2002 (#42, 43, 44, 45)

Evolution & Development **Spring 2002**

Joint with Genetical Society **University of York**

The BSDB/Genetics Society Spring Meeting

University of York, 20-23rd March 2002

The Evolution of Developmental Mechanisms

In the past 15 years, the interface between developmental biology and evolution has re-emerged as an exciting and productive area of research. The topic has received an added impetus as complete, or near complete, genomes have been acquired for a diversity of organisms. The spring 2002 symposium, organised jointly by The Genetics Society and BSDB, will focus at the interface between development, evolution and genomics. The partnership between GenSoc and BSDB means that we have been able to invite a wide range of speakers from Europe, USA and Japan, and we can look forward to a high quality and very timely symposium. It is hoped that several contributed talks can also be included in the program, selected from submitted abstracts. Posters describing research on all areas of the subject are encouraged.

The meeting will focus on four themes that lie at the core of this subject, yet that have been under-represented at similar meetings in the past. These are (together with speakers confirmed to date):

(1) Microevolution of development
David Kingsley (Stanford), John Doebley (Madison), Paul Brakefield (Leiden), Enrico Coen (Norwich), Michael Akam (Cambridge), Susan Lindquist (Chicago), David Stern (Princeton).

(2) Genomes and evolution
Nori Satoh (Kyoto), John Postlethwait (Eugene), Jonathan Hodgkin (Oxford), Paul Nurse (London), Virginia Walbot (Stanford), Peter Holland (Reading).

(3) Molecular mechanisms of phenotypic evolution
Vivian Irish (Yale), Jane Langdale (Oxford), Mike Levine (Berkeley), Denis Duboule (Geneva), Sean Carroll (Madison), Richard Lenski (Michigan).

(4) Life histories and life cycles
Mark Martindale (Hawaii), James Truman (Seattle), Linda Partridge (London), Detlev Arendt (Heidelberg), Simon Conway Morris (Cambridge), David Gems (London)

A discussion session on Phylogenetic Methods and Applications will also take place, involving Sandra Baldauf (York) and several other speakers.

The Balfour Lecture for 2002 will be given by Adam Eyre-Walker (University of Sussex).

Organisers: Peter Holland, Enrico Coen, Michael Akam, Paul Nurse, Vivian Irish, Jane Langdale, Jayne Richards

BSDB Spring Meeting 2002

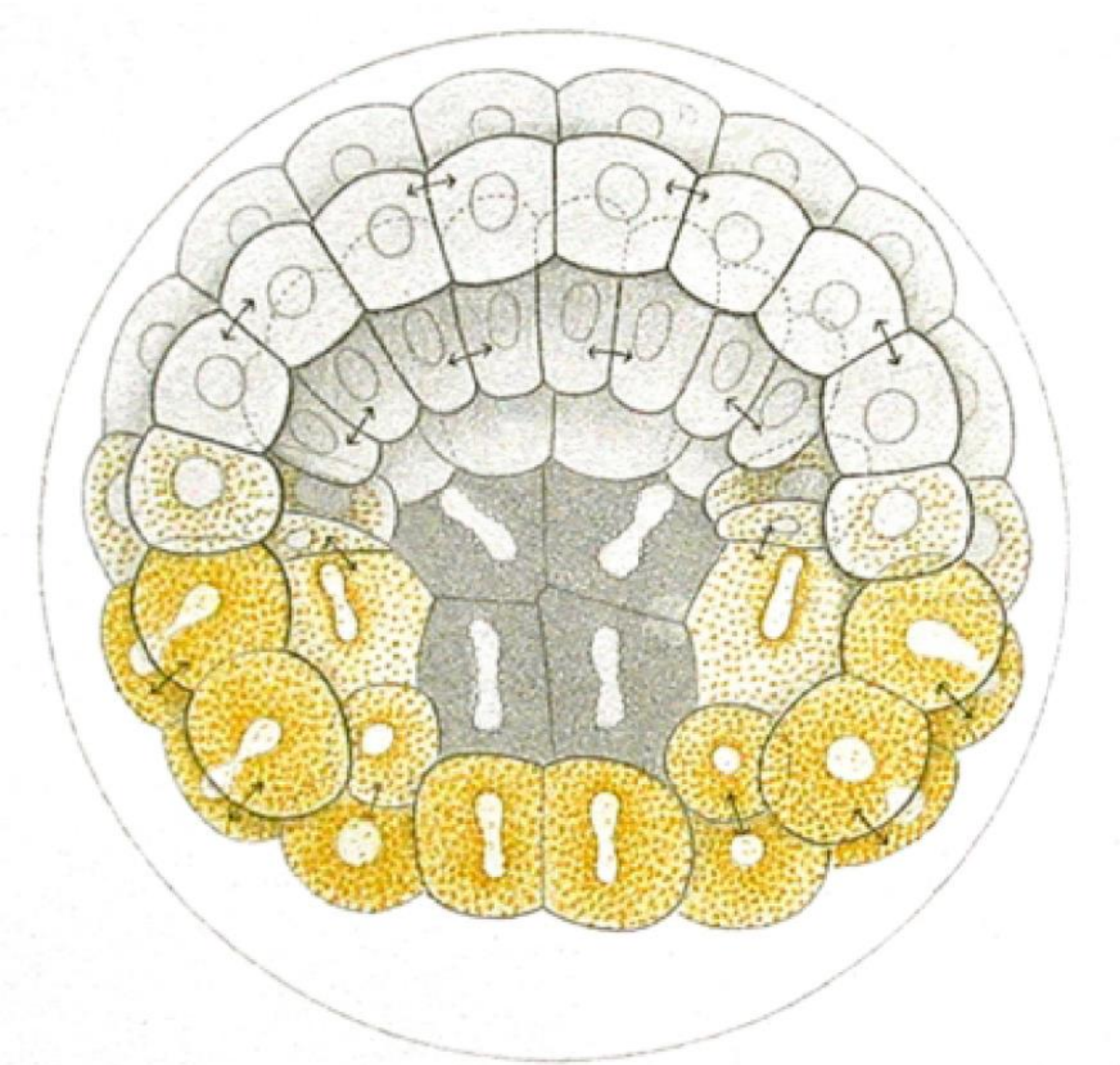
Evolution of Developmental Mechanisms

York, 20th – 23rd March

See pages 8 & 9 for details. Registration and Abstract Submission will be online:

www.ana.ed.ac.uk/BSDB/
or
www.bscb.org

Registration and Abstract Deadline 18th January, 2002



Evolution of Developmental Mechanisms

Spring Meeting 2002

Cover Legend: an ascidian embryo drawn by Conklin and from E G Conklin (1905) "The organisation and cell lineage of the ascidian egg." J Acad Nat Sci, Philadelphia ser 2, 13:1-119. Reproduced with permission of the Academy of Natural Sciences of Philadelphia

BSDB/ Genetics Society/ BSCB Joint Spring Meeting

EVOLUTION OF DEVELOPMENTAL MECHANISMS

University of York, Wednesday 20th – Saturday 23rd March, 2002

Scientific Organizers:
Peter Holland (Chair), Michael Akam, Enrico Coen, Paul Nurse, Vivian Irish, Jayne Richards, Jane Langdale

In the past 15 years, the interface between developmental biology and evolution has re-emerged as an exciting and productive area of research. The topic has received an added impetus as complete or near complete genomes have been acquired for a diversity of organisms. The spring 2002 symposium, organised jointly by The Genetics Society and BSDB, will focus at the interface between development, evolution and genomics. The partnership between GenSoc and BSDB means that we have been able to invite a wide range of speakers from Europe, USA and Japan, and we can look forward to a high quality and very timely symposium. It is hoped that several contributed talks can also be included in the program selected from submitted abstracts. Posters describing research on all areas of the subject are encouraged.

Provisional Programme

Wednesday 20th

Registration
GS/BSCB Committee meetings
Drinks reception
Dinner

Abstract/Registration Deadline 18th January, 2002

Thursday 21st

9-9.50	**BSCB Plenary**
10-10.50	**Genomes, Evolution and Development** *Chair:* ***Peter Holland*** **Jonathan Hodgkin**: Lessons from insect and nematode genomes **Nori Satoh**: The ascidian genome project
10.50-11.20	Coffee
11.20-12.35	**Paul Nurse**: Fission yeast genome a nd development **Virginia Walbot**: Plant genome evolution **John Postlethwait**: Chordate genome evolution
12.35-2	Lunch and Posters
2-2.45	**Balfour Lecture** **Adam Eyre-Walker**
3-3.50	**Evolution of gene regulation** *Chair:* ***Paul Nurse*** **Denis Duboule**: Hox gene regulation **Mike Levine**: Evolution of gene networks
3.50-4.30	Tea/Posters
4.30-6.30	**Parallel a: Promega Young Life Scientist of the Year** **Parallel b: Workshop on Molecular Phylogeny** Sandra Baldauf, Peter Holland et al
7.30-11.00	Drinks reception and banquet dinner at Railway Museum Announcement of Promega winner

PhD students (& Supervisors) Don't miss the Graduate Student of the Year Award announcement See page 4

Friday 22nd

9-10.40 **Microevolution of development**
Chair: ***Enrico Coen***
Paul Brakefield: Butterfly wing spots: evolution, ecology and development
David Stern: Microevolution of Drosophila morphology
John Doebley: Microevolution of maize morphology
David Kingsley: Sticklebacks as a model for evolution of development

10.40-11.20 Coffee

11.20-12.30 **Susan Lindquist**: hsp90 and evolutionary capacitors
Richard Lenski: Experimental evolution in a test-tube
Contributed talk

12.30-2 Lunch and Posters

2-3.30 **Evolution of pattern and form**
Co-chairs: ***Vivian Irish/Jane Langdale***
Enrico Coen: Flower development and evolution
Vivian Irish: Comparative analysis of flower development genes
Sean Carroll: Evolution of animal body plans
Contributed talk

3.30-4.15 Tea and Posters

4.15-5.15 **Jane Langdale**: Leaf origins and evolution
Michael Akam: Evolution of arthropod body plans

5.30–6.30 **Waddington Medal Lecture**

6.30-7 BSDB and GenSoc **AGMs**

7.00 Dinner

PhDs, Post-docs

We would like a couple of volunteers to write reviews of the Spring Meeting. To encourage you, we are offering **£50** upon publication. Interested? Contact Andy Furley: a.j.furley@sheffield.ac.uk

Saturday 23rd

9-10.30 **Larvae and life cycles**
Chair: ***Michael Akam***
Linda Partridge: Evolution of size, life history and reproductive traits
Simon Conway Morris: Body plans in the Cambrian
Mark Martindale: Diversity of metazoan embryos larvae
Contributed talk

10.30 – 11.10 Coffee

11.10-12.30 **James Truman**: Insect metamorphosis
David Gems: Genes, ageing and longevity in nematodes
Detlev Arendt: The ancestor of bilaterians

12.30-2 Lunch and depart

For the latest details and for registration information see the BSDB or BSCB websites*:
BSDB: http://www.ana.ed.ac.uk/BSDB/ BSCB: http://www.bscb.org

* If web access not available, contact Victoria Milner, Procon Conferences Ltd, Ashbourne House, 2 South Park Road, Harrogate, North Yorkshire, HG1 5QU, United Kingdom. Tel: +44 (0)1423 564488 Fax: +44 (0)1423 701433

Sci-Art at the BSDB Spring meeting 2002 in York

The BSDB Committee is supporting the creation of a small science-art exhibition which will run throughout the annual spring meeting in March 2002 at the University of York. This is a novel and exciting venture, with serious intentions, though to some it will seem a surprise item and to others perhaps even a travesty of science. But what is the idea?

The term sci-art embraces a broad field of artistic endeavour in which the theme, the inspiration or starting point for the artist's work comes from within science. Some sci-art is the outcome of long-term collaboration between, and discussion within, a partnership formed between a practising artist and scientist. Other artwork may have been prompted by ideas coming to an artist from science but 'at arm's length' from the science, perhaps via the media. Yet other pieces may have been commissioned from within the world of science, specifically to illustrate and publicise a scientific idea or event, and in this sense are rather closer to the outcome of a graphic design brief or the commissioning of art. This spectrum of origins and inputs means that some sci-art may pursue and explore the conceptual ideas of

York on the Run

This year's Spring Symposium was again a resounding success, marred only by the outbreak of food poisoning which seems to have afflicted a large number of delegates following the meal on Friday evening. This unfortunate occurrence was reported to York City Council's Environmental Health Department. Despite going to some length to contact delegates and collect samples for analysis, the Department was unable to identify the cause of the infection, a failure they attributed to the length of time that elapsed before samples could be obtained due to the intervening Bank Holiday. I expect this is one Bank Holiday that many of you will want to forget! I can only say how sorry I was to hear about your discomfort – luckily for me the scheduling of the Committee meeting on Friday evening meant I escaped exposure to the contaminated food!

In any event the scientific organisers of the meeting can clearly be exonerated from any blame for the quality of the catering and are to be congratulated for putting together such an excellent programme. The interaction with the Genetics Society was so positive that we have

Art for Art's Sake

Another successful component of the York meeting was the Sci-Art exhibition staged by **Paul Martin**, **Jenny Whiting**, **Kate Storey** and **Robert Whittle**. This fascinating collection of paintings, high fashion and installation art attracted large numbers of visitors both from amongst the conference delegates and the local community, with visits from several schools. It is very pleasing that the exhibition connected with the general public in this way – but should we always have to portray science as art to make it so accessible? A recent survey of television viewing preferences revealed– somewhat surprisingly – that there is a great appetite for science amongst the general population, with respondents expressing a preference for science and natural history programmes over game shows and soap operas. This should remind us, if we need reminding, that the pursuit of scientific knowledge for its own sake has an intrinsic value for the intellectual vitality of the nation. If the public are prepared to put their hands in their pockets to support the arts or sport, why then should they not be persuaded to support science in a similar way? It's a sobering thought that the gate receipts from a single Premiership football match in England would fund two five year Programme grants, the results of which could probably form the basis of a TV documentary that could entertain millions. We should resist the pressure always to justify our research in terms of its medical or commercial applications. To paraphrase my favourite philosopher: science isn't just a matter of life and death – it's much more important than that!

Phil Ingham

Spring Meeting Reports

Evolution of Developmental Mechanisms was the subject of the 2002 BSDB Spring meeting, held jointly with the Genetical Society in York. It was a cracker. The meeting was packed (with a waiting list of late registrants) and had a constant lively buzz about it.

The diversity of subject matter covered during the meeting gave a real sense of the variety of topics encompassed by Evo-Devo, and the vibrancy of the field. During the course of the two and a half days we were treated to choice samples of genomics and genome evolution, gene regulation, phylogenetics, palaeontology, and evolution of development and developmental mechanisms, in organisms as diverse as bacteria and humans.

The fact that we are in the "post-genomic" era shaped the first morning of talks. It is clear though that from a comparative point of view we are actually still in a genomic era. The sequencing of more genomes from organisms around the select few is greatly improving our understanding of those select genomes, as well as showing us how genomes are organised, how they evolve and how there is a surprising amount of diversity amongst them. Nematodes and flies have altered the relative abundances of different gene families, to suit their different needs (Jonathan Hodgkin), and the two yeasts Saccharomyces cerevisiae and Schizosaccharomyces pombe, despite their superficially similar appearances (ie. they are both yeasts!), have hundreds of genes that are unique to one or other of them (Paul Nurse). A particularly impressive achievement is the Japanese Ciona intestinalis project (Nori Satoh). Not only is the genome sequenced, but there are thousands of ESTs for five different developmental stages, hundreds of which have already been analysed by embryonic in situ hybridisation. This huge amount of data is being rapidly placed into the public domain (http://ghost.zool.kyoto-u.ac.jp), greatly furthering the case for Ciona intestinalis as one of the model organisms of choice for developmental biology. Two of the selected talks (Clare Hudson and Jean-Philippe Chambon) actually dealt with brain development and tail regression in Ciona. The role of gene and genome duplication in evolution was also a prominent theme, in plants (Virginia Walbot), and chordates (John Postlethwait, Peter Holland and Georgia Panopoulou).

A workshop on Molecular Phylogenetics took place in the middle of the programme, and was both well attended and well received. The crash course on the basics and pitfalls (Sandra Baldauf) was appreciated by the many folk who simply put their sequences into Clustal or PAUP and hit 'Go'! It was also exciting to see that the Acoel flatworms are shaping up to be basal bilaterians much more robustly (Jaume Baguña), thus offering the hope that an even closer examination of these animals should bear fruit in understanding what was there when the bulk of the animals (the triploblast Bilateria) arose. What went before were the diploblasts (hydra, sea anemones, jellyfish and comb jellies). How the axes and cell layers of these basal animals relate to those of the Bilateria is a conundrum which is being clarified by some careful embryology and analysis of such genes as the Hox genes (Mark Martindale). The continued importance and pervasiveness of Hox genes within Evo-Devo was illustrated by their prominence at this meeting (Denis Duboule, Victoria Prince, Sean Carroll, Michael Akam). How morphologies have been pieced together during evolution, rather than how the molecular mechanisms have been assembled, is predominantly the realm of palaeontology (Simon Conway-Morris). It is clear that we need to keep the findings of palaeontology to the front of our minds when forming ideas about Evo-Devo, as no description or understanding of animal evolution is complete without it.

The interface between what could be viewed as the more traditional face of Evolutionary Biology (Microevolution at the population and species levels) and Developmental Biology, was well represented. We heard about the constraints, or rather their absence, on butterfly eyespots (Paul Brakefield), the evolution of 'naked' flies (David Stern), the domestication of maize (John Doebley), the impact of QTL analysis on the evolutionary development of the classic evolutionary model of the stickleback (David Kingsley), and the difficulty of building a genotype-phenotype map even in such an amenable system as bacteria (Paul Rainey), finishing off with nematode vulvas (M.L. Dichtel). Much food for thought.

Evolution not only effects morphology, but also life history. We were reminded of this by considerations of ageing (Linda Partridge and David Gems) and insect metamorphosis (James Truman). Returning to morphology however the benefits of the candidate gene approach, comparing homologous genes between taxa for which a phenotypic effect is established in more traditional model systems first, is having a significant impact in understanding the evolution of segmentation, particularly in insects (Sarbjit Lall), and the relationships between the eyes and brains of different bilaterians (Detlev Arendt). The approach is also bearing fruit in plants, in understanding the evolution of flower asymmetry (Enrico Coen), and flower and leaf form (Vivian Irish and Jane Langdale).

Other events included the award of the Waddington medal to Prof. Johnathan Slack, and an interesting new feature to BSDB meetings of a Sci-Art exhibition. This was excellent, and certainly stimulating. Unfortunately it was somewhat hidden away in a small side room. Perhaps if such exhibitions are to feature in future meetings a more prominent position might be sought, perhaps in an area where delegates cannot help but wander past. This would increase the number of folk who will have their senses prodded in a different and welcome way from the stimulation of the talks.

No review of the meeting would be complete without a mention of the incredibly virulent stomach bug that seems to have hit the majority of the conference within days of the departure from York, setting us up nicely for all of that Easter chocolate! Hopefully this particular feature of the meeting will never be repeated.

Dave Ferrier, Reading

This year's spring meeting was held at York University with the BSCB and the Genetical Society and included four keynote lectures. The conference opened with the BSCB Plenary Lecture by Hugh Pelham, who described a number of mechanisms cells utilize to sort different membrane proteins from the Endoplasmic Reticulum into different cellular compartments. The Gensoc Balfour lecture was given by Adam Eyre-Walker who discussed deleterious and adaptive mutations in the human genome; Andrea Brand gave the BSCB Hooke Medal Lecture and talked about asymmetric cell division in the Drosophila embryonic CNS and the BSDB Waddington Medal lecture was given by Jonathan

Spring Meeting Reports

Slack, who gave us an interesting overview of his career.

The BSDB talks focused on Evolution and Development. The first session included a number of genome analysis talks, starting with Jonathan Hodgkin comparing Caenorhabditis elegans and Drosophila and Paul Nurse summarizing the Fission yeast genome. We heard that nematodes have taken over the world: constituting 80% of all individual animals and 80% of all species; that the fission yeast (S. Pombe) genome is the smallest eukaryotic genome sequenced so far; and that 60% of identified human disease genes have homology to S. Pombe genes. Both speakers estimated that there are about 3000 genes that encode core eukaryotic functions. Despite the similarities between different organisms there are also some striking differences. For example C. elegans does not appear to have a Hh signalling pathway and it has only some components of the Toll signalling pathway. C. elegans also has about ten fold more putative nuclear hormone receptors and G protein coupled receptors than Drosophila, though Drosophila has twice as many C2H2 Zinc finger proteins as C. elegans.

Not surprisingly, a number of talks discussed Hox genes. Denis Duboule talked about the Hox D complex and its role in mouse limb development. His lab is undertaking a detailed analysis of the effects of mutating, deleting and duplicating individual genes in the Hox D complex. Their results suggest that a digit enhancer 180-250 KB upstream of this complex, acts in a position specific rather than promoter specific manner, so that the closer a gene is to the enhancer the higher is its level of transcription. In addition, reducing the distance between the Hoxd11 coding region and the enhancer, and hence increasing the levels of Hox d11 transcription, causes extra digits to form, suggesting that the chromosomal position of this gene is important in determining digit number.

Michael Akam discussed the complexities of Hox expression, function and evolution. Particularly striking was his description of how Drosophila Ubx represses bristle formation in different ways at different times in development. In one case Ubx represses the prepattern stage of bristle development, in another it acts just before the lateral inhibition step, and in yet another it represses bristle development after the parent stem cell has divided.

In the session on Microevolution of Development we heard how influential a previous BSDB Evolution and Development conference had been. Paul Brakefield described "jumping up and down" after Sean Carroll's talk at the 1994 Edinburgh meeting, and how this conference resulted in a great collaboration between himself, Sean Carroll, Vernon French and Antonia Monteiro investigating butterfly eyespot development. This year Brakefield showed that variation of eye spot size in the African Squinting Brown butterfly is not developmentally constrained, despite the fact that certain eye spot patterns are not normally seen.

A common theme emerging from a number of talks was the importance of evolutionary changes in cis-regulatory regions of transcription factors. David Stern told us how mutations in separable enhancers for Drosophila shaven baby/ovo have resulted in its function in bristle development evolving separately from its role in germ cell development. He also discussed results from Nipam Patel's lab, which show that there have been substantial genetic changes in the stripe 2 enhancer region of eve in different Drosophila species, but without changing its expression pattern, as assayed in Drosophila Melanogaster. Chimaeric analysis suggests that these enhancers have acquired complementary changes maintaining the original expression pattern of eve rather than evolving new expression patterns or levels. This raises the question of why some enhancer changes acquire compensatory changes while others cause phenotypic changes that evolution acts on.

John Doebley discussed how the different branch lengths of Maize and its ancestor Teosinte can be explained by different expression levels of a transcription factor, TB1, that normally represses organ growth; and Sean Carroll described how changes in cis-regulatory regions of particular genes have produced different pigment patterns in different Drosophila species. Sean Carroll also gave us an example of a transcription factor acquiring different functions through coding region changes: in some insects Ubx has a domain that can repress the distalless gene, and in some it doesn't.

Then the topic turned to aging, that "intrinsic state that leads to an increase in death rate and decline in fertility with advancing age". Linda Partridge described two key theories of aging – Medawar's hypothesis that aging is due to an accumulation of mutations and Williams theory that a mutation that is advantageous early in life, but that causes aging later, will be kept in the population, as early survival and fertility are under more selective pressure than longevity. A lot of the research done so far suggests that early fecundity = early aging, supporting Williams hypothesis. Two mechanisms for slowing down aging are caloric restriction, and reducing signalling through the insulin/IGF pathway. Both act through either the same, or overlapping, mechanisms to slow down normal aging.

David Gems discussed sex differences in longevity in C. elegans. In the lab, males normally die earlier than hermaphrodites. However, this is because their life span is reduced by sex: males maintained on single occupancy plates live substantially longer than males maintained with other worms of either sex, and live about 20% longer than hermaphrodites. Blocking neurological functions related to mating (unc mutations) can increase the lifespan even of solitary males, suggesting that self-mating behavior also reduces longevity.

The posters spanned the whole spectrum of cell, evolutionary and developmental biology. In addition, there was the first ever BSDB Sci-Art exhibition. The subject matter and media were amazingly varied, including dresses and hats based on embryonic development; oil paintings; digital media; stained glass; an installation art piece with HeLa cells, Drosophila and reflective text; and an exhibit of real butterflies with wing patterns modified experimentally by the artist. It was a great exhibition with some beautiful and thought provoking exhibits.

All in all it was a great conference, though the experience was unfortunately tainted for many by food poisoning the day after it ended. The culprit is rumored to be the prawns at the Friday evening formal dinner.

Kate Lewis, Oregon

BSDB Autumn Meeting, 2002

T-box genes in development

Organizer Jim Smith, Venue: Nottingham, Dates 16-18 September

The BSDB Autumn Meeting 2002
University of Nottingham, 16th –18th September

T-box genes in development

Scientific Organizers:
Jim Smith, Ginny Papaioannou

The T box family of transcription factors plays an important role in many aspects of development, including mesoderm formation and limb and heart development. This is the first meeting devoted to this important gene family, and it addresses evolutionary aspects of T box protein function, the structure of the T box proteins, T box specificity, and many examples of T box genes in development and disease. It promises to be an important and exciting meeting.

Confirmed speakers include:

David Brook
Jacques Drouin
Colin Goding
Janet Heasman
Bernhard Herrmann
Malcolm Logan
Christof Muller
Ginny Papaioannou
Gert Pflugfelder
Nori Satoh
Jim Smith
Alison Woollard

BSDB Autumn Meeting 2002

T Box Genes in Development and Disease

Nottingham, 16th – 18th September

See pages 6 & 7 for details of registration and abstract submission

Registration and Abstract Deadline
5th August, 2002

BSDB Autumn Meeting 2002
T Box Genes in Development and Disease

University of Nottingham, Monday 16th – Wednesday 18th September, 2002

Scientific Organizers: **Jim Smith, Ginny Papaioannou**

MONDAY 16 SEPTEMBER

Introductory Session

2.00 – 2.15	**Jim Smith** and **Ginny Papaioannou**: Welcome
2.15 – 3.00	**Bernhard Herrmann**, Max-Planck-Institut für Immunbiologie, Germany *Brachyury in paraxial mesoderm development in mouse*
3.00 – 3.40	**Jeremy Gibson-Brown**, Washington University, USA *Evolution of T-box genes and their functions*
3.40 – 4.10	Tea
4.10 – 4.50	**Christoph Müller**, EMBL, France *Structural insight into DNA recognition by T-box transcription factors*
4.50 – 5.30	**Jim Smith**, Wellcome Trust/Cancer Research UK Institute, UK *Regulation of T-box targets*

TUESDAY 17 SEPTEMBER

T-Box Genes & Development (1)

09.00 – 09.40	**Janet Heasman**, Children's Hospital Medical Center, USA *The interplay between T-box genes and Wnt signaling pathways in Xenopus*
09.40 – 10.00	Poster speaker
10.00 – 10.40	**Nori Satoh**, Kyoto University, Japan *T-box genes in the basal chordate, Ciona intestinalis*
10.40 – 11.10	Coffee
11.10 – 11.50	**Gert Pflugfelder**, University of Wuerzburg, Germany *Drosophila optomotor-blind: one gene - many functions*
11.50 – 12.10	Poster speaker
12.10 – 12.50	**Deborah Chapman**, University of Pittsburgh, USA *Generation of an allelic series of Tbx6 mutant phenotypes in the mouse*
12.50 – 2.20	Lunch

T-Box Genes & Development (2)

2.20 – 3.00	**Malcolm Logan**, National Institute for Medical Research, UK *T-box genes and limb-type specification*
3.00 – 3.20	Poster speaker
3.20 – 4.00	**Alison Woollard**, University of Oxford, UK *T-box genes in C. elegans*
4.00 – 4.30	Tea
4.30 – 5.10	**Colin Goding**, Marie Curie Research Institute, UK *Regulation of T-box factor function*
5.10 – 5.50	**Jane Sowden**, University College London, UK *T-box genes as regulators of eye development*

Conference Dinner

PhDs, Post-docs

We would like a volunteer to write a review of the Autumn Meeting. To encourage you, we are offering **£50** upon publication. Interested? Contact Andy Furley: a.j.furley@sheffield.ac.uk

WEDNESDAY 18 SEPTEMBER

T-Box Genes & Disease

09.00 – 09.40	**Ginny Papaioannou**, College of Physicians & Surgeons, Columbia University, USA *Mouse models and human syndromes: Tbx1 and DiGeorge syndrome*
09.40 – 10.00	Poster speaker
10.00 – 10.40	**David Brook**, University of Nottingham, UK *TBX5 and heart development*
10.40 – 11.10	Coffee
11.10 – 11.50	**Jonathan Seidman**, Harvard Medical School, USA *Tbx5 deficiencies in mice and man*
11.50 – 12.10	Poster speaker
12.10 – 12.50	**Jacques Drouin**, Institut de Recherches Cliniques de Montreal, Canada *Role of Tpit in pituitary cell differentiation and transcription*
12.50 – 1.00	**Jim Smith/Ginny Papaioannou**: Summary & farewell

Meeting Reports

BSDB Autumn Meeting: T-box Genes in Development and Disease

Nottingham University, Sept 16-18.

This autumn's BSDB meeting was designed to bring together different aspects of research on the T-box genes. Talks covered topics such as evolution, structure, function and disease models, which brought together different angles for discussion and enlightenment!

The T-box gene family, so called after the first to be identified, the T gene or Brachyury, encode developmentally regulated transcription factors. The family is characterised by a region of homology of around 180-200 amino acids, a DNA binding domain called the T-box. The T-box domain is conserved from C. elegans to humans and mutations in the T-box genes have been associated with developmental defects in all animal species.

Evolution of the T-box genes

In the attempt to understand the origins of T-box gene function in vertebrates, work was undertaken to clone all the T-box genes of the amphioxus, a primitive chordate, that is the closest living invertebrate relative of the vertebrates. It was found that there was roughly one amphioxus T-box gene for every T-box subfamily of vertebrates (Genetics 2000 156: 1249-1257). The T-box family then expanded through duplication in the vertebrate lineage.

Most amphioxus genes are orthologous to two or three vertebrate genes. The ancestor of the vertebrate eomes/tbr/tbx21 subfamily was a single gene that had been duplicated to give rise to three genes in vertebrates. The original gene was thought to be involved in anteriorisation of the neural domain. Together the members of the Tbx21 subfamily are expressed in the telencephalon of the mouse. They have overlapping, but specific sites of expression. However, in amphioxus the anterior neural domain has now been lost. Mapping the loss and gain of expression domains onto the phylogenetic species tree allowed **Jeremy Gibson-Brown** (Washington University, USA) to map the inferred character states for the evolution of developmental functions by this subfamily.

Comparative analysis has also led to the understanding of vertebrate innovations, for example, in the study of the Tbx1/Tbx10 subfamily. On examination of the Tbx1/Tbx 10 subfamily it appears that although amphioxus lacks neural crest and sclerotome, the expression pattern of the Tbx1 gene in amphioxus is in a segmental pattern, which, it was theorised, was later utilised in vertebrates, where it could have evolved migratory properties.

Structural insight into DNA recognition by T-box transcription factors

Christoph Müller (EMBL, France) gave us insight into the structure of the T- box domain. The T-box transcription factors appear to be different to other transcription factors in the way they form complexes with the DNA. The T-box transcription factors complex to a T-site, a 24-meric palindromic DNA duplex, as a dimer. The interaction occurs in the major and minor groove of the DNA. But unlike most other minor- groove bound protein-DNA complexes, the hydrophobic contacts do not cause an overall bend in the DNA. The binding of each T monomer to one strand in the inner region and to the opposite strand in the outer region of each half site could prevent DNA bending (Nature 1997: 389, 884-888).

Xbra binds as a dimer to the T-domain, stabilised through hydrophobic interactions, whereas TBX3 binds as two independent monomers to the palindromic T-site. The dimer forms a large arc that spans the DNA and allows it to recognise the two half site consensus sequences. The importance of the dimer formation was discussed. Is there the possibility of heterodimer formation, and therefore a degree of redundancy to the T-box transcription factors?

Mutations in Tbx5, insights into Holt-Oram Syndrome

A number of talks provided a molecular insight into clinical syndromes in which known mutations in the T-box genes have been the primary cause. Holt-Oram syndrome, characterised by malformations of the heart and upper limb, occurs due to truncated variants of the TBX5 protein. Both **David Brook** (University of Nottingham, UK) and **George Nemer** (Institut de Reserches Cliniques de Montreal, Canada) provided new insights into downstream targets of TBX5. It was found that TBX5 binds to target sites in the enhancer of Atrial Natriuretic Factor (ANF), explaining the reduction of ANF expression in Holt-Oram syndrome. TBX5 also acts synergistically with NKX2.5 and GATA4 to enhance activation.

However, there are two TBX5 variants, the longer isoform has a stronger binding to the DNA. The short form is expressed in the adult. It was proposed the short form may be cytoplasmic, therefore non- functional, whilst the longer form is functionally active during embryogenesis. The functionally active isoform may not be required in the adult and therefore becomes truncated.

Along with George Nemer, **Jonathan Seidman** (Harvard Medical School, USA) revealed that Connexin 40 (Cx40) was also a downstream target of Tbx5. The connexins are a family of proteins that form pores in the cell membrane, to allow small molecule transmission. Cx40 null mice show heart defects and conduction system abnormalities similar to those found in Tbx5 mutants in mouse and humans. Jonathan Seidman stated that'Cx40 deficiency is the primary cause of cardiac defects in Holt-Oram syndrome patients.'

T-box genes involved in other human hereditary diseases

Models for other syndromes were also represented: disruption of Tbx1 and Tbx3 are implicated in DiGeorge Syndrome and Ulnar-Mammary syndrome, respectively. **Ginny Papaioannou** (College of Physicians & Surgeons of Columbia University, USA) described the Tbx3 mutation in the mouse, there were hardly any abnormalities found in the heterozygote mice (although this is the dominant condition in humans). The homozygote mice lack mammary gland induction, they lack the ulna and digits and have severe hindlimb abnormalities. Homozygote mice share similarity with human Ulnar-mammary syndrome patients although exhibit a more severe condition.

A model was proposed which aimed to embark providing an explanation for the abnormalities seen in the Tbx3 null mutant mice. Tbx3 has a key repression domain in the C-terminus. It was proposed that absence of Tbx3 might release repression of p19, a cell cycle inhibitor protein, in the mutant embryo. p19 binds and inhibits Mdm2, which normally promotes p53 degrada-

tion. Increasing levels of p19 by release of repression effectively increases p53 in the cell. p53 induces apoptosis or cell cycle arrest, and could be seen to be the cause of the loss of structures observed in the areas where Tbx3 is normally expressed.

The poster session provided another great opportunity for discussion. Posters were of a very high standard, and both complimented talks and provided information on other areas of research of the T-box genes. The T-box genes are a fundamental gene family, critical in development, and found in a vast array of developmental processes. Sept 16-18 saw researchers at the leading edge of T-box research come together for the first time to discuss current understanding of this important gene family. With good food, great talks, and of course rastaball, who could ask for a better conference!

Lucy Smith, Sheffield

Meeting for Martin Raff

Between July 3-5th a special meeting took place at UCL to celebrate the career of Martin Raff, who is due to retire later this year. The mouth-watering programme of speakers reflected the huge esteem in which Martin Raff is held and the outstanding contributions that he has made throughout his life in science. The meeting covered a wide range of topics that have interested Martin over the years and was split broadly into sessions covering, stem cells and neurobiology, cell biology and disease, behaviour/psychiatry and finally, policy and ethics in science. There was also a poster session given by old friends, collaborators and current lab members. To do justice to the many fantastic talks and discussions in a brief review such as this is impossible. Thankfully, however, BioMedCentral filmed the entire meeting and most of the talks are now available online and are well worth viewing:

http://www.biomedcentral.com/meetings/2002/raff+bscb/

The meeting began with a session on stem cells and neural development, which has been of great interest to the Raff lab in recent years. **Ruth Lehmann** discussed mechanisms of germ cell fate and migration in Drosophila and then **David Anderson** presented a summary of many years of work from his lab dissecting cell fate choices using rat neural crest stem cells as a model system. He spoke of Martin as a major influence on his approach to this problem following conversations at the early stages of his career. A former postdoc (**Ben Barres**) presented exciting data suggesting that co-culture of astrocytes with retinal ganglion cells results in a marked increase in synapse number and consequently activity. **Josh Sanes**, followed and discussed the problem of how axons and synapses become restricted to particular laminae within the brain, and how Sidekick proteins may be determinants of this within the retinotectal system.

Many co-authors of "Molecular Biology of the Cell", were present and spoke over the course of the meeting. All praised Martin's efforts and incredible powers of concentration (revealed by his son, Jordan, as an attribute fine-tuned during periods in charge of the children!). The first to speak was **Keith Roberts**, who described initial work from his lab on a system for studying transdifferentiation in plants (conversion of mesophyll cells to vascular cells), and interspersed his talk with photos of Martin through the ages closely monitoring his "bilateral" ectopic hair during the 70's!

The afternoon session started with axon guidance (**Marc Tessier-Lavigne**), then patterning of neural tube, for which **Tom Jessell** presented data showing how knowledge of DV patterning within the embryo can be used to direct embryonic stem cells to produce motor neurons. The final two talks of the day dealt with neural disease. **Paul Patterson**, presented preliminary data on an interesting investigation into the effects of viral infections of the mother, which can lead to offspring mice exhibiting schizophrenic and autistic behaviour. **Charles Weissman** completed the day with a discussion of prion diseases and their transmission.

The next morning brought the first of two cell biology sessions, with talks initially on Notch signalling (**Julian Lewis**), and then control of cell cycle, by **Jordan Raff**, who presented data using GFP fusion proteins in fly, to address the issue of spatial and temporal regulation of cyclin B destruction during the cell cycle. He also paid tribute to his father, putting his success down to a fascination with all areas of science. **Alan Hall** mentioned the draw of many scientists (himself included) to the LMCB in order to interact with Martin, and his influence on the introduction of 4-year PhD programs in the UK.

In the afternoon three speakers discussed issues relating to cancer. First, **Gerard Evan** discussed an astonishing recent study from his lab, where invasive and angiogenic pancreatic ß cell tumours could be induced in mice by just two molecular changes, activation of c-myc and suppression of apoptosis. **Ron Laskey** followed, and described DNA replication controls and their usefulness as a basis for cancer diagnosis. **David Lane** finished the day highlighting the need to translate basic knowledge of cancer into practical treatments and how frustrating this can sometimes be.

The final day saw the second Cell biology session, which included two talks dealing with the related problems of cell shape (**Paul Nurse**) and cell size control (**Tim Mitchison**). The later described some experiments (motivated by discussions with Martin) to try and understand how the size of the mitotic spindle is determined, as a step towards understanding the problem of how cell size is controlled.

The final talks dealt with more general topics and the questioning and discussions could have continued all night! Initially, there were two talks dealing with sexual behavior (**Simon Levay** and **Richard Axel**), and then **Lewis Wolpert** spoke, as always, engagingly, about depression and its devastating effect and the long way we are from a complete understanding of its causes. A lively open forum followed, dealing with scientific publishing, particularly those changes brought about by the Internet and the effect on relationships between publishers and scientists.

Gerald Fischbach spoke highly of Martin and the legacy that he will leave in cell and developmental biology, before reviewing science policy and ethical issues with regard to stem cell therapies. **Bruce Alberts** gave an overview of the role that National Acadamy plays in both the US and internationally, especially in the promotion of science education. Finally, euthanasia was discussed by **Paul van der Maas**, who gave a frank and honest review of the approaches to it taken in the Netherlands.

There was time left, however, for the man himself to have the final word and give us a brief reflection on his scientific career. Initially he sincerely thanked **Anne Mudge** for her great efforts in organising the meeting

and all of the speakers for their kind words, and fantastic talks. Although "like being present at your own funeral", he enjoyed the meeting immensely, being "by far the best meeting" he's ever been too. He thanked all those who had influenced his career, and described how very lucky he has been, especially early on with the mentorship of **Av Mitchison**.

Martin is looking forward to his retirement, and will keep an office at LMCB where he'll work on issues, such as euthanasia, about which he feels passionately. The next generation of scientists will also be thankful that he will work on one more edition of Molecular Biology of the Cell.

In summary, this unique meeting was a huge success, full of great science and lively discussion - and also a lot of fun. A fitting tribute, then, to a man with incomparable qualities!

Steve Pollard, ISCR, Edinburgh