Trophoblast Stem Cells (TSCs), a stem cell population that represents the building block of all placental trophoblast cell types. We find that their self-renewal capacity is tightly controlled by a stoichiometry-sensitive network of interacting transcription factors centered around Elf5. At the same time, we are pursuing a CRISPR-Cas9-driven knockout screen in TSCs to determine the origins of developmental abnormalities that may have a placental origin. These efforts will help elucidate the gene complexity required for normal placentation.

O30 10:45 – 11:00
Poster Number: P091
Coordinate Regulation of Development by a Shared RNA Element
A Zaucker[1], A Nagorska[1], Y Wang[1], S Huang[1], L Cooper[1], P Kumari[1], N Hecker[2], J Brosens[1], J Gorodkin[2], K Sampath[1]

[1]Division of Biomedical Sciences, University of Warwick, Coventry, UK; [2]Center for Non-coding RNA in Technology and Health, University of Copenhagen, Copenhagen, Denmark

Developmental gene expression is regulated at the level of DNA and/or RNA. We find that an RNA element we previously identified in the zebrafish *nodal /squint* (*sqt*) 3'UTR is shared by multiple Nodal signalling pathway components: *lefty1/2* inhibitors, *acvr2a* receptor and *smad2* effector RNAs. Reporter assays for localization and translation in early embryos suggest that the RNA elements function similarly to the *nodal* 3'UTR. Y-box binding protein1 (Ybx1) binds to the RNA element and the translation pre-initiation complex, resulting in translational repression of *nodal* and *lefty*. Whereas *Mybx1* mutant embryos show premature Nodal translation and gain-of-Nodal signalling, *Mybx1;nodal* compound mutants display premature and elevated Lefty protein expression and loss-of-Nodal signalling. Thus, multiple components of a developmental pathway are translationally regulated by a shared RBP/RNA element "regulon". This module also regulates human *NODAL*. Computational analysis identified >800 zebrafish transcripts harbouring similar elements, and preliminary assays indicate broader roles for this regulon.

Date: Wednesday 5 April, 2017
Session: Cell Competition
Time: 09:30 – 11:00
Venue: Woods Scawen Lecture Theatre

S36 09:30 – 10:00
Two transmissible cancers in Tasmanian devils
E P Murchison

Department of Veterinary Medicine, University of Cambridge, Cambridge, UK

Tasmanian devils are marsupial carnivores endemic to the Australian island of Tasmania. Tasmanian devils are considered endangered due to the emergence of a transmissible facial cancer that is spread between animals by the transfer of living allogeneic cancer cells by biting. This cancer, known as DFT1, was first observed in 1996, and has spread through devil populations across most of the island. In 2014, a second transmissible facial cancer, DFT2, was observed in devil populations in Tasmania's south-east. Considering the rarity of transmissible cancers in nature, it is surprising to find two transmissible cancers in the same species. We have reconstructed the genomes of both DFT1 and DFT2, and are using these to understand the origins and evolution of transmissible cancers in Tasmanian devils.

O31 10:00 – 10:15
Poster Number: P001
Differential EphA2 drives segregation and extrusion of Ras-transformed epithelial cells from normal tissues
S Porazinski[1], J de Navascues[1], Y Yako[2], W Hill[1], M Jones[1], R Maddison[1], Y Fujita[2], **C Hogan**[1]

[1]European Cancer Stem Cell Research Institute, School of Biosciences, Cardiff University, Cardiff, UK; [2]Division of Molecular Oncology, Institute for Genetic Medicine, Hokkaido University Graduate School of Chemical Sciences and Engineering, Sapporo, Japan

In epithelial tissues, cells expressing oncogenic Ras (RasV12) are detected by normal neighbours and are subsequently extruded from the tissue. The mechanism underlying detection of the mutant cell has remained elusive. Here, we identify differential EphA2 signalling as the mechanism by which RasV12 cells are detected and eliminated from simple epithelia. Cell-cell interactions induce an EphA2-ephrin-A signalling cascade that triggers cell repulsion between RasV12 and normal cells, and a concomitant increase in RasV12 cell contractility. Together, these processes drive extrusion of clusters of RasV12 cells. We also show that Drosophila Eph (DEph) receptor signalling is functionally required to drive segregation of RasV12 cells in vivo. Our data indicate that expression of RasV12 in epithelial cells creates ectopic EphA2 boundaries, which promote the segregation and elimination of RasV12 cells from tissues. Thus, deregulation of Eph/ephrin expression would allow RasV12 cells to go undetected and expand within an epithelium.

S37 10:15 – 10:45
Cell competition promotes bilateral symmetry through a Dilp8/Lgr3-dependent mechanism
A Kodra[1], C Bergantinos[1], K Kanakousaki[1], J Colombani[2], D Andersen[2], P Leopold[2], **L A Johnston**[1]

[1]Genetics and Development, Columbia University Medical Center, New York, USA; [2]Inserm, CNRS Univ. Cote d'Azur, Institut de Biologie Valrose, Nice, France

Drosophila development is a robust process that yields remarkably reproducible body size and bilaterally symmetric appendages, even in the face of environmental or genetic perturbations. Developmental stability is tightly regulated and even small deviations from bilateral symmetry – known as fluctuating asymmetry (FA) – are rare. Dilp8, a secreted peptide that coordinates organ growth with developmental timing, promotes developmental stability in Drosophila. Loss of *dilp8* or its receptor *lgr3* leads to strong wing FA. Cell competition, a conserved process that optimizes tissue fitness, is required for the precision of wing size control. Mutations that prevent cell competition also induce wing FA, suggesting a mechanistic link with the Dilp8/Lgr3 system. We will present results from experiments designed to reveal how Dilp8 and cell competition function together to reduce developmental instability and promote animal fitness.

O32 10:45 – 11:00
Poster Number: P112
Interplay between Notch signaling and ID proteins during adult and embryonic neurogenesis
M Boareto[1], D Iber[1], V Taylor[2]

[1]BSSE, ETH Zurich, Basel, Switzerland; [2]DBM, University of Basel, Basel, Switzerland

During neurogenesis, multipotent neural stem cells (NSCs) give rise to the correct number and types of neurons and glia. Notch signaling and inhibitor of DNA binding (ID) factors are recognized as pivotal during neurogenesis, but the underlying mechanism of their interactions and the differences between embryonic and adult neurogenesis remain to be elucidated. We combined mathematical modeling with single-cell transcriptomics to elucidate key interactions between the Notch and ID pathways in embryonic and adult NSCs. We show how both pathways regulate adult neurogenesis in a complementary and independent manner. In contrast, during brain development, Notch signaling directly regulates the expression of IDs and this regulation precludes ID-induced quiescence. Our analyses unveil the molecular interactions underlying NSC quiescence, maintenance and differentiation, highlighting key mechanistic differences between embryonic and adult NSCs. Similar mechanisms are expected to be critical in other stem cell systems during development and disease.

Date: Wednesday 5 April, 2017
Session: Cell Division and Genome Stability
Time: 09:30 – 11:00
Venue: Cinema

S38 09:30 – 10:00
Generating a dynamic kinetochore-microtubule interface
I M Cheeseman

Department of Biology, MITI, Whitehead Institute, Cambridge, MA, USA

Facilitating proper chromosome segregation during mitosis requires the ability of the kinetochore to generate and maintain attachments to dynamic microtubule polymers, and to harness the force from microtubule depolymerization to drive chromosome movement. The kinetochore-microtubule interface is composed of several key players in human cells, but the individual and combined properties of these factors remains imcompletely defined. I will describe our recent work to analyze the molecular properties and principles associated with microtubule binding components of the kinetochore.

O33 10:00 – 10:15
Poster Number: P009
DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression
A R Barr[1], S Cooper[1], F S Heldt[2], F Butera[1], H Stay[1], J Mansfeld[3], B Novak[2], C Bakal[1]

[1]Division of Cancer Biology, Institute of Cancer Research, London, UK; [2]Department of Biochemistry, University of Oxford, Oxford, UK; [3]Biotechnology Centre, TU Dresden, Dresden, Germany

Following DNA damage caused by exogenous sources, such as ionising radiation, p53 mediates cell cycle arrest via expression of the CDK inhibitor, p21. However, the role of p21 in maintaining genomic stability in the absence of exogenous DNA damaging agents is unclear. Using live, single-cell imaging of p21 protein in proliferating cultures, we show that stochastic, naturally-occurring DNA damage in S-phase causes p53-dependent accumulation of p21 during mother G2- and daughter G1-phases. High p21 levels promote quiescence via CDK inhibition, yet low-intermediate levels have no impact on G1 progression, and the ubiquitin ligases $CRL4^{Cdt2}$ and SCF^{Skp2} couple to degrade p21 prior to the G1/S transition with different rates and timings. Mathematical modelling reveals that a bistable switch, created by $CRL4^{Cdt2}$, promotes irreversible S-phase entry by keeping p21 levels low, preventing premature S-phase exit upon DNA damage. Thus, we characterise how p21 regulates the proliferation-quiescence decision to maintain genomic stability.

S39 10:15 – 10:45
Regulation of the spindle assembly checkpoint by mitotic phosphatases
U Gruneberg, D Hayward, J Bancroft

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

The ultimate goal of mammalian cell division is the correct segregation of the duplicated chromosomes into the nascent daughter cells. The spindle assembly checkpoint (SAC) is instrumental in monitoring the

accuracy of microtubule-kinetochore attachments required for faithful chromosome segregation. Detection of unattached kinetochores results in cell cycle arrest until the problem has been resolved. Once all chromosomes are correctly tethered to microtubules the SAC signal is extinguished and anaphase entry is initiated. Important questions are whether the checkpoint can be re-established shortly after the initial silencing, if required, and at what point this is not possible anymore ("the point of no-return"). We have investigated the contributions of different PPP family phosphatases to the regulation of the spindle assembly checkpoint and the metaphase-to-anaphase transition and have identified distinct roles for PP2A-B56, PP2A-B55 and PP1 in controlling SAC silencing, the time window for possible SAC re-activation and anaphase onset.

O34 10:45 – 11:00
Poster Number: P016
Biased Mis-segregation of Human Chromosomes
J T Worrall, T van Lingen, **S E McClelland**

Barts Cancer Institute, Queen Mary University of London, London, UK

Human chromosomes vary greatly in size, gene density, heterochromatin content and structure among other properties, however, it is not currently known whether certain chromosomes are more prone to mis-segregation. We have performed the first comprehensive examination of chromosome mis-segregation rates of individual human chromosomes under different cellular stresses that promote aneuploidy (the wrong number of chromosomes). We have employed fluorescence *In-Situ* hybridization (FISH) imaging of specific centromeres coupled to high throughput analysis using the ImageStream$^{®X}$ cytometer, allowing us to generate highly accurate rates of chromosome gain or loss for each chromosome. Using this approach we have demonstrated that human chromosomes are mis-segregated in a biased fashion. Moreover the mechanism leading to aneuploidy dictates the chromosomes that are most affected. Taken together this new approach to comprehensively analyzing aneuploidy patterns following different cellular insults may have the power to predict mechanistic causes of aneuploidy in cancer and aging.

Date: Wednesday 5 April, 2017
Session: Plenary Session
Time: 11:30 – 12:30
Venue: Main Lecture Theatre

PL08 11:30 – 12:30
Illuminating biology at the nanoscale and systems scale using single-molecule and super-resolution imaging
X Zhuang

Howard Hughes Medical Institute, Harvard University, Cambridge, MA, USA

Fluorescence microscopy is a powerful imaging modality for investigating biological systems. However, the diffraction-limited resolution of light microscopy is substantially larger than molecular length scales in cells, making many sub-cellular structures difficult to resolve. We developed a super-resolution imaging method, stochastic optical reconstruction microscopy (STORM), which overcomes the diffraction limit. This approach has allowed multicolor and three-dimensional imaging of living cells with nanometer-scale resolution and enabled discoveries of novel sub-cellular structures. I will present both technological advances of STORM and some recent biological discoveries enabled by STORM. I will also describe our recently developed single-cell transcriptome imaging method, multiplexed error-robust FISH (MERFISH), which allows thousands of RNA species to be imaged in individual cells. This approach enables single-cell transcriptomic analysis in the native context of tissues, facilitating the delineation of gene regulatory networks, the mapping of RNA distributions inside cells, and the mapping of distinct cell types in complex tissues.

POSTER ABSTRACTS

Cell competition

Poster Number: P1
Differential EphA2 drives segregation and extrusion of Ras-transformed epithelial cells from normal tissues
S Porazinski[1], J de Navascues[1], Y Yako[2], W Hill[1], M Jones[1], R Maddison[1], Y Fujita[2], **C Hogan**[1]

[1]European Cancer Stem Cell Research Institute, School of Biosciences, Cardiff University, Cardiff, UK; [2]Division of Molecular Oncology, Institute for Genetic Medicine, Hokkaido University Graduate School of Chemical Sciences and Engineering, Sapporo, Japan

In epithelial tissues, cells expressing oncogenic Ras (RasV12) are detected by normal neighbours and are subsequently extruded from the tissue. The mechanism underlying detection of the mutant cell has remained elusive. Here, we identify differential EphA2 signalling as the mechanism by which RasV12 cells are detected and eliminated from simple epithelia. Cell-cell interactions induce an EphA2-ephrin-A signalling cascade that triggers cell repulsion between RasV12 and normal cells, and a concomitant increase in RasV12 cell contractility. Together, these processes drive extrusion of clusters of RasV12 cells. We also show that Drosophila Eph (DEph) receptor signalling is functionally required to drive segregation of RasV12 cells in vivo. Our data indicate that expression of RasV12 in epithelial cells creates ectopic EphA2 boundaries, which promote the segregation and elimination of RasV12 cells from tissues. Thus, deregulation of Eph/ephrin expression would allow RasV12 cells to go undetected and expand within an epithelium.

Poster Number: P2
Transcriptional factors of trophectoderm (TE) and inner cell mass (ICM) in rabbit embryos obtained in vivo, compared with mice model
K Barłowska[1], Z Madeja[2], P Pawlak[2], A Piliszek[1]

[1]Department of Experimental Embryology, Institute of Genetics and Animal Breeding PAS, Jastrzębiec, Poland; [2]Department of Genetics and Animal Breeding, Poznan University of Life Sciences, Poznan, Poland

Differentiation of trophectoderm (TE) and inner cell mass (ICM) is the first cell fate decision in mammalian embryogenesis. Trophectoderm forms placenta, while ICM gives rise to epiblast and primitive endoderm. Transcripton factors present from the onset of TE in mouse embryo are Cdx2, Gata3 and Eomes, while the markers of ICM and pluripotency are Nanog, Oct4, Sox2. In mouse embryos Gata3 and Cdx2 are present in nuclei from 16-cells stage, localising to TE after formation of the blastocyst. In rabbit 3.5 dpc embryos, Gata3 and Eomesodermin ware not detected, while most of the cells (including TE) expressed Oct4. Gata3 was first observed in 4.5 dpc embryos and at 5 dpc was expressed in all TE cells. In rabbit embryos formation of blastocyst is followed by expression of specific markers of trophectoderm, so rabbit embryos seem to form blastocyst without expression of transcriptional factors associated with TE in the mouse embryos.

Cell division and genome stability

Poster Number: P3
Binary fission: from archaea to unicellular eukaryotes
G Dey[1], G Risa[1], S Culley[1], R Henriques[1], R Desai[2], B Baum[1]

[1]MRC Lab for Molecular Cell Biology, University College London, London, UK; [2]Biological Making Lab, The Francis Crick Institute, London, UK

Eukaryotes evolved from a genomic merger between an archaeal host and a bacterial endosymbiont. Since the first eukaryote was therefore topologically linked to its putative archaeal ancestor by an unbroken sequence of cell divisions, understanding division mechanisms that survived the transition from archaea to eukaryotes could shed new light on the origins of the eukaryotic cell cycle. The thermophilic model archaeon *Sulfolobus* uses homologs of eukaryotic proteins to regulate a phasic eukaryote-like division cycle. We are leveraging novel super-resolution imaging approaches and microfluidics to better understand the role of ESCRTIII homologs in *Sulfolobus* binary fission. In parallel, we are investigating the dynamics of, and a possible role for ESCRTIII in, nuclear division (‘closed mitosis’) in fission yeast. I will present our latest experimental results, hoping in the future to probe ‘inside-out’ models for eukaryogenesis that envisage the eukaryotic nucleus as the topological equivalent of an archaeal cell.

Poster Number: P4
Mitotic centrosome assembly in flies requires conserved domains in Cnn that assemble into micron-scale structures
Z Feng, **A Caballe**, A Wainman, S Johnson, A F M Haensele, M A Cottee, P T Conduit, S M Lea, J W Raff

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

In flies, Centrosomin (Cnn) forms a scaffold that recruits proteins to the mitotic centrosome, but how Cnn assembles into a scaffold is unclear. Here we show that scaffold assembly requires conserved Leucine Zipper (LZ) and Cnn-Motif 2 (CM2) domains that co-assemble into a 2:2 complex *in vitro*. We solve the crystal structure of the LZ:CM2 complex and show that both proteins form helical dimers that assemble into an unusual tetramer. A slightly longer form of the LZ forms large micron-scale assemblies with CM2 *in vitro*, and mutating individual residues that perturb LZ:CM2 tetramer assembly perturbs the formation of these micron-scale assemblies *in vitro* and Cnn scaffold assembly *in vivo*. Thus, Cnn molecules have an intrinsic ability to form LZ:CM2-interaction-dependent assemblies that are critical for mitotic centrosome assembly. These studies provide the first atomic insight into a molecular interaction required for mitotic centrosome assembly.

Poster Number: P5
Adhesion, not cortical tension, is vital for successful cytokinesis in RPE-1 cells
C L Dix, H K Matthews, L Wolf, S McLaren, B Baum

MRC Laboratory for Molecular Cell Biology, UCL, London, UK

Cells entering mitosis round up before undergoing cytokinesis and respreading post-anaphase. Previous studies have shown that the activity of the Rho GEF, Ect2, is a key requirement for successful rounding and cytokinesis. Here we study mitotic rounding and cytokinesis in motile RPE1 cells that leave bipolar integrin-dependent adhesions when they enter mitosis. We find that, when spread, these cells undergo Ect2 independent cytokinesis. This is achieved by tension across the bridge connecting daughter cells as they migrate away from each other following mitotic exit - and fails when respreading is inhibited through restrictive micropatterning or by inhibition of Rac or Arp2/3. This contrasts with normal abscission, which requires relaxation of tension across the bridge. Notably, RPE1 cells also fail to divide in the absence of adhesion. Strikingly, these data identify a strict requirement for adhesion, but not actomyosin ring formation, for cell division in adherent, migratory human cells.

Poster Number: P6
Dynamic tracking of centriole elongation reveals key aspects of how centrioles grow in *Drosophila* embryos
M G Aydogan[1], A Wainman[1], **S Saurya**[1], T L Steinacker[1,2], Z A Novak[1], J Baumbach[1,3], N Muschalik[1,3], J W Raff[1]

[1]Sir William Dunn School of Pathology, University of Oxford, Oxford, UK; [2]Research Institute of Molecular Pathology (IMP), Vienna Biocenter (VBC), Vienna, Austria; [3]MRC Laboratory of Molecular Biology (LMB), University of Cambridge, Cambridge, UK

Centrioles are barrel-shaped organelles that are developmentally important in many metazoans, as centrioles give rise to the formation of cilia and centrosomes. A tight regulation for the number of centrosomes and cilia (therefore centrioles) is essential, as numerical aberrations are linked to human disease. Biochemical pathways that lead to the formation of centrioles are well studied in different organisms, however there is little dynamic information about how centrioles assemble from nano-scale building blocks and precisely determine their own size. Here we describe several assays we developed that can dynamically track centriole growth in live *Drosophila* embryos, using genetics, quantitative live imaging, super-resolution microscopy and mathematical modelling. Live monitoring of centriole growth revealed a set of key working principles for the dynamic machinery that controls centriole elongation in early embryogenesis.

Poster Number: P7
Imaging chromatin dynamics reveals a novel mechanism for nuclear organisation after cell division
A S Sherrard, A K Kaidi

Cellular and Molecular Medicine, University of Bristol, Bristol, UK

Re-establishment of nuclear structure and chromatin organisation after cell division is integral for genome regulation and cell function. However, the mechanisms underlying this process remain incompletely understood. Given the dramatic re-organisation of the nucleus during and after mitosis, we hypothesised that nuclear organisation after mitosis may be driven by filamentous structures such as polymerised actin (F-actin). Accordingly, we discovered a transient and pronounced assembly of F-actin in the nuclei of daughter cells upon exiting mitosis. By developing a quantitative method for imaging chromatin dynamics in intact cell using florescent lifetime imaging microscopy (FLIM), we identified a key role for this F-actin in chromatin de-condensation after mitosis. A combination of quantitative biochemical and cell imaging assays revealed that interference with this nuclear F-actin assembly impairs the re-establishment of nuclear structure and chromatin organisation post mitosis, and influences transcription and replication in the daughter cells.

Poster Number: P8
Integrin beta 3 regulates cellular senescence by activating the TGFβ pathway
V Rapisarda, M Borghesan, **A O'Loghlen**

Centre for Genomics and Child Health, Blizard Institute, London, UK

Cellular senescence is an important in vivo mechanism that prevents the propagation of damaged cells. However, the precise mechanism(s) regulating senescence are not well characterized. Here, we find that *ITGB3* (integrin beta 3 or β3) is epigenetically regulated by the Polycomb protein CBX7. β3 expression accelerates the onset of senescence in human primary fibroblasts, by activating the TGFβ pathway in a cell autonomous and non-cell autonomous manner. β3 levels are dynamically increased during oncogene-induced senescence (OIS) through CBX7 epigenetic regulation and downregulation of β3 levels override OIS and therapy-induced senescence (TIS), independently of its ligand-binding activity. Moreover, cilengitide, an αvβ3 antagonist, has the ability to block the SASP without affecting proliferation. Finally, we show an increase in β3 levels in a subset of tissues during aging. Altogether, our data show that integrin β3 subunit is a marker and regulator of senescence.

Poster Number: P9
DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression
A R Barr[1], S Cooper[1], F S Heldt[2], F Butera[1], H Stay[1], J Mansfeld[3], B Novak[2], C Bakal[1]

[1]Division of Cancer Biology, Institute of Cancer Research, London, UK; [2]Department of Biochemistry, University of Oxford, Oxford, UK; [3]Biotechnology Centre, TU Dresden, Dresden, Germany

Following DNA damage caused by exogenous sources, such as ionising radiation, p53 mediates cell cycle arrest via expression of the CDK inhibitor, p21. However, the role of p21 in maintaining genomic stability in the absence of exogenous DNA damaging agents is unclear. Using live, single-cell imaging of p21 protein in proliferating cultures, we show that stochastic, naturally-occurring DNA damage in S-phase causes p53-dependent accumulation of p21 during mother G2- and daughter G1-phases. High p21 levels promote quiescence via CDK inhibition, yet low-intermediate levels have no impact on G1 progression, and the ubiquitin ligases $CRL4^{Cdt2}$ and SCF^{Skp2} couple to degrade p21 prior to the G1/S transition with different rates and timings. Mathematical modelling reveals that a bistable switch, created by $CRL4^{Cdt2}$, promotes irreversible S-phase entry by keeping p21 levels low, preventing premature S-phase exit upon DNA damage. Thus, we characterise how p21 regulates the proliferation-quiescence decision to maintain genomic stability.

Poster Number: P10
Stomatin: a plasma membrane protein involved in late stages of cytokinesis
F Dona, S J Terry, U Eggert

Randall Division of Cell and Molecular Biophysics, King's College London, London, UK

Cytokinesis is the final step of cell division that is tightly regulated to ensure equal division of cellular components into two identical daughter cells, requiring the coordination of cell cycle, cytoskeleton and membrane trafficking systems. We used an RNAi based screen to discover new possible contributors to cytokinesis. We identified Stomatin as hit from the screen, as depletion gave significant increases in binucleated cells indicating a failure of cytokinesis. Depletion also resulted increases of F-actin with changes in actin morphology in interphase cells, with cells having increases in actin stress fibres that can be reversed by inhibition of Rho Kinase using a small molecule inhibitor. Live cell imaging of Stomatin depleted cells resulted in defective cytokinesis, where the predominant defect is during abscission. We hypothesise that the membrane associated protein Stomatin contributes to the later stages of cytokinesis via the Rho signalling pathway.

Poster Number: P11
Untangling Polo kinase recruitment during centrosome maturation
I Alvarez Rodrigo, L Gartenmann, J W Raff

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

Centrosomes are organelles composed of two centrioles surrounded by a cloud of proteins known as pericentriolar matrix (PCM). Centrosome biogenesis must be tightly regulated, or abnormalities can lead to diseases like microcephaly or cancer. One major regulator of centrosome assembly and maturation is Polo kinase. Amongst other processes, Polo regulates the formation of a scaffold over which the PCM is organised. We have used a screen based on mRNA injection into *Drosophila* embryos to study what centrosomal protein(s) recruit Polo to its PCM targets. In addition to loss of Polo recruitment, positive hits often presented PCM defects, abnormal distribution of pericentriolar proteins Cnn and γ-tubulin, and centrosome clustering. Our results highlight the importance of centrosomal protein Spd-2 in Polo recruitment and PCM assembly.

Poster Number: P12
Cell cycle regulation of Trunk Neural Crest migration
Z Alhashem, C Linker

Randall Division of Cell and Molecular Biophysics, King's College London, London, UK

Collective cell migration is fundamental for life and a hallmark of cancer. Trunk Neural Crest cells (TNCs) migrate collectively, leader cells at the front of the group determine the directionality, while followers track leaders. Cell cycle progression has been shown to regulate migration initiation. Moreover, experiments in

chick have suggested that progression through the cell cycle is required for neural crest migration initiation. Here we investigate the relation between cell cycle progression and the establishment of leader and follower cells identity in TNCs. Our results show that upon S phase arrest, TNCs migration is halted. Live imaging revealed that cell motility is not affected, but migration initiation is impaired.We are now characterising TNCs cell cycle progression in vivo and dissecting the specific phase of the cell cycle that that controls TNCs migration initiation. We postulate that differences in cell cycle progression rate control TNCs identity and the initiation of migration.

Poster Number: P13
A robust DNA damage response to ionizing radiation ensures genome stability in planarian stem cells
S Sahu[1], P Abnave[1], N Kosaka[1], A Dattani[1], J Thompson[2], M Hill[2], A A Aboobaker[1]

[1]Department of Zoology, University of Oxford, Oxford, UK; [2]CRUK/MRC Oxford Institute for Radiation Oncology, University of Oxford, Oxford, UK

Radiotherapy using ionizing radiation (IR) is routinely used to kill cancerous cells. There is growing evidence that tumour-initiating cancer stem cells survive and adapt to repeated rounds of IR eventually leading to cancer recurrence. This radiation resistance often depends on an efficient DNA damage response (DDR) that repairs DNA breaks. Here we utilised the pluripotent stem cells in planarian *Schmidtea mediterranea* to study DDR. Exposure to usually non-lethal IR doses of 15 Gy, following knockdown of putative DNA repair genes is lethal, providing a proof of principle that DDR genes have a role in stem cell survival post IR. We also investigated the critical dose that triggers DDR in stem cells and a dose as low as 5 Gy also sensitises the pASCs of *BRCA2* RNAi worms. Our study establishes planarians as a novel and experimentally tractable invertebrate model to study DNA damage response mechanism in the context of stem cells.

Poster Number: P14
Tip60 histone acetyltransferase targeted small molecule inhibitor (TH1834) induces genomic instability and apoptosis in breast cancer but not normal cells
A McGuire[1], A Shalaby[2], O Kalinina[3], E Holian[3], M Webber[2], M Scobie[4], L Eriksson[5], E Bourke[2], M J Kerin[1], **J A L Brown**[1]

[1]Dept Surgery, School of Medicine, National University of Ireland Galway, Galway, Ireland; [2]Dept Pathology, School of Medicine, National University of Ireland Galway, Galway, Ireland; [3]Dept Mathmatics, School of Medicine, National University of Ireland Galway, Galway, Ireland; [4]Division of Translational Medicine and Chemical Biology, Dept Medicine, Karolinska Institute, Stockholm, Sweden; [5]Department of Chemistry and Molecular Biology, University of Gothenburg, Gothenburg, Sweden

A key fundamental process regulating genome maintenance, gene regulation and metabolism is acetylation by histone acetyltransferases (HAT). Importantly, dysfunctional acetylation is implicated in cancer. Within the HAT superfamily, key MYST sub-family members are directly involved in the DNA damage response and repair pathways and crucially key members down-regulated in some cancers (including breast cancer). We describe modelling, development and application of novel lysine (K) acetyltransferase inhibitors (KATi) targeting the essential MYST family member Tip60, a key mediator of the DNA damage response and repair pathways and transcriptional co-activator. We demonstrate that Tip60 protein expression is significantly and differentially reduced in patient samples from each breast cancer subtype. We demonstrate TH1834 significantly inhibits Tip60 activity *in vitro*, and results in cytotoxicity, apoptosis and increased DNA double strand breaks in breast cancer, but importantly not in normal control-cell lines. KATi represent a powerful new tool for investigating the essential roles of Tip60 in cancer.

Poster Number: P15
Parallel deubiquitylase family screens identify OTUD6B and JOSD2 as regulators of KIFC1/HSET expression and centrosome clustering in breast cancer cells
A B Fielding, D Sabat-Pospiech, I A Prior, J M Coulson

Cellular and Molecular Physiology, University of Liverpool, Liverpool, UK

Many cancer cells contain supernumerary centrosomes that often cluster in mitosis to allow bipolar spindle formation, a process that requires the kinesin KIFC1/HSET. KIFC1 can be targeted for ubiquitin-mediated degradation yet regulation of its reversible ubiquitylation remains unknown. The aim of this project is to investigate how members of the deubiquitylase (DUB) family regulate centrosome clustering. Two

DUB-family wide siRNA screens have been performed, firstly to identify DUBs that affect KIFC1 protein expression, and secondly to directly identify DUBs whose depletion causes multipolar mitoses. Two DUBs were identified and subsequently validated as required to maintain KIFC1 protein levels. Depletion of six DUBs were validated to cause an increase in multipolar spindle formation. Combining data from the two screens identifies OTUD6B and JOSD2 as having KIFC1-dependent effects on centrosome clustering. We are now investigating the mechanism of action of these DUBs and the effect of their depletion on cancer cell proliferation.

Poster Number: P16
Biased Mis-segregation of Human Chromosomes
J T Worrall, T van Lingen, **S E McClelland**

Barts Cancer Institute, Queen Mary University of London, London, UK

Human chromosomes vary greatly in size, gene density, heterochromatin content and structure among other properties, however, it is not currently known whether certain chromosomes are more prone to mis-segregation. We have performed the first comprehensive examination of chromosome mis-segregation rates of individual human chromosomes under different cellular stresses that promote aneuploidy (the wrong number of chromosomes). We have employed fluorescence *In-Situ* hybridization (FISH) imaging of specific centromeres coupled to high throughput analysis using the ImageStream$^{®X}$ cytometer, allowing us to generate highly accurate rates of chromosome gain or loss for each chromosome. Using this approach we have demonstrated that human chromosomes are mis-segregated in a biased fashion. Moreover the mechanism leading to aneuploidy dictates the chromosomes that are most affected. Taken together this new approach to comprehensively analyzing aneuploidy patterns following different cellular insults may have the power to predict mechanistic causes of aneuploidy in cancer and aging.

Poster Number: P17
Cell size regulation in *Drosophila* sensory organ precursor asymmetric cell divisions
N Ramkumar[1], N Rodrigues[2], B Baum[1]

[1]MRC LMCB, University College London, London, UK; [2]Crick Institute, London, UK

Asymmetric cell division is the unequal segregation of cell fate determinants into daughter cells following mitosis. Additionally, some asymmetric divisions lead to daughter cells of unequal sizes. The regulation and functional significance of the unequal daughter cells size are unknown. To study this, we are using *Drosophila* sensory organ precursor (SOP) cells which give rise to the cells of the mecahnosensory organ in the notum. Alongwith cell fate determinant segregation, SOP division results in cells of unequal sizes. This would require communication between the spindle and the cortex. The Chromosome passenger complex (CPC), owing to their dynamic localization, on the kinetochores during metaphase and spindle midzone during anaphase, are ideal candidates. We are investigating their role during division using loss of function analysis and by mislocializing individual components. Additionally, using genetic tools, we aim to perturb the daughter cell size to determine the significance of cell size during lineage specification.

Poster Number: P18
A new tool for identifying substrates of Aurora kinases
J Deretic[1], A R Kerr[1], T Ly[2], J P Welburn[1]

[1]The Wellcome Trust Centre for Cell Biology and Institute of Cell Biology, University of Edinburgh, Edinburgh, UK; [2]Centre for Gene Regulation and Expression, College of Life Sciences, University of Dundee, Dundee, UK

The Aurora kinases control multiple steps of mitosis via phosphorylation of different mitotic players. Although many proteins have been confirmed as in vivo substrates of Aurora kinases by mass spectrometry studies, the role of substrate phosphorylation is poorly understood. We demonstrate that the Aurora kinases regulate many more substrates based on the large abundance of their phosphorylation consensus sites. We have used bioinformatics to predict possible kinase substrates based on the consensus sequence for Aurora kinases and focused on candidates with multiple consensus motifs clustered together. I have validated four proteins - SPICE1, TTLL4, AHCTF1 and CLASP2 - as in vitro substrates of Aurora A and Aurora B kinases using radiolabelled kinase assays. This demonstrates the high accuracy of our bioinformatics approach and the potential of this approach for the identification of other candidates. We are currently characterizing phosphorylation of SPICE1 in HeLa cells.

Cytoskeleton and transport

Poster Number: P19
A link between planar polarity and staircase-like bundle architecture in hair cells
A Tadenev[1], N Devanney[1], M Cayouette[2], **B Tarchini**[1]

[1]The Jackson Laboratory, Bar Harbor, USA; [2]Cellular Neurobiology Research Unit, Institut de Recherches Cliniques de Montreal, Montreal, Canada

Sensory perception in the inner ear relies on the hair bundle, the polarized brush of movement detectors crowning hair cells. We previously showed that the edge of the forming bundle is defined by the 'bare zone', a microvilli-free region of apical membrane specified by the mInsc-LGN-Gai protein complex. We now report that LGN and Gai also occupy the tip of stereocilia directly abutting the bare zone. We demonstrate that LGN and Gai are essential to promote the elongation and differential identity of stereocilia across rows. Interestingly, we also uncover that total LGN-Gai protein amounts are actively balanced between the bare zone and stereocilia tips, suggesting that early planar asymmetry of protein enrichment at the bare zone confers adjacent stereocilia their tallest identity. We propose that LGN and Gai participate in a long-inferred signal originating outside of the bundle to model its staircase-like architecture, a property essential for hearing.

Poster Number: P20
Regulation of microtubule function in endothelial cells
K Naylor, A Lampropoulou, J Brash, C Raimondi, C Ruhrberg

Institute of Ophthalmology, UCL, London, UK

Neuropilin 1 (NRP1) is a transmembrane protein located in endothelial cells (ECs) that promotes blood vessel growth induced by the vascular endothelial growth factor (VEGF) and extracellular matrix (ECM). However, it remains poorly understood how NRP1 helps to transduce these signals into intracellular responses that modulate the behaviour of ECs to drive vessel growth. We have recently shown that NRP1 facilitates actin remodelling for filopodia extension and cell migration. The aim of our current research is to determine whether NRP1 also influences microtubule morphology and function. Our analysis shows that NRP1 regulates microtubule dynamics in response to ECM and during cytokinesis in primary ECs. Future work will define the molecular mechanism by which NRP1 interacts with the microtubule network. A better understanding of processes that integrate cell surface signals with the behaviour of microtubules is expected to shed light on EC behaviour during blood vessel growth and maintenance.

Poster Number: P21
Cooling evokes spatial and functional rescue of vascular alpha 2C-Adrenoceptors: Role of ROS, Rho and filamin
K Issa[1], M Fardoun[2], **A Eid**[1]

[1]Pharmacology and Toxicology, American University of Beirut, Beirut, Lebanon; [2]Biology, American University of Beirut, Beirut, Lebanon

Augmented cold-induced vasoconstriction is entirely mediated by vascular alpha 2C-adrenoceptors (alpha 2C-ARs). We previously showed that the cAMP-Rap1 signaling in microvascular smooth muscle cells evokes a spatial (from the Golgi to the plasma membrane) and a functional rescue of alpha 2C-ARs, concomitant with increased interaction between alpha 2C-AR and filamin-2. This association then mobilizes the receptor to the membrane along actin filaments. Here, we show that cooling cells (to 28 C) increases production of reactive oxygen species (ROS), followed by activation of RhoA and increase in actin polymerization. Cooling leads to phosphorylation of filamin-2 and promotes its association with alpha 2C-AR. We show that this association promotes translocation of this receptor to the membrane where it becomes responsive. Together, our data show that cooling, as a physiologic stressor, rescues the receptor via ROS production, Rho activation and rearrangement of the actin cytoskeleton.

Poster Number: P22
Paracrine-mediated invasion induced by centrosome amplification
T Arnandis[1], V Rajeeve[2], C H Brennan[3], P R Cutillas[2], S A Godinho[1]

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Human tumours contain supernumerary centrosomes, which can induce CIN, promote invasion and accelerate tumourigenesis. However, in a heterogeneous tumour it is unclear how centrosome amplification impacts tumourigenesis. We found that conditioned medium (CM) collected from cells with extra centrosomes induces a robust invasive phenotype in 3D culture models. Using zebrafish as a model, we found that, when co-injected, cells with extra centrosomes are able to induce invasion of normal cells, supporting a role for centrosome amplification in cooperative invasion in vivo. Secretome analysis followed by a siRNA screen identified factors responsible for this paracrine invasion. Activation of RTK signaling is the cause of paracrine invasion, and we are currently investigating how pro-invasive factors are secreted and promote RTK activation. This is the first demonstration of a positive interaction between cells with different number of centrosomes and point towards a novel role for supernumerary centrosomes in modulating paracrine-signaling pathways in tumours.

Poster Number: P23
Ciliopathy protein TMEM67 regulates laminin-dependent cell migration via formation of the perinuclear actin cap
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Ciliopathies are caused by malfunction/malformation of the primary cilium, a microtubule-based structure built by almost every cell type in the human body, which acts as a cellular “radio mast”. TMEM67/Meckelin is implicated in four ciliopathies: Meckel syndrome (MKS), Joubert syndrome, nephronophthisis, and COACH syndrome. Fibroblasts isolated from a MKS patient with a mutation in TMEM67 ([c.653 G>T p.R217X]+[c.785 T>C p. M216T]) show several non cilium-associated phenotypes, including altered actin organisation and RhoA hyperactivation. We show here that these defects impact on cell migration. Patient cells migrate faster, but with impaired directionality. This correlates with loss of the perinuclear actin cap, and nuclear rotation and centrosome positioning defects. We find that these cellular defects stem from altered extracellular matrix composition, and are rescued by growth on laminin-containing matrices. We propose that failure in laminin-dependent directional cell migration may help to explain aspects of MKS pathology, such as cleft palate.

Poster Number: P24
The Exocyst component EXOC4 is required to position the centrosome during primary cilium biogenesis
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Ciliopathies encompass a broad range of syndromes with overlapping symptoms associated with dysfunction or dysgenesis of primary cilia. Recently, mutation in *EXOC4* was discovered in a ciliopathy patient presenting with Meckel-Gruber syndrome, a lethal malformation disorder with multiorgan involvement. EXOC4 is a component of the exocyst complex, which tethers secretory vesicles to membranes. Here, we show that EXOC4 localises to the centrosome in interphase cells. Loss of EXOC4 results in a ciliogenesis defect due to alterations in the position of the centrosome. This cellular defect is a hallmark of Meckel-Gruber syndrome, but the mechanism remains unknown. We performed GFP-Trap combined with quantitative proteomic analyses and identified novel EXOC4 interacting proteins. Cross comparison of this dataset reveals overlap with a recent screen for ciliogenesis regulators, and provides candidate proteins for further analysis. We propose that EXOC4 acts in concert with other ciliopathy proteins to regulate the early stages of cilium biogenesis.

Poster Number: P25
Investigating biomechanical forces in zebrafish brain morphogenesis
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The accessibility and transparency of the zebrafish embryo make it an excellent model system for investigating the morphogenesis of complex vertebrate organs *in vivo*. Understanding morphogenesis may help us to understand some of the many birth defects that afflict human infants. We are investigating biomechanical forces in neural tube formation. Cells from each side of the zebrafish neural primordium initially interdigitate but then rearrange to meet and adhere precisely at the tissue midline. We hypothesise that biomechanical forces could help align cell interfaces to the midline. Rapid cell retraction from laser cuts demonstrates tension is present at the neural midline both along and across the apicobasal axis. Apicobasal retraction results from cell shortening rather than whole tissue movement. Pharmacological treatment suggests actinomyosin contractility underlies tissue tension. Tissue tension decreases over time as cells align to the midline, suggesting forces are more able to manipulate the cell alignment at early stages.

Poster Number: P26
How human cytoplasmic dynein-1 can be auto-inhibited and activated
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Cytoplasmic dynein-1 binds dynactin in the presence of cargo adaptor proteins to form a transport machine capable of long distance processive movement along microtubules. However, it is unclear why human dynein-1 cannot move on its own and how dynactin activates movement. We present a cryo-electron microscopy (cryo-EM) structure of the complete 1.4 MDa human dynein-1 complex in an inhibited conformation known as the phi-particle. We reveal the 3D structure of the cargo binding dynein tail and show how self-dimerization of the motor-domains locks them in a conformation with low microtubule affinity. Disrupting dimerization with structure-based mutagenesis drives dynein-1 into an open-form with higher affinity for both microtubules and dynactin. We find the open-form is also inhibited for movement and that dynactin relieves this by reorienting the motor domains to interact correctly with microtubules. Our model explains how dynactin binding to the dynein-1 tail stimulates its motor activity directly.

Poster Number: P27
A change in the polarity of a contractile actomyosin network underlies behaviourial change during *Drosophila* morphogenesis
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During animal development, cells undergo various behaviours, such as migration and shape change, which need to be coordinated. How this coordination is achieved is still elusive. During morphogenesis of the adult abdominal epidermis of *Drosophila*, the larval epithelial cells (LECs) are replaced by the adult histoblasts. The LECs migrate directedly and, subsequently, cease migration, constrict apically and die. Here, we use *in vivo* 4D microscopy to study the mechanisms that underlie this behavioural change. We show that the LEC's apical actomyosin network is planar polarized during migration, undergoing pulsed contractions in the back of the cell, while protruding at the front. Contractions re-localise to the cell centre during constriction. Behavioural change thus involves a change in the polarity of the contractile network. We further characterize network dynamics and show how interfering with actomyosin contractility impacts on cell behaviour. We will discuss the role of pulsed contractions in apical constriction.

Poster Number: P28
A Novel GTPase System Regulates β-Catenin Nuclear Transport in Development and Disease
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Canonical Wnt signaling coordinates many critical aspects of embryonic development, while dysregulated Wnt signaling contributes to numerous common diseases, including congenital malformations and cancer. The nuclear localization of β-catenin is fundamental in pathway activation. However, despite intensive investigation, the mechanisms regulating β-catenin nuclear transport remain undefined. β-catenin nuclear transport is energy (GTP) dependent but β-catenin lacks a classic "NLS" nuclear localization signal and does not require the karyopherin/Ran GTPase transport system. Here, we describe a nuclear localized guanine nucleotide exchange factor (GEF) that is an unexpected regulator of β-catenin nuclear transport. Identified in a patient with congenital heart disease and heterotaxy, we show that this GEF alters left-right patterning via Wnt signaling and the nuclear localization of β-catenin, rather than β-catenin degradation. Together, our results define a novel GTPase based nuclear transport system, and suggest new targets for the modulation of Wnt signaling in disease.

Poster Number: P29
Centrosome amplification drives nuclear deformability and translocation during 3-D cell migration
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Centrosome amplification, a common feature of human tumours, can induce cell invasion via a process involving increased microtubule (MT) nucleation and Rac-1 activation. However, how these mechanisms contribute to cell invasion remains unclear. We recently found that cells that carry extra centrosomes exhibit higher nuclear deformability and translocation in 3D environments, essential for efficient cell invasion. Nuclear deformations in cells with extra centrosomes require MTs and nucleus-MTs attachment through Nesprin-1 and MT motors kinesin-1 and dynein. Interestingly, extra centrosomes increase the centrosome-nucleus distance, suggesting that active pulling forces applied by the extra centrosomes on the nucleus contribute to the nuclear deformability. To test this hypothesis, we are developing FRET-based probes to measure the forces applied to the nucleus and assess the role of MTs in this process. Studying the contribution of extra centrosomes to nuclear deformability will provide new insights into the mechanisms that regulate nuclear translocation during cell invasion.

Poster Number: P30
Fission Yeast Sec3 Bridges the Exocyst Complex to Exo- and Endocytosis
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Cell shape and polarity are important for the function and survival of cells. Higher eukaryotes often adopt complex morphologies which are crucial for their function in tissues. Establishing cell shape involves the trafficking of secretory vesicles and the remodelling of the actin cytoskeleton. The exocyst, a conserved hetero-octameric complex, is thought to tether post-Golgi secretory vesicles to the plasma membrane during exocytosis. The exocyst component Sec3 binds to membranous PIP2 and is thought to target the assembly of the exocyst at sites of secretion. In fission yeast, mutation of Sec3 leads to the accumulation of secretory vesicles, but also alters all three actin structures. Using a GFP-Trap approach, we show that Sec3 associates with endocytic actin patches and that these interactions are lost in sec3 mutants. This highlights a novel role for Sec3 at the interface between exocytosis and endocytosis and places it as a key regulator of cell shape.

Poster Number: P31
Subcellular dynamics and genetic regulation of dense core granule compartment formation and maturation using live-cell imaging of *Drosophila* secondary cells
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Many secretory cells release bioactive molecules that are pre-packaged in dense-core granules (DCGs). There are currently only limited in vivo genetic systems available to analyse the mechanisms underlying DCG biogenesis pathways. We utilise secondary cells (SCs) of the *Drosophila* male accessory gland, each containing numerous large (3-10 µm diameter) DCG compartments. Here we show that DCG formation in SCs is regulated via similar genetic programmes to those found in mammalian secretory cells. Furthermore, using live-cell imaging, we follow DCG biogenesis in real-time and demonstrate that it involves the interaction between Golgi- and recycling endosome-derived membranes and compartments. Our data reveal novel links between DCG production and the biogenesis of secreted endosomal vesicles called exosomes. These results may also provide an explanation for the lipid-dependent processes and acidification events that accompany DCG biogenesis and maturation, highlighting processes that might be affected in diseases of secretion such as diabetes and neurodegenerative disorders.

Poster Number: P32
'Exosome signatures' as biomarkers for centrosome-targeted therapy in pancreatic ductal adenocarcinoma (PDAC)
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Centrosome amplification has been observed in many human cancers, including both early and late stage PDAC. Despite progress in the development of novel centrosome-targeted therapeutics, our inability to rapidly identify suitable patients highlights the need for a biomarker of centrosome amplification. Recent studies have identified small extracellular vesicles (sEV) as promising new biomarkers for cancer. We have identified a significant correlation between centrosome amplification and exosome secretion in pancreatic cancer cells lines. Additionally we have observed an increase in sEV secretion when centrosome amplification is induced in PDAC cells. Our preliminary data suggests that exosomes originating from cells with extra centrosomes play a role in pancreatic fibroblast activation. We are currently performing a proteomic analysis of the isolated sEV, to identify the specific cargos secreted by cells with extra centrosomes. This will enable us to determine how these sEV activate fibroblasts and to define an exosome signature for centrosome amplification.

Poster Number: P33
The role of actomyosin in the transition from migratory to constrictive cell behaviour during *Drosophila* abdominal morphogenesis
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During morphogenesis of the *Drosophila* abdominal epidermis, the larval epithelial cells (LECs) undergo a transition from migration to constriction, while they are replaced by the adult histoblasts. During this process, the LECs apical actomyosin network undergoes pulsed contractions, which are associated with changes in apical cell area and constriction. How this contractile network is regulated is poorly understood. Here, we manipulate contractility in the LECs. We show that knock down of RhoGEF2 function interferes with pulsed contractions. Increasing contractility by activation of Rho kinase inhibits cell migration and cells constrict displaying cortical stress fibre-like actin bundles. Overexpression of actin disrupts the apical network reducing contractility and interfering with apical constriction. Interestingly, increasing contractility can rescue this phenotype. Our results show that the level of a cells contractility not only impacts on the contractile networks behaviour but also on the networks architecture and the cells behaviour.

Poster Number: P34
Regulation of E-cadherin endocytosis downstream of p120 catenin
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Adhesions between cells are vital for the formation of multicellular structures and cell-cell communication. E-cadherin is the principal transmembrane protein which provides such adhesions between cells in the epithelium. The correct regulation of E-cadherin expression, in space and time, is indispensable for proper development. Conversely the dysfunction of E-cadherin is implicated in multiple disease processes, particularly cancer metastasis. E-cadherin is a highly dynamic protein, which is constantly being turned over at the plasma membrane by endocytosis and recycling. The p120 catenin protein has been identified as the key regulator of E-cadherin presentation and stability at the membrane. However, the mechanism of how p120 catenin promotes E-cadherin endocytosis is as yet unknown. We have identified two p120 catenin interacting proteins: Rho-kinase and Arf79F. Both are mislocalised and their amounts are reduced in the absence of p120ctn. Currently, we are investigating how these two proteins are regulating E-cadherin endocytosis.

Poster Number: P35
The molecular basis determining organ accessibility: systemic versus local growth factors
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The size of organs is determined by both systemic and local growth signals. While patterning signals with growth factor activity seem to be restricted to their organ of origin, systemic signals are released into the circulation to reach a variety of tissues. My hypothesis is that the basement membrane of developing tissues could act as a selective filter to regulate signal diffusion. I use *Drosophila* as a model system to compare the systemic Drosophila insulin-like peptide 2 (Dilp2) to the local growth factor Decapentaplegic (Dpp) and their ability to cross the BM between wing disc epithelium and hemolymph *in vivo*. In addition, I develop an *ex vivo* system to test different selective criteria for penetrance, such as size, charge and ECM-binding domains. My ambition is to identify and modify the physicochemical properties that control passage of peptides through the BM in developing tissues.

Poster Number: P36
Molecular mechanisms regulating human CENP-E and chromosome movement in mitosis
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During mitosis, chromosomes congress to the metaphase plate before being segregated into two daughter cells. Centromere protein E (CENP-E) is a 230 nm-long and flexible plus-end directed protein from the kinesin-7 family that localises to the kinetochore. CENP-E transports misaligned chromosomes to the metaphase plate and is essential for dynamic kinetochore-microtubule coupling in metaphase and anaphase. The interacting partners of CENP-E at the kinetochore are not clearly identified. We are therefore investigating the molecular mechanisms regulating the recruitment of CENP-E to the kinetochore, using a biochemical approach. Using single molecule assays, we are studying how the activity of the full length human CENP-E is regulated as most *in vitro* work was done using the *Xenopus* orthologue. We have identified both the kinetochore- and the centrosome-targeting domains of CENP-E. Here we show that the kinetochore- and centrosome-targeting domains are mainly alpha-helical rod-shaped proteins.

Poster Number: P37
Orchestrated patterning of a group of cells: the fly ommatidium as a case study
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During development, the actomyosin cytoskeleton drives cell shape changes to shape organs. However, how such cellular morphogenetic activity is integrated at the tissue level is not well understood. To examine this issue, we took advantage of the fly ommatidium, a highly patterned group of 24 genetically tractable neuro-epithelial cells, which is the building block of the fly retina. We combined molecular genetics, live

imaging and *in silico* modelling, and show patterning of the ommatidium is orchestrated by extensive actomyosin-dependent mechanical cross-talk between ommatidial cells. In addition, we find a pro-eminent role for transcriptional regulation downstream of the Notch signalling pathway and endocytosis in regulating cell intercalation during ommatidia patterning. Interestingly, our results reveal instances of cell intercalation that show very little requirement for the ROCK-Myosin/Bazooka canonical epithelial cell intercalation pathway, indicating alternative regulation of cell-cell contact remodelling can operate in developing neuro-epithelial tissues.

Poster Number: P38
The family specific α4 helix of the kinesin-13, MCAK, is critical to microtubule end recognition
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Kinesins which influence the dynamics of microtubule growth and shrinkage require the ability to distinguish between the microtubule end and the microtubule lattice. The microtubule depolymerizing kinesin MCAK has been shown to specifically recognize the microtubule end. This ability is key to the action of MCAK in regulating microtubule dynamics. We show that the α4 helix of the motor domain is crucial to microtubule end recognition. Mutation of the residues K524, E525 and R528, which are located in the C-terminal half of the α4 helix, specifically disrupts the ability of MCAK to recognize the microtubule end. Mutation of these residues, which are conserved in the Kinesin-13 family and discriminate members of this family from translocating kinesins, impairs the ability of MCAK to discriminate between the microtubule lattice and the microtubule end.

Poster Number: P39
Four-stranded mini microtubules formed by Prosthecobacter BtubAB show dynamic instability
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Eukaryotic microtubules are dynamic, yet stiff hollow tubes built from αβ-tubulin protein heterodimers. Stabilised microtubules provide tracks for cellular cargo, and dynamic instability is crucial for spindle function during mitosis. Although microtubules are thought to be absent from other organisms, it has been shown that certain bacterial *Prosthecobacter* species contain BtubAB proteins that are closely related to tubulin and that also form hollow tubes. Here we show by near-atomic resolution helical reconstruction cryoEM and *in vitro* TIRF microscopy that *Prosthecobacter dejongeii* BtubAB form seamed four-stranded 'mini microtubules' that show dynamic instability, suggesting that as few as four protofilaments recapitulate distinctive microtubule behaviour. The third protein BtubC in the *btub* gene cluster inhibits BtubAB mini microtubule catastrophe, increases rescue and binds along protofilaments every 8 nm. Our work reveals that some bacteria make use of complex cytoskeletal systems that were once thought to be only useful in much larger and sophisticated eukaryotic cells.

Poster Number: P40
An actomyosin ring allows for differential release of pro-inflammatory and pro-haemostatic molecules from endothelial cells
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Following vascular injury endothelial cells respond by secreting both pro-haemostatic molecules (e.g. von Willebrand Factor (vWF); a highly multimeric protein composed of >60 individual ~250kDa subunits) and smaller pro-inflammatory molecules (e.g. P-selectin) - both of which are stored in organelles termed Weibel Palade Bodies (WPBs). Recent evidence has shown that the efficient secretion of vWF, and to a lesser extent P-selectin, is dependent upon an actomyosin ring being recruited to the WPBs. This fits with a model whereby mechanical force is required to squeeze out large vWF molecules from the WPBs and offers the possibility that pro-haemostatic or pro-inflammatory molecules can be differentially released. Ongoing experiments are now focused on identifying the molecular pathway involved in regulating actomyosin formation and function. It is hoped that this information will be used to develop novel therapeutic agents to minimise harmful thrombus formation in patients exhibiting excessive vWF secretion, whilst still retaining an effective inflammatory response.

Poster Number: P41
Radixin Mediates E-cadherin Localisation and Acinar-like Morphogenesis of Prostate Cancer Spheroids
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Prostate Cancer (PC) is the second most common cause of cancer death in UK men. Radixin (RDX) is a cytoskeletal linker protein associated with PC. Here, we show that non-neoplastic (RWPE-1) and tumorigenic (WPE-1 NB26) cells formed prostate acini-like structures in 3D-cell culture. However, WPE-1 NB26-derived acini showed dispersed E-cadherin expression at cell-cell contacts. RDX knockdown (KD) in WPE-1 NB26 acini re-localised E-cadherin to cell-cell contact regions, resembling those observed in non-neoplastic acini. Inhibition of atypical protein kinase C (aPKC) reduced RDX phosphorylation in WPE-1 NB26 cells and increased localisation of E-cadherin at cell-cell contacts. Furthermore, upon RDX KD or inhibition of aPKC there was an increase in biotinylated E-cadherin in tumourigenic cells. We propose that aPKC participates in RDX activation, facilitating the ability of the latter to keep E-cadherin away from cell-cell contacts as a mechanism to maintain the mesenchymal phenotype observed in PC cells.

Poster Number: P42
Characterising intracellular trafficking and ubiquitylation of Junctional Adhesion Molecule C (JAM-C)
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Tissue infiltration of leukocytes requires transmigration from venules, usually by squeezing through endothelial cell-cell junctions. These junctions must be remodelled to allow leukocyte passage, then reform to maintain vessel integrity. One junctional molecule, Jam-C, has a role in polarised transmigration, angiogenesis, and vascular permeability, yet little is understood about the molecular mechanisms regulating Jam-C trafficking. We show that in endothelial cells, Jam-C is present at the cell surface and in intracellular vesicles. We have begun to define residues of Jam-C affecting trafficking. We show for the first time that JamC is ubiquitylated under non-stimulated conditions and, using a ubiquitylation-deficient mutant, that this ubiquitylation controls JamC degradation and recycling. We have further begun to characterise the ubiquitin linkages. We also demonstrate that JamC internalisation is clathrin- and caveolin-independent. As Jam-C is associated with numerous inflammatory diseases, mechanistic insights into Jam-C trafficking are an essential step in characterising its physiological role.

Poster Number: P43
Mutational analysis of the regulation of Notch receptor trafficking and signalling in *Drosophila melanogaster*
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Notch signalling is an evolutionarily conserved developmental signalling pathway. Notch can be activated in different subcellular locations and trafficking regulation is a key controlling mechanism. Our research focuses on the highly conserved Ankyrin domain of Notch, which plays a scaffolding role interacting with numerous regulatory components at different times and in different sub-cellular locations. Several *Drosophila* developmental and human cancer-associated mutations are found in different conserved residues within the ankyrin region, but the mechanistic links to altered phenotypic outcome are not known. Using the genetically amenable *Drosophila* model we aim to compare *in vivo* and *in vitro* how differently located ankyrin domain mutations disrupt the structure, regulation and signalling of Notch. This project will provide us with a deeper understanding of Notch structure/function relationships and could lead to the identification of new personalised therapeutic strategies, which reflect mutant-specific differences in underlying pathological mechanisms.

Poster Number: P44
Cdc42 controls epithelial polarity by coordinating cortical polarization and plasma membrane specialization through Par6
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How cortical polarity arises and translates into plasma membrane specialization during epithelial morphogenesis is not fully understood. To study this question, we used the cellularizing embryo and fly photoreceptor to show that partitioning of the cortex into a sub-apical domain and apical junctional belt (*Zonula Adherens, ZA*) relies on two convergent pathways, connected through Par6. Cortical polarity arises through Par6-aPKC segregating away from Bazooka (Baz), a molecular sorting mechanism that we show is controlled by the small GTPase Cdc42. Moreover, we find that Par6 binds to Exo84 to promote exocyst-dependent delivery of Crumbs, which enables sub-apical membrane and ZA morphogenesis. We conclude that polarization of the apical cortex is an emergent property of the Cdc42-Par6-aPKC-Baz biochemical module, with Cdc42 regulating the apical localization of Par6-aPKC. Translating cortical polarity into membrane specialization relies on a delivery-based positive feedback loop, which also acts as a cortical asymmetry amplifier through Crumbs.

Poster Number: P45
ABSTRACT WITHDRAWN

Poster Number: P46
Localising mRNA drives assembly of *in vitro* reconstituted mRNPs and stimulates their transport through activation of cytoplasmic dynein
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Cytoplasmic dynein-1 is a versatile microtubule-based motor that mediates the majority of minus end-directed processes in the cell. The diversity of these processes demands strict spatial, temporal and compositional regulation of dynein motility, though little is understood about how this is achieved. To investigate the regulation of dynein-cargo complexes, we have reconstituted a minimal transport competent mRNP *in vitro* and analysed its behaviour by single-molecule microscopy. Our results show that the RNA-binding protein Egalitarian, the adaptor BicD, and the dynactin complex are sufficient for robust dynein-dependent mRNA transport. Remarkably, the presence of mRNA is essential for robust activation of long distance dynein motion by Egalitarian and BicD. Our findings suggest that cargo association with adaptor proteins is a key step in the activation of dynein motility in cells. We are currently investigating how RNA activates motility and will present our latest findings at the meeting.

Poster Number: P47
Assembly Mechanisms of Dynein Motors
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Dynein motors power the essential beating of small microtubular structures called cilia and flagella. In mammals, ciliary motility is critical for proper embryonic development and homeostasis of vital tissues such as the lungs and the brain. Defective ciliary motility can lead to a severe disease called Primary Ciliary Dyskinesia, characterized by respiratory distress in newborns which may progress to life-threatening complications. A major cause of PCD is a failure in dynein motor functions or assembly. Most PCD causing mutations directly affect structural sub-units of the outer dynein arm (ODA) motor complex. However, several other PCD causing mutations impact the functions of proteins which do not form structural subunits of dyneins. The roles of these so called dynein axonemal assembly factors (DNAAFs) is poorly understood but they likely promote cytoplasmic pre-assembly of dyneins. Here, we describe the molecular roles of a newly discovered assembly factor and propose a revised model of the dynein assembly pathway.

Poster Number: P48
Rab27a co-ordinates actin-dependent long-range organelle transport by integrating the activity of motors and track assembly proteins
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Cell biologists generally consider that microtubules and actin play complementary roles in long- and short-distance transport in animal cells. On the contrary, using melanosomes of melanocytes as a model, we recently discovered that motor myosin-Va, works with dynamic actin tracks, to drive long-range transport in microtubule depleted cells. This suggests that in animals, as in yeast and plants, myosin/actin can drive long-range transport. Here we show that the actin assembly activity of spire and formin (Fmn-1) proteins is required for myosin-Va-dependent transport. Moreover we show that, in addition to recruiting myosin-Va, Rab27a recruits spire/Fmn-1 to melanosomes, thereby integrating motor and track assembly activity at the organelle membrane. Based on this we suggest a model in which organelles and force generators (motors and track assemblers) are linked forming a cell-wide network that allows the collective activity of the force generators to rapidly disperse the population of organelles long-distance throughout the cytoplasm.

Poster Number: P49
Dual nucleotide recognition underlies tip-binding specificity of mammalian EB proteins
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EB proteins track the ends of growing microtubules and regulate microtubule dynamics both directly and by acting as the hub of the tip-tracking network. Mammalian cells express cell type-specific combinations of three EB proteins with different cellular roles. Here we compare the plus end-tracking behaviour of EB1, EB2 and EB3 in cells and in vitro. We find that the signal from all three EBs correlates strongly to the microtubule assembly rate, but the three signals differ in their maxima and the position from the microtubule tip. Using microtubules built with nucleotide analogues, simulations and site-directed mutagenesis, we explore the molecular basis for these differences. Our experiments strongly support the idea that EBs bind between 2 protofilaments and sense the nucleotide state of both flanking beta-tubulins. Different specificities are conferred by amino acid substitutions at the right hand side interface of the EB microtubule-binding domain with tubulin.

Poster Number: P50
Location, location, location: PKD2 in the cilium prevents renal cyst formation
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Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a common inherited disease which leads to end stage renal failure in most patients before their 6th decade. PKD2 is an essential Ca^{2+} permeable cation channel, the loss of which results in ADPKD. PKD2 localises to the primary cilium in renal tubules, yet the role of this localisation in cyst prevention remains undetermined. Here we investigate the effects of aberrant cellular localisation of PKD2, specifically the loss of ciliary localisation. Using a non-ciliary localising mutant allele (*Pkd2*^{lrm4}) which retains channel function, for *in vitro* and *in vivo* mouse studies, we demonstrate an absolute requirement for the protein within the cilium. Embryonically, *Pkd2*$^{lrm4/lrm4}$ kidneys exhibit gross cystic development. In vitro studies show specific accumulation of the protein at the mother centriole. This work indicates an essential role for PKD2 in the cilium and that non-ciliary function alone is not sufficient to prevent cyst formation.

Poster Number: P51
Switching On and Off the Motor Activity of Intraflagellar Transport Dynein
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Cilia are multi-functional organelles that are constructed using intraflagellar transport (IFT) of cargo to and from their tip. It is widely held that the retrograde IFT motor, dynein-2, must be controlled in order to reach the ciliary tip and then unleashed to power the return journey. However, the mechanism is unknown. Here, we systematically define the mechanochemistry of human dynein-2 motors as monomers, dimers, and multi-motor assemblies with kinesin-II. Combining these data with insights from single-particle electron microscopy, we discover that dynein-2 dimers are intrinsically autoinhibited. Inhibition is mediated by trapping dynein-2's mechanical "linker" and "stalk" domains within a novel motor-motor interface. We find that linker-mediated inhibition enables efficient transport of dynein-2 by kinesin-II *in vitro*. These results suggest a conserved mechanism for auto-regulation among dimeric dyneins, which is exploited as a switch for dynein-2's recycling activity during IFT.

Poster Number: P52
Unravelling the roles of kinesin-1 during neuronal growth and maintenance
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Neurons electrically wire the nervous system through meter-long protrusions called axons, which can last for decades in humans. For this, axons actively maintain parallel bundles of microtubules (MT) constituting their structural backbones and transport tracks. In cultured *Drosophila* neurons, the loss of MT motor proteins kinesin-1 reduces axon growth and induces MT bundle disorganisation, reminiscent of axon swellings observed in kinesin-1-linked spastic paraplegias. To dissect underlying pathomechanisms, we study contribution of three molecular subfunctions of kinesin-1 (vesicle/organelle transport, mitochondrial dynamics and MT sliding), by analysing kinesin-1 mutations or interaction partners (KLC, Milton, Miro, Pav) specific to these subfunctions. Surprisingly, depletion of any of these leads to MT disorganisation. By extending studies to include relevant subcellular readouts (mitochondria, synapses, and ER), we aim to compare and constrast different phenotypes within one standardised neuron system. This systematic approach offers the oppportunity to unravel the specific contribution of kinesin-1 subfunctions towards MT bundle maintenance.

Poster Number: P175
GSK3 roles during murine neural crest cell migration
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Neural crest (NC) cells are a vertebrate multipotent cell population that migrate extensively within the embryo and contribute to numerous tissues. While the migratory properties of NC have been extensively studied in *Xenopus* and chick, investigation of mammalian NC migration has been hindered by technical limitations. Here, we use an *ex vivo* system, coupled with confocal imaging, to overcome these challenges and investigate GSK3 requirements in migrating mouse NC. Single cell tracking revealed a reduction in NC migration distance and velocity following GSK3 pharmaceutical inhibition, and analysis of time lapse movies demonstrated that the formation of lamellipodia was perturbed in migrating cells. Furthermore, localization of both branched actin and pFAK were lost from the leading edge, while the total cellular amount of pFAK associated with stress fibres increased. Our data identify new roles for GSK3 in actin cytoskeletal rearrangements and focal adhesion turnover during mammalian NC migration.

Epigenetics

Poster Number: P53
Investigating the role of lysine acetyltransferase *cbp-1* in regulating the lifespan of*Caenorhabditis elegans*
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cbp-1, a gene encoding for the mammalian homolog of the CBP/p300 lysine acetyltransferase, was recently identified to be involved in regulating lifespan of the nematode *Caenorhabditis elegans*, as decrease of *cbp-1* activity was observed to extend lifespan in worms. While *cbp-1* has been heavily studied from a developmental perspective, its role in ageing is not well understood. *cbp-1* was discovered in an unbiased genetic screen, suggesting that further mechanistic studies need to be pursued to understand how *cbp-1* regulates lifespan in worms. Null mutations of *cbp-1* are embryonically lethal, necessitating the use of *cbp-1* heterozygous mutants. The dominance of the longevity phenotype is likely caused by haploinsufficiency of *cbp-1*, suggesting that *cbp-1* activity makes a large contribution to lifespan regulation. Importantly, mobility assays suggest that *cbp-1* knockdown extends worm healthspan as well as lifespan. These preliminary findings have prompted investigations to determine the mechanism for *cbp-1* mediated lifespan extension.

Poster Number: P54
Higher-order chromatin structure in the ground state of pluripotency
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Mouse embryonic stem cells (mESCs) are an excellent model for studying epigenetics and chromatin structure. Recently refined culturing conditions (2i) can harness mESCs in a pluripotent 'ground state'. This growth environment generates a naïve and homogenous cell population, in contrast to heterogeneous and metastable serum-cultured cells. Epigenetically, 2i culture promotes global hypomethylation and redistribution of polycomb marks. We investigated the effects of this altered epigenetic landscape on chromatin structure. We used a targeted, single-locus approach (FISH) and a genome-wide approach (HiC) to analyse differences in chromatin structure between conventionally serum-cultured and ground state mESCs. We find that chromatin structure is globally altered in mESCs in 2i. Mechanistically, we suggest that the epigenetic changes – not the pluripotency status of the cell population – are responsible for driving these structural changes.

Poster Number: P55
The role of chromatin helicase homolog Lsh in *de novo* DNA methylation during mouse embryonic development
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DNA methylation undergoes global reprogramming during early mammalian embryonic development, when it is almost completely erased after fertilisation of the zygote, then re-established in the implanting blastocyst. *De novo* DNA methyltransferases are the major enzymes involved in depositing methylation during development. However, exactly how DNA methylation patterns are determined remains unclear. Lsh (lymphoid specific helicase), a putative chromatin remodelling helicase, has been implicated in facilitating *de novo* DNA methylation during embryonic development. This study aims to define the requirement for Lsh in establishing DNA methylation patterns during early development. Culture conditions were varied to model early stages of development ('ground state', postimplantation epiblast and differentiation) in Lsh knockout mouse embryonic stem cells. Our results suggest that Lsh is not required for initial re-establishment of DNA methylation, but may be important for facilitating methylation at certain loci in epiblast-like stem cells and during the early stages of differentiation.

Poster Number: P56
R-loop, regulator of gene expression by epigenetic modification
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Epigenetic control can shape chromatin structure and genomic activities. Chromatin contains histone proteins wrapped around by DNA. Active promoter regions harboring high levels of CG dinucleotides are marked by H3K4me3, an active promoter mark, and the R-loop structure, a transient RNA:DNA hybrid. The three-stranded structure of R-loop pose a hindrance to transcription and replication, but paradoxically they modify the epigenetic landscape with active transcription marker. An overabundance of these three stranded structures leads to genomic instability while the lack of them hinders the proper execution of certain biological processes. Due to the significant effect R-loops have on the transcription pattern of highly active genes, it makes them an interesting research target. We investigate the relationship between the transcription-promoting histone modifications and R-loops. Uncovering the function of R-loops can potentially give an insight into the regulatory events including genomic instability that underlie human diseases including cancer.

Poster Number: P57
O-GlcNAcylation of Host Cell Factor is essential for *Drosophila* development
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O-GlcNAcylation of nucleocytoplasmic proteins is an essential post-translational modification. In *Drosophila*, null mutants of the polycomb gene *O*-GlcNAc transferase (OGT, also known as *super sex combs, sxc*) display homeotic phenotypes. Using CRISPR/Cas9 gene editing technology we have generated *sxc/OGT* hypomorphic point mutants to dissect the requirement of O-GlcNAc signaling in *Drosophila* development. One of the mutants sxc/OGT^{H537A}, retains only about 5% catalytic activity and is homozygous viable. Reduced *O*-GlcNAc levels in the sxc/OGT^{H537A} homozygotes are associated with phenotypes in trachea, wings and the nervous system. To establish whether *O*-GlcNAcylation of a well-established OGT substrates, Host Cell Factor (Hcf) is essential for its function, genetic interaction between sxc/OGT^{H537A} and a *Hcf* null allele, Hcf^{HR1} was assessed. sxc/OGT^{H537A}, Hcf^{HR1} double homozygotes displayed increased variance in scutellar bristle number as compared to either sxc/OGT^{H537A} or Hcf^{HR1} homozygotes. Current experiments are focused on establishing the molecular link between hypo-O-GlcNAcylated Hcf and the observed phenotypes.

Poster Number: P58
Depletion of DNMT1 in differentiated human cells highlights key classes of dependent genes
K M O'Neill[1,2], **R E Irwin**[1], S J Mackin[1], J Loughery[1], D McArt[5], C P Walsh[1], A Thakur[1,3], S J Thursby[1], C Bertens[1], L Masala[1,4]

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DNA methylation plays a vital role in the cell, but loss-of-function mutations of the maintenance methyltransferase DNMT1 in human cells are lethal, precluding target identification, and the only existing hypomorphic lines are tumorigenic. We generated a hypomorphic series in normal hTERT-immortalised fibroblasts depleted in DNMT1. Most sites showed demethylation, with a minority showing hypermethylation. Enrichment analysis indicated significant losses at mainly four gene classes: 1) protocadherins, key to neural cell identity; 2) genes involved in fat homeostasis; 3) olfactory receptors, responsible for smell 4) sex-chromosome encoded TSPY and MAGE genes, implicated in cancer. Many of the targets are monoallelically expressed. Effects on transcription were relatively small, but some genes showed robust derepression. Upregulation was accompanied by significant loss of methylation at the promoters of MAGE genes and increased gene body methylation, consistent with direct transcriptional control. Our results highlight the sensitivity of key neural, adipose, and cancer-associated genes to deficient maintenance methylation activity.

Poster Number: P59
Regulation of LINE1 retrotransposons by 2-oxoglutarate-dependent dioxygenases
L de la Rica, K C Cheng, O Deniz, **M R Branco**

Blizard Institute, QMUL, London, UK

Expression of retrotransposons such as LINE1 elements is kept under tight control via epigenetic mechanisms such as DNA methylation. Yet in tissues such as the brain and embryonic stem cells (ESCs), LINE1s undergo a loss of DNA methylation and increase in expression. TET enzymes, which can mediate DNA demethylation, are highly expressed in these tissues, suggesting a possible involvement of TETs in LINE1 activation. We found that TETs target evolutionarily young LINE1 elements in ESCs and drive LINE1 demethylation. Surprisingly, LINE1s are kept repressed through additional TET-dependent activities. On the other hand, addition of ascorbate and alpha-ketoglutarate, two key co-factors of 2-oxoglutarate-dependent dioxygenases such as TETs, drives LINE1 activation in ESCs. We found that ascorbate-mediated activation of LINE1s is independent of TET activity, suggesting the involvement of other 2-oxoglutarate-dependent dioxygenases. Our data raise the possibility that retrotransposition can be modulated by nutritional and metabolic inputs via epigenetic mechanisms.

Poster Number: P60
Chromatin-remodelling ATPase central subunits and plant defence
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Plants can detect pathogen microorganisms and build up defences accordingly. In order to survive and guarantee the provision of seeds for the next generation, the limited plant resources need to be finely tuned in the trade-off between growth and defence upon pathogen perception. Gene reprogramming is therefore a major component of the innate plant defence. Chromatin remodelling complexes have been pinpointed as regulators of immunity. Here we report a susceptibility screening, using the *Arabidopsis – Pseudomonas siryngae* pathosystem, for chromatin remodelling ATPases as novel regulators of plant immunity. We characterise the biological function and we are interested in describing its molecular mechanism of action. Our preliminary data highlights chromatin remodelling as a target for gene silencing via a negative feed-back loop mechanism, allowing the plant to recover pre-defensive genetic program in order to re-gain successful growth and reproduction.

Poster Number: P61
Analysis of a knock-out mouse model for the microcephaly-associated *Trappc9* gene and its epigenetic regulation by genomic imprinting
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Homozygous mutations of *TRAPPC9* cause microcephaly, intellectual disability, white matter hypoplasia and developmental delays in human. Trappc9 forms part of the trafficking protein particle II complex, which mediates vesicle transport at the ER/Golgi. It also interacts with the dynactin/dynein motor complex involved in retrograde transport and signalling along microtubuli. The *Trappc9* gene is located within the *Peg13/Kcnk9* cluster of imprinted genes on mouse chromosome 15 / human chromosome 8. In a first *Trappc9* knock-out (KO) mouse model we found brain weights and volumes (via MRI) to be reduced by 10% at 3-months of age. *Trappc9* is expressed in neurons and neural progenitor cells (NPCs), and Sox2-positive NPCs are reduced by 15% in the hippocampal dentate gyrus. Female KOs show a 20% increase in body weight. Pyrosequencing of brain cDNA SNPs show imprinted expression of *Trappc9* preferentially (70%) from the maternal allele, which is not associated with promoter DNA methylation.

Poster Number: P62
Identification of long non-coding RNAs in planarian pluripotent stem cells – a combined transcriptomic and epigenetic approach
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Planarians have emerged as a tractable model system to study regeneration because of their remarkable capacity to recover missing tissue following amputation or fission. Although various transcriptome assemblies have shed light on the protein coding content of planarians, very little is known about the identity or control of long non-coding RNAs (lncRNAs). Our study aims to identify novel as well as conserved lncRNAs in regenerating planarians. As putative lncRNAs are difficult to define, we use epigenetic histone modification markers as an additional factor to classify them. Putative lncRNAs were identified by applying a series of filters on the genome annotations to assess coding potential and then classified into single exon and multi-exon depending on the annotations structure. RNA-seq data from previous experiments were used to check for enrichment of these lncRNAs in different planarian cell types.

Poster Number: P176
Parp1 is required for imprint methylation maintenance
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Poly ADP-ribosylation is a posttranslation modification of proteins catalysed by Parp family of enzymes in response to cellular stress and DNA damage. Parp1 and Parp2 family members are directly activated by DNA strand breaks and mediate base excision repair. In addition to critical roles in DNA repair, Parp1 and Parp2 have been shown to be involved in chromatin remodelling and has been reported to play a role in maintaining ES cell pluripotency. In order to elucidate the molecular mechanisms of Parp1 function in ES cells we performed a genome wide DNA methylation analysis of Parp1 null ESCs leading to a serendipitous discovery of DNA methylation loss specifically at imprinted genes. We further confirmed the tendency of Parp1 and Parp1/2 DKO ES cells to lose methylation at multiple imprinting control regions using CRISPR-Cas9 gene disruption methods. Currently, we are investigating the mechanism by which this loss of methylation occurs.

Evodevo

Poster Number: P63
Endoderm on the face: Pre-oral expansion of the primitive gut in non-teleost fishes and its evolutionary implications
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In vertebrate embryos, the ectoderm gives rise to the skin, nervous system, and non-neural neural crest derivatives such as craniofacial skeleton and pigment cells, whereas the endoderm is usually considered to form the inner epithelial lining of the alimentary tract and its derivative organs. Interactions between the ectoderm and endoderm occur within strictly defined locations: primary mouth, pharyngeal slits and anus. Our fate-mapping experiments in non-teleost fishes – bichir, sturgeon and gar – reveal extensive endodermal contribution to facial surface, establishing an additional ecto-endodermal interface prior to the opening of mouth and pharyngeal slits. Micro-CT imaging allowed us to trace the origin of this external facial endoderm back to a pre-oral diverticulum of the primitive gut. These pre-oral gut diverticula share their developmental origin and gene expression patterns with rostral gut derivatives of invertebrate chordates and hemichordates, hence may represent an ancient blueprint for rostral pharynx development in deuterostomes.

Poster Number: P64
Conditional deletion of WT1 using *Prx1-Cre* causes congenital diaphragmatic hernia in mice
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Congenital diaphragmatic hernia (CDH) is a severe birth defect with a prevalence of approximately 1/3000 live births. Incomplete diaphragm development permits herniation of the liver, spleen, intestines or stomach into the pleural cavity. Bochdalek-type CDH accounts for 80-90% of cases, and is characterised by hernias in the posterolateral region. *Wt1*-null mice develop CDH, however, the causative mechanisms are unknown, and the embryos die at mid-gestation due to heart defects. We have developed a mouse model of CDH, using the *Prx1-Cre* line to drive WT1 deletion. ~70% of $Prx1^{Cre/+};Wt1^{loxP/loxP}$ embryos present with Bochdalek-type hernias. The embryos survive *in utero* but die at birth, making this murine model of CDH one of the few that survive gestation. The etiology of CDH remains largely unknown. We are investigating the cellular and molecular mechanisms responsible for the defect in our model, which should inform us more about the processes leading to human CDH.

Poster Number: P65
Regulatory mechanism of *Tbx5* in the forelimb and its adaptation in flightless birds
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The acquisition of limbs in primitive vertebrates was an important event as it allowed this group of animals to diversify, by adapting new feeding and breeding methods and colonising new environments. Forelimbs and hindlimbs in vertebrates are particularly diverse because their forms are directly linked to the ability and mode of locomotion. A striking example is found in a group of flightless birds, the ratites, that includes ostrich, emu and rhea. Ratites are spread widely across the continents of the southern hemisphere, but all share common characteristics; their wings are small, and unable to power flight, and their legs are usually well developed and adapted for running. We will discuss our preliminary results on the mechanisms responsible for forelimb reduction in ratites.

Poster Number: P66
Staging mouse embryos harvested on embryonic day 14 (E14.5)
S H Geyer[1], R Wilson[2], F Prin[2], D Szumska[3], R Ramirez-Solis[4], C Tudor[4], J White[4], **J Lane**[2], T J Mohun[2], W J Weninger[1]

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Identifying gene function remains a central goal of developmental biology. Comparison of mutant with wild-type embryos forms the basis for this and is central to “Deciphering the Mechanisms of Developmental Disorders (DMDD)”, a programme studying embryonic lethal gene mutations in the mouse (dmdd.org.uk). DMDD has found that many structures change rapidly as development proceeds. Current staging systems for embryos reaching the end of organogenesis (E14.5) are inadequate. We have therefore developed a simple alternative. Based on the external appearance of the forelimb, it can distinguish six developmental sub-stages amongst embryos harvested at E14.5. We have analysed 215 wild-tpye E14.5 embryos and identified differences of many organs, especially the palate, gut and heart. Applying the new staging system to E14.5 embryos of 58 embryonic lethal mutant lines reveals that comparison of mutant embryos with wild type littermates is likely to be seriously misleading, unless these are at the identical developmental stage.

Poster Number: P67
Break down of Meckel’s cartilage provides clues to the evolution of mammals
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The separation of the middle ear ossicles from the mandible by the breakdown of the Meckel’s cartilage is a key anatomical change during the evolution of mammals. Fossilised pre-mammalian synapsids posses a persistent ossified Meckel’s cartilage. These fossils are believed to be transitory forms, since only non-mammalian extant gnathostomes maintain Meckel’s cartilage to adulthood. We present biological mechanisms underlying the breakdown of Meckel’s cartilage, including the recruitment of chondroclast cells . Genetic or drug induced perturbations of clast cells in mice and opossums results in the persistence Meckel’s cartilage. Furthermore, we demonstrate that the Meckel’s undergoes ossification in mutant mice, in doing so phenocopying the Mesozoic pre-mammalian synapsids.

Poster Number: P68
Axial skeletal development in the skate, *Leucoraja erinacea*
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The vertebral column is a defining feature of vertebrates, but its early evolutionary history remains poorly understood. Vertebral centra in zebrafish are composed of notochord-secreted acellular bone, while amniote centra develop exclusively from sclerotome. To identify patterns general for jawed vertebrates (gnathostomes), we examined vertebral development in a cartilaginous fish, the skate, *Leucoraja erinacea*. We show that the skate axial skeletal anlage is an initially continuous mesenchymal condensation that surrounds the notochord. This condensation differentiates into a continuous tube of cartilage before subdividing into discrete vertebrae. Skate vertebral centra comprise three tissue layers: inner hyaline cartilage, middle areolar tissue, and outer hyaline cartilage. Using cell lineage tracing, we demonstrate that all of these tissue layers, as well as neural and haemal arches, derive from sclerotome. Our findings demonstrate that sclerotome ancestrally contributed to all components of gnathostome vertebrae, but highlight striking diversity in mode of gnathostome axial skeletal development.

Poster Number: P69
Establishing the mechanism of the calcium wave at *Drosophila* egg activation
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Egg activation is an essential process in development that typically accompanies fertilisation and collectively regulates major cellular processes. Concomitant with these events is a change in the intracellular concentration of calcium. However, a full understanding of the role of calcium in the regulation of the events at egg activation remains unclear. To address this we use mature *Drosophila* egg chambers, taking advantage of their amenability to imaging, genetic and *ex vivo* experimentation. We show that osmotic pressure, the actin cytoskeleton and internal calcium sources are required for a calcium wave, while physical pressure is not. Our work, together with other labs, supports a model where changes in osmotic pressure trigger the calcium wave via stretch-sensitive calcium channels, and the wave is relayed by the nearby channels via the actin cytoskeleton. We are currently testing this change in intracellular calcium and its relation to spindle orientation and translation of maternal transcripts.

Poster Number: P70
ABSTRACT WITHDRAWN

Poster Number: P71
The role of *hairy* in the genetic regulatory network for posterior segment addition in the spider *Parasteatoda tepidariorum*
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Arthropods, annelids and vertebrates undergo a time and space-controlled patterning developmental mechanism that differentiates body segments. Much about segmentation in arthropods has come from *Drosophila melanogaster*. However, this model shows a derived mode of segmentation, because most other arthropods display short germ sequential addition of segments from an undifferentiated posterior zone, such as the common house spider *Parasteatoda tepidariorum*. In this spider involves dynamic interplay between the Delta-Notch and Wnt signalling pathway, which in turn direct the downstream expression of segmentation genes. *hairy* (*h*) also exhibits dynamic expression in SAZ associated with formation of new segments, and interestingly requires *Wnt8*, that when perturbed segmentation is blocked. This suggests *h* is an integral component of the SAZ GRN. Further experimentation utilising RNAi knockdowns of other genes will provide insights into the role and regulation of *h* and the architecture of the GRN for segment addition in this short germ arthropod.

Poster Number: P73
Analysis of the expression and function of *Wnt10* in *Drosophila melanogaster*
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There are 13 subfamilies of Wnt ligand genes in metazoans and they are crucial for a wide range of developmental processes. In *Drosophila melanogaster* the best described and functionally analysed Wnt gene is *wingless*, however, the functions of several other Wnt ligands are not well understood: for example, *Wnt10* which is highly conserved in metazoans. In *Drosophila*, *Wnt10* is expressed in the developing gut and other tissues – however its specific function remains unclear. Therefore we have verified the expression of *Wnt10* in *Drosophila* embryos and larvae and analysed its function using RNAi knockdown. Additionally we have designed a CRISPR/Cas9 strategy to create a *Wnt10* knockout strain via introduction of an integrase site into this locus. This project will provide new insights into the function of *Wnt10* and its roles in developmental processes in *D. melanogaster*.

Poster Number: P74
Investigating the role of gene duplication and divergence during the evolution of spiders and other arachnids
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Gene duplication underlies the origin and evolution of novel genes with new functions that can contribute to organismal divergence. Relaxed selection on the duplicates allows the accumulation of mutations, modifying both coding and regulatory sequences. This can lead to subfunctionalization or neofunctionalization. Recent studies of spiders and scorpions show a high prevalence of duplicated genes, including two Hox clusters and approximately 40% of other homeodomain containing genes, which is suggestive of a whole genome duplication event in the common ancestor of scorpions and spiders. With a sequenced genome and an increasing array of molecular tools, the spider *Parasteatoda tepidariorum* readily allows the study of the impact of this duplication event during arachnid evolution. Therefore I have analysed the expression of duplicated homeodomain genes in spiders and other arachnids to infer the extent of sub and neofunctionalization upon duplication.

Poster Number: P75
The shortest germ: Evolution of an extreme short-germ mode of segmentation within the beetles
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A segmented body plan is one of the key traits underlying the immense evolutionary success of insects. However, the manner in which segments are generated embryonically varies greatly between species. The best studied mode of segmentation (“long-germ”) is seen in flies like *Drosophila melanogaster*, where all segments are specified near simultaneously at the blastoderm stage. However, most insects only generate some segments at the blastoderm stage, while the rest are generated sequentially during posterior elongation of the embryo (“short-/intermediate-germ”). The long-germ mode has seemingly evolved several times from the ancestral short-germ mode, but the opposite has never been described. I will present my results from the previously uncharacterised beetle *Atrachya menetriesi*, which I have found to display the most extreme-short-germ mode ever described. This finding is remarkable because, based on current data, *Atrachya* seems to represent an actual example of the “re-evolution” of the short-germ mode from a long-/intermediate-germ ancestor.

Poster Number: P182
Investigating gene regulatory network architecture and evolution in different developmental contexts
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Changes in gene regulatory networks (GRNs) underlie morphological evolution. However, it is unclear how different developmental contexts affect the nodes at which GRNs can evolve. To investigate this question we studied the GRN underlying trichome development in *Drosophila*. The larval trichome GRN is well characterised, and changes in the regulation of *shavenbaby* underlies the convergent loss of larval trichomes among *Drosophila* species. Trichome patterns on the second leg of *Drosophila* have also evolved within and between species through changes in *mir-92a* and *Ultrabithorax*. To determine the architecture of the leg trichome GRN to compare to the larval trichome GRN, we performed RNA-Seq and ATAC-seq followed by functional assays. This allowed us to identify key genes and their putative enhancers used in the leg trichome GRN, including Ubx, SoxN, Svb and Sha, which may help to decipher why evolutionary change occurs at different nodes of GRNs in different developmental contexts.

Poster Number: P187
Telling good segmentation from bad
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Somitogenesis is the process by which the developing vertebrate embryo segments its body axis. While in amniotes somitogenesis instructs the metamery of the vertebral column, in zebrafish it is not clear.
To investigate the relationship between somitogenesis and vertebral segmentation, we have generated a mutant line that is null for her1 and her7. These genes function as a transcriptional genetic oscillator that gives rise to the periodicity of somitogenesis. We confirm the loss of dynamic gene expression and disordered muscle boundaries. However, the vertebral column is not correspondingly affected.
One hypothesis that can explain this paradox is that residual periodic information is still present in the mutant. A second hypothesis is that the vertebral column patterns by an independent mechanism. To enable testing of these hypotheses, we are devising methods to quantitatively describe segmentation defects and differentiate between phenotypes that have residual periodic information and those that have none.

Mechanisms in gene expression

Poster Number: P76
Developmental genes and impacts on human diseases
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Studying gene expression and regulation is crucial for understanding the biology of human diseases. The human body is governed by a complex of gene regulatory networks to exert its necessary functions in harmony. Despite the major advances in genomic technologies, these networks are still not fully understand especially how they precisely orchestrate to perform the body functions. There is some evidence indicating that human diseases develop by disruption of embryonic genes. Here, we aimed at analyzing 7500 developmental genes in human diseases using ingenuity pathway analysis software (IPA) to elucidate the shared genes in development and diseases. We validated our findings by identifying developmental genes in a human colorectal cancer microarray analysis. We identified a number of important developmental genes that are common in different types of human diseases. We believe that this analysis could broaden our understanding about the common grounds between genes in development and human diseases.

Poster Number: P77
Highly variable penetrance of abnormal phenotypes in embryonic lethal knockout mice
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Characterising the changes in mouse embryos that result from the knockout of genes essential for embryonic development and survival is an important first step towards uncovering their role and establishing any correlates amongst human congenital abnormalities. The Deciphering the Mechanisms of Developmental Disorders (DMDD) programme has catalogued the morphological defects identified from comprehensive imaging of 220 homozygous mutant embryos from 42 lethal and subviable lines, analysed at E14.5. Virtually all embryos show multiple abnormal phenotypes and within each mutant line the phenotypes of individual embryos form distinct but overlapping sets. Subcutaneous edema, abnormalities of the heart, great vessels, forebrain and musculature of the eyes are all prevalent, as is loss or abnormal size of the hypoglossal nerve. Most strikingly, no matter how profound the malformation, each phenotype shows highly variable penetrance within and between mutant lines. These findings have challenging implications for efforts to identify human disease correlates.

Poster Number: P78
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 the molecular mechanisms underlying neural crest differentiation into OECs, as opposed to Schwann cells, which are less effective in spinal cord repair. To achieve this, I am taking 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 should identify candidate genes that may be important specifically for OEC differentiation and that distinguish different OEC subpopulations.

Poster Number: P79
Seperable control of growth and patterning by Dpp in *Drosophila* wing precursors
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Decapentaplegic (Dpp), a member of the BMP family, is a morphogen that specifies positional information in Drosophila wing precursors. However, it has also been shown to play a vital role in regulating the growth of this tissue. The spatial and temporal requirements of Dpp for normal cell proliferation have been the subject of debate, which has intensified recently with the suggestion that the endogenous stripe of Dpp is not required for growth during the third larval instar. We use an independent, conditional allele to show that removal of the Dpp stripe is deleterious to wing disc growth. Furthermore, we show that low-level, uniform Dpp expression is sufficient to promote normal growth in the prospective wing region or pouch. These results suggest that the stripe of Dpp generates a gradient that specifies cell fates, but also promotes cell proliferation by ensuring that Dpp signalling stays above a certain threshold.

Poster Number: P80
The regulation of embryonic stem cell differentiation by Nrf2
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Oxidative stress is closely related to stem cell differentiation. Oxygen availability is usually different between the niche of stem cells and differentiated cells. In addition, the change towards oxidative metabolism in differentiated cells could cause oxidative stress. We focused on Nrf2, the master antioxidant response regulator, and its role during embryonic stem cell (ESCs) differentiation. We evaluated five stages of differentiation from mouse ESCs to neural progenitor cells (NPCs) for Nrf2 levels, oxidative metabolism, and reactive oxygen species. Additionally, we conducted gain and loss of function experiments using a small molecule Nrf2 activator and CRISPR-Cas9 genome editing. We found that, independently of oxidative stress level, Nrf2 expression decreased during neural differentiation both in transcriptional and protein levels, and that elevation of Nrf2 levels inhibited the differentiation of ESCs towards NPCs. Moreover, Nrf2 null ESCs could not be derived, suggesting an essential role for this gene in pluripotent cells.

Poster Number: P81
The effects of exogenous expression of MyoD fusion proteins on the myogenic regulatory factors (MRFs) in fibroblasts - development of a tool to identify MRF target genes in somites of chicken embryo
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Background: Vertebrate myogenesis is orchestrated by the myogenic regulatory factors (MRFs); MyoD, Myf5, myogenin (MyoG) and MRF4. This research aimed to identify the effect of exogenous MyoD expression in fibroblasts, particularly the expression of endogenous MRF genes. Methods: A MyoD-glucocorticoid receptor fusion including a HA-tag was cloned in RCAS retroviral vector. DF1 chicken fibroblasts were infected, incubated for 48 hours, followed by RT-PCR expression analysis or immunofluorescence microscopy (anti-HA antibody). Results: Elevated gene expression of the MyoD-GR fusion was achieved in DF1 cells, along with fusion protein expression and a dexamethasone influenced translocation to the nucleus. The gene expression of MyoD in DF1 was associated with a dexamethasone treatment induction of MRF4 and Myf5 but not MyoG. Conclusion: Exogenous express of MyoD in fibroblasts induces expression of selected MRFs. The infection of chick embryo somites with this vector will examine effects of the four MRFs on *in situ* mRNA expression.

Poster Number: P82
Role of the transcription factor Odd-skipped in neural arbour formation in *Drosophila*
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The genetic code underlying neural connectivity remains unclear for many lineages in the brain. One such lineage is the Odd neurons in the *Drosophila* brain that are characterised by expression of the transcription factor Odd-skipped. Using loss and gain-of-function approaches we show that Odd-skipped is crucial for neurite formation and controls cell numbers in the Odd neural lineage. Overexpression of Odd-skipped in the Odd-neurons causes severe truncation of axonal outgrowth whereas dendrites are completely absent. Loss of Odd-skipped expression using the MARCM approach abolishes neurite outgrowth all together. Overexpression of Odd-skipped in the Odd neurons results in a decrease in the number of Odd-skipped expressing cells whereas loss-of-Odd-skipped function terminates cell division in the lineage. This data shows that manipulating the levels of Odd-skipped expression affects neurite formation and cell numbers suggesting that levels of Odd-skipped expression is tightly controlled to ensure the correct development of the Odd neural lineage.

Poster Number: P83
Interpreting Neonatal Lethal Phenotypes in Mouse Mutants: A New Screen to Gain Insights into Gene Function and Human Diseases
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The Wellcome Trust Sanger Institute (WTSI) is a major contributor towards the worldwide effort in developing mouse models to help understand human genetic disease. To date, 32% of over 1000 lines studied within the WTSI primary phenotyping screen are classified as lethal or sub-viable at postnatal day 14 (P14). For the majority of those lines, embryos die before birth, however 5-10% die around birth or in the immediate post-natal period. Embryonic lethality assessed within the Deciphering Mechanism of Developmental Disorders (DMDD) programme has so far focussed on in-utero development. During the neonatal period, there are also major physiological processes which are critical to mouse new-born survival. By using a relatively small, focussed set of in vivo and ex vivo tests, we will systematically phenotype perinatal lethal and sub-viable lines in order to obtain greater insight into whether lethality in such lines results from defects in parturition, breathing, feeding or homeostasis.

Poster Number: P84
Gremlin, gradients and ectoderm patterning
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Positional information is essential for the development of complex structures. Signalling gradients established by long-range communication are used as foundations for pattern formation. Intricate networks of signalling molecules underlie this process, involving a multitude of extracellular, cell surface and intracellular components with feedback loops at every step. Regionalisation of the ectoderm in *Xenopus laevis* is an ideal model system to investigate patterning mechanisms. This study examines the role of the bone morphogenetic protein (BMP) antagonist Gremlin in the formation of the dorsoventral axis that subdivides the ectoderm into neural plate, border and non-neural regions. Differential diffusivity of signalling complexes is a key determinant of gradient formation. Heparan sulfate proteoglycans (HSPGs) are a class of cell surface macromolecules that may be important regulators of diffusion. Their role is addressed using mutant Gremlin constructs with impaired HSPG binding.

Poster Number: P85
A long undecodable transcript isoform mediates transcriptional repression of the *NDC80* gene during early meiosis in budding yeast
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To ensure faithful chromosome segregation during budding yeast meiosis, expression levels of the outer kinetochore protein Ndc80 are tightly controlled. During early meiosis, transcription of a long undecodable transcript isoform (*NDC80^{luti}*) represses expression of the canonical *NDC80* protein coding isoform (*NDC80^{ORF}*) in cis. *NDC80^{luti}* transcription establishes a repressive chromatin state at the 5' end of NDC80 and repression depends on the Set2/Rpd3S and the Set3C pathways. Furthermore, multiple upstream open reading frames in *NDC80^{luti}* prevent its translation into Ndc80. This repression mechanism is highly dynamic because *NDC80^{luti}* transcription is quickly switched off and *NDC80^{ORF}* is rapidly de-repressed when cells are returned to the mitotic cell cycle. In conclusion, repression of *NDC80^{ORF}* by a long isoform is mediated through a combination of transcriptional interference, repressive chromatin, and translational control. We propose that this could be a generic mechanism for temporal transcriptional repression in cell fate-regulatory programs.

Poster Number: P86
SEMA3E and SEMA3C Cooperate to establish vascular boundaries
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The process by which blood vessels grow in response to vascular endothelial growth factor A (VEGFA) is well established. However, it is poorly understood how tissues with widespread VEGFA expression can generate avascular areas. We demonstrate that two axon guidance cues of the class 3 semaphorin family, SEMA3C and SEMA3E, establish vascular boundaries in developing tissues. *In vitro* assays with endothelial cells showed that SEMA3C and SEMA3E collapse endothelial cells via their respective receptors, NRP1 and PLXND1. *In vivo* analyses with complementary sets of ligand and receptor mouse mutants showed that SEMA3E and SEMA3C cooperate to establish avascular areas in the lung and somites, whereby signalling from only one of these ligands is sufficient to maintain appropriate vascular boundaries, but loss of both signalling pathways causes ectopic vessel growth. We conclude that vascular boundaries are established in developing organs through the concerted action of class 3 semaphorins.

Poster Number: P87
Mechanism of expression regulation by STR (microsatellite)
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Microsatellites (STR) are common genetic vairation and had been considered biological inert in the human genome in the past. We have intensively studies the STR in IGF1 and showed that it interacts with adjacent SNPs in the IGF1 promoter in regulation of IGF1 expression in epidemiology study. Using a extensive array of plasmids contructure of the IGF1 promoter. A in-vitro luciferase reporter system was optimized to reveal the transactivation capacity of an individual plasmid construct. We showed that there was a gradational transactivation capacity of promoters of reducing number of repeat units. However, this gradational property is only found in a particular haplotype of adjacent SNPs. When the SNPs were swapped to the minor allele, the gradation property was lost. The results confirmed and provided an plausible mechanism on how the STR variation could affect gene regulation. And it is likely work together with adjacent TF-DNA complexes to deliver a regulation effect.

Poster Number: P88
CSL DNA-binding dynamics are a major point of regulation in determining the functional consequences of Notch activation
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Notch pathway is a major signalling pathway involved in development. Upon activation, Notch, the transmembrane receptor, undergoes two cleavages, releasing its intracellular domain (NICD). NICD forms a complex with a DNA-binding transcription factor, CSL, and the co-activator Mastermind to stimulate transcription. Chromatin immunoprecitation studies of CSL binding, indicates that Notch activation is accompanied by changes in the genomic occupancy of CSL, suggesting that NICD stimulates CSL movement and/or binding kinetics. To investigate this, we studied CSL nuclear dynamics using live imaging techniques, including Fluorescence Recovery After Photobleaching and Single Molecule Tracking. Our results revealed that in Notch-OFF cells, only a small fraction of CSL molecules are bound to DNA at anytime, and their binding is highly dynamic. In Notch-ON cells, CSL becomes highly enriched at target loci. Two different mechanisms operate: Notch induced "assisted loading" increases the number of CSL complexes recruited, and Mastermind functionality favours an increased dwell time.

Poster Number: P89
Exploiting Notch regulation to probe alternative mechanisms of TSC signaling
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Tuberous sclerosis is caused by mutations in Tuberous Sclerosis Complex (TSC)-1 and TSC-2 genes, and manifests in hamartomas throughout the body. The TSC proteins form a complex that is involved in the control of cell growth and division by repressing the Rheb GTPase and thus controlling mTOR signaling on the surface of lysosomes. Inhibiting mTOR has demonstrated clinical efficacy in treating TSC-associated tumors, however, responses are usually only partial and regrowth occurs after drug withdrawal. Work in *Drosophila* suggests that the partial success is due to the fact that Rheb also targets Tor-independent mechanisms. Following a genome-wide RNAi screen in *Drosophila*, we found that TSC knockdown specifically downregulates a form of ligand-independent Notch signaling. Moreover, we observed that this is independent of Tor, but dependent of Rheb. We are now exploiting the mechanistic links between TSC/Rheb and Notch, which can provide new opportunities in the search for better drug targets.

Poster Number: P90
The Gene Expression Database (GXD): an integrated resource for gene expression information for the developing mouse
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The Gene Expression Database (GXD) (www.informatics.jax.org/expression.shtml) is an extensive and freely available community resource for mouse developmental expression data acquired by curation of published literature and from large-scale expression studies. GXD maintains an up-to-date, searchable index of publications, and annotates results from RNA in situ, immunohistochemistry, knock-in reporter, RT-PCR and blot assays. Experiment details, including genetic/allelic backgrounds, probe or antibody information, ages and/or stages, and tissue(s) of expression, are recorded in standardized ways. Currently GXD contains ~1.5 million results, for >14,000 genes, with >300,000 expression images. Query forms enable searches using one or multiple parameters, resulting in data summaries defined by search criteria, with options including interactive matrix views and image summaries, and filters enabling iterative query refinement. As an integral part of Mouse Genome Informatics, expression information in GXD is fully integrated with genetic, functional, phenotypic and disease-oriented data in MGI. GXD is funded by NIH grant HD062499.

Poster Number: P91
Coordinate Regulation of Development by a Shared RNA Element
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Developmental gene expression is regulated at the level of DNA and/or RNA. We find that an RNA element we previously identified in the zebrafish *nodal /squint* (*sqt*) 3'UTR is shared by multiple Nodal signalling pathway components: *lefty1/2* inhibitors, *acvr2a* receptor and *smad2* effector RNAs. Reporter assays for localization and translation in early embryos suggest that the RNA elements function similarly to the nodal 3'UTR. Y-box binding protein1 (Ybx1) binds to the RNA element and the translation pre-initiation complex, resulting in translational repression of nodal and *lefty*. Whereas *Mybx1* mutant embryos show premature Nodal translation and gain-of-Nodal signalling, *Mybx1*;nodal compound mutants display premature and elevated Lefty protein expression and loss-of-Nodal signalling. Thus, multiple components of a developmental pathway are translationally regulated by a shared RBP/RNA element "regulon". This module also regulates human *NODAL*. Computational analysis identified >800 zebrafish transcripts harbouring similar elements, and preliminary assays indicate broader roles for this regulon.

Poster Number: P92
Molecular logic behind Satellite cells specification in Drosophila
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Adult stem cells are important for tissue maintenance and repair. One key question is how such cells are specified and then protected from differentiation. Similar to vertebrates, Drosophila have a population of residual satellite cells (SCs) in adult muscles that retain characteristics of muscle progenitors. We have uncovered a role for *zfh1*, a Notch target, in keeping these progenitors/SCs undifferentiated. Their differentiation into functional muscles is accompanied by expression of a conserved micro RNA, *mir-8/mir-200*, which targets the major "long" *zfh1* isoform and decrease Zfh1 protein. Importantly, an alternate, *zfh1-short* isoform is produced at high level in the SCs. Because short *zfh1* lacks the target-site for *mir-8*, Zfh1 protein is maintained in SCs and they can escape differentiation. This type of regulatory logic, utilizing RNA isoforms with differential sensitivity to mIRs, may be of general relevance for progenitor maintenance in other tissues.

Poster Number: P93
Cell identity switching in zebrafish hindbrain segmentation
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During development of the vertebrate hindbrain, the neuroepithelium becomes subdivided into seven morphological units, known as rhombomeres. It is necessary that rhombomeres have sharp, well-defined boundaries, which are established from initially rough gene expression domains during early hindbrain segmentation. Evidence suggests that this sharpening process involves both cell identity switching and Eph/ephrin-mediated cell sorting. To assess the relative contributions of these two mechanisms in zebrafish, we have generated a novel transgenic reporter line by CRISPR/Cas9-mediated reporter integration at the *egr2b* locus. This enables us to visualise cell identity and cell intermingling in live embryos during border sharpening. Time lapse imaging in this novel reporter line indicates that cell identity switching does contribute to border sharpening in zebrafish. We have also observed that the contribution of cell identity switching to border refinement is enhanced when Eph-ephrin signalling is perturbed.

Poster Number: P94
Understanding gene specific regulation of RNA polymerase pausing by Groucho family proteins
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The evolutionarily conserved family of Groucho/Transducin-Like Enhancer of split (Gro/TLE) proteins act as co-repressors for numerous transcription factors. They act in several key pathways during development

(including Notch and Wnt signalling) and are implicated in the pathogenesis of several human cancers. The molecular mechanisms underlying Gro/TLE-mediated repression remain largely unknown. Gro is enriched at transcription start sites that exhibit RNAP II pausing, and loss of Gro in cells leads to a decrease in RNA polymerase pausing at a validated target locus of Gro repression (E(spl)mβ-HLH). This raises the possibility that at least one mechanism of Gro function is through the promotion of RNA polymerase pausing. We are currently screening various genes encoding candidate factors known to directly regulate transcriptional pausing for genetic interactions with gro. These factors will be further investigated for physical interactions with Gro to help elucidate Gro's mechanism of repression.

Poster Number: P95
Exploring the connection between Oct4 and adhesion molecules in the pluripotent state
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The transcription factor Oct4 (Pou5f1) is highly expressed in Embryonic Stem Cells (ESCs) and supports ESC self-renewal and maintenance of pluripotency. The Oct4 network is complex due to collaboration with many factors and regulation of thousands of target genes by activation or repression. In addition, evolutionary studies have revealed that a significant part of Oct4 targets are involved in cell adhesion. E-cadherin, a cell-cell adhesion protein, is strongly expressed in ESCs and can partially replace Oct4 in sustaining pluripotency and blocking differentiation. These data suggest a connection between Oct4 and E-cadherin but how they regulate each other remains unknown. We have been exploring this link using a dual-reporter line (Oct4mCherry/EcadGFP) and isolated different populations of ESCs with distinct properties in adhesion, self-renewal and differentiation. We are exploring how adhesion impacts on Oct4 occupancy of its targets, and how Oct4 targets regulate adhesion.

Poster Number: P96
Regulation of transcription in mESC Differentiation
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FGF signalling via Erk activation has been associated with ESC differentiation to primitive endoderm (PrE) by suppressing core nodes of the pluripotency network. Several mechanisms have been proposed, including transcription factor (TF) phosphorylation and degradation. However, analysis of nascent RNA expression shows that promoter inhibition proceeds any detectable loss in TF abundance and promoter occupancy. Our data suggest, that Erk phosphorylates core enhancer components such as p300, CBP and Med24, decommisioning enhancers, while leaving specific TF bound to their sites in the early stages of Erk induced PrE differentiation. This state would represent a novel intermediate in transcription regulation and we will now examine the nature of promoter-enhancer interactions in this state by chromosome FISH and ChIA-PET.

Poster Number: P97
Gene family expansion allows diversification of transcriptional bursting dynamics
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During the evolution of gene families, diversification often follows gene duplication which can result in the generation of novel protein functions. However, in some instances, notably histones, gene families can expand while preserving protein sequence. Why would a cell need to maintain multiple copies of the same gene? Here we have addressed this question for an actin gene family containing 17 genes encoding an identical protein. We show that family members display different transcriptional dynamics with strong 'bursty' behaviours contrasted by more stable transcriptional activity. These differences in transcription dynamics could play a functional role with constitutive protein production supplemented by more transient responses to environmental stimuli enabling precise regulation within a highly compact genome. We are now investigating the downstream effects of these differential dynamics at both the mRNA and protein level as well as probing the genetic determinants by promoter switching.

Poster Number: P98
m6A potentiates Sxl alternative pre-mRNA splicing for robust Drosophila sex determination
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Methylation of adenosine (m6A) is the most common internal modification of eukaryotic mRNA and decoded by YTH proteins. The functions of m6A in alternative splicing regulation, however, remain uncertain.
Here we show that Drosophila lacking dIME4 do not have m6A in mRNA. In contrast to mouse and plant knock-out models, Drosophila dIME4 mutants remain viable, though flightless and show a sex bias towards maleness. This is because m6A is required for female-specific alternative splicing of Sex-lethal (Sxl), which determines female physiognomy, but also translationally represses male-specific lethal to prevent dosage compensation normally occurring in males. We further show that lack of the m6A reader YT521-B decodes m6A in the sex-specifically spliced intron of Sxl and phenocopies lack of dIME4. Requirement of m6A and its reader YT521-B for female-specific Sxl alternative splicing reveal this hitherto enigmatic mRNA modification as constituting an ancient and specific mechanism to adjusts levels of gene expression.

Poster Number: P100
Regulatory principles governing enhancer function
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Enhancers are genomic elements that encode the instructions for when and where genes are expressed during development and homeostasis. The majority of mutations leading to disease are thought to reside within enhancers. However, we do not understand which changes in enhancer sequence are inert sequence variations between individuals and which mutations impact gene regulation and cell identity. These fundamental questions remain unsolved because we cannot relate enhancer sequence to gene expression patterns and phenotype. To address this problem, we developed high-throughput assays to test millions of enhancer variants for function in millions of embryos. The model organism that enables such in-depth functional approaches is the marine chordate *Ciona intestinalis*. I will discuss our recent experiments using this approach to identify organizational constraints and other regulatory principles governing enhancer function. I will also discuss how we are using these principles to pinpoint mutations associated with disease.

Poster Number: P177
The tectonics of inner ear cristae formation: rift and break-up of an initial pan-sensory domain
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The inner ear contains multiple sensory organs separated by non-sensory epithelial domains. Here, we studied in the embryonic chick inner ear the changes in cell shape occurring during the formation of the anterior and lateral cristae. We found that the cristae arise at the edge of a larger Sox2-expressing pan-sensory domain, the bulk of which gives rise to the utricle. Interestingly, enlarged cells appear at the interface between the cristae progenitors and the pan-sensory domain. As the cristae segregate, those enlarged cells down-regulate Sox2 expression and form the non-sensory cells at their lateral border. These observations suggest that the cristae form by a 'rift and break-up' process, occurring in parallel to the specification of new sensory-competent cells at the border of the initial pan-sensory domain. They also suggest that signals conveyed by mechanical forces could play a role in the diversion of the prospective border cells from a sensory fate.

Poster Number: P178
Establishing the chick as a model for anterior segment development
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Anterior segment dysgenesis and glaucoma are a group of human ocular disorders that may severely affect the cornea, iris, retina and lens. Their pathogenesis is often associated with disruptions to normal embryonic development of the anterior segment of the eye. A detailed insight about how this region develops could provide a better understanding of the origin, and potential treatments, of ASD and glaucoma. To date, few studies have focused on chicken eye development, which offers several advantages over traditional systems. The principal aim of this project is to investigate the utility of the chick for long-term studies of AS development and disease through: histological AS analysis during embryogenesis and early post natal stages, mapping the spatial-temporal expression of causative genes for human ASD and glaucoma, and to develop a transcriptome dataset for the developing anterior segment.

Poster Number: P180
Notch and Lmx1a: An antagonistic partnership during formation of inner ear sensory patches
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The inner ear contains multiple sensory organs, separated by non-sensory structures. We found that during development, Notch signalling and Lmx1a have opposing effects on sensory patch formation: Jagged1/Notch signalling promotes sensory commitment by lateral induction; conversely, Lmx1a antagonizes Notch and is required for the normal segregation of sensory organs. To understand how these two signals regulate sensory and non-sensory development and interact with one another, we manipulated Notch and Lmx1 function in the developing chick and mouse inner ear and used RNA-seq to analyse the resulting changes in gene expression. We will present the results of our preliminary analyses to identify genes specifically regulated by Notch and Lmx1a, and our cross-comparison strategy to discover new candidate genes and pathways involved in the early formation of inner ear sensory patches.

Neurons, networks and behaviour

Poster Number: P101
Genomic Relation of Human Aggression Behavior in Convicted Offenders for Physical Assault and Terrorism
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Genomic association of human negatively driven behavior lies under the control of Serotonergic system derived by *MAOA* gene responsible for criminal violence and aggression. In this context, following study was planned to evaluate the genetic variants in MAOA gene associated with the violence in convicted offenders of Physical assault and terrorism from Central Jail in Lahore, Pakistan. Blood/Saliva /Buccal swabs samples were collected from Jail of Punjab, Pakistan and organic method of DNA extraction was used. Exonic regions of the gene were amplified and sequences. Analysis of region indicated two polymorphisms. The exon 13 having heterozygous SNP, AT instead of TT. This SNP was found strongly associated with level of aggression score calculated on a specially designed proforma. These SNPs can be potential markers for detecting the level of eggression and to design a national stretegic plan for controlling the risk factors behind this raising concern regarding aggression.

Poster Number: P102
Identifying additional protein interactors of members of the Sm protein family and the implications in Spinal Muscular Atrophy pathogenesis
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The inherited neurodegenerative disease Spinal Muscular Atrophy (SMA) is caused by a reduction in functional Survival of Motor Neuron protein (SMN), and predominantly affects motor neurons. SMN is an essential housekeeping protein, required in all cells to assemble a ring of Sm family proteins around small nuclear RNA during the biogenesis of splicing snRNPs (small nuclear ribonucleoproteins).
It has been proposed that SMN has additional functions in motor neurons, transporting mRNA towards growth cones. We have previously identified vesicles containing SMN and SmB, an Sm family protein, that are trafficked along microtubules.
Using proteomics to identify interactors of SmB and SmN, a neural Sm family protein, we have identified an interacting protein that may be involved in cell polarity and neural signaling pathways. This protein localises to a subset of vesicles containing Sm proteins, interacts with SMN and may be important for correct localization of SMN in neural cells.

Poster Number: P103
Control of Cell-Cell interactions in Forebrain Morphogenesis
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Cell segregation and establishment of boundaries are key processes in development. Despite the importance of this phenomenon, the cellular and molecular basis of boundary formation has yet to be unravelled. During neurulation, telencephalic cells at the anterior neural border of the neural plate converge towards the midline, on top of eye field progenitors that maintain a cohesive state before moving outwards to form the primordium of the optic vesicles. Although the patterning mechanisms leading to the determination of the different forebrain territories have been well described, how these cell populations are physically segregated and acquire different dynamic behaviours has not been studied. Combining time-lapse video microscopy and functional analyses in the zebrafish embryo, this study aims at describing the cell movements inducing the separation of telencephalon and eye field, and deciphering the interplay between the different actors leading to the organisation of the forebrain during neurulation.

Poster Number: P104
Microautophagy-mediated degradation of Arouser regulates lipid metabolism and feeding behaviour in *Drosophila*
A C Jacomin[1], Z Hussain[1], A Varga[2], A Jain[3], M Eddison[4], K G Moffat[1], T Johansen[3], G Juhasz[2], I P Nezis[1]

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The coordination of metabolism and feeding behaviour related to the nutrient source is crucial for maintaining organism homeostasis, health and survival. Elucidation of the physiological and molecular bases of appetite and energy mobilisation in *Drosophila* may contribute to a better understanding of human pathologies such as obesity or feeding disorders. Lipids constitute an essential source of energy for the cell, that can be mobilised during fasting by autophagy. We have identified Arouser protein which is degraded by microautophagy (a subtype of autophagy) during larval feeding stages but is stabilised under nutrient starvation. Furthermore, we observed that *arouser*-deficient flies are more sensitive to hunger and present a deregulation of the food intake behaviour. Finally, we showed that *arouser*-deficient flies have a defective lipid metabolism. Altogether, our results suggest that Arouser is involved in lipid storage and mobilisation during fasting periods.

Poster Number: P105
Splicing factor proline-glutamine rich (SFPQ) in motor axon development and neurodegeneration
R Taylor[1,2], T Fielding[1,2], P Gordon[1,2], C Houart[1,2]

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RNA processing ensures expression of the correct complement of proteins, facilitating cellular homeostasis. Performed in the nucleus, pre-mRNA splicing requires the spliceosome. Misexpression of genes regulating splicing, results in various biological abnormalities. Recently, extranuclear expression of the neural-specific splicing factor, SFPQ, and other spliceosomal proteins has been observed in motor neuron axons. Although the nuclear functions of SFPQ have been well explored, its extranuclear roles remain enigmatic. SFPQ null zebrafish embryos display a striking phenotype including no motility – coincidentally accompanied by failed motor neuron development. These abnormalities are rescued upon expression of an exclusively cytoplasmic SFPQ variant. Using a cell transplantation approach, we now show that SFPQ null motor axons grow in a wild-type background. These axons appear later than SFPQ-expressing axons, and exhibit abnormal morphology. These early observations reveal that axons, although morphologically abnormal, are capable of extension in absence of SFPQ, providing the environmental conditions are permissive.

Poster Number: P106
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: P107
Automated animal tracking and quantitative analysis of *C. elegans* social behaviour
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Social behaviour is common in the animal kingdom, but studies are often limited to the observational level, as few systems allow for perturbation in a controlled environment. To this end, we use the nematode *C. elegans* to dissect the behavioural mechanisms of aggregation, a simple social behaviour. *C. elegans* natural isolates aggregate into tight groups, whereas the laboratory strain forms looser groups or feeds alone; the difference is due in part to a mutation in the neuropeptide receptor gene *npr-1* which arose during laboratory domestication. We quantified the behaviour of the laboratory strain and an *npr-1* mutant using fluorescence imaging and automated animal tracking, and built an agent-based mathematical model to identify the key differences.

Poster Number: P108
The role of the splicing factor SFPQ in motor neuron development and degenerative disease
P M Gordon, T Fielding, S Jinu-Thomas, C Houart

Department of Developmental Neurobiology, King's College London, London, UK

mRNA splicing and processing plays a key role in neuronal development, impacting synapse formation, neurotransmission, synaptic plasticity, and cell recognition. The importance of these processes has been highlighted in recent years with findings that changes in RNA processing are associated with neurodegenerative diseases. Here, we examined the effects of the ubiquitously expressed splicing factor SPFQ on motor neuron development. We found that mutations in SFPQ cause cell-autonomous defects in zebrafish motor neuron maturation. In addition, we examined two single-base variants of *sfpq* that have been identified in patients with ALS. We found that rescue of an *sfpq* null mutant with either of these two variants lead to changes in motor axon length and branching. Using CRISPR, we genocopied these point mutations in the zebrafish *sfpq* gene and analyzed changes in axon development and maintenance. This work expands our understanding of the role of splicing proteins in neuron maturation and degeneration.

Poster Number: P109
formin-like regulates terminal branching in multidendritic neurons
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Neuron morphogenesis requires the polarized specification of the axon and dendrites. However, the mechanisms driving neuron polarization and axon growth remain poorly understood. To address this issue we have conducted a reverse genetic screen in the *Drosophila melanogaster* larval photoreceptors, the Bolwig's organ. We identified 83 genes that regulate axon growth *in vivo*. Here we will present one candidate gene, *formin-like* (*frl*), which we find regulates nerve growth in the Bolwig's photoreceptors. *frl* is an F-actin nucleating protein with homologues in mice and humans. Our preliminary results indicate that *frl* is a broad regulator of neuron morphogenesis as, in addition to regulating axon growth, we find that it modulates dendritic arborisation in daIV sensory neurons. We hypothesise that in daIV neurons, *frl* may act downstream of the negative regulator of dendritic branching, RhoA. Ongoing work aims to produce an integrated view of how *frl* regulates neuronal morphogenesis.

Poster Number: P110
Chemical and mechanical signals interact to direct axon growth
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Department of Physiology, Development, and Neuroscience, University of Cambridge, Cambridge, UK

During brain development, growing neurons navigate through a highly complex environment as they extend towards their synaptic targets. Studies of axon pathfinding have focused primarily on chemical guidance, but neurons also sense and respond to mechanical properties of their environment such as the local tissue

stiffness, and such mechanical signals strongly influence axon growth and guidance. Growing neurons must integrate these diverse signals present in their environment. We find that substrate stiffness modulates the response of *Xenopus laevis* CNS neurons to the repulsive guidance signal semaphorin3A (Sema3A), with softer substrates attenuating the Sema3A response. Cyclic GMP – a critical regulator of chemical guidance cue signalling – is elevated on soft substrates, and pharmacological studies indicate that cGMP plays a role in the stiffness-dependent modulation of the Sema3A response.

Poster Number: P111
Piezo Proteins in Axon Growth and Pathfinding
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Neuronal growth in the developing brain is regulated not only by chemical signals but also by the mechanical properties of the environment. Mechanosensitive ion channels (MSCs) are potential key players in transducing mechanical cues into intracellular signals. Inhibiting MSCs caused severe pathfinding errors in the optic tract of developing *Xenopus laevis*. We identified a number of putative MSCs and are studying their distribution in retinal ganglion cell axons (that form the optic tract) and the whole brain. We then focused on a particular type of MSC, piezo proteins. We perturb piezo function *in vivo* and observed changes in optic tract morphology. This study will thus contribute to understanding the role of mechanosensitive ion channels in axon growth and pathfinding, which may be crucial in development and in regeneration of neural processes in the adult CNS.

Poster Number: P112
Interplay between Notch signaling and ID proteins during adult and embryonic neurogenesis
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During neurogenesis, multipotent neural stem cells (NSCs) give rise to the correct number and types of neurons and glia. Notch signaling and inhibitor of DNA binding (ID) factors are recognized as pivotal during neurogenesis, but the underlying mechanism of their interactions and the differences between embryonic and adult neurogenesis remain to be elucidated. We combined mathematical modeling with single-cell transcriptomics to elucidate key interactions between the Notch and ID pathways in embryonic and adult NSCs. We show how both pathways regulate adult neurogenesis in a complementary and independent manner. In contrast, during brain development, Notch signaling directly regulates the expression of IDs and this regulation precludes ID-induced quiescence. Our analyses unveil the molecular interactions underlying NSC quiescence, maintenance and differentiation, highlighting key mechanistic differences between embryonic and adult NSCs. Similar mechanisms are expected to be critical in other stem cell systems during development and disease.

Poster Number: P113
Four-dimensional dense reconstruction of retinogenesis in zebrafish
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The vertebrate CNS is arranged into exquisitely organized strata from a diverse collection of neuronal types. Long-term imaging of whole zebrafish retinas during development can delineate the processes by which organized layers appear from RPCs that migrate and differentiate stochastically. We use light-sheet microscopy to image the developing retina at a high temporal resolution and produce reliable tracks of nuclear movements and divisions. We have created tracks of early retinogenesis (24-31 hpf) for tightly packed nuclei using automated tracking software and manual curation. Furthermore, we have begun analyzing the kinetic behavior of these nuclei (velocities, apico-basal vs lateral displacement, etc.) to understand the contribution of each nucleus to the collective migration dynamics within the retina. By extending these tracks to the later stages of retinogenesis (72 hpf), we aim to reveal any possible connections between these early dynamics and RPC decision-making processes giving rise to variable clone sizes and compositions.

Poster Number: P114
Neurotransmitter specification in the ventral nerve cord of *Drosophila melanogaster*
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Neuroblasts constitute the fundamental developmental units of the *Drosophila melanogaster* 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. Mapping neurotransmitter type to neuroblast lineage will allow us to discover the 'rules' of neurotransmitter patterning, both within a segment and within a lineage. For the vast majority of lineages it is unknown which neurotransmitters their progeny produces (GABA, Acetylcholine, or Glutamate). We have identified a collection of neuroblast-specific Gal4 lines that we are now screening in conjunction with either genetic or immunological reporters for neurotransmitter production. Preliminary analysis of several neuroblast lineages screened thus far suggests that while some lineages appear to give rise exclusively to neurons expressing the same major transmitter, others are capable of producing cells of different neurotransmitter types.

Poster Number: P115
Studying the role of Bod1 in the development and function of iPS derived neuronal tissue
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We previously identified Bod1 as a small protein regulator of the phosphatase PP2A-B56. Specifically, Bod1 inhibited phosphatase activity at kinetochores during mitotic progression, allowing proper congression and segregation of chromosomes. Recently we identified a stop-mutation in BOD1 which co-segregates with intellectual disability in a large consanguineous family. Individuals homozygous for the mutation have no detectable BOD1 mRNA or protein. Cognitive disability was also observed in *Drosophila* models where neuron-specific knockdown of BOD1 caused pronounced learning deficits and abnormalities in synapse morphology. To determine the molecular role of Bod1 in the development and function of neurons we have established dopaminergic and motor neuron tissues derived from HiPSC embryoid bodies. Bod1 is expressed throughout these tissues, localising apically in neural rosettes and along microtubules in differentiated neurons. Using CRISPR-Cas9 we generated two independent Bod1$^{-/-}$ HiPSC clones and using the above methodology are comparing tissue development in these cells with WT derived tissues.

Poster Number: P116
Optogenetic activation of mechanical forces to control neuronal polarisation
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Neuronal polarisation is fundamental for the functioning of the nervous system. However, despite the importance of this process, the mechanisms driving axon formation have not been discovered. While currently no molecules are known that initiate neuronal polarisation, axon formation can be induced experimentally by applying tensile ('pulling') force to a neurite. Based on these 'classical' experiments, my hypothesis is that intrinsic cellular forces determine the fate of a neurite and drive neuronal polarisation. To test this idea, I use traction force microscopy to quantify forces in developing neurons. By correlating tensile forces, growth velocities, and maturation of neurites, I test whether growth cone-mediated forces predict which neurite will become an axon. Furthermore, I perturb local forces to control which neurites turn into axons by means of optogenetics, which enables the local and specific recruitment of proteins thought to be crucially involved in controlling cellular force generation using fluorescent light.

Poster Number: P117
The sex of specific neurons controls female body growth in *Drosophila*
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Sexual size dimorphism is widespread throughout the animal kingdom but its underlying mechanisms are not well characterised. Here, we use tissue-specific genetics in the fruit fly *Drosophila* to investigate how this type of size dimorphism is established. We find that the larger female body size in this species is established very early in larval development via an increase in the mass-specific growth rate. We demonstrate that the female sex determination gene, *Sex-lethal* (*Sxl*), functions in the nervous system as part of a relay that increases growth remotely in peripheral larval tissues. Surprisingly, neuronal Sxl is both necessary and sufficient to increase larval body size in females. Sxl acts specifically in peptidergic and GABAergic neuronal subsets to regulate female growth, and this is selective for larval not imaginal tissue types. We conclude that sex-specific growth patterns in insects, as in mammals, are specified via both tissue-autonomous and non-autonomous mechanisms.

Poster Number: P118
Characterizing the role of foxm1 during tail regeneration in *Xenopus tropicalis*
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In contrast to most vertebrates *Xenopus* tadpoles have the ability to regenerate their central nervous system upon injury or amputation. Using bio-informatics we have identified a gene encoding for the transcription factor Foxm1, as being upregulated specifically in the outgrowing cord. Knocking down *foxm1* expression using morpholinos or Crispr/Cas9 reduces *cyclinb3* expression in the regenerating spinal cord. Furthermore, we observe an increase in the number of neuronal progenitors (Sox3+ve) and a decrease in differentiated neurons (Myt1+ve) in the regenerating spinal cord when *foxm1* expression is knockdown. Finally using chemical inhibitors of signalling pathways acting early during regeneration, we have identified reactive oxygen species (ROS) as being required for upregulating of *foxm1* expression. Altogether, our experiments show that Foxm1 is required to control the equilibrium between proliferation and differentiation in the regenerating neural tube. In the future, we will use transcriptomics approaches to identify downstream target of Foxm1 during neuronal regeneration.

Poster Number: P119
Transcriptional regulator Nolz1 is required for establishment of dopaminergic circuitry during embryonic development
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Midbrain dopaminergic neurons form axonal projections towards several forebrain areas including the striatum. However, the molecular mechanisms involved in establishing dopaminergic connectivity are not well defined. We identified the transcription factor Nolz1 (Zfp503) as a key regulator of dopaminergic circuitry formation. In Nolz1$^{-/-}$ mutant embryos a large proportion of dopaminergic axons are misguided in the diencephalon and cross the ventral midline. In addition, dopaminergic axons that reach the striatum fail to innervate their target area. Although general factors involved in dopaminergic axon guidance are expressed normally, we identified alterations in expression of genes not associated with dopaminergic axon guidance before. In addition, the expression of several genes required for the specification of striatal projection neurons is reduced, which may underlie the lack of dopaminergic innervation. We are currently further investigating the molecular mechanism of Nolz1 in regulating these processes.

Poster Number: P120
Developing new Drosophila models to understand Dystonia pathogenesis
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DYT-11 dystonia is a movement disorder caused by loss-of-function mutations in the SGCE gene. Epsilon sarcoglycan (Scge) is a type-I transmembrane glycoprotein broadly expressed in the mammalian brain. However, its function remains poorly understood. We use *Drosophila* as a genetic model to characterize Scge function in vivo to gain insight into the mechanism underlying DYT-11. A GFP-tagged Scgae was used to analyze protein distribution in all life stages of the animal. This revealed expression in different tissues including CNS, fat body and prothoracic gland. We have generated loss-of-function mutants for the *Drosophila Scgae* gene based on homologous recombination and the CRISPR technique. The mutants display significant size increases implicating *Scgae* in growth regulation, for which *Scgae* appears required in the CNS. Given the impact on growth, we hypothesize that *Scgae* is required in regulating insulin signaling and are currently pursuing possible mechanisms by which *Scgae* might mediate this effect.

Poster Number: P121
4D lineage based temperature sensitive embryonic lethal screen to identify regulators of left-right asymmetric neurogenesis
T W Mullan[1], R F Wademan[1], T J Felton[1], O Kasem[1], R Schnabel[2], R J Poole[1]

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We are interested in uncovering cellular and molecular regulators of proneural gene expression and left-right asymmetric neurogenesis. We focus specifically on the *Caenorhabditis elegans* C-lineage which consists of two near left-right symmetric sides with two glutamatergic tail neurons, DVC and PVR, arising only on the left. Taking advantage of *C. elegans*' invariant cell lineage and single-cell resolution we are performing a 4D-lineage based embryonic screen for C-lineage mutants which phenocopy the precocious DVC neuroblast division seen in mutants of the proneural *acheate/scute* homologue *hlh-14*, required for neurogenesis in the lineage. Of 70 strains screened four mutants of interest have been identified. These are being mapped, cloned and characterised in detail. Presented here are our latest results, including a mutant demonstrating early blastomere identity defects leading to ectopic DVC neurons, for which WGS has identified a candidate not previously implicated in early blastomere specification.

Poster Number: P122
Sexy learning in *C. elegans*
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A central goal in neuroscience is to understand how neural circuits integrate conflicting experiences that need to be behaviourally resolved. To shed light into this process, we are dissecting a circuit for associative learning in the nematode *C. elegans*. Previously, Sakai et al. (2013) and us (Sammut et al. 2015) have shown that *C. elegans* males undergo sexual conditioning, a form of associative learning by which a rewarding experience with mates overrides an aversive association with starvation. Sexual conditioning leads to a switch in behavioural responses to an environmental stimulus from avoidance to attraction. These studies showed conditioned responses to salt. Here we demonstrate that odorants can also be sexually conditioned, indicating that sexual conditioning is a general strategy to increase reproductive success in males. Moreover, we have identified the MCM interneurons and the neuropeptide PDF as mediators of the sexually conditioned behavioural switch.

Poster Number: P123
A direct glia-to-neuron cell fate switch in the *C. elegans* male
R C Bonnington[1], M Sammut[1], L Molina Garcia[1], K Khambhaita[1], D J Elliott[1], B Kim[2], S J Cook[2], D H Hall[2], S W Emmons[2], A Barrios[1], R J Poole[1]

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Whether cell fate is restricted or plastic during development is a central question in developmental biology. In vertebrates, differentiated glia give rise to neurons, but how they can remain plastic and retain neurogenic potential remains poorly understood. Here, we describe a novel glia-to-neuron cell-fate switch in *C. elegans*, where a fully differentiated glial cell undergoes a direct change in cell fate, becoming a cholinergic sensory neuron, PHD. Using transgenic reporters and electron microscopy, we describe the morphology, gene expression and connectome of PHD and demonstrate that the cell-fate switch occurs during male sexual maturation and is cell-intrinsically regulated by the sex determination pathway. This is the first well-described example of a direct naturally-occurring glia-neuron switch in invertebrates. Combined with our recent demonstration that the MCM neurons derive from the division of fully-differentiated glia, this provides us with a paradigm to investigate the mechanisms of plasticity during glia-to-neuron cell fate switches.

Poster Number: P124
Decoding a Glia-to-Neuron Cell Fate Switch in *C. elegans*
M Sammut, K Khambaita, R Bonnington, D Elliott, A Barrios, R J Poole

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

We have recently described the first instance of glia-derived neurogenesis in an invertebrate (Sammut et al., 2015). In the *C. elegans* male, the MCMs interneurons are born from the asymmetric division of fully differentiated AMso glial cells, whereas hermaphrodite AMso cells do not divide. In order to uncover the molecular mechanisms that regulate this sex-specific cell fate plasticity we have performed a GFP-based forward genetic screen for mutants in which the MCMs fail to be specified. Using a battery of glial and neuronal markers we have identified mutants that affect sequential stages of MCM formation such as AMso division, neuronal specification and MCM neuronal subtype specification. Two AMso division mutants, *nom-5* and *nom-8* were mapped-by-sequence to the *cdk-4* locus; no acquisition of neuronal characteristics in the AMso was observed. This suggests that DNA replication is a prerequisite for the cell fate plasticity.

Poster Number: P125
Cellular and molecular mechanisms of left-right asymmetric neurogenesis
T Felton[1], T Mullen[1], J Tam[1], J Yeung[1], O Kasem[1], A Aldabergenova[1], R Scnabel[2], R J Poole[1]

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Little is know about the mechanisms that regulate the development of left-right asymmetric neuronal structures. We focus on how neuronal potential is asymmetrically inherited in *C. elegans*' C-lineage. Through forward genetic screening, we have isolated several mutants that affect the expression of *hlh-14/ac-sc*, the key proneural gene required for neuronal identity in this lineage. Through 4D-lineage analysis and cell size measurements, we observe three successive unequal divisions within the C-lineage, that lead up to the neuroblast. *let-19/mdt-13*, a member of the Mediator, regulates the first two unequal divisions resulting in loss of neuronal potential; the last division is regulated by *hlh-14* itself. Furthermore, *hlh-2/daughterless* mutants lack *hlh-14* however, it's required in the neuroblast. Together these results suggest that asymmetric segregation of currently unidentified neuronal determinants has an important role in this lineage and that the Mediator, as well as proneural genes, can regulate cell fate and cell size concomitantly.

Poster Number: P126
Role of Fgf signalling in positioning neurogenic regions in the early embryonic vertebrate brain
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In early amniote brain development, neurogenesis is limited to three distinct neurogenic regions in the hypothalamus, ventral pretectum and dorsal mesencephalon. This provides an excellent model to

investigate the spatial and temporal regulation of the neurogenic regions. A prime candidate regulatory signal is Fgf8, which is secreted by the isthmic organiser and the anterior neural ridge. We used pharmacological inhibitors to specifically investigate its role in positioning the early-forming neurones of the medial longitudinal fascicle (MLF), and the signal transduction pathways involved. Our results indicate that Fgf signalling prevents premature neurogenesis in the mesencephalon, thereby restricting the MLF neurones to the ventral pretectum. The Ras-MAPK pathway is sufficient, but not necessary to mediate this effect, indicating the involvement of a further Fgf signal transduction pathway. To identify targets of Fgf signalling, we analysed the transcriptomes following receptor inhibition and will present data on the transcriptional effects.

Poster Number: P174
ABSTRACT WITHDRAWN

Poster Number: P179
Establishing the inside out axis of the vertebrate brain
V Vijayakumar, L Ward, J Clarke

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The vertebrate central nervous system is derived from the polarized neuroepithelium of the embryonic neural tube. Two of the major axes; the antero-posterior and the dorso-ventral are well studied, but understanding the third major axis - the apico-basal or inside out axis – has received little attention so far. We have analysed apico-basal polarisation of neural progenitor cells in vivo using the developing hindbrain of the zebrafish as a model and demonstrate an important role for the extracellular matrix (ECM). We provide strong evidence that the ECM component laminin1 is required to establish the orientation of apico-basal polarity in the neural tube. Laminin1 loss from the basement membrane results in a nearly total reversal of the apico-basal polarity of the brain's neuroepithelium. The inverted neuroepithelium can be rescued by local application of ECM-rich Matrigel, and is independent of apical signaling and of centrosome dependent microtubule traffic.

Poster Number: P186
The role of NFκB in early neural specification of human embryonic stem (hES) cells
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Nuclear factor kappa B (NFκB) is a family of transcription factors most notable its role in inflammation. In recent years, a number of studies have demonstrated that NFκB plays an integral part in neurogenesis and ageing. In terms of neural specification, activation of the canonical NFκB signalling pathway is necessary for early neural stem cell (NSC) differentiation and inhibition of NFκB activity in vitro blocks neural maturation. The aim of this project is to clarify the role of NFκB throughout neural specification of hES cells using a reproducible targeted differentiation protocol. We have found that as neural stem cells are passaged, they upregulate canonical NFκB signalling. Transcriptomic microarray analysis at key stages of neural differentiation indicates that many NFκB targets, which are involved in a number of processes such as metabolism and cell cycle regulation, are significantly increased in expanding neural progenitor cells.

New methods to study cell biology

Poster Number: P127
Rapid profiling of interactome dynamics by analysis of protein-protein colocalisations on a global scale
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Localisation and protein function are intimately linked in eukaryotes, as proteins are localised to specific compartments where they come into proximity of other functionally relevant proteins. Significant co-localisation of two proteins can therefore be indicative of their functional association. We here present COLA, a proteomics based method coupled with a bioinformatics framework to detect protein-protein co-localisations on a global scale. COLA reveals functional interactions by matching proteins with significant similarity in their subcellular localisation signatures. The rapid nature of COLA allows mapping of interactome dynamics across different conditions or treatments with high precision.

Poster Number: P128
Invadolysin: A novel secreted metalloprotease is enriched in the extracellular vesicle fraction of human plasma
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Invadolysin is a novel zinc metalloprotease, which is conserved amongst metazoan species and plays an important role in the cell cycle, cell migration and metabolism. Invadolysin is the only protease so far shown to localize to lipid droplets, an intracellular lipid storage organelle. We have shown that invadolysin is important for mitochondrial function, angiogenesis and the maintenance of normal chromosome structure. Invadolysin has an N-terminal signal sequence and a C-terminal GPI anchor site. Here we show that a secreted form of invadolysin is present in the soluble fraction of vertebrate blood and invertebrate hemolymph. We additionally show that invadolysin is enriched in the extracellular vesicle fraction of human plasma. Strikingly, invadolysin mutant Drosophila larvae have reduced overall gelatinase activity. These findings open a new avenue of research into secreted invadolysin, a metalloprotease that does not belong to either the MMP or the ADAM families of secreted metalloproteases.

Poster Number: P129
Functional characterisation of metachronous cell state transitions
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Recent data shows that mouse embryonic stem (ES) cells have to acquire the capacity to respond to lineage inducing signals over time, in a 'formative' phase that precedes lineage choice. Understanding these phase transitions requires studying how functional and molecular properties change over time at single cell resolution. To study the dynamics of this transition, we have developed an encapsulation system in which ES cells are encased in hydrogel beads. In these beads, the extracellular matrix composition, degradability and stiffness can be controlled and ES cells can self-renew or be induced to differentiate towards different lineages. We combined this encapsulation system with a new micruofluidic trap device, which allows culture of cells/beads in a controlled environment and extraction of individual beads for downstream analysis at specific times. These two combined platforms provide a unique opportunity to understand how cells transit form one state to another.

Poster Number: P130
'Car Sharing' – Intracellular Co-Trafficking of Junctional Adhesion Molecule C and its Neighbouring Proteins in Endothelial Cells
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Interendothelial junctions are dynamic structures consisting of junctional proteins imperative to vascular permeability, leukocyte extravasation and angiogenesis. The junctional adhesion molecule C (JAM-C) is pivotal during junctional remodelling and faulty expression/function has been associated with multiple inflammatory diseases including atherosclerosis and heart disease. Following an inflammatory stimulus dynamic changes of JAM-C levels can be observed at endothelial junctions and in intracellular vesicular pools. This might serve to regulate JAM-C functions, however, little is known regarding JAM-C internalisation and redistribution. To gain deeper insight into its intracellular trafficking we generated a JAM-C-horseradish peroxidase fusion protein and identified neighbouring proteins of JAM-C using a novel biotinylation-based pull-down and mass spectrometry approach. By mapping the proteomic inventory surrounding vesicular as well as surface JAM-C we distinguished co-trafficked from non-co-trafficked proteins. We can now identify key players involved in dynamic trafficking of JAM-C and support further elucidation of its function at interendothelial junctions.

Poster Number: P131
The biomechanics of cells and the 3D structures they form: novel tools for mechanobiology
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During development and disease progression, cells undergo mechanical changes and respond differently to physical cues. Understanding these changes requires novel tools to measure mechanical properties of 3D tissues. Furthermore, related computational techniques are needed to show how properties of individual cells generate the mechanical properties of 3D structures they form. We used atomic force microscopy (AFM) to compare the mechanical properties of cells in 2D monolayers and in 3D cysts. However, AFM requires contact with the sample, making measurements in cysts difficult and unreliable. Microultrasound is an alternative approach that does not require contact. Preliminary results show that microultrasound can measure size and mechanical properties of living 3D structures. We are currently using markers for mechanical stress to determine the effect of compression created by ultrasound radiation pressure. Eventually, this approach could permit measurement of mechanical properties of tissue *in situ* to reveal how mechanics influences tissue behaviour.

Poster Number: P132
The versatile application of cultured insect cells in cell biology research and Higher Education cell biology teaching
M Figgitt

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The use of insect cell culturing techniques, such as those using SF9 cell lines, providing a huge opportunity not only in the study of cell biology, but in the teaching of cell biology. One of the chief challenges of teaching cell biology in the higher education environment is too provide a means for students to acquire key cell biology skills and an avenue for students to conduct a wide range of investigative projects. Culturing insect cells can have huge benefits is in higher education chiefly because of the less restrictive measures, making them a means not only to teach cell culturing techniques to "en masse", but also provide a very cost effective means for research led teaching, which is an increasing aspiration of Higher Education

Poster Number: P133
Understanding the phenotypic and pathological outcomes of Notch mutations
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Notch is a key pathway involved in development and tissue homeostasis and its misregulation has been associated with many pathological conditions, such as cancer. Genetic analysis of *Drosophila* Notch has revealed that mutations affecting specific domains of the protein have distinct outcomes on the pathway. This suggests different mutations may affect diverse regulatory processes. Using *Drosophila*, we aim to classify Notch mutations depending on their position in the protein and predict their outcome. This will be particularly meaningful in cancer where Notch mutations have being often found to cluster in specific domains of Notch. Our study focuses on mutations affecting domains in the extracellular region of Notch. Interestingly, according to our data, these mutations not only have an impact on extracellular events, but also disrupt specific intracellular events in the pathway. These findings provide new insights into the mechanism behind these mutations and suggest new ways to reverse their outcome.

Poster Number: P134
Biomimetic hydrogels to steer stem cell fate choices
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Wellcome Trust/MRC Stem Cell Institute, University of Cambridge, Cambridge, UK

We developed fully functionalisable stem cell substrates called StemBond hydrogels, which can be mechanically tuned over the physiologically relevant range, while also allowing independent control over the density of extracellular matrix (ECM) linkage points to control cell adhesion. Using these substrates, we have performed two studies showing that our technology optimally steers stem cell fate. First, we showed, both functionally and with molecular data, that self-renewal of embyronic stem cells is significantly enhanced with these substrates. We identified several potential mechanisms. Embryonic priming genes are also suppressed, and we have used them alongside minimal media conditions to show that the substrates support self-renewal in the most minimal conditions yet shown. We have also investigated oligodendrocyte progenitor cells to show, both functionally and with RNA sequencing, that the soft StemBond substrates rejuvenate the ageing phenotype. This opens the tantalizing possibility that ECM stiffness is a primary driver of the ageing phenotype.

Poster Number: P135
ABSTRACT WITHDRAWN

Poster Number: P136
Putative interactors of a rhomboid protease
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Rhomboid proteases are intramembrane serine proteases belonging to the superfamily of rhomboid-like proteins. Rhomboid-like proteins mostly reside in the secretory pathway wherefrom they determine the fate of other proteins. Recently, they have been shown to be involved in shedding and trafficking of proteins, and endoplasmic reticulum associated degradation (ERAD). Among the rhomboid-like proteins is RHBDL4, a vertebrate rhomboid protease with roles in ERAD. For instance, preTCR alpha is targeted to ERAD upon cleavage by RHBDL4; APPL1 and APPL2 are shown to be substrates, too. RHBDL4 coimmunoprecipitates with Transitional endoplasmic reticulum ATPase (VCP/p97), an AAA ATPase with multiple roles, among of which is to power ERAD. We screened for proximal proteins of RHBDL4 by using BioID and identified more than 100 candidates. Many of those are related to VCP/p97 and ERAD. Here we present the studies conducted on those potential candidates.

Poster Number: P181
Mechanisms of skull expansion
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The skull, or neurocranium, is essential to human life as it protects the brain from damage. The neurocranium forms from sheet-shaped mesenchymal condensations that rapidly expand over the growing brain. Despite the skull's importance, little is known about the cell behaviours of osteoblasts within these condensations which drive morphogenesis. To address this problem, we developed a novel live imaging system for performing quantitative *ex vivo* analyses of early skull growth. We find that osteoblasts spread as a sheet towards the apex of the head. Oriented cell division and proliferation contribute to this collective spread of osteoblasts, suggesting apexical tissue flow. Our *ex vivo* imaging system provides insights into mechanisms of morphogenesis in a mesenchymal-derived, sheet-shaped tissue.

Newly tractable systems

Poster Number: P137
Early Detection of Ovarian Cancer (*BARCA 1* & *BARCA 2* Mutation) risk prediction for Bangladesh
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This study was carried out in 521 cancer and non-cancer patients' data was collected from different diagnostic center and data pre-processed. Then a structured questionnaire was used containing details of ovarian cancer risk factors including age, menopause end age, problem during pregnancy, late Menopause, early Menopause, exercise, previous exposure to other sexually transmitted infections (STIs), marital status, genetic risk, outdoor activities and affected any cancer before based on the previous studies. Results: After pre-processing data is clustered using K-means clustering algorithm for identifying relevant and non-relevant data to ovarian Cancer. Next significant frequent patterns are discovered using AprioriTid algorithm. Abnormal menstruation and problem during pregnancy were found most highly significant risk factor using data mining. This ovarian cancer risk prediction system will be helpful in detection of a patient's predisposition to ovarian cancer. Specifically there were no work of ovarian cancer risk prediction system using data mining or Statistical approaches.

Poster Number: P138
Conserved long non-coding RNAs in the switch to flowering
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Since their discovery, long non-coding RNAs (lncRNAs) have in turn been described as essential genomic regulators or as transcriptional noise. We are interested in the functional significance of a group of lncRNAs (*COOLAIR*) that are transcribed in the antisense direction at an important *Arabidopsis thaliana* floral repressor gene, *FLC*. Previous work has revealed a role for *COOLAIR* antisense RNAs in regulation of *FLC* sense expression levels and, consequently, flowering time. We found *COOLAIR* secondary structure and transcription, but not primary nucleotide sequence, to be conserved across multiple flowering plants, supporting a regulatory role. Natural variation across and within species creates subtle changes in *COOLAIR* secondary structure and transcript architecture that may modulate its activity. We propose an evolutionarily conserved lncRNA that is neither essential regulator nor transcriptional noise, but rather fine-tunes the switch to flowering.

Poster Number: P139
Prevalence of agrochemical resistance-associated natural variation in wild populations of *C. elegans*
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Resistance to pesticides is a growing global food security problem and an emerging issue for the agrochemical sector, yet little is known about the prevalence, molecular mechanism and evolutionary biology of resistance. Using *Caenorhabditis elegans* as a model organism and utilising the existing bank of over 200 wild isolates, we have assessed natural variation in pesticide resistance, an idea supported by a previous report linking natural variation in the Hawaiian strain CB4856 to resistance to a commonly used anthelmintic (PMID:22301316). We looked at the development of 25 *C. elegans* wild isolates upon exposure to 21 different pesticides and demonstrated both increased sensitivity as well as increased resistance to particular chemicals in different wild strains. We plan to identify the genetic basis of particular variation in resistance as well as to model the emergence of agrochemical resistance in an experimental evolution approach.

Poster Number: P140
DNA extraction from oak heartwood: motivation and challenges
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Forest trees are large, long-living organisms, experiencing a wide range of biotic and abiotic stress factors. Adaptive mechanisms are fundamental to mitigate the effects of such factors. These mechanisms include changes in wood anatomy. Endogenous and environmental stimuli are integrated through multiple and cross-talking molecular pathways into the wood forming cells. These pathways include epigenetic modifications of the genome: DNA methylation and histone modifications. Forest tree heartwood is a terminal tissue but remains a viable source of DNA. Heartwood DNA extraction is challenging due to the high content of polyphenols usually present in the DNA extracts. Polyphenols inhibit DNA polymerase activity which is essential for PCR and library preparation success. Here, I report and test protocols for the extraction of oak heartwood DNA. The obtained sapwood and heartwood DNA yield is compatible with library preparation. Bisulfite converted heartwood DNA libraries will be generated and sequenced to obtain whole-genome methylation maps.

Poster Number: P141
***Gastruloids* develop the three body axes in the absence of extraembryonic tissues and spatially localised signalling**
D A Turner[1], L Alonso-Crisostomo[1], M Girgin[2], P Baillie-Johnson[1], C R Glodowski[1], P C Hayward[1], J Collignon[3], C Gustavsen[4], P Serup[4], B Steventon[1], M Lutolf[2], A Martinez Arias[1]

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Establishment of the three body axes is a critical step during animal development. Using *Gastruloids*, embryonic organoids, as a model system we find that they are able to develop an AP and DV axis, break bilateral symmetry and undergo axial elongation in a manner that mirror embryos. Our experiments show that Nodal, together with Wnt/β-Catenin signalling, is essential for the localised expression of T/Bra at the poserior of *Gastruloids* but that Wnt signalling has a separable activity in the elongation of the axis. Furthermore, AP axis specification occurs in the absence of both extraembryonic tissues and localised sources of signalling. These results lead us to suggest that, in the embryo, the role of the extraembryonic tissues might not be to induce the axes but to bias an intrinsic ability of the embryo to break its initial symmetry and organise its axes.

Poster Number: P142
High-throughput discovery of novel developmental phenotypes
J Cleak[1], S Johnson[1], Z Szoke-Kovacs[1], N Horner[2], J Brown[2], S Wells[1], H Westerberg[2], **L Teboul**[1]

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We established a high throughput programme for the generation and phenotypic characterisation of embryonic lethal and sub-viable mice at the Mary Lyon Centre (MLC), MRC Harwell Institute, as part of the International Mouse Phenotyping Consortium. We developed analysis strategies that maximize resources to efficiently define the window of lethality and implemented 3D imaging modalities to capture embryo morphology at large scale, as well as to document the transcriptional activity of the targeted loci. We will present the embryonic lethal screen currently run at the MLC, how the data can be accessed and the initial analysis from over 1700 mouse lines generated by the consortium. We will discuss the findings of this initial screen and their value for the understanding of human developmental defects.

Poster Number: P143
Primitive endoderm and epiblast specification during preimplantation development of rabbit embryos
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Preimplanation development of mammalian embryos comprises two consecutive cell fate decisions, and their proper execution is necessary for the formation of three cell lineages: pluripotent epiblast (EPI), and extraembryonic primitive endoderm (PrE) and trophectoderm. Here we present stage-by-stage analysis of the formation of EPI and PrE during rabbit preimplantation development. Our data suggest that reciprocal repression of GATA6 and NANOG might not be essential for initiation of PrE versus EPI specification in the rabbit, and that FGF/ERK inhibition is not sufficient to sustain naive pluripotency in the rabbit epiblast. Consistent with that observation, we show that FGF/ERK inhibition (2i/3i treatment), although proven successful in the murine ES cell derivation, does not support derivation of pluripotent ES cell lines in the rabbit. These results suggest differences in PrE versus EPI specification and in mechanisms regulating pluripotency between different mammals.

Poster Number: P184
Using metatherians to elucidate the evolution of mammalian epigenetic pathways
B Leeke, F Decarpentrie, S K Mahadevaiah, J Zohren, S Wood, S Horswell, M N Sangrithi, J M A Turner

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Metatherians diverged from eutherian mammals 160-180Mya, and are an excellent model system for researching mammalian evolution. We have recently used the metatherian Monodelphis domestica, to understand the evolution of mammalian epigenetic pathways. We focus on X-chromosome inactivation (XCI), the silencing of one X chromosome that ensures an equal dosage of X-gene products between females (XX) and males (XY). Eutherian XCI is mediated by the non-coding RNA Xist, and maintenance of XCI relies on epigenetic marks on the inactive X (Xi), particularly hypermethylation of CpG islands. Metatherians have no Xist gene, and examination of specific Xi-genes suggests that they do not exhibit CGI hypermethylation. We will describe our ongoing characterisation of a potential metatherian Xist equivalent, Rsx, and the application of methylation sequencing to generate genome-scale methylation maps in this species. Our findings suggest both shared and distinct epigenetic mechanisms driving the silencing of the X chromosome between metatherians and eutherians.

Poster Number: P188
Investigating diet-induced renal lipotoxicity using Drosophila models
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One hallmark of disrupted lipid homeostasis in diseases such as metabolic syndrome is the accumulation of lipid droplets (LDs) in peripheral tissues. The presence of these ectopic lipids often correlates with organ dysfunction and is referred to as lipotoxicity. However, it is unclear if LDs are a cause or consequence of organ damage, and the mechanisms of LD accumulation in different tissues are poorly understood. I am investigating both questions using newly established Drosophila models of LD accumulation in renal cells. We find that nephrocyte LDs can be triggered by low protein, high sugar or high fat diets. Interestingly, LDs accumulate in renal cells in a ROS- and JNK-independent manner, unlike those reported in glial cells1,2. We also show that nephrocyte LD accumulation requires acetyl-CoA carboxylase in all three dietary models, and we are now investigating the mechanisms by which this enzyme regulates LDs and nephrocyte functions.

Stem cells in vivo

Poster Number: P144
Is there a role for Neuronal Cell Adhesion Molecule in the hypothalamus?
A W Moore, A J Furley, M Placzek

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The hypothalamus is a brain region dedicated to coordinating homeostasis. It consists of multiple discrete nuclei built around the third ventricle and above the median eminence. Recent research describes proliferative activity and de novo neurogenesis in the adult hypothalamus, and reveals that specialised radial glial-like cells called tanycytes derive from embryonic cells that maintain constitutive stem cell activity throughout life. Changes in local signals and circulating levels of physiological signals can modulate a proliferative and neurogenic response in tanycytes, suggesting a plasticity that may be important postnatally. Our work investigates whether the Neuronal Cell Adhesion Molecule (NrCAM) plays a role in the development and/or regulation of hypothalamic tanycytes. Our studies show that NrCAM is expressed on subsets of tanycytes and analysis of NrCAM knockout mice reveals abnormal tanycyte and neuron distribution in the adult hypothalamus. These observations point to a role for NrCAM in the regulation of hypothalamic stem cells.

Poster Number: P145
Conserved principles of primordial germ cell (PGC) specification and development between the human and pig highlight the porcine as a reliable and accessible model for investigation
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We recently showed that pigs share conserved features of PGC development with humans. Here we investigated the transcriptome of single PGC isolated from 13.5 old embryos. We identified unique PGC genes expressed during early PGC development. Furthermore, pig PGCs repressed SOX2 and PRDM14, unlike mice but consistent with human data. Gene Ontology revealed enrichment for terms consistent with known PGC identity. We identified shared differential expression between pPGCs, hPGCs and hESC-PGCs, which were investigated using molecular approaches. PGCs have the greatest numbers of downregulated genes compared to soma, involving DNA methylation, mesoderm formation and cell fate commitment, and the WNT signalling was significantly downregulated. Using an in vitro system of dissected epiblast cultures we show that BMP4 is required for PGC induction and that WNT signalling confer germ cell competency. These findings enable development of novel approaches for generating hPGC-like cells and provide a new platform for in vivo investigation.

Poster Number: P146
The abrogation of condensin function provides independent evidence for defining the self-renewing population of pluripotent stem cells
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Heterogeneity of neoblast stem cells in highly regenerative flatworms has been categorised on the basis of gene expression patterns, replicative behaviour and potency. Without the ability to perform transgenesis and i*n vivo* lineage analysis, we took an alternative approach to provide independent evidence for defining self-renewing stem cell populations. We exploited the role of highly conserved condensin proteins to functionally assay neoblast self-renewal properties. Condensins are proteins involved in mediating structural changes of chromosomes during cell division, and their abrogation can lead to repeated endoreplication of the genome in dividing or self-renewing cells. We show that planarian condensins are required for normal stem cell function and whole body regeneration. Interruption of condensin function led to stem cell depletion accompanied by the appearance of enlarged cells with increases DNA content. We show that these enlarged cells are always stem cells from the sigma-class of neoblasts.

Poster Number: P147
A genome-wide approach to characterize spatial pattering of neurogenesis in the zebrafish hindbrain
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How cells are precisely specified in space and time is a crucial question in developmental biology and it is key for the correct establishment of the central nervous system. The zebrafish hindbrain is a great model to investigate spatial patterning of neurogenesis since progenitors are stereotypically arranged in neurogenic and non-neurogenic zones within each hindbrain segment. Previous work has shown that hindbrain boundaries and Fgf20-expressing neurons are signalling centres that contribute to such precise patterning. In order to understand the molecular mechanisms used by FGF to inhibit neurogenesis a genome-wide screen was performed, allowing us to establish some of its transcriptional targets in this context. Furthermore, taking advantage of the powerful technology of single-cell gene expression profiling, we aim to identify the molecular signature of the different cell population present in the developing hindbrain to further provide molecular insights into the process of neurogenesis.

Poster Number: P148
Esrrb complementation rescues development of *Nanog*-null germ cells
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The transcription factors Nanog and Esrrb play important roles in embryonic stem cells (ESCs) and during primordial germ cell (PGC) development. *Esrrb* is a positively regulated direct downstream target of Nanog in ESCs that can substitute qualitatively for *Nanog* function in ESC self-renewal and reprogramming. Whether this functional substitution extends to the germline is unknown. Here we show that specific germline deletion of *Nanog* dramatically reduces the PGC number detectable at midgestation. Despite this quantitative depletion, Nanog-null PGCs, can complete germline development. Knock-in of Esrrb to Nanog restores PGC numbers to wild type levels. These effects are recapitulated in vitro: PGC-like cell (PGCLC) differentiation of *Nanog*-null ESCs is impaired. However, induced expression of either Esrrb or Nanog restores PGCLC numbers to normal levels. These findings indicate that Esrrb can substitute fully for Nanog function in PGCs.

Poster Number: P149
Uncovering a central role for Id4 in the regulation of adult hippocampal neural stem cell quiescence
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Within the adult mammalian hippocampus, there exists a population of mostly-quiescent neural stem cells. However, the precise mechanisms controlling the quiescence/activation switch are poorly understood, partly due to the complexity of their sub-granular zone (SGZ) niche. Therefore we aim to investigate the signals and transcriptional mechanisms regulating adult hippocampal (AH)NSC quiescence. In order to study this, we have developed an *in vitro* system of BMP4-induced AHNSC quiescence. By analysing the genome-wide transcriptional profile of quiescent AHNSCs *in vitro*, we have identified Inhibitor of differentiation-4 (Id4) to be one of the highest and specifically expressed genes in the quiescent state. Moreover, Id4 protein is highly expressed in >95% of stem cells in the adult SGZ *in vivo*. Therefore we are investigating a mechanism whereby Id4 induces and maintains NSC quiescence by negatively regulating the bHLH transcription factor Ascl1, a crucial factor for NSC activation[1].
[1] Andersen, J. et al., (2014) Neuron. doi: 10.1016/j.neuron.2014.08.004.

Poster Number: P150
The blueprint of primate preimplantation development
T E Boroviak[1], G G Stirparo[1], S Dietmann[1], I Herraez[2], H Mohammed[2], W Reik[2], A G Smith[1], E Sasaki[3], J Nichols[1], P Bertone[1]

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Preimplantation development in rodents and primates establishes the founding cell population of the foetus in the epiblast and segregates two extraembryonic lineages, trophoblast and hypoblast. Most of our knowledge about these cell-fate decisions is derived from studies in mouse. Here, we set out to delineate the primate-specific aspects of preimplantation development. We present a high-quality single-cell RNA-seq dataset from zygote to late blastocyst in marmoset (*Callithrix jacchus*). In addition, we generated stage-matched samples in mouse and re-analysed three human single-cell datasets. Weighted gene network analysis identified primate-specific factors of the pluripotency network in vivo, including *KLF17*, *ARGFX*, *KHDC3L*, *LEFTY2* and *CTSF*. Global features exclusive to primate epiblast and hypoblast segregation were BMP and WNT signalling. Strikingly, the mouse epiblast marker Otx2 is specifically expressed in human and marmoset hypoblast. Our cross-species analysis demarcates conserved and primate-specific features of mammalian preimplantation development and provides a rich resource for comparative embryology.

Poster Number: P151
The Role of SUMOylation of Sox2 in the Regulation of Neural Stem Cells Proliferation and Multipotency
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Sox2 is known to play a major role in maintaining neural stem cells in a multipotent state, functioning both as transcriptional activator and repressor. We are interested in understanding how Sox2 can switch between these two functions and, in particular, we want to determine whether this activity change is linked to SUMOylation. Our preliminary results suggest that SUMOylation of Sox2 could cause a loss of its transcriptional activator activity or, potentially, that it causes a switch from activator to repressor function. We successively performed RNA sequencing on hNSC transfected with wt Sox2 or different Sox2 SUMO-mutant constructs and we are comparing the results with data collected from published literature. In addition, in order to determine whether SUMOylation of Sox2 plays a role in regulating hNSC proliferation or multipotency, we performed cell cycle analysis and proliferation assays on hNSC transiently transfected with either Sox2 or different Sox2 SUMO-mutant constructs.

Poster Number: P152
***Transmembrane protein 33* (*tmem33*) is essential for VEGF-mediated calcium signalling during angiogenesis in zebrafish embryos**
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TMEM33 is a 3-transmembrane domain protein, uncharacterised in vertebrates, and is expressed in kidney and endothelial cells (ECs). TMEM33 interacts with PKD1and PKD2 in mice and *tmem33* and *pkd2* knockdownin zebrafish embryos induce cystic kidneys. Furthermore, *tmem33* knockdown attenuates EC calcium signalling downstream of VEGF, reduces EC filopodia numbers and delays EC migration, suggesting *tmem33* mediates the EC response to VEGF. VEGF overexpression does not rescue angiogenesis in *tmem33* morphants, suggesting *tmem33* lies downstream of VEGF. Conversely, *mindbomb* mutants display increased *tmem33* expression, while *tmem33* morphants exhibit attenuated Notch signalling, indicating Notch may regulate *tmem33* via negative feedback. Interestingly, *tmem33* mutants display nonsense-mediated decay of *tmem33* and are phenotypically normal. *tmem33* mutants are resistant to *tmem33* morpholinos, suggesting transcriptional adaptation exists in *tmem33* mutants. Conditional knockdown of *tmem33* in ECs by CRISPR-interference recapitulates angiogenic defects induced by global knockdown, demonstrating *tmem33* is required cell-autonomously in ECs during angiogenesis.

Poster Number: P153
***foxc1a* and *foxc1b* exhibit distinct compensatory requirements during brain and trunk angiogenesis and haematopoietic stem cell formation in zebrafish**
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In mammals, *Foxc1/Foxc2* are critical for cardiovascular and haematopoietic development. How these genes interact with endothelial signalling pathways to elicit these functions remains unclear. We have generated novel zebrafish mutants in orthologues of mammalian *Foxc1* (*foxc1a/foxc1b*) to determine their function during angiogenesis and haematopoietic stem cell (HSC) formation. *foxc1a* mutants display aberrant cranial angiogenesis with loss of central arteries (CtAs). Reduced expression of VEGFreceptors in *foxc1a* mutant endothelial cells suggests *foxc1a* is required for VEGF-mediated cranial vessel remodelling. Interestingly, dorsal aorta Notch expression is substantially reduced in *foxc1a* and *foxc1a;foxc1b* doublemutants, leading to ectopic trunk angiogenesis and reduced HSC numbers. Our data also suggests *foxc1a* caninstruct HSC formation via a non-cell-autonomous somitic *wnt16-dlc/dld* pathway. Collectively, our studies indicate *foxc1a* and *foxc1b* play compensatory and context-dependent roles during co-ordination of angiogenesis and HSC formation and may influence these processes via differential regulation of VEGF and Notch signalling.

Poster Number: P154
Early-life remodelling of the gut microbiome promotes intestinal homeostasis and longevity in *Drosophila*
F Obata, C Fons, A P Gould

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There is now strong evidence that transient environmental stresses during development can influence ageing and alter the long-term risk of acquiring adult metabolic diseases. The underlying mechanisms, however, are poorly understood. We took advantage of the abundant genetic tools and rapid lifecycle of *Drosophila* to investigate the effect of various early-life stressors upon adult lifespan. We observed that larval exposure to sub-lethal doses of a widely used oxidative stressor, tert-butylhydroperoxide (tBH) significantly increases starvation resistance and extends medianadultlifespan by up to 30%. Surprisingly, we found that these long-term effects of developmental exposure to tBH are accounted for by a stable change in gut microbiota that persists in adult flies. This study opens up the possibility that early-life interventions that stably reprogramme the microbiome could be used to achieve long-term beneficial effects upon healthspan and lifespan.

Poster Number: P155
Decoding the molecular identity of neural stem cell types: a single-cell transcriptomic approach
J Gil-Ranedo, T Bossing, C S Barros

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An increasing number of studies provide evidence of diversity among NSCs in the developing and adult mammalian brain. Given our poor understanding of their molecular identity, it is advantageous to use the Drosophila larval brain as a simpler model, in which different NSC types are known. We generated a transgenic fly line with two major NSC types (I and II) permanently labeled, harvested individual type I and type II NSCs from live brains, and performed a single-cell transcriptome comparative analysis at two fate-restrictive temporal windows. We identified transcripts differentially expressed in each NSC type and specific for 24h and 72h after larval hatching (-0.7<Log2Fold-Change<0.7; p<0.05), which potentially confer both molecular and temporal identity. Transcription factors and nucleic acid-binding proteins are the most represented protein classes, ranging from 14 to 31% of identified targets. We are curating candidates with highly conserved mammalian orthologues, validating their expression and initiating functional analysis.

Poster Number: P156
Capturing emerging pluripotency in the pig early embryo by modulation of WNT and ERK signalling pathways
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Despite multiple attempts, germline competent pig ESCs have not yet been established. Here we set out to elucidate how pluripotency emerges during pig embryo development and investigated how WNT and ERK (PD0325901) modulation can promote NANOG expression in the epiblast and support the establishment of pESC. t2iGö inhibition during the morula to blastocyst transition prevented hypoblast segregation, resulting in ICM enriched for NANOG+ cells and devoid of SOX17+ cells. WNT inhibition alone did not affect SOX17 expression in the ICM, whereas in combination with PD resulted in no SOX17 expression. Pig ESC derivations using t2iLGö and WNTi + PD were unsuccessful, however cell lines could be established when cultured with WNTi + FGF with or without Activin A (7 passages). These experiments demonstrate contrasting roles of ERK and WNT signalling during the formation of the ICM and in self-renewing pig ESC cultures.

Poster Number: P157
dMob4 is required for mitotic reactivation of Drosophila neural stem cells
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Neural Stem Cells (NSCs) in the postembryonic or adult brain can leave quiescence and mitotically reactivate. The Hippo and Insulin pathways were implicated in this process but the underlying mechanisms are not fully understood. We identified Drosophila monopolar spindle-one-binder 4 (dMob4) as one of the transcripts upregulated upon NSC reactivation on a single-cell transcriptome microarray. We show that loss of dMob4 leads to reduction in NSC enlargement and division, while overexpression of dMob4 or its human orthologue, causes premature NSC reactivation. We also demonstrate that inactivation of Hippo signaling or activation of the Insulin pathway in NSCs of dmob4 mutants can rescue reactivation defects. dMob4 is part of the STRIPAK protein complex, of which members are involved in regulating both Insulin and Hippo pathways. Our current work focuses on how dMob4/ STRIPAK complex may contribute as a switch between Hippo and Insulin signaling to promote NSC mitotic reactivation.

Poster Number: P158
***Tfec* controls cytokine expression in the haematopoietic stem cell vascular niche and expands haematopoietic stem cells**
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[1]Department of Pathology and Immunology, CMU, Geneva, Switzerland; [2]Department of Internal Medicine Specialties, HUG, Geneva, Switzerland

Rare haematopoietic stem cells (HSCs) can self-renew, establish the entire blood system and are used in regenerative medicine to treat haematopoietic conditions. However, current protocols expand HSCs *ex vivo* inefficiently, limiting their therapeutic potential, creating a need to further understand HSC expansion, which takes place during embryonic development. In zebrafish, HSCs emerge from the aorta, colonise the caudal haematopoietic tissue by interacting with endothelial cells and expanding, before they seed the kidney marrow. We find that *tfec* controls cytokine expression in the zebrafish caudal HSC niche and augments HSC proliferation. In contrast, *tfec*$^{-/-}$ mutants have reduced haematopoiesis and become anaemic. We also find that *tfec* regulates the expression of *oncostatin M* (*osm*), a previously uncharacterised haematopoietic zebrafish gene. *osm* increases HSC proliferation and inhibits differentiation. Fully understanding *osm* is an important step in fully characterising zebrafish haematopoiesis. We are now using human TFEC to expand donated human cord blood HSCs.

Poster Number: P159
Drosophila neural stem cells are polarised by their daughter cells
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Drosophila neural stem cells (neuroblasts) divide asymmetrically to both self-renew and generate Ganglion Mother Cells (GMCs) daughter cells. A noticeable feature of larval neuroblasts is the fact that their division orientation is maintained from one cell cycle to the next, even when isolated from their niche in neuroblast/GMCs clusters. This relies on an apical microtubule network acting as an intrinsic polarising cue which disruption, however, only partially affects division orientation maintenance. Here, we used live imaging of cultured *Drosophila* larval brains, genetics and laser ablation to demonstrate that the GMC acts as an additional – this time external – polarity cue also participating to neuroblasts division axis maintenance. We further investigated the role of the midbody, a structure forming at the neuroblast/GMC interface following cytokinesis, which likely participates to this mechanism and allows neuroblasts to distinguish their latest daughter cells from the previous ones.

Poster Number: P160
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 tumor initiation and growth. Brat is a Drosophila brain tumor suppressor. Loss of Brat or its human orthologue, Trim3, increases neural stem cell-like properties and promotes brain tumor growth in the fly brain and in human glioblastomas (GBMs). We performed a single-cell transcriptome screen comparing brat tumour-initiating cells to normal neural cells, harvested directly from Drosophila brains. Over 70% of identified transcripts with differential expression levels have highly conserved human orthologues. We selected one candidate, HeatR1, highly upregulated in both Drosophila 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 and growth of human GBM cell lines. Our data suggests HeatR1 to be a potential novel player promoting brain tumour growth.

Poster Number: P161
Hormonal regulation of neural stem cell proliferation in _Drosophila_
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An important and conserved strategy for surviving nutrient deprivation during development is to spare the growth of the CNS at the expense of other organs. In *Drosophila*, we previously found that the remarkable ability of stem cells in the developing CNS to maintain proliferation during starvation is conferred by Anaplastic lymphoma kinase (Alk). We now show that Alk-dependent sparing is progressively acquired as neural stem cells increase their cell cycle speed during development. Cell cycle acceleration requires the temporal transcription factors Castor and Seven-Up but these do not specifically regulate sparing. In contrast, the steroid hormone ecdysone is a critical temporal regulator of both cell cycle speed and sparing. Importantly, this involves the ecdysone signalling pathway acting in the neural stem cell niche as well as in the stem cells themselves. This study demonstrates how systemic, niche and cell-autonomous timing cues are integrated during neural stem cell proliferation and sparing.

Poster Number: P162
Disticnt roles of two pax7 stem cell populations in larval zebrafish muscle repair
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Heterogeneity of stem cells or their niches is likely to influence tissue regeneration. We reveal stem/precursor cell diversity during wound repair in larval zebrafish somitic body muscle using time-lapse 3D confocal microscopy on reporter lines. Skeletal muscle stem cells expressing Pax7 marker regenerate muscle fibres effectively post injury. Analysis of pax7a and pax7b transgenic reporter fish reveals that cells expressing each of the duplicated pax7 genes are distinctly localized in an un-injured larvae and each behaves differently in wounds. While low numbers of pax7a-only cells form nascent fibres, the more numerous Pax7b-marked cells frequently fuse to fibres contributing more strongly than pax7a-only cells to repair of damaged fibres. Ablation of a substantial portion of nitroreductase-expressing pax7b cells with metronidazole prior to wounding triggered rapid pax7a-only cell accumulation, but this neither inhibited nor augmented pax7a-only cell derived myogenesis and thus altered the cellular repair dynamics during wound healing.

Poster Number: P163
A novel and unusually dynamic progenitor cell population integrates the transition zone between pseudostratified and squamous epithelium
F Campo-Paysaa, J D Clarke, R J T Wingate

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Epithelial transition zones are characterised by an abrupt transition in epithelial morphology, for example the transition from columnar to squamous epithelium. They are proposed to contain a stem cell niche and are susceptible to tumour formation. Here we take advantage of the transparency of the zebrafish embryo to characterise the development of cellular architecture and cell behaviours in an epithelial transition for the first time. The transition zone between pseudostratified columnar epithelium of the rhombic lip and squamous epithelium of the expanded rhombencephalic roof plate consists of a single novel cell type that we have named the veil cell. Veil cells constitute a lineage restricted stem zone that generates the squamous roof plate. These neural progenitor cells are very dynamic and have a previously undescribed morphology that accomodates a single cell transition between pseudostratified and squamous epithelia to integrate the growth of two distinct epithelia.

Poster Number: P164
KLF4 supports establishment of pluripotency in vivo by controlling levels of endoderm specific GATA6 transcription factor
A Al-Anbaki, **B Plusa**

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Kruppel-like factor 4 (KLF4) is known to play a role in somatic cells reprogramming and is associated with pluripotency control in embryonic stem cells. However, little is known, about its role in establishment/maintenance of pluripotent cell population in vivo. Here, we tested the role of KLF4 in the formation of pluripotent mouse epiblast by altering levels of KLF4 in a random blastomere of 8-cell stage embryos. Alteration of KLF4 levels had no direct effect on the ability of affected clone to contribute to epiblast. However, very clear effect was observed when levels of other well-established pluripotency marker, SOX2 were changed. Co-injection of mRNA for Sox2 and Klf4 attenuated Sox2 over-expression effects, directing majority of the cells towards epiblast. The Klf4 overexpression did not alter expression levels of any major pluripotency transcription factors but it had a profound effect on the levels of primitive endoderm marker, GATA6.

Poster Number: P165
Quantifying the effective range and modelling in vivo signals regulating germ cell migration
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To understand the effects of extracellular signalling molecules it is important to have quantitative information about their range of influence *in vivo*. In *Drosophila*, embryonic germ cell migration requires spatial information provided by diffusible signals dependent on two pathways: Wunen and HMG-CoA reductase (HMGCR). Wunen expression effectively repels germ cells whilst HMGCR expression attracts. To explore the nature of the HMGCR-dependent signal and we ectopically expressed HMGCR-GFP in wild type embryos and also those otherwise null for HMGCR or Wunen. Using germ cell positioning relative to the ectopic domains in fixed tissue, and trajectories of migration from live light sheet microscopy we have determined that the HMGCR dependent signal operates over a long range *in vivo* and acts competitively with that provided by Wunen. These characteristics are feeding into mathematical models that we are developing to infer the chemotactic gradients and explain the behaviour of the germ cells.

Poster Number: P166
The role of Deltex modulation of Notch signalling in regulating homoeostasis of the Drosophila midgut
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The tight regulation of intestinal stem cell (ISC) proliferation and differentiation is essential for normal intestinal homeostasis and repair after injury. ISCs divide asymmetrically into one daughter cell for ISC self-renewal and one enteroblast daughter, which migrates away and differentiates into either an absorptive-enterocyte or a secretory enteroendocrine cell. The evolutionary conserved Notch pathway is known to regulate ISC maintenance and differentiation. Notch can signal by ligand-dependent or ligand independent means. We found that one positive intracellular regulator of ligand-independent Notch signalling called Deltex, could alter midgut homeostasis in Drosophila. We show that in adult flies lacking Deltex, ISC divisions produce tumour-like un-differentiated cell clumps, which accumulate with age, express a reporter for Notch signalling, but remain localised adjacent to the stem cell expressing the Notch-ligand Delta. To understand the role of Deltex further we are exploring effects on Notch localisation and genetic interactions with Notch pathway mutants.

Poster Number: P167
Modulation of *gata2a* levels through an endothelial enhanceris required for generation of definitive haematopoietic stem cells
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Haematopoietic stem cells (HSCs) maintain the vertebrate blood system throughout life. They arise during embryogenesis from the haemogenic endothelium (HE), located in the floor of the dorsal aorta. Our understanding of HE specification remains incomplete, but regulation of Gata2 is crucial for its programming. Here we investigate whether *gata2a* is required for HSCs emergence in zebrafish. We found that the endothelial-specific intronic *gata2a* enhancer (i4 enhancer) is conserved throughout vertebrates and established a transgenic line driven by this enhancer to monitor the activity of *gata2a in vivo*. Homozygous deletion of the i4 enhancer (*gata2a*$^{\Delta i4/\Delta i4}$) led to endothelial-specific loss of *gata2a* expression, including the HE. This correlated with a decrease in *gata2b* and *runx1* in the HE of *gata2a*$^{\Delta i4/\Delta i4}$ mutants, suggesting that Gata2a is an upstream regulator of the *gata2b/runx1* axis that programmes the HE to become haematopoietic. Thus, endothelial Gata2a activity is required to programme the HE and generate HSCs.

Poster Number: P168
Investigating the role of the ARF GTPase arf-3 in regulating seam cell development and secretion
A Walker, A Woollard

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The promoter region of *arf-3*, a small GTPase implicated in intracellular trafficking, drives the expression of the tissue-specific seam cell marker *scm::gfp*, a transcriptional reporter commonly used in the study of the development of the stem-like seam cells in *C. elegans*. Knockdown of *arf-3* by RNAi leads to variable seam cell numbers suggesting a possible failure in the regulation of asymmetric seam cell divisions during larval development. We found that knockdown of *apr-1*, an ortholog of human APC alters the localisation of the translational reporter ARF-3::mCherry in an RNAi screen for potential interactors of arf-3. Simultaneous knockdown of *arf-3* and apr-1 results in variable seam cell numbers and morphological defects. Finally we discuss the generation of an *arf-3* knockout strain by Cas9 mediated deletion of the *arf-3* coding region and an ongoing co-localisation study of ARF-3::mCherry with other intracellular trafficking components to determine the nature and function of ARF-3::mCherry vesicles.

Poster Number: P169
Probing the skeletal stem cell niche through functional investigation of Prx1 expressing cells
S V Pretorius

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Previous work by M Logan and others have shown that Prx1 marks an early population of mesenchymal cells that give rise to all the skeletal and connective components of the limb. As development progresses the expression of this marker becomes specified to a subpopulation of cells within the periosteum and these cells contribute to callus formation during skeletal repair. Using a Prx1-eGFP reporter mouse line this project aims to characterise these Prx1 expressing cells. Immunohistochemistry is used to identify the locations of the Prx1+ cells within the periosteum. Using FACS to isolate GFP+ cells a full genome transcriptomic analysis will be used to compare Prx1 positive and negative cells of the periosteum to identify biomarkers of Prx1+ cells that will be utilised for enrichment strategies. Additionally Prx1+ cells will be analysed for their endochondral differentiation potential in vitro to further characterise the skeletal stem cell nature of this subpopulation.

Poster Number: P170
Studying consequences of vascular dementia CADASIL Notch3 mutations in cell culture and iPS derived in vitro differentiated tissue models
S S Hosseini Alghaderi, W Zhang, M Baron, T Wang

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Notch signalling is highly important to develop and maintain vasculature. CADASIL, an adult-onset autosomal dominant vascular dementia disease, is caused by human Notch3 mutations. A likely pathological mechanism is the misregulation of Notch3 trafficking because the CADASIL is associated with an excessive accumulation of the Notch extracellular domain. Here we aim to develop an *in vitro* model using patient-derived induced pluripotent stem cells (iPSCs) to study the role of Notch trafficking in CADASIL pathogenesis. Initially, signalling and protein localisation assays using expressed protein will be established to identify locations in Notch where a fluorescent tag can be inserted for live image analysis, without compromising Notch function, and to compare wild type and CADASIL mutant Notch. For more physiological studies using endogenous Notch3 we will also use patient derived iPS cell and CRISPR approaches and establish *in vitro* models of vascular differentiation to investigate mutant Notch mislocalisation and CADASIL phenotypes.

Poster Number: P171
Asymmetric localization of Miranda in *Drosophila* neuroblasts involves the cognate mRNA independent of local translation
A Ramat, J Januschke

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How cells position their proteins is a key problem in cell biology. Targeting mRNAs to distinct regions of the cytoplasm contributes to protein localization by providing local control over translation. We tagged with GFP endogenous mRNA and protein of *miranda*, a factor required for fate determination in mitotic *Drosophila* neural stem cells. We find that the mRNA localizes, like the protein, in a basal crescent in mitosis. We used GFP-specific nanobodies fused to localization domains to alter the subcellular distribution of the GFP-tagged mRNA. Altering the localization of the mRNA resulted in mislocalization of the protein and *vice versa*, suggesting that protein and cognate mRNA asymmetric distribution are interdependent. Protein localization defects caused by mislocalization of the cognate mRNA was rescued by introducing untagged mRNA coding for mutant non-localizable protein. Therefore, mRNA can contribute to the localization of the encoded protein independent of serving as the source of local translation.

Poster Number: P172
Using C. elegans stem-like epithelial development to study mechanisms of biological robustness
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Biological robustness is the process whereby living systems are able to reliably produce the same outcome in the face of differing internal (genetic) and external (environmental) conditions. *Caenorhabditis elegans* is an ideal candidate in which to study mechanisms of robustness due to its genetic tractability and defined cell lineage (eutely), allowing development to be studied at single cell resolution. We have chosen to focus on studying robustness of the epithelial seam cell lineages, which during development undergo stereotypical rounds of stem-like divisions. We carried out an EMS forward genetic screen to isolate mutants with a high degree of seam cell number variance within isogenic populations due to stochastic noise. Here I present the design of this screen and our findings on the nature of the causative loci and developmental basis of phenotypic variability.

Poster Number: P173
Protection of embryonic muscle stem cells in vivo
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Embryonic muscle stem cells (eMuSC), in contrast to their adult counterpart, self-renew and produce muscle all the time. They thus have properties that cells for the therapy of muscle diseases should emulate. We are interested in understanding the molecular basis of eMUSC's properties, and we challenged the cells with molecular constructs to force them into untimely differentiation. These constructs can recruit pluripotent cells in the early Xenopus embryo into myogenesis, but fail to inflict myogeneis on chicken eMuSC. This suggests that the stem cell state of eMuSC is actively protected.

Poster Number: P183
Single cell expression profiling of neural crest-derived cells identifies partially-restricted intermediate pigment progenitor cell
T Subkhankulova[1], M Nikaido[1], G Aquino[2], H Schwetlick[3], T Sauker-Spengler[4], A Rocco[2], **R N Kelsh**[1]

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The neural crest (NC) is a major model for understanding stem cell differentiation. Controversy over how individual NC fates are specified concerns whether fate choice proceeds via a Progressive Fate Restriction model. The latter model posits sets of partially-restricted intermediates, but these remain poorly characterised *in vivo*. Zebrafish NC generates three distinct pigment cells – melanocytes, iridophores and xanthophores – which have been proposed to share a common cellular origin from a partially-restricted chromatoblast, or a bipotent melanoiridoblast. We are using NanoString technology to profile expression of 45 neural crest/pigment cell genes in FACS-isolated freshly *ex vivo* single NC-derived cells. Clustering analysis of the expression profiles identifies cells showing expression patterns consistent with multipotent NC cells, differentiated cell-types (melanocytes, iridophores), but also common precursors for all pigment cells. Consistent with new fate-mapping data, these cells appear to also have neural potential, identifying a highly multipotent partially-restricted intermediate *in vivo*.

Poster Number: P185
CXCR4 and c-Kit signalling are required for directed migration of chicken primordial germ cells through the chick embryonic vascular system
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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 that CXCR4-knockout PGCs completely fail to migrate to the genital ridges in vivo whereas c-Kit-knockout PGCs colonise the developing gonads in reduced numbers. Our result shows conserved roles for CXCR4 and c-Kit signalling during vascular migration of chicken PGCs.

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York-Andersen, A H - P69*

Z

Zak, M - P180
Zaucker, A - O30* & P91*
Zhang, H - P145
Zhang, K - O15, P26 & P46
Zhang, M - P148
Zhang, W - P170
Ziukaite, R - P79*
Zohren, J - O20 & P184

INVITED SPEAKER BIOGRAPHIES

Sunday 2 April 2017

Plenary Session 19:00 – 20:00

Bonnie Bassler
Bacterial Quorum Sensing and its Control
Bonnie Bassler is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. She is a Howard Hughes Medical Institute Investigator and the Squibb Professor and Chair of the Department of Molecular Biology at Princeton University. Bassler received a B.S. in Biochemistry from the University of California at Davis, and a Ph.D. in Biochemistry from the Johns Hopkins University. She performed postdoctoral work in Genetics at the Agouron Institute, and she joined the Princeton faculty in 1994. Dr. Bassler was awarded a MacArthur Foundation Fellowship in 2002. She was elected to the American Academy of Microbiology in 2002 and made a fellow of the American Association for the Advancement of Science in 2004. She is the 2009 recipient of the Wiley Prize in Biomedical Science for her paradigm-changing scientific research. She is the 2011 recipient of the National Academies' Richard Lounsbery Award. She is the 2012 UNESCO-L'Oreal Woman in Science for North America. In 2012, Bassler was elected to the Royal Society and to the American Philosophical Society. She received the Shaw Prize in Life Sciences and Medicine in 2015. Bassler was the President of the American Society for Microbiology in 2010-2011, and she chaired the American Academy of Microbiology Board of Governors from 2011-2014. She was a member of the National Science Board from 2010-2016 and was nominated to that position by President Barack Obama. The Board oversees the NSF and prioritizes the nation's research and educational activities in science, math and engineering.

The Genetics Society Medal Lecture 2017 20:00 – 21:00

Marisa Bartolomei
Epigenetic Regulation of Genomic Imprinting in Development and Disease
Marisa Bartolomei is a Professor of Cell & Developmental Biology and co-Director of the Epigenetics Program at the University of Pennsylvania Perelman School of Medicine. Marisa S. Bartolomei received her BS in Biochemistry at the University of Maryland and then obtained her PhD from the Johns Hopkins University School of Medicine under the guidance of Dr. Jeffry Corden. She trained as a postdoctoral fellow with Dr. Shirley Tilghman at Princeton University. In 1993, Dr. Bartolomei was appointed as an Assistant Professor at the University of Pennsylvania and was promoted to Associate Professor with tenure in 1999 and Professor in 2006. In 2006, Dr. Bartolomei received the Society for Women's Health Research Medtronics Prize for Contributions to Women's Health. In 2011, Dr. Bartolomei received the Jane Glick Graduate School Teaching Award for the University of Pennsylvania School of Medicine and a MERIT award from the NIH. She was elected as a Fellow of the American Association for the Advancement of Science in 2014 and was recently elected Member-At-Large of the Section on Biological Sciences for AAAS (2016-2020 term). Dr. Bartolomei previously served on the Science Board of Reviewing Editors and is currently a member of the Human Molecular Genetics and Molecular and Cellular Biology editorial boards and is an Associate editor for PLOS Genetics. Dr. Bartolomei's research addresses the epigenetic mechanisms of genomic imprinting and X inactivation, as well as the impact of adverse environmental insults on epigenetic gene regulation using the mouse as a model.

Monday 3 April 2017

Session 1 09:00 – 12:30
Epigenetics

Julie Ahringer
Genome architecture and transcription regulation in C. elegans
Julie Ahringer is a Senior Group Leader at the Gurdon Institute at the University of Cambridge. Her group investigates chromatin structure and function using molecular genetic and high-throughput genomic approaches in C. elegans. Their interests include the organization of the genome into domains, functions and interactions between enhancers and promoters, and chromatin regulation at developmental transitions. She pioneered genome-wide RNAi screening, carrying out the first systematic inactivation of genes in an animal by creating the widely-used C. elegans RNAi feeding library. She is a member of EMBO, a Fellow of the Academy of Medical Sciences and she received the Francis Crick lecture prize of the Royal Society in 2004.
http://www.ahringer.group.gurdon.cam.ac.uk/

Didier Trono
Mobile elements, polydactyl proteins and the genesis of human-specific regulatory networks
Didier Trono, M.D., completed a clinical training in pathology, internal medicine and infectious diseases in Geneva and at Massachusetts General Hospital before performing post-doctoral work with David Baltimore at the Whitehead Institute. In 1990, he moved to the Salk Institute to launch a center for AIDS research. From 1997 to 2004, he was at the University of Geneva as professor and then head of the Department of Genetics and Microbiology. He then joined the EPFL as dean of its newly launched School of Life Sciences, a position he held for eight years. He now leads the Health 2030 Initiative, a joint venture of the EPFL, the Universities of Geneva, Bern and Lausanne and their affiliated hospitals to promote the advent of personalized health in Switzerland.
Didier Trono's research has long gravitated around interactions between viruses and their hosts and the development of tools for gene therapy. This led him to epigenetics, and to explore the impact of transposable elements and their controllers on transcriptional networks governing human development and physiology.

Dirk Schubeler
Reading and writing DNA methylation
Dirk Schübeler's group at the FMI in Basel studies the function of chromatin and DNA methylation in gene regulation in higher eukaryotes. Dirk performed his PhD in Germany and his postdoctoral work in Seattle. He started his own group in Basel in 2003 expanding his effort to genome-wide analysis of chromatin, DNA methylation and replication. This has lead to the first comprehensive maps of histone modifications, replication timing and DNA methylation in metazoan genomes.
His group is applying stem cell differentiation as a cellular model to monitor epigenome changes during cellular commitment. These experiments are combined with targeted genome perturbation in order to generate better predictive models. Recent efforts are aimed to define the interplay between transcription factors and chromatin in the nucleus.

Recent publications:
Domcke, S.*, Bardet, A. F.*, Ginno, P., Hartl, D., Burger, L., and Schübeler, D. Competition between DNA methylation and transcription factors determines binding of NRF1. Nature, 2015 528(7583):575-9.
Tuncay Baubec, Daniele F. Colombo, Christiane Wirbelauer, Juliane Schmidt, Lukas Burger, Arnaud R. Krebs, Altuna Akalin and Dirk Schübeler. (2015) Genomic profiling of DNA methyltransferases reveals a role for DNMT3B in genic methylation. Nature. 520 (7546):243-8.
Arnaud R. Krebs, Sophie Dessus-Babus, Lukas Burger and Dirk Schübeler. (2014) High-throughput engineering of a mammalian genome reveals building principles of methylation states at CG rich regions. eLife, Sep 26;3. doi: 10.7554/eLife.04094.
Tuncay Baubec, Robert Ivanek, Florian Lienert and Dirk Schübeler. Methylation-dependent and – independent genomic targeting principles of the MBD protein family, Cell 153, 480–492.

Vincent Colot
Transgenerational Epigenetics, transposable elements and heritable phenotypic variation
Vincent Colot has a long-standing interest in the study of DNA methylation and epigenetic processes. His research focuses on determining the extent as well as the molecular and phenotypic impact of transposable element-based transgenerational epigenetic variation in the model plant Arabidopsis.
Vincent graduated from the Institut National Agronomique in Paris. He did his PhD at the Plant Breeding Institute in Cambridge (UK). He joined the French Centre National de la Recherche Scientifique (CNRS) in 1990 and has been a CNRS Director of Research since 2004.

Session 1 09:00 – 12:30
Neurons, Networks and Behaviour

Gregory Jefferis
Development, Structure and Function of Neural Circuit Motifs
Gregory's first taste of science was a year working on C. elegans apoptosis with Michael Hengartner (Cold Spring Harbor). He then read Natural Sciences at Cambridge, where he joined the MRC LMB worm group and spent a summer at Caltech with Gilles Laurent, all highly formative experiences.
During his Neurosciences PhD with Liqun Luo at Stanford, Gregory uncovered a number of developmental principles using the olfactory system of the fly. They found that central neurons in the brain were pre-specified to form connections with specific incoming sensory neurons. Surprisingly, they found that central dendrites could target independently of the incoming sensory axons, suggesting a principle of independent coarse maps refined by contact-mediated matching.
Returning to Cambridge as a Wellcome research fellow based in the Zoology Department, Gregory combined genetic and computational approaches to build a 3D atlas of higher olfactory centres in the fly, showing that odours of different behavioural significance are spatially segregated.
In 2008 he opened his lab at the MRC LMB in Cambridge. Their work supported by the MRC and ERC has combined anatomical and physiological characterisation of circuits underlying instinctive fly behaviour. They are also well known for tool development and a commitment to open science. He was elected an EMBO YIP in 2012, tenured in 2014, was a Caltech Moore Scholar in 2015 and was elected a FENS-Kavli Scholar in 2016. Gregory is also a Principal Research Associate in the Cambridge Dept of Zoology, where he directs the Wellcome-funded Drosophila Connectomics Group.

Laure Bally Cuif
Spatio-temporal control of neural stem cell activity and pallium construction in the teleost zebrafish
Laure Bally-Cuif is CNRS Research Director and is leading a Research Unit at the Pasteur Institute in Paris. Her research interests focus on the mechanisms controlling the formation and activity neural progenitor cells (NPs) / neural stem cells (NSCs) in the vertebrate central nervous system, using as main model the embryonic and adult zebrafish brain. Her group notably contributed to promoting the zebrafish adult as a powerful model for the study of adult NSC properties. She is using this model to probe the molecular and cellular mechanisms controlling NSC pools' formation, maintenance and recruitment, and driving the NSC quiescence/activation cycle. Among recent findings, her lab identified Notch signaling and microRNA-9 as key pathways controlling homeostasis of the NSC pool of the dorsal telencephalon (pallium), and traced the developmental source of adult pallial and midbrain NSCs, highlighting different NSC properties based on NSC origin. Her lab also developed a live imaging approach permitting to record over weeks the behaviour of adult pallial NSCs in their endogenous niche, opening unprecedented possibilities to analyse NSC behaviour in vivo.

Stephen Goodwin
Neural circuitry coordinating male copulation
Stephen studied genetics as an undergraduate at the University of Glasgow, and researched Drosophila learning and memory for his Ph.D. After a postdoctoral stint in Jeff Hall's lab at Brandeis University (USA), where he used molecular-genetic and behavioural approaches in the fruit fly to understand how the sexual identity of a nervous system and its behaviours are specified, he returned to the UK and spent 10 years leading a research group at the University of Glasgow. He arrived in Oxford in 2009, where he is a Professor of Neurogenetics, a Wellcome Trust Senior Investigator, and a Tutorial Fellow in Genetics at Magdalen College. He is part of the Centre for Neural Circuits and Behaviour along with the groups of Gero Miesenböck, Martin Booth, Scott Waddell, Korneel Hens and Tim Vogels.
Stephen's group uses the fruit fly, Drosophila melanogaster, to study the genetic, developmental, and neural mechanisms that underlie sex-specific behaviours in higher animals. In particular, the elaborate

courtship ritual performed by the male fly has provided remarkable insights into how the neural circuitry underlying sexual behaviour, which is largely innate in flies, is built into the nervous system during development, and how this circuitry functions in the adult. The fly has the advantages of advanced molecular genetics approaches along with well-defined anatomy and physiology.

Gilles Laurent
Born in Casablanca Morocco, French National.
1986 DVM and PhD, Toulouse, France.
1985-89 Postdoc and Royal-Soc. Locke Research Fellow, U. Cambridge, UK.
1990-2010 Professor California Institute of Technology, USA.
2009- Director, Max Planck Institute Brain Research, Frankfurt, Germany.

Arantza Barrios
Glia developmental plasticity couples behaviour to reproductive needs
After studying Biology at Universitat de Barcelona, Arantza joined the lab of Prof Steve Wilson at UCL to pursue a PhD in Developmental Biology. Her work focused on the role of Eph/ephrin signaling in somite specification and morphogenesis in zebrafish.
For her postdoc, she moved into the field of Neuroscience. Arantza joined the laboratories of Prof Scott Emmons at Albert Einstein (NY) (2005) and later Prof Maureen Barr at Rutgers University (NJ) (2009) to study the molecular and cellular mechanisms underlying behavioural state transitions and decision-making in a sexually dimorphic manner using C. elegans.
Since September 2012, Arantza has had her research group at UCL in the Department of Cell and Developmental Biology where they continue to use C. elegans to understand the genetic mechanisms and neural circuits underlying innate and learned behavior.

Session 1 09:00 – 12:30
New Methods to Study Cell Biology

Manuel Théry
Microtubule rejuvenation
Manuel Théry has developped microfabrication tools and methods to investigate the relationship between cell shape, cytoskeleton architecture and centrosome positioning. Recently he developped new assays to control the growth of actin filaments and microtubule from purified components in biochemical assays on micropatterned chips. He believes our understanding of cell architecture self-organization will stem from the effort to bridge cell biology and biochemistry (with some help from numerical simulations).

John Briggs
Determining structures of coated vesicles in vitro and in cells using cryo-electron tomography
DPhil Oxford University.
Postdoctoral research at the University of Munich.
Group Leader at European Molecular Biology Laboratory (EMBL) since 2006.
Group Leader at MRC Laboratory of Molecular Biology since 2017.

Sebastian Deindl
Structural Insights into the Autoinhibition of the Oncogenic Human Chromatin Remodeler Alc1
Sebastian Deindl's group studies how the molecular structures and dynamics of molecular machines together enable their function and regulation. Molecular machines are proteins or protein complexes that convert chemical energy into conformational changes to carry out work in the cell. One major focus are nucleic-acid interacting enzymes whose aberrant function or dysregulation is often associated with severe diseases such as cancer. Sebastian Deindl's fascination for the workings of protein machines at a molecular level began during his PhD training in John Kuriyan's laboratory at the University of California, Berkeley. There he studied the allosteric control of protein kinases and developed a passion for correlating protein structure with function. For his postdoctoral research Sebastian decided to venture into another important area of biology and study dynamic aspects of chromatin remodeling enzyme mechanisms using single-molecule imaging techniques in Xiaowei Zhuang's laboratory at Harvard. Sebastian Deindl's group now develops and applies single-molecule fluorescence methodologies and combines them with a range of structural approaches, biochemistry and computer simulations in order to understand the function and regulation of nucleic-acid interacting proteins at a molecular level.

Thijn Brummelkamp
Haploid Genetics to study disease-related networks
Thijn Brummelkamp received his Msc in biology from the Free University in Amsterdam, in 1998. He did his graduate research at The Netherlands Cancer Institute in the group of René Bernards and received his PhD cum laude from Utrecht University in 2003. After his PhD he was appointed as group leader (Whitehead Fellow) at the Whitehead Institute for Biomedical Research in Cambridge, USA. In 2011 his laboratory moved to the Netherlands Cancer Institute in Amsterdam and he became an Adjunct PI at Center for Molecular Medicine (CeMM) in Vienna.
For his studies he received the Antoni van Leeuwenhoek Award (2003), The Annual NVBMB Award (2004, Dutch Association for Biochemistry and Molecular Biology), he was chosen as one of the world's top 35 Young Innovators by MIT's Technology Review Magazine (2005) and received the Kimmel Scholar Award (2006). He received an ERC starting grant from the European Research Council (2012), the 2012 Molecular Biosystems Early Career Award and the EMBO Gold Medal 2013.

Session 2 14:00 – 15:30
Stem Cells in Vivo

David Traver
Ontogeny of hematopoietic stem cells
The Traver laboratory studies the formation and function of hematopoietic stem cells in the early embryo, and how the progeny of these cells provide immunity to the developing animal. Through direct imaging approaches in the zebrafish embryo, we have recently demonstrated that HSCs derive from the transdifferentiation of hemogenic endothelium comprising the aortic floor. A major goal is to understand the genetic hierarchies that regulate this event. Recently, we have demonstrated that signals from the somite are required to instruct HSC fate during the early migration of their shared vascular precursors.
Dr. Traver has received a Career Development Award from the National Institutes of Health, a New Faculty Award from the California Institute for Regenerative Medicine, and Scholar Awards from the March of Dimes Foundation, the American Society of Hematology, the Sidney Kimmel Foundation for Cancer Research, and the Leukemia and Lymphoma Society.

Marella de Brujin
Elucidating the birth of blood stem cells
Marella de Bruijn obtained her BSc from Leiden University and her PhD from Erasmus University Rotterdam, the Netherlands. After her postdoctoral training she joined the faculty of the MRC Molecular Haematology Unit at the Weatherall Institute of Molecular Medicine, University of Oxford, where she currently is Associate Professor of Developmental Hematopoiesis. Marella's main research interest is the birth of blood stem cells during embryonic development. Work in her group focuses on the cellular processes and gene regulatory interactions that underlie the de novo generation of blood stem cells.

Session 2 14:00 – 15:30
Newly Tractable Systems

Reiner Schulz
Exploring the epigenomic archive of environmental exposure preserved in the wood of forest trees
Reiner graduated with a PhD in Computer Science from the University of Maryland, College Park. He then became a postdoctoral bioinformatician in the Epigenetics group of Rebecca Oakey at King's College London.
After EMBO long-term and RCUK fellowships, he was appointed a Senior Lecturer at King's in 2012. His main areas of expertise are genomics and epigenetics. Current projects cover subjects such as CD4 T cell (post-)transcriptional regulation and the identification of (epi)genetic correlates of rare human diseases. With his current project on the potential of forest tree wood as an epigenetic archive, he is exploring new and unexpectedly difficult territory.

Richard Buggs
Rising from the ashes: can genomic research help tree populations to recover from epidemics?
Richard Buggs is Senior Research Leader (Plant Health) at Royal Botanic Gardens Kew, and Reader in Evolutionary Genomics at Queen Mary University of London. His group works on plant population genomics and phylogenomics, in the context of tree health. He currently runs projects on ash, hazel and birch. He sits on the Department for Environment, Food and Rural Affairs' "Future Proofing Plant Health" project management board. He is on the committee of the London branch of Christians in Science. He advises the UK Native Tree Seeds Project. He did post-doctoral research in the lab of Doug and Pam Soltis at University of Florida, on whole genome duplication. His DPhil was with John Pannell at University of Oxford on plant evolutionary ecology. He read Plant Sciences in the Natural Sciences Tripos at Cambridge University.

Session 2 14:00 – 15:30
Nucleic Acids

Marvin Tanenbaum
Dynamics of Translation of Single mRNA Molecules in Vivo
Marvin Tanenbaum received a PhD in 2010 from Utrecht University for his work on cell division in the group of Prof. René Medema. During his PhD work, Marvin used live-cell microscopy to study the molecular mechanism of chromosome segregation during cell division, focusing on a small group of proteins called microtubule motor proteins. After obtaining his PhD, he received KWF and EMBO fellowships to perform his postdoctoral research in the group of Prof. Ron Vale at UCSF in the United States. As a postdoc, Marvin developed a keen interest in studying the control mechanisms and dynamics of gene expression in single cells, focusing on gene expression control during the cell cycle. He pioneered several new techniques using protein engineering that enabled direct observation of single protein molecules in action, and developed methods to observe gene expression in single living cells by fluorescence microscopy. In 2015, he became a group leader at the Hubrecht Institute and was awarded an ERC Starting grant. His group uses genetic engineering combined with single molecule microscopy to dissect the temporal and spatial control of gene expression.

David Tollervey
Nuclear RNA decay pathways aid rapid remodeling of gene expression in yeast
David Tollervey has directed a research group studying RNA Biology for over 30 years, including extended periods in the USA, France and Germany. In this time he worked in the University of Cambridge, the University of California at San Francisco, Institut Pasteur in Paris and EMBL in Heidelberg. He is currently Director of the Wellcome Trust Centre for Cell Biology in Edinburgh.

Jerne Ule
Exon Junction Complex inhibits recursive splicing of canonical exons
Jernej Ule obtained his PhD in Molecular Neuroscience from the Rockefeller University, New York. In 2006, he started his research group at the MRC Laboratory of Molecular Biology in Cambridge. In 2013 he joined the UCL Institute of Neurology as Professor of Molecular Neuroscience, and in 2016 the group has been seconded to the Francis Crick Institute. His group developed iCLIP and hiCLIP, methods that identify protein-RNA and RNA-RNA interactions in living cells. This provided insights into diverse transcriptome-wide functions of RNPs, their dynamics and evolution. Currently, the group studies non-canonical splicing at transposable elements and recursive splice sites, mechanisms of long-range secondary structures within the 3' UTRs of mRNAs, and the role of aberrant RNPs in neurodegenerative diseases.

The Mendel Medal Lecture 2017 16:00 – 16:45

David Baulcombe
When genomes meet: RNA, epigenetics and the phenotypes of hybrid plants
David Baulcombe was a student in Botany at Leeds (BSc) and Edinburgh (PhD) Universities. After periods in Montreal, the University of Georgia and the Cambridge Plant Breeding Institute he spent 20 years at the Sainsbury Laboratory, Norwich. He joined Cambridge University in 2007 as Royal Society Research Professor and now as Regius Professor of Botany. David is a Fellow of the Royal Society and a foreign associate member of the US National Academy of Sciences. His awards include the 2006 Royal Medal of the Royal Society, the 2008 Lasker Award for basic biomedical sciences, the Wolf Prize for Agriculture in 2010 and the 2012 Balzan Prize. He was knighted in June 2009.
Research interests of David Baulcombe involve plants and he focuses on gene silencing and epigenetics – the science of how nurture can influence nature. His discoveries changed thinking about the role of RNA in the regulation of gene expression of animals, plants and fungi.

Hooke Medal Lecture 16:45 – 17:30

Ewa Paluch
Cell morphogenesis across scales, from molecular processes to cell-scale behaviours
Ewa Paluch studied Physics and Mathematics at the École Normale Supérieure in Lyon, France. She did her PhD (2001-2005) at the Curie Institute in Paris, under the supervision of Cécile Sykes and Michel Bornens, investigating actin networks mechanics in vitro and in cells. In 2006, she moved to Dresden to start her own Research Group at the Max Planck Institute of Molecular Cell Biology and Genetics, as a joint appointment with the International Institute of Molecular and Cell Biology in Warsaw. She was appointed Professor of Cell Biophysics and MRC programme leader at the MRC Laboratory for Molecular Cell Biology, University College London, in January 2013. Since 2014, she has also been the head of the Institute for the Physics of Living Systems (IPLS), a new cross-faculty initiative aiming to promote collaborations between physicists and biologists at UCL. In 2014, she received a Philip Leverhulme Prize in Biological Sciences for her contributions to Cell Biophysics.
Ewa's laboratory investigates the principles underlying cellular morphogenesis. Since cell shape is ultimately defined by cellular mechanical properties and by the cell's physical interactions with its environment, biophysical approaches are essential to understand cell shape control. The lab combines cell biology, biophysics and quantitative imaging, and works in close collaboration with theoretical physicists, to investigate cell shape regulation.

Tuesday 4 April 2017

Session 3 09:00 – 12:30
Evodevo

Angela Hay
Explosive seed dispersal
Current position: Group leader, MPIPZ, Köln
Education: B.Sc. Massey University, New Zealand; Ph.D. UC Berkeley, USA
Awards and career history:
Max Planck Society Minerva Research Fellow, MPIPZ, Köln, Germany
Royal Society University Research Fellow, University of Oxford, UK
Junior Research Fellow, Balliol College, University of Oxford, UK
Glasstone Research Fellow, University of Oxford, UK
Fulbright Ph.D. Scholar, UC Berkeley, USA

Nipam Patel
Germline regeneration in the crustacean, Parhyale hawaiensis
Nipam Patel grew up in the West Texas town of El Paso, received an A.B. in Biology from Princeton University and a Ph.D. in Biology from Stanford University. Before moving to Berkeley, he was a Staff Associate in the Department of Embryology at the Carnegie Institution and a Professor at the University of Chicago. At UC Berkeley, he is jointly appointed in the Dept. of Molecular Cell Biology (and is currently Dept. co-Chair) and the Dept. of Integrative Biology. He is co-author of an undergraduate textbook on Evolution, and has taught in the summertime Embryology Course at the Marine Biological Lab at Woods Hole for the past seventeen years.

Linda Holland
Hybrids Between the Two Most Phylogenetically Distant Genera of Cephalochordates Give Insights into the Evolution of Pharyngeal Development
Linda Z. Holland received her BA and MA in biology from Stanford University and her PhD in marine biology from the University of California San Diego (UCSD). Because of the “two jobs problem,” her early research ranged from sea urchin reproductive physiology, to Drosophia developmental genetics, to the electrical polyspermy block in the marine worm Urechis caupo, to protein chemistry of human blood clotting, to fertilization and evodevo of pelagic tunicates, and, finally, starting in 1988 to evodevo of the cephalochordate, amphioxus. In 1998, she was promoted to a research professorship in the department of Scripps Institution of Oceanography at UCSD and began supervising graduate students and postdoctoral fellows. She led the community effort to sequence the genome of the Florida amphioxus, Branchiostoma floridae. To date, she has published 178 research papers, reviews and book chapters. Her work on amphioxus has been featured on public television in both Japan and the United States and she is frequently asked to speak on amphioxus in countries ranging from Japan, China and Taiwan to the USA, U.K., France, Germany, Italy and Brazil. In She was co-recipient of the 2014 Kowalevsky medal, an international award for research in evolutionary developmental biology.

Ralf Sommer
The mechanisms of developmental plasticity: from switch genes and epigenetics to the interplay of organisms and their environment
Ralf J. Sommer works in the field of evolutionary developmental biology on nematodes. He has developed and established the nematode Pristionchus pacificus as a model system for integrative studies in evolutionary biology. His research program focuses on the evolutionary analysis of developmental processes and mechanisms and has identified developmental systems drift as general principle for the evolution of development. In the last decade his work focuses on integrative evolutionary biology. That is, his lab tries to link and integrate laboratory studies in nematode genetics and development with fieldwork in ecology and population genetics using the island of La Réunion as a case study. Most recent studies focus on the evolution of novelty and developmental (phenotypic) plasticity. This work reveals how a novel predatory feeding behavior in nematodes is regulated by developmental switch genes and epigenetic regulatory mechanisms.
Sommer is the Director of the Department Integrative Evolutionary Biology at the Max Planck Institute (MPI) for Developmental Biology in Tübingen, Germany since 1999. Previously he worked as Young Investigator at the MPI for Developmental Biology from 1995-1999, as EMBO Research Fellow at the California Institute of Technology, Pasadena, USA in Paul W. Sternberg's lab from 1993-1995 and at the Ludwig Maximilians University in Munich, where he earned his PhD at Prof. Dr. Diethard Tautz’ lab in 1992.

William Jeffrey
From Genotype to Phenotype: Evolution and Development of Cavefish Eye Loss
William Jeffery is Professor of Biology and Cell Biology and Molecular Genetics at the University of Maryland, College Park. He has also been a Professor at The Pennsylvania State University (Biology), The University of California, Davis (Molecular and Cellular Biology), and The University of Texas at Austin (Zoology). He is also a Whitman Investigator in the Bell Center for Regenerative Biology and Tissue Engineering at The Marine Biological Laboratory, Woods Hole, Massachusetts. Dr. Jeffery studies phenomena at the interface of developmental and evolutionary biology, including the evolution of larval forms and regeneration in ascidians and the mechanisms of eye and pigment degeneration in subterranean animals. He has pioneered use of the cavefish Astyanax mexicanus as a model system in EvoDevo research. He received the 2012 Alexander Kowalevsky medal for distinguished contributions to evolutionary developmental biology.

Session 3 09:00 – 12:30
Cytoskeleton and Transport

Bruce Goode
Mechanisms of microtubule-actin coordination: a journey from yeast to mammals
Bruce Goode is a Professor of Biology at Brandeis University. Dr. Goode earned a B.S. in Biology from the University of California Santa Barbara, received his Ph.D. at the same institution working in the laboratory of Stuart Feinstein, and conducted his postdoctoral research in the laboratories of David Drubin and Georjana Barnes at the University of California Berkeley. In 2000, Dr. Goode started his lab at Brandeis University, where his research focuses on dynamic rearrangements of the actin and microtubule cytoskeletons that drive cell motility, cell morphogenesis, and intracellular transport. Specific areas of interest include defining mechanisms of actin filament assembly, actin filament disassembly and turnover, and coordination of microtubule and actin dynamics. Work is equally divided between yeast and mammalian systems. Projects in the lab are multi-disciplinary in nature, combining in vitro single molecule TIRF imaging, genetics, biochemistry, and live cell imaging. Dr. Goode has received scholar awards from the Pew Charitable Trust, March of Dimes, and American Cancer Society, and a Research Career Development Award from the NIH. Dr. Goode is on the F1000 advisory board and the editorial boards of The Journal of Cell Biology and Molecular Biology of the Cell, and he was the Editor-in-Chief of Cytoskeleton from 2009-2016. His lab's accomplishments include the initial discovery that formins nucleate actin assembly, defining formin mechanism and regulation by in vivo ligands such as APC, CLIP-170, Bud6, Bud14, Smy1, and Hof1, and single-molecule level characterization of the roles of Cofilin, AIP1, Coronin, Twinfilin, and Srv2/CAP in actin disassembly.

Sam Reck-Peterson
Regulation of human cytoplasmic dynein revealed through a proteomics approach
Samara Reck-Peterson received her Ph.D. from the Department of Cell Biology at Yale University and did postdoctoral research with Ron Vale at the University of California, San Francisco. She was an Assistant and Associate professor of Cell Biology at Harvard Medical School and the Associate Director of the Biological and Biomedical Sciences Graduate Program at Harvard Medical School. She joined the UCSD faculty in 2015, where she is a Professor of Cellular and Molecular Medicine and a member of the Division of Biological Sciences. Her research interests are focused on determining the mechanisms of intracellular transport. Dr. Reck-Peterson was the recipient of an NIH New Innovator Award and is currently an HHMI-Simons Faculty Scholar.

Anna Akhmanova
Regulation of microtubule minus-end dynamics at spindle poles by microcephaly-related proteins ASPM and katanin
Anna Akhmanova is a Professor of Cell Biology at the Department of Biology, Faculty of Science, Utrecht University, the Netherlands. She studied biochemistry and molecular biology at the Moscow State University and obtained her PhD at the University of Nijmegen, the Netherlands. Akhmanova studies cytoskeletal organization and trafficking processes, which contribute to cell polarization, differentiation, vertebrate development and human disease. The main focus of the work in her group is the microtubule cytoskeleton. Research in the group relies on combining high-resolution live cell imaging and quantitative analysis of cytoskeletal dynamics with in vitro reconstitution experiments. Her work has resulted in identification and characterization of a broad variety of factors which control microtubule organization and dynamics and motor attachment to membrane organelles. Anna Akhmanova is an elected member of the European Molecular Biology Organization and the Royal Netherlands Academy of Arts and Sciences.

Tarun Kapoor
Examining how nanometer-sized proteins assemble dynamic micron-sized structures needed for successful cell division
Dr. Kapoor graduated with honors from the California Institute of Technology with bachelor's degrees in chemistry and biology in 1993. He received both his M.S. in 1994 and Ph.D. in 1998 in chemistry from Harvard University and did his postdoctoral research at the Harvard Medical School. In 2001 he began his career at The Rockefeller University as an Assistant Professor and Head of the Laboratory of Chemistry and Cell Biology. He was named Associate Professor in 2005 and in 2008 became the Pels Family Professor. In 2012 he also became the Associate Director of The Tri-Institutional Program in Chemical Biology and Program Director of the Training Grant (T32): Mechanisms of Cell Regulation and Transformation. In 2016 he was appointed Director of the Pels Family Center for Biochemistry and Structural Biology and Head of the Selma and Lawrence Rubin laboratory of Chemistry and Cell Biology.
Dr. Kapoor has applied multi-disciplinary approaches to decipher fundamental cellular mechanisms, focusing on cell division and cancer. He received the 2012 Irving Sigal Young Investigator Award from The Protein Society and the Leukemia and Lymphoma Society Scholar Award in 2008. He was an Irma T. Hirschl/Monique Weill-Caulier Trust Scholar from 2004-2009 and a Pew Scholar in the Biomedical Sciences from 2002-2006.
Dr. Kapoor is an Editorial Board Member of Cell, Cell Reports, Developmental Cell and Chemistry and Biology; and a member of the Review Boards of the Damon Runyon-Rachleff Innovation Award and Pew Biomedical Scholar Award. Dr. Kapoor has published 75 papers and 18 reviews.

Session 3 09:00 – 10:30
Newly Tractable Systems

Eamonn Mallon
The power behind the throne: epigenetics in social insects
Eamonn carried out his undergraduate studies in Zoology at Trinity College, Dublin. He studied for a PhD in ant colony self organisation with Professor Nigel Franks at the University of Bath. A move to Switzerland and bumblebees followed, where he worker with Professor Paul Schmid-Hempel at the ETH Zurich. At the ETH, Eamonn studied the role of immunity in pollinator behaviour. This continued when he started his research group at the University of Leicester. His current research involves studying epigenetic factors in social insects, specifically establishing the bumblebee, Bombus terrestris, as a model for methylation.

Mike Goodisman
DNA Methylation in Social Insects
Dr. Michael A. D. Goodisman is Associate Professor and Associate Chair in the School of Biological Sciences at Georgia Tech in Atlanta, USA. He received his BA from Cornell University in Genetics & Development and conducted postdoctoral research as an NSF fellow in insect genetics at James Cook University and as an NIH fellow in insect genomics at the University of Arizona. Dr. Goodisman's research focuses on understanding the causes and consequences of sociality. Increases in biological complexity resulted from major evolutionary transitions that altered how biological information was stored and transmitted. One of the most recent major evolutionary transitions occurred when solitary organisms came together to form social groups. Dr. Goodisman's research program explores the causes and consequences of sociality. His primary research subjects are the social insects, which include ants, termites, social bees, and social wasps. Social insects 'are among the greatest achievements of organic evolution' because they display extreme cooperative and helping behaviors. Thus social insects represent key models for understanding advanced social behavior. Dr. Goodisman's research program has four foci. First, he investigates how social behavior affects patterns of molecular evolution. Second, he studies epigenetic inheritance in social insects. Third, he investigates the ecology of social animals using molecular techniques. And finally, he collaborates to study the physics of social insect interactions. Together, this research program helps advance our understanding of the evolutionary, ecological, and molecular processes underlying sociality

11:00 – 12:30
Mechanisms in Gene Expression

Axel Visel
Distant-Acting Enhancers in Development, Disease, and Evolution
Dr. Visel received his Ph.D. in 2004 from the Max Planck Institute in Hanover, Germany, where he developed novel tools for large-scale in situ gene expression analysis in multicellular organisms. During his postdoctoral training at Lawrence Berkeley National Laboratory, he developed and applied novel computational and experimental sequence-based methods for elucidating the gene regulatory landscape of vertebrate genomes, which led to the discovery of thousands of genetic switches implicated in developmental and disease processes in the human genome. In addition to his position as a Senior Staff Scientist at Lawrence Berkeley National Laboratory Dr. Visel is currently serving as Interim Director of the Joint Genome Institute where he is also the Deputy for Science Programs, focusing on the development and implementation of strategic initiatives at the JGI and overseeing the scientific directions and administration of the JGI User Programs. Dr. Visel also hold an appointment as an Associate Adjunct Professor at the School of Natural Sciences at the University of California, Merced.

Rebecca Oakey
Transcription of intragenic CpG islands and their associated epigenetic marks as regulators of tissue- and developmental-stage specific transcription of related host genes
Rebecca completed her DPhil in the Department of Biochemistry at the University of Oxford with Chris Tyler-Smith. She undertook her post-doctoral training and first faculty post in the USA and in 2002 moved to King's College London. Rebecca's research interests have centred around identifying novel imprinted genes and understanding the epigenetic mechanisms involved in their regulation. She is currently interested in the mechanisms involved in tissue-specific gene regulation, and she utilises a family of intron-less imprinted retrogenes as models to study this. Her interest in epigenetics extends to finding out how endocardial cells in the developing heart are directed to form values through the use of genome-wide sequencing technologies and techniques for assaying genomic architecture. Identifying essential factors in endocardial cell specification contributes towards efforts to understand biological repair and regeneration.

Beddington Medal Lecture 17:15 – 17:45

Erik Clark
The evolution and development of Drosophila segment patterning
Erik studied Biological Sciences at the University of Oxford, followed by a MSc in Bioinformatics and Theoretical Systems Biology at Imperial College London. He then moved to the Department of Zoology at the University of Cambridge, to work with Michael Akam in the Laboratory for Development and Evolution. He completed his PhD, on the Drosophila pair-rule system, in 2016. Erik is now continuing to research arthropod segmentation as a post-doc in the Akam lab, and will soon take up a Junior Research Fellowship from Trinity College, Cambridge.

Women in Cell Biology Medal Lecture 17:30 – 18:00

Victoria Sanz Moreno
Connecting actomyosin dynamics to transcriptional responses for efficient cancer cell migration and invasion
Victoria holds a BSc in Chemistry from the Faculty of Chemistry and an MSc in Biochemistry from the Faculty of Medicine (Oviedo University, Spain).
During her PhD, Victoria focused on studying signalling pathways regulating cancer cell proliferation in Cantabria University (Spain). She was awarded a University of Cantabria Scholarship and a Lady Tata Memorial Trust Fellowship.
She did her postdoctoral training at the Institute of Cancer Research (London, UK), where she was supported by a Cancer Research UK and Marie Curie Intra European Fellowships. For her postdoctoral work, she received the European Association for Cancer Research 40th Anniversary Research Award in her effort to understand Rho GTPase signalling in different modes of cancer cell migration.
Victoria Sanz-Moreno is currently a group leader at the Randall Division of Cell and Molecular Biophysics, King's College London. As an independent researcher, Victoria was awarded a Cancer Research UK Career Development Fellowship and The Royal Society University Research Fellowship (which she

declined to accept Cancer Research UK). More recently and for her work communicating science to the public through media, she was highly commended by Cancer Research UK Communications and Brand Ambassador Research Engagement Prizes.
Victoria's group investigates molecular mechanisms involved in the regulation of cancer cell migration and its connections to the transcriptional machinery. Victoria's group has discovered how signalling pathways regulated by the cytoskeleton crosstalk with transcription factors to sustain cell migration during cancer metastatic dissemination.

Cheryll Tickle Medal Lecture 18:15 – 19:00

Jenny Nichols
Jennifer Nichols began her research career in early mammalian development with Richard Gardner at the University of Oxford. She then joined Austin Smith for a long and fruitful collaboration to develop strategies for efficient derivation of embryonic stem cells from murine embryos. She is now a group leader at the Wellcome Trust-Medical Research Council Cambridge Stem Cell Institute and the department of Physiology, Development and Neuroscience. Her group is interested in early mammalian development, in particular, how lineage decisions are made and how the embryo accommodates fluctuations in environment, signals and cell number to produce a foetus. The establishment of a population of cells that must be protected from inappropriate differentiation, whilst retaining the capacity to respond to instructive cues in a timely manner is the main focus. To this end, her group studies genes associated with epiblast specification, embryonic stem cell derivation and maintenance, mainly using genetic deletion, expression analysis and chimaeras.

Wednesday 5 April 2017

Session 4 09:30 – 11:00
Mechanisms in Gene Expression

Joan Barau
The novel de novo DNA methyltransferase DNMT3C protects male fertility against transposon activity
Joan Barau was born in 1981, Rio de Janeiro, Brazil. He was awarded a bachelor degree in Biological Sciences (2006), followed by a PhD in Molecular Biology (2012), both at the Unicamp university located in the São Paulo state, Brazil. During his PhD he became interested in the biology of transposable elements and their impact on the evolution and regulation of eukaryotic genomes. He moved to Paris, France in 2013 to join the laboratory of Deborah Bourc'his at the Institut Curie as a postdoctoral researcher. There he combined state of the art molecular biology and mouse genetics to make recent contributions to the understanding of the relationship between the epigenetic regulation of transposable elements and the development of the male germline in mammals.

Myriam Hemberger
The critical role of the placenta for normal development
Myriam Hemberger trained at the University of Freiburg and Max-Planck Institute for Molecular Genetics, Berlin, Germany, (PhD) and as postdoctoral fellow in Dr. Jay Cross' lab at the Samuel Lunenfeld Research Institute in Toronto and at the University of Calgary, Canada. Since 2004 she has been group leader at the Babraham Institute in Cambridge, UK, first as MRC Career Development Fellow and since 2009 on a tenured position as part of Babraham's Epigenetics Programme. Her research interests are on molecular mechanisms of the genetic – epigenetic crosstalk that ensures formation of a functional placenta. In 2007 she was awarded the IFPA Award in Placentology for her contributions to the field.
Her current research focuses on early developmental processes that lead to normal placentation and consequently a healthy reproductive outcome. Of particular interest is the regulation of trophoblast stem cells by signalling pathways, transcriptional networks and epigenomic hallmarks. Insights from these studies are being translated to study physiological and environmental influences on the trophoblast's differentiation potential and resulting pregnancy defects.

Session 4 09:30 – 11:00
Cell Competition

Elizabeth Murchison
Two transmissible cancers in Tasmanian devils
Elizabeth Murchison is Reader in Comparative Oncology and Genetics at the University of Cambridge, Department of Veterinary Medicine. Her laboratory, the Transmissible Cancer Group, studies the genetics, evolution and host interactions of clonally transmissible cancers in dogs and Tasmanian devils.
Elizabeth grew up in Tasmania and performed her undergraduate studies in genetics and biochemistry at the University of Melbourne. She subsequently joined the graduate programme at Cold Spring Harbor Laboratory, New York, and was awarded her PhD there in 2007. After a period at the Australian National University, in 2009 she was awarded an Australian government postdoctoral fellowship to join the Cancer Genome Project at the Wellcome Trust Sanger Institute. At Sanger, she was involved in sequencing the genome of the Tasmanian devil and its transmissible cancer. She started her laboratory at the University of Cambridge in 2013, and in 2014 she was awarded a Wellcome Trust Investigator Award to support her research.
Elizabeth was the recipient of the 2014 Genetics Society Balfour Prize Lecture and the 2014 Cancer Research UK Future Leaders in Cancer Research award. She was a recipient of a 2014 Philip Leverhulme Prize, awarded by the Leverhulme Trust, and in 2016 she received an honourable mention in the Genetics Society of America Rosalind Franklin Young Investigator Awards. Elizabeth is a keen science communicator, and in 2011 she delivered a TED talk entitled "Fighting a Contagious Cancer" which has been translated into 29 languages and viewed by a global audience more than 480,000 times.

Laura Johnston
Cell competition promotes bilateral symmetry through a Dilp8/Lgr3-dependent mechanism
Laura Johnston is Professor of Genetics & Development at Columbia University in New York. Her lab at Columbia University uses Drosophila to study the dynamics of tissue growth and size control in development, during regeneration and in models of cancer. The Johnston lab is particularly interested in the cooperative,

competitive and homeostatic processes by which cells sense and respond to growth changes in their local environment. Laura serves on the Editorial Advisory Board for the journal Development, and currently serves as the President of the US National Drosophila Research Board of Directors.

Session 4 09:30 – 11:00
Cell Division and Genome Stability

Iain Cheeseman
Generating a dynamic kinetochore-microtubule interface
Iain Cheeseman is a Member of Whitehead Institute and Associate Professor of Biology at MIT. He did his graduate work with David Drubin and Georjana Barnes at UC Berkeley and conducted his post-doctoral work with Arshad Desai at the Ludwig Institute for Cancer Research/UCSD. The Cheese lab focuses on the mechanisms of chromosome segregation and cell division in human cells using a combination of proteomics, biochemistry, and cell biology. In particular, they are excited about understanding kinetochore composition, structure, organization, and function. Mostly, Iain is a big nerd who thinks that science and kinetochores in particular are frigging cool. He also has two amazing daughters, who kept him honest and occasionally laugh at his dad jokes.

Uli Gruneberg
Regulation of the spindle assembly checkpoint by mitotic phosphatases
Ulrike Gruneberg trained initially as an immunologist in the lab of John Trowdale at the Cancer Research UK London Institute, investigating antigen presentation via MHC class II molecules.
After obtaining her PhD she decided to change research direction and pursue her interest in basic cell biology and cell division, first in Elmar Schiebel's lab at the Beatson Institute for Cancer Research in Glasgow and then in the Department of Erich Nigg at the Max-Planck Institute of Biochemistry in Munich. At the Max-Planck Institute Ulli analysed the mechanisms of cytokinesis in mammalian cells and in particular the role of the chromosomal passenger complex in this process.
In 2007, supported by a Cancer Research UK Career Development Award, Ulli set up her own lab at the University of Liverpool with the goal of understanding the role of phosphatases in the regulation of chromosome segregation. One outcome of her lab's research was the identification of the conserved PP2A-family phosphatase PP6 as a key regulator of bipolar spindle formation in mammalian cells. In 2011 Ulli's lab moved to the University of Oxford, initially to the Department of Biochemistry and in 2013 to the Dunn School of Pathology where she is now an Associate Professor and holds an MRC Senior Research Fellowship. Ulli's current research is focused on the regulation of mammalian chromosome segregation by kinases and phosphatases.

Plenary Session 11:30 – 12:30

Xiaowei Zhuang
Illuminating biology at the nanoscale and systems scale using single-molecule and super-resolution imaging
Xiaowei Zhuang is the David B. Arnold Professor of Science and the director of Center for Advanced Imaging at Harvard University. She is an investigator of Howard Hughes Medical Institute. Her lab develops advanced optical imaging techniques, in particular single-molecule and super-resolution imaging methods, and applies these methods for biological studies. In particular, she invented STORM, one of the first single-molecule-based super-resolution imaging methods, and discovered novel cellular structures using STORM. She invented a single-cell transcriptome imaging method, MERFISH. Her lab has also developed and applied single-molecule approaches to investigate the dynamics and function of biomolecules.
Zhuang received her B.S. degree from the University of Science and Technology of China, her Ph.D. degree from the University of California at Berkeley, and her postdoctoral training at Stanford University. She joined Harvard University as an assistant professor in 2001, and was promoted to full professor in 2006. In 2005, Zhuang joined the Howard Hughes Medical Institute as an investigator.
Zhuang is a member of the US National Academy of Sciences and the American Academy of Arts and Sciences, a foreign member of the Chinese Academy of Sciences and the EMBO, a fellow of the American Association of the Advancement of Science and the American Physical Society, and an honorary fellow of the Royal Microscopical Society. Among her awards are the MacArthur Fellowship, the Pure Chemistry Award, the Max Delbrück Prize in Biological Physics, the Raymond and Beverly Sackler International Prize in Biophysics, and the National Academy of Sciences Award in Molecular Biology.

CAREER WORKSHOP BIOGRAPHIES

Dr Aidan Maartens
Community Manager and Online Editor for The Node
Aidan manages the Node, the community site for developmental biologists hosted by the journal Development, for whom he is also an online editor, helping with social media and some front section content. They are based in The Company of Biologists offices in Histon, Cambridge, and he came into the job from a postdoc. Running the Node involves commissioning, writing and editing pieces, as well as some basic web management, and a lot of social media. Aidan also goes to a lot of conferences, and film and edit videos.

Dr Georgina MacKenzie
Science Portfolio Adviser, Neuroscience and Mental Health
Georgina completed her PhD in Neuroscience at Imperial College London in 2011 before moving to Tufts University in Boston where her postdoctoral research focused on the mechanisms underlying stress exacerbated epilepsy. In 2015, she worked within the Neuroscience and Pain Research Unit at Pfizer as a postdoctoral fellow before joining Wellcome as a Science Portfolio Advisor in 2016. Science Portfolio Advisors contribute to the management of Wellcome's research portfolio and contribute to the assessment, development and implementation of new strategic activities and partnerships. An important part of the role is liaising with researchers and providing scientific advice on grant and fellowship proposals.

Mark Abthorpe
Patent Attorney
Mark joined Carpmaels & Ransford LLP as a trainee patent attorney in autumn 2005, having studied Natural Sciences at the University of Cambridge, where he specialised in chemistry with materials science. He qualified as a European patent attorney in 2009 and a chartered patent attorney in 2010. Nowadays, he works for a wide range of clients – from individuals, universities and SMEs to multinationals – on an even wider range of subject matter, including contact lenses, absorbent articles, small-molecule pharmaceuticals, industrial-scale polymer synthesis, and diagnostic devices. He spends most of his time in the office in London, but his work also takes him to science and technology parks in the UK, the east coast of the USA and the European Patent Office in The Hague and Munich, where he represents his clients at hearings before the Examining and Opposition Divisions and Boards of Appeal.

Dr Alicia Greated
Director of Research and Enterprise, Heriot-Watt University.
Prior to that, Alicia led the Newton Fund (a £735 million research and innovation fund to enhance the UK's engagement with global emerging economies) delivery team at the UK's Department of Business, Innovation and Skills (BIS – now BEIS).
In 2008, Alicia moved to Delhi, India where she was founder and Director of Research Council UK (RCUK) India at the British High Commission. After four years in India, she moved to Beijing to become Director RCUK China at the British Embassy in Beijing.
Alicia has worked as acting Director of Research for the Arts and Humanities Research Council, and Head of Engineering at the Engineering and Physical Sciences Research Council. Alicia has a PhD in Molecular Genetics.

Dr Joanna Huddleston
Civil Service
Following her PhD in Cancer Genetics working at the Cancer Research UK Cambridge Institute, Joanna joined the Civil Service through the fast stream graduate recruitment process.
She has had a number of roles in the Civil Service in Business Energy and Industrial Strategy (formally BIS) and the Intellectual Property Office. She has worked on a range of policy areas including STEM engagement, migration policy, text and data mining and copyright policy with relation to the Digital Single Market. My current role is focused on European Research Policy.
Post PhD and prior to working in the Civil Service, Joanna also worked as an Assistant Editor on Nature Reviews Molecular Cell Biology and Nature Reviews Microbiology.

Ben Steventon
Sir Henry Dale Fellow
Ben began mhis studies in Developmental Biology as a PhD student with Roberto Mayor at UCL in 2004. After graduating in 2008 he moved to KCL to work with Andrea Streit. During this time he was interested in the mechanisms that pattern and orchestrate cell fate decisions and movements of the early embryonic ectoderm. Subsequently Ben moved to the lab of Jean-Francois Nicolas and Estelle Hirsinger at the Institut Pasteur, Paris. Here, he began to work with zebrafish embryos in order to get a complete understanding of the tissue deformations that lead to the elongation of the embryonic body axis. In order to develop imaging and analytical techniques to study this process at the cellular and molecular levels, Ben was awarded a Marie-Curie fellowship to work with Scott Fraser (University of California, USA) and Alfonso Martinez-Arias (University of Cambridge). With his Sir Henry Dale fellowship, he is now applying these techniques to investigate how cell fate decisions are orchestrated in space and time during axis patterning in zebrafish embryos. While zebrafish perform this with little overall growth in embryo size, higher vertebrates like mammals undergo a large degree of growth. Ben is interested in how such fundamental differences in embryo size, cell number and energy supply have influenced the interpretation of conserved regulatory networks and patterning mechanisms by individual cells. What are the limits of adaptability and developmental constraint that are encoded within developmental systems during vertebrate evolution?

Dr Kathryn Woodfine
Field Applications Specialist for Agilent Technologies
Kat did a PhD in Molecular Genetics at the Wellcome Trust Sanger Institute during which she worked on the Human Genome Project and was an early adopter of array CGH for chromosomal and epigenetic studies. She then did two postdocs, both looking at Genomic Imprinting at Kings College London and The CRUK Cambridge Research Institute.
Kat then moved to the commercial world as a Field Applications Specialist for Roche Sequencing Solutions. This involved advising and training academic and clinical customers on next generation sequencing workflows. She then progressed to become a Technical Sales Specialist for Roche Molecular Systems working to implement new laboratory developed molecular tests. However, her love of genomics took me back to become a Field Applications Specialist for Agilent Technologies where she enjoys discussing cutting edge science with customers.

Dr Victoria Sanz-Moreno PhD
Cancer Research UK Career Development Fellow/ Head of the Tumour Plasticity Lab, King's College London
Vicky received her first degree in chemistry and later a master's degree in biochemistry from the University of Oviedo in Spain, followed by a PhD in chemical sciences in the laboratory of Piero Crespo at the University of Cantabria, awarded in 2002. After a short postdoc in the same lab with a Lady Tata Memorial Trust Fellowship, she moved to the Institute of Cancer Research in London as a CRUK and Marie Curie Intra-european Fellow with Chris Marshall. In 2008, she received the Applied Biosystems and EACR 40th Anniversary Research Award. In 2011, Vicky started her independent research group with a CRUK Career Development Fellowship at King's College London in the Randall Division of cell and molecular biophysics. In 2015, she was highly commended by CRUK Communications and Brand Ambassador Prizes for communicating science to the public through media. Vicky has been awarded the 2017 BSCB Women in Cell Biology Early Career Award Medal. Her group is interested in the actomyosin cytoskeleton and in transcription factors, and how the crosstalk between the two influences invasive and metastatic behaviour in cancer cells.

Dr Hayley McCulloch
Science teacher, Chesterton Community College
Before moving to Chesterton Community college, Cambridgeshire, Hayley completed her PhD in the lab of Professor Andrew Hudson at the University of Edinburgh. She discovered novel allelic variation in natural accessions of Arabadopsis thaliana during a study of local variation in flowering time. She then went on to a post-doctoral researcher position with Professor Ottoline Leyser at the Sainsbury Laboratory, University of Cambridge, where she studied the evolutionary genetics of plants.

Dr Ann LeGood
Senior Editor, Nature Communications
Ann started a career in Publishing by joining the first Open Access Publisher, BioMed Central, as an Assistant Editor in 2006. She worked on several journals both in the areas of biology and medicine (including BMC Developmental Biology, BMC Cell Biology, BMC Cancer and BMC Gastroenterology), learning how to be an Editor and overseeing peer review of manuscripts, and later, to managing a team of Editors, becoming Deputy Editor for the BMC series biology journals. In this role, she provided guidance and training to Editors on the ethics of publishing and resolving difficult editorial decisions. Four years later, she joined the team of BMC Biology, the flagship biology journal of BioMed Central, covering the areas of molecular cell and developmental biology. This role included commissioning Review, Forum and Opinion articles for the journal and launching journal series, ranging in topics from stem cells and cell geometry to quantitative biology. She is currently a Senior Editor at Nature Communications (since March 2015) covering the areas of stem cell, developmental biology and regeneration. Before becoming an Editor, after studying Biochemistry at the University of Oxford, Ann obtained a PhD at the Imperial Cancer Research Fund on how atypical PKCs (aPKC) are regulated, and then examined how aPKCs cause tumorigenesis in postdoctoral work at the University of Alberta. She subsequently studied the role of Nodal in early mouse development at the Swiss Institute for Experimental Cancer Research.

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