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# GENETICS SOCIETY NEWS

*the*  
**genetics**society

[www.genetics.org.uk](http://www.genetics.org.uk)



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Genetics Society News is edited by Steve Russell. Items for future issues should be sent to Steve Russell, preferably by email to [s.russell@gen.cam.ac.uk](mailto:s.russell@gen.cam.ac.uk), or hard copy to Department of Genetics, University of Cambridge, Downing Street, Cambridge CB2 3EH. The Newsletter is published twice a year, with copy dates of 1st June and 26th November.

Cocoons of the parasitoid wasp *Cotesia vestalis* on cabbage leaf in Taiwan. From the fieldwork report by Jetske G. de Boer on page 36.

# A word from the editor

**H**ow soon until the \$1000 genome is actually with us and individual sequencing is widespread? The publication of increasing numbers of individual human genome sequences suggests that we should start to consider some of the implications associated with the availability of personal genetic information. In this issue we present two articles reflecting on his issue: a report from a Genetics Society sponsored meeting recently held in Cambridge organised by The Triple Helix, an international undergraduate organisation, as well as our Taxi Driver column by Andrew Grierson. In relation to the societal implications of personal genetic information, on May 21st this year, the U.S. President signed into law the Genetic Information Non-discrimination Act (GINA). The new legislation will prohibit employers and health insurers from discriminating against individuals on the basis of their personal genetic information and was driven by the joint efforts of the American Society of Human Genetics, the Coalition for Genetic Fairness, the Genetic Alliance and other organizations in the genetics community. See the NHGRI website [www.genome.gov/24519851](http://www.genome.gov/24519851) for more details of this important step forward in preventing discrimination

based on the results of tests we barely understand! Here in the UK there is currently a moratorium, adhered to by most insurers, on the use of genetic testing information for assessing life insurance applications. It is important that this remains in place and its effectiveness is reviewed well before the current moratorium expires in 2011. The Human Genetics Commission (<http://www.hgc.gov.uk>) monitor issues relating to genetic discrimination in the UK and are a point of contact for those with any concerns in this area.

The implications of using personal sequence data in society has some echoes with the eugenics movement prominent in the early 20th Century and in this issue Mike Majerus reviews the recent publication of a volume of lectures marking the Centenary of the Galton Institute that provides some historical context to this important current debate.

We are happy to report a flurry of awards for current and past presidents of the Genetics Society. Our current president, Brian Charlesworth, receives the Weldon Memorial Prize, former president Michael Ashburner receives the Thomas Hunt Morgan Medal and Alex Jeffries has been nominated for



the Millennium Technology Prize. On a less happy note, the Society was sad to learn of the recent death of John Evans, a much-respected figure in international genetics. Our president Elect, Veronica van Heyningen, presents an appreciation of his life in science.

We have a report of the recent Genetics Society meeting on epigenetics along with other society-sponsored meetings and a selection of reports from members who received travel or fieldwork grants. I hope you enjoy this issue and, as always, anything you want to get off your chest, scientifically speaking, can be published in our Taxi Driver column. I also welcome any other material you feel would be of interest to the Society membership and you can contact me to sound out potential articles.

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University of Cambridge

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The Genetics Society Journals  
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# Evolution of Sex and Asexual Reproduction

**One day meeting. Friday 5 September 2008 at the University of Bath, UK**

While the maintenance of sex and recombination remains an intellectual challenge, the long term persistence of some asexuals is equally puzzling. What if anything can be learnt about the former issues by studying the latter and vice versa? There are multiple contrasting approaches to these problems: theoretical versus empirical approaches, genetical versus ecological explanations, field versus laboratory systems. This meeting will bring together all of these strands in current research.



**Speakers:**

Christina Burch (North Carolina, USA)  
Jukka Jokela (Zurich, Switzerland)  
Peter Keightley (Edinburgh, UK)  
Ryszard Korona (Krakow, Poland)  
Dunja Lamatsch (Mondsee, Austria)  
Thomas Lenormand (Montpellier, France)  
Mike Lynch (Indiana, USA)  
Stefan Scheu (Darmstadt, Germany)

**Scientific organisers:**

Laurence Hurst (Bath) and Roger Butlin (Sheffield)

**Featuring:**

2008 Mendel Medal winner,  
Matthew Meselson (Harvard, USA)

2008 Balfour Lecture by  
Daven Presgraves (Rochester, New York)

**Registration Fees:** Genetics Society members £30, non-members (academic) £80, non-members (non-academic) £135  
Student members can apply for travel grants to offset the cost of attending this meeting (see website for details).

Visit the Genetics Society website for further details and to register for the meeting: [www.genetics.org.uk/home](http://www.genetics.org.uk/home).

A Joint One Day Genetics Society and  
British Society for Human Genetics Meeting

# Human Genetic Disease: From model organism to the clinic

Friday 28th November 2008, The Royal Society, London

## SCIENTIFIC ORGANISERS

### Genetics Society:

Lizzy Fisher (UCL) and Andrew Ward (Bath)

### BSHG:

Phil Beales (ICH, London), Eamonn Maher (Birmingham)  
and Andrew Wilkie (IMM, Oxford)

## SPEAKERS

Robin Ali (University College London, UK)

Kathryn Anderson (Sloan-Kettering Institute, New York)

Han Brunner (Nijmegen, Netherlands)

Juan Botas (Baylor College of Medicine, Texas, USA)

Neal Copeland (Institute of Molecular and Cell Biology, Singapore)

Wofgang Driever (Freiburg, Germany)

Jill Helms (Stanford University, USA)

Jenny Morton (University of Cambridge, UK)

Nadia Rosenthal (EMBL, Monterotondo, Italy)

The 2008 Genetics Society Medal  
will be awarded to Nick Hastie  
(MRC Human Genetics Unit, Edinburgh)

Further details will be made available at

[www.genetics.org.uk](http://www.genetics.org.uk)

A meeting of The Genetics Society

# The Mammalian Genetics and Development Workshop

20th - 21st November 2008 . Institute of Child Health, UCL, 30 Guilford Street, London WC1N 1EH

The Mammalian Genetics and Development Workshop is a small annual meeting that aims to cover any aspects of the genetics and development of mammals. Meetings are based on the submitted abstracts, and usually include diverse topics ranging from early mammalian development (not exclusively human or mouse), imprinting and positional cloning of disease genes to human population genetics and association studies. In recent years, presentations on other model systems (such as chick and zebrafish) have also been included where these relate to general developmental questions or disease models.

The meeting is traditionally a venue for post-docs and PhD students to talk rather than laboratory heads and so is an excellent training ground and friendly, informal forum for discussing new results. In keeping with this objective, we offer TWO PRIZES of £150 to individual post-graduate/post-doctoral presenters who, in the opinion of a panel of judges, have given an outstanding presentation. A further prize is also offered, thanks to the generosity of the editors of Mammalian Genome (Springer). The prizewinner receives £150, a book of choice from the Springer range plus a year's subscription to Mammalian Genome. One additional prize of £200 will be awarded to the speaker judged to have given the best presentation of a genetics-based research project. Promega, who will also sponsor the wine reception at this meeting, generously contributes this prize.

## Registration

A £10 registration fee is payable by all attendees on arrival at the meeting. The fee entitles registrants to attend all of the scientific sessions, to receive the abstract booklet and tea/coffee refreshments on both days. Speakers and chairpersons will be provided with lunch, free of charge, on the day of their presentation. Other participants will be expected to make their own arrangements for lunch. All participants are responsible for organising their own overnight accommodation, if required, although we can advise on places to stay. There will also be a wine/cheese reception (sponsored by Promega) on the first day of the meeting.

## Abstract Submission

All Workshop presentations will be in lecture format (15 or 30 minutes), chosen from abstracts submitted prior to the meeting. If you would like to present a paper at the Workshop please send your abstract by e-mail to the following address: [MGD.Workshop@ich.ucl.ac.uk](mailto:MGD.Workshop@ich.ucl.ac.uk). With the authors' permission, abstracts will be published in *Genetical Research*.

If you would like to announce a meeting that you think may be of interest to Genetics Society members, please contact the newsletter editor Steve Russel [s.russell@gen.cam.ac.uk](mailto:s.russell@gen.cam.ac.uk).

XX International Congress of Genetics

12th – 17th July 2008

Berlin, Germany

further info [www.geneticsberlin2008.com/](http://www.geneticsberlin2008.com/)

International Society for Animal Genetics 2008

20th – 24th July 2008

Amsterdam, The Netherlands

further info [www.isag2008.nl/](http://www.isag2008.nl/)

DNA Topology and Topoisomerases (Topo2008)

20th – 23rd July 2008

John Innes Centre, UK

further info [www.liv.ac.uk/sbs/Topo2008/Register.html](http://www.liv.ac.uk/sbs/Topo2008/Register.html)

2008 Yeast Genetics and Molecular Biology Meeting

22nd – 27th July 2008

Toronto, Canada

further info [www.yeast-meet.org/](http://www.yeast-meet.org/)

19th International Conference

on Arabidopsis Research

23rd – 27th July 2008

Montreal, Canada

further info [www.plantconferences.org/Arabidopsis2008/](http://www.plantconferences.org/Arabidopsis2008/)

International Symposium on Induced

Mutations in Plants

12th – 15th August 2008

Vienna, Austria

further info [www-pub.iaea.org/MTCD/Meetings/Announcements.asp?ConfID=167](http://www-pub.iaea.org/MTCD/Meetings/Announcements.asp?ConfID=167)

RNA 2008

28th July – 3rd August 2008

Berlin, Germany

further info [www.rna2008.mpg.de/](http://www.rna2008.mpg.de/)

Mycological Society of America 2008

9th – 13th August 2008

Pennsylvania, USA

further info [www.outreach.psu.edu/programs/mycology/](http://www.outreach.psu.edu/programs/mycology/)

Molecular Biology of Archaea 2008

19th – 20th August 2008

St Andrews, UK

further info [www.biochemistry.org/meetings/programme.cfm?Meeting\\_No=SA079](http://www.biochemistry.org/meetings/programme.cfm?Meeting_No=SA079)

9th International Conference on Systems Biology

22nd – 28th August 2008

Göteborg, Sweden

further info <http://icsb-2008.org/>

Agricultural Biotechnology International Conference

24th – 27th August 2008

Cork, Ireland

further info [www.abic.ca/abic2008/html/program.html](http://www.abic.ca/abic2008/html/program.html)

GARNet/SEB Plant Symposium

8th – 10th September 2008

Nottingham, UK

further info <http://garnet.arabidopsis.info/>

ESF-EMBO Symposium on Bacterial Networks

13th – 18th September 2008

Sant Feliu de Guixols, Spain

further info [www.esf.org/index.php?id=4565](http://www.esf.org/index.php?id=4565)

**4th London Fly Meeting****19th September 2008****London, UK****further info** <http://lfm2008.org.uk>**Molecular Genetics of Aging****24th – 28th September 2008****Cold Spring Harbor Laboratory, USA****further info** <http://meetings.cshl.edu/meetings/aging08.shtml>**HUGO 13th Human Genome Meeting****27th – 30th September 2008****Hyderabad, India****further info** <http://hgm2008.hugo-international.org/>**10th Human Genome Variation Meeting****15th – 17th October 2008****Toronto, Canada****further info** [www.tcag.ca/hgv2008/](http://www.tcag.ca/hgv2008/)**Advances in Nucleic Acid Detection & Quantification****28th – 29th October 2008****Hinxton Hall, Cambridge, UK****further info** [www.biochemistry.org/meetings/programme.cfm?Meeting\\_No=SA092](http://www.biochemistry.org/meetings/programme.cfm?Meeting_No=SA092)**Mouse Genetics & Genomics: Development & Disease****29th October – 2nd November 2008****Cold Spring Harbor Laboratory, USA****further info** <http://meetings.cshl.edu/meetings/mouse08.shtml>**58th American Society for Human Genetics Meeting****11th – 15th November 2008****Philadelphia, USA****further info** [www.ashg.org/2008meeting/index.shtml](http://www.ashg.org/2008meeting/index.shtml)**IV International Conference on Legume Genomics and Genetics****7th – 12th December 2008****Puerto Vallarta, Mexico****further info** [www.ccg.unam.mx/iclgg4/](http://www.ccg.unam.mx/iclgg4/)**Annual Symposium: DNA damage: From Causes to Cures****15th – 17th December 2008****Robinson College, Cambridge, UK****further info** [www.biochemistry.org/meetings/programme.cfm?Meeting\\_No=SA084](http://www.biochemistry.org/meetings/programme.cfm?Meeting_No=SA084)**Epigenetics, Development and Human Disease****5th – 10th January 2009****Breckenridge, USA****further info**[www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=978](http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=978)**Fourth Biennial Conference of the International Biogeography Society****8th – 12th January 2009****Mérida, México**

Invited symposia will feature talks on the biogeography of disease, patterns and processes in biotic transition zones, disjunct distributions in Asia and America, and the biogeography of species extinction. Attendees are invited to submit abstracts for oral and poster presentations. The conference will also include workshops, field excursions, and social events. Registration, contact, and additional information may be found at:

<http://www.biogeography.org>.**further info** <http://www.biogeography.org>**Miami Winter Symposium 2009: Interpreting the Human Genome****24th – 28th January 2009****Miami, USA****further info** [www.nature.com/natureconferences/MWS2009](http://www.nature.com/natureconferences/MWS2009)**Cancer Genetics and Epigenetics****25th – 30th January 2009****Ventura, USA****further info** [www.grc.org/programs.aspx?year=2009&program=cancer](http://www.grc.org/programs.aspx?year=2009&program=cancer)

The Genetics Society helps support several sectional interest groups by providing meeting sponsorship. We currently have 8 groups who organise sectional interest meetings with the organizers and dates of any forthcoming meetings are listed below. We include short reports from two of our groups on their recent activities. If you are interested in any of these areas, please contact the relevant organiser. Groups who wish to be considered for sectional interest group status should contact the Treasurer, Josephine Pemberton, in the first instance.

#### Arabidopsis

Organiser: Ruth Bastow (ruth@arabidopsis.info)  
 GARNet/SEB Plant Symposium 8th – 10th September  
 2008, University of Nottingham.  
<http://garnet.arabidopsis.info/>

#### Archaea group

Organiser: Thorsten Allers  
 (thorsten.allers@nottingham.ac.uk)  
 Molecular Biology of Archaea 2008  
 19th – 20th August 2008, University of St Andrews.  
[http://www.biochemistry.org/meetings/programme.cfm?Meeting\\_No=SA079](http://www.biochemistry.org/meetings/programme.cfm?Meeting_No=SA079)

#### British Yeast Group

Organiser: Alistair Goldman  
 (a.goldman@sheffield.ac.uk)

#### C. elegans

Organiser: Stephen Nurrish (s.nurrish@ucl.ac.uk)

#### Ecological Genetics Group

Organiser: Barbara Jones (b.jones@ccw.gov.uk)

#### Genetics Society Pombe Club

Organiser: Jacky Hayles (j.hayles@cancer.org.uk)

#### Mammalian Genetics & Development

Organisers: Elizabeth M. Fisher and Nick Greene  
 Contact: mgd.workshop@ich.ucl.ac.uk

#### POP group

Organiser: Deborah Charlesworth  
 (Deborah.Charlesworth@ed.ac.uk)

#### Drosophila

Organiser: David Ish-Horowicz  
 (david.horowicz@cancer.org.uk)  
 Monthly meetings are organised by:  
 Joe Bateman (joseph\_matthew.bateman@kcl.ac.uk)

London Fly Meetings: The London Fly Meetings (LFMs) are monthly gatherings of *Drosophila* groups in the London area held at the Cancer Research UK London Research Institute on the third Wednesday of each month, and are organised by the London Fly Group. Recent attendance at the monthly meetings has been excellent, frequently topping 50 participants. The meetings start with an informal mixer, during which fly stocks and stories are often exchanged, followed by one or two speakers. Usually, the speakers are from participating labs, but we also occasionally host external speakers, such as Ulrike Gaul from Rockefeller University on September 5th 2007 who presented her latest work on glial cell development. Topics covered by our local speakers in 2007 included Src signalling in imaginal discs (Paul Langton, Tapon lab, CRUK), DIAP2 in the control of cell death (Paulo Ribeiro, Meier lab, Breakthrough Cancer Centre), the circadian clock and light (Nikolai Peschel Stanewsky lab, Queen Mary's) and insulin signalling in the CNS (Irene Miguel-Aliaga Gould lab, NIMR). Finally, we enjoyed a fabulous Lebanese buffet for our festive December meeting, and even more fabulous science as Andrea Brand (Gurdon Institute, Cambridge) presented her lab's exciting new work on stem cell populations in the nervous system. In addition to the monthly meetings, the London Fly Group also organises the highly successful biannual international London Fly Meetings. The 4th London Fly Meeting will be on Fri 9th September 2008 at King's College (<http://lfm2008.org.uk/>).

#### The Zebrafish Forum

Organiser: Rachel Ashworth (r.ashworth@ucl.ac.uk), Caroline Brennan (C.H.Brennan@qmul.ac.uk), Corinne Houart (corinne.houart@kcl.ac.uk). There are meetings at 5:30pm-8.00pm on the first Thursday of every other month. Room G12, New Hunt's House, King's College - London SE1 1UL

## The Zebrafish Forum from two different perspectives

Manuela Lahne and Rachel Ashworth, QMUL.



In this report we bring a roundup of past meetings: December and February as described by Rachel Ashworth, along with an overview of the March meeting from Manuela Lahne, a new member of the zebrafish community. We would also like to draw your attention to an upcoming meeting on zebrafish welfare, husbandry, and maintenance, to be held at UCL in October.

The December meeting, held at Queen Mary University of London, had a packed programme including 3 speakers and posters. Tessa Peterkin from University of Oxford described her investigation of the role of GATA transcription factors, GATA 4, 5 and 6, in vertebrate heart development. Gavin Wright from The Sanger Institute presented work on large scale screening for novel low affinity transient extracellular-ligand pair interactions. The group is using zebrafish to determine the functional significance of identified cell surface interactions *in vivo*. Robert Kelsh from University of Bath gave an overview of their work examining how pluripotent

progenitor cells become specified to one of several distinct fates, using the vertebrate neural crest as a model system. In February the zebrafish forum was held at UCL, thanks to Masa Tada, and included three speakers. Manuel Batista, University of Cambridge, described his work examining Pax2 and its role in the specification of interneurons. Issac Bianco, University College London talked about his work on analysis of lateralised circuitry in the zebrafish brain, with focus on the habenular nuclei. Helen Bodmer, from the Home Office, led a group discussion regarding defining developmental stages.

In March I had the pleasure of attending the fish forum at the Weatherhall Institute of Medicine in Oxford, organized by Roger Patient and co-hosted with the monthly developmental biology club. This was the first zebrafish forum I attended after only recently moving into a research area that uses this model organism. The three speakers, Sally Stringer, Tom Chipperfield and Rachel Ashworth, are investigating very different topics and talked about some of their most recent discoveries. Sally Stringer described vascular development in zebrafish with the specific focus on heparan sulfates. She used morpholinos in order to knock down two groups of enzymes, the hexosulfate-6-O-

transferase and sulfatases both of which are involved in the regulation of heparan sulfatation and showed vascular phenotypes ranging from vascular oedema to reduced branching. This presentation was followed by Tom Chipperfield, who identified targets of the transcription factor Sox10 in neural crest cells. He carried out his research using microarray techniques and *in situ* hybridisation. The final speaker, Rachel Ashworth, is investigating the role of neural activity induced calcium signals on the development of slow muscle fibres. She used calcium imaging techniques as well as immunocytochemistry to determine muscle phenotypes in zebrafish mutants. The meeting gave me an opportunity to gain insight into the versatility of research questions that are tackled using zebrafish, as well as the techniques that are used to carry out this research. Moreover, attending the meeting allowed me to acquire and consolidate basic knowledge regarding zebrafish anatomy and development. It was also helpful to meet with researchers in the field and discuss related subjects in a relaxed environment with a glass wine. I am now looking forward to zebrafish forums in the future.

### Forthcoming events:

October 2008 Zebrafish Forum at UCL (date to be confirmed).

Zebrafish welfare, husbandry, and maintenance: this is a one-off meeting designed as a forum for both technical staff and researchers, involving subjects interesting and useful to all groups with an interest in zebrafish. The meeting will involve aspects of zebrafish welfare, husbandry and maintenance, alongside more research-based topics. The aim is to encourage discussion of some of the more practical but often overlooked aspects of this model organism. There will be a presentation of posters and people are encouraged to bring along any appropriate work. Please contact the event organizers of this one off event for more information: Carly Nicholls [c.nicholls@qmul.ac.uk](mailto:c.nicholls@qmul.ac.uk)

## Annual General Meeting

The Annual General Meeting of the Society, where new members are admitted and committee members elected, was formally held during the recent Epigenetics meeting in Norwich. In addition to the

physical event, many members took advantage of the new electronic voting system, for which we are very grateful. The AGM is an essential part of the running of the Society and we thank all of the members

who took the time to register their votes.

The AGM admitted 218 new members and voted in favour of the committee nominees for new committee members.

The new committee members are:

President-Elect (to succeed Brain Charlesworth in 2009):

Vice-President (Corporate Affairs):

Vice-President (External Relations):

Honorary Secretary:

Postgraduate Representative:

Committee area "E"  
(evolutionary, ecological & population genetics)

Committee area "F"  
(corporate genetics & biotechnology)

**Veronica van Heyningen**

**Ian Jackson**

**John Brookfield**

**Patty Kuwabara**

**Tom Nowakowski**

**Adam Eyre-Walker**

**Tom Weaver**

## Committee News

This year, the time has come to bid farewell to several long-serving officers of the Society: the Honorary Secretary, John Armour, the Vice-President for External Relations, Bill Hill, and the Vice-President for Corporate Affairs, Helen Sang. They have all given outstanding, and unremunerated, service to the Society. The Society

owes a particular debt of gratitude to John and Helen, who unselfishly volunteered last year for an extra year's service. This was done in order to help us through the difficult period when the Society's office lacked an Executive Officer, with the result that a considerable burden of work fell upon their shoulders. We should also be

grateful to Hazel Hutchison for her work in the office during this period. Fortunately, we now have a new Executive Officer, Christine Fender, and I am confident that the new officers that have come onto the Committee can look forward to a smoothly running operation. I am delighted to welcome them aboard. I am sure that John, Bill and Helen will enjoy their well-deserved leisure hours, if their other duties allow them to have any.

Brian Charlesworth, President

# Genetics Society Awards

## Winner of the 2009 Balfour Lectureship

The Balfour Lecture, named after the Earl of Balfour, the Society's first President, is awarded annually to mark contributions to the field of genetics by an outstanding young investigator. We are delighted to announce that the 2009 Balfour Lecturer will be Dr. Matthew Hurles, Wellcome Trust Sanger Institute, Hinxton, Cambridge. Matt's research career has been devoted to understanding the basis of human variation from both a genetic and archaeological perspective.

Matt became a group leader at the Sanger Institute in 2003, where he quickly demonstrated both flair and imagination for genomic analysis. He was the senior author on an influential paper published in *Nature* (2006), which highlighted the importance of global variation in copy number on the human genome; he was also a member of a team that published an analysis of the impact of copy number variation on gene expression and disease susceptibility in *Science* (2007). Matt's study of human evolution has also led him to assess how genome dynamics mediated by mechanisms such as homologous recombination have affected human evolution.



## The Sir Kenneth Mather Memorial Prize

This is an annual prize of £150 to reward a BSc, MSc or PhD student of any UK University or Research Institution who has shown outstanding performance in the areas of quantitative or population genetics.

Nominations should be made between July 1st and November 1st inclusive of each year through the local Head of Department or School of the nominee. Nominations should consist of no more than one page of A4, setting out the case for the nomination, including relevant comparison with other students where possible. Nominations should be sent to the Head of School, School of Biosciences, The University of Birmingham, Birmingham, B15 2TT, clearly labelled as a nomination for "The Sir Kenneth Mather Memorial Prize".

Nominations will be assessed by a panel of two people with experience in the area of quantitative/population genetics, one from the University of Birmingham and the other nominated by the UK Genetics Society. Decisions will be announced in December each year.

## Winner of the 2009 Genetics Society Medal

The GS medal is awarded annually to recognise outstanding research contributions in genetics and the Genetics Society is delighted to announce that the winner of the 2009 medal is Professor Stephen Brown FMedSci, MRC Mammalian Genetics Unit, Harwell. Steve is internationally recognised for his seminal contributions to mouse and mammalian genetics, and he has been one of the driving forces behind the development of the MRC Harwell site, where he is currently director. Steve has

played a leading role in generating high-resolution genetic and physical maps of the mouse genome, and he continues to foster the development and application of functional genomic tools in the post-genomic era. Steve is perhaps most closely identified with the large-scale mouse ENU mutagenesis programme at Harwell. This project was designed to identify mutations in genes that produced disease phenotypes, which could be exploited in order to learn about the basis of human disease. To this end, Steve's research group has successfully identified and studied the developmental genetics of gene mutations underlying hearing loss in humans.



# Presidents Recognised

We are happy to report on the international recognition the current and past presidents of the Genetics Society have recently enjoyed:



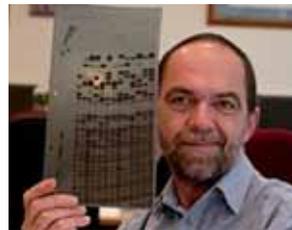
Brian Charlesworth

Current society president Prof. Brian Charlesworth, Edinburgh University, has received the Weldon Memorial Prize, awarded by the University of Oxford to recognise the most noteworthy contributions to the development of mathematical or statistical methods applied to biological problems.



Prof. Michael Ashburner

The Genetics Society of America has awarded the Thomas Hunt Morgan Medal to past president, Prof. Michael Ashburner, University of Cambridge. The medal recognises lifetime contributions in the field of genetics.



Prof. Alex Jeffreys

Another past president, Prof Alex Jeffreys, has been selected as one of the four final nominees for the Millennium Technology Prize, a very prestigious Finnish award that recognises innovators who contribute to improvements in quality of life. The final result should be available by the time you get the newsletter and is available at: [www.millenniumprize.fi/](http://www.millenniumprize.fi/)

## Postgraduate Representative

During the 2008 spring meeting of the Genetics Society I was elected to the position of postgraduate representative for the Genetics Society. During my two-year tenure I will be aiming to strengthen the involvement of the Genetics Society in the issues of postgraduate students to help young scientists actively participate in scientific meetings, symposia and conferences. On this occasion I would like to outline the strategies for the near future.

Following the positive feedback from students after the workshops and the social event organised during the joint meeting of the Genetics Society,

BSDB and BSCB in Edinburgh in spring 2007, the Genetics Society wishes continue its engagement in organising postgraduate symposia, workshops and social events; perhaps extending their scope by organising meetings with academic staff at different stages of their scientific careers. I believe providing opportunities for students to meet junior postdocs, principal investigators setting up their laboratories and senior members of academia in a friendly environment will make students feel they can ask questions about their specific project, future job opportunities in other labs, or simply how they feel about their positions

as principal investigators or a postdocs. This kind of interaction is of vital importance for students who have to consider their future careers.

Furthermore, we hope that Promega will continue to sponsor awards for young scientists to mark their excellence in postgraduate research much in line with the 2008 Young Geneticist of the Year Award competition. The Genetics Society would like to be involved in selecting finalists for such competitions.

We are also happy to consider applications for support in organising student events at scientific meetings at conferences, not necessarily organised by the Society. Such applications and other suggestions for ways in which the Genetics Society could support students should be directed to me, the postgraduate students' representative, in the first instance (s0454833@sms.ed.ac.uk). Tom Nowakowski.

# Heredity News

A joint venture by NPG and The Genetics Society has just completed scanning all of the back issues of the Societies' journal, *Heredity*. These are now all freely available from the Journal Web Site (<http://www.nature.com/hdy/index.html>) as fully searchable PDF files. This is an excellent resource for the community and encompasses some of the most vibrant research in UK genetics. The very first article, Genetic Research in Britain 1939 – 1945. (1047) *Heredity* 1: 1-17, provides an overview of genetic research during the war years via a series of abstracts from a 1945 Genetical Society conference. The contributor list reads like the cast list of *Giants in Genetics* – (DG Catcheside, MB Crane, CD Darlington, F

Engledow, RA Fisher, EB Ford, A Greenwood, JBS Haldane, J Hammond, H Hunter, TJ Jenkin, DE Lea, K. Mather, LS Penrose, RR Race, W Robb, CH Waddington) and is well worth perusing to see the state-of-the-art at the time. There are many fabulous papers in the archive, a few that caught my eye from the early issues include: *The Genetic Component of Language* by Cyril Darlington (1: p269), *Problems in Microbial Genetics* by Joshua Lederberg (2: p145), *Morphism and Evolution* by Julian Huxley (9: p1) and *On the Change in Population Fitness by Natural Selection* by Motoo Kimura (12: p145). Along with these and many more fascinating papers there are some very interesting book reviews (a review by Peter Medewar of *Evolution as a Process* edited by J Huxley, AC

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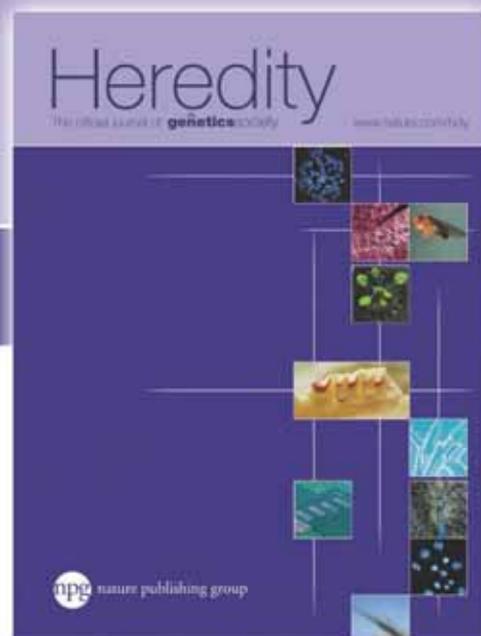
The first article in the first issue of *Heredity* summarises the genetic research at UK institutions.

Hardey and EB Ford was particularly entertaining). Overall the quality of the scanning is very good, a few pages I examined are at a slight angle, but as I mention above, all the text is fully searchable. Just search the journal site for your favorite genetic term or author and revel in these classic papers.

This is an excellent resource for the community and encompasses some of the most vibrant research in UK genetics.

# Heredity

The official journal of the **Genetics Society**



cs, functional genomics and proteomics • population genetics (including human) • biometrical and statistical genetics • ec  
ics • ecological and evolutionary genetics • animal and plant breeding • cytogenetics • genomics, functional genomics and

Genetics Society members can access *Heredity* free of charge through [www.genetics.org.uk](http://www.genetics.org.uk)

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# News From The Biosciences Federation

[www.bsf.ac.uk](http://www.bsf.ac.uk)

Steve Russell . University of Cambridge

An important new development for UK bioscience comes with the joint announcement by the Biosciences Federation and the Institute of Biology that they are working together with the aim of joining forces to form a single body representing British biology. With the IoB currently representing individual scientists and the BSF more focused on organisations, the proposed new body will provide a broad platform for representing Biosciences on the political stage. Both organisations are consulting their respective memberships to ensure broad support for the proposed merger and it is hoped that the new organisation will come into being next year. Society Presidents Prof. Raymond Dwek (IoB) and Prof Dame Nancy Rothwell (BSF) set out some of the key challenges that face the biosciences in the 21st Century at a meeting held at the Royal Society in May. These include: maximising the social and economic benefits of new discoveries and addressing challenging

**With the IoB currently representing individual scientists and the BSF more focused on organisations, the proposed new body will provide a broad platform for representing Biosciences on the political stage.**

environmental problems such as the consequences of climate change. Constructively engaging with both the public and politicians. Assessing the provision of adequate resources for life sciences research, especially in emerging areas where new tools and skills are essential. Exploring how biology education from the schoolroom to the workplace can be effectively structured. Figures from industry and biological science funding bodies are supportive of the proposal and believe that biology will benefit from a unified voice in policy forums.

The BSF continues its policy work in a variety of areas, responding to a range of consultation exercises and their input can be accessed at the BSF website ([www.bsf.ac.uk](http://www.bsf.ac.uk)).

Activities include reports on open access publishing, systematics and taxonomy, genomic medicine, the research excellence framework and biosecurity.

Nominations are being accepted for the 2008 BSF Science Communication Awards for research-active scientists who make outstanding and consistent contributions in the area of public science communication. There are two categories: one for young scientists, PhD or masters students or graduates with less than a year of postdoctoral experience and one for established researchers. Nominations close of the 24th August 2008, with the prizes awarded in November this year. The nomination form can be obtained at the BSF website.

# Promega Young Geneticist of the Year

As we announced in the last Newsletter, the Promega Young Geneticist of the Year competition was judged at the 18th Mammalian Genetics and Development Workshop last November. The winner and runners-up were invited to the Genetics Society Epigenetics meeting this May where

Dr Paul Glands of Promega presented their awards. The winner, Carol Anne Edwards gave a talk on her work at the meeting and we present an abstract of her fascinating investigations into the evolution of Genomic imprinting here.



Carol Anne Edwards delivers her talk at the Epigenetics meeting (right)

## The Evolution of Genomic Imprinting: A comparative analysis of the *DLK1/DIO3* domain in extant vertebrates.

Carol Anne Edwards . Department of Physiology, Development and Neuroscience, University of Cambridge



Carol Anne Edwards delivers her talk at the Epigenetics meeting

Genomic imprinting is a process by which certain mammalian genes are expressed from only one parentally inherited copy, with the other allele being repressed. Imprinted genes therefore lose the advantages that diploidy provide against recessive mutations. This has led to much speculation on how and why imprinting evolved. Functional data indicates that genomic imprinting arose alongside placentation in therian

mammals. This theory predicts that oviparous monotremes will not imprint but viviparous marsupials will. The *DLK1/DIO3* cluster (approximately 1 million base pairs long) is ideal for investigating the evolution of imprinting as all of the protein coding genes within the cluster are expressed in the placenta, including a gene related to a Ty3-gypsy retrotransposon, *RTL1*. In addition, this region contains many functionally significant genomic features

such as differentially methylated regions (DMRs), long non-coding RNAs (*GTL2*), small functional RNAs (C/D snoRNAs and microRNAs) and antisense transcripts.

The *DLK1/DIO3* imprinted domain was mapped and sequenced in a marsupial (tamar wallaby) and monotreme (platypus). *DLK1* and *DIO3* genes were identified in both species and found to be biallelically expressed. Imprinted expression of genes within this region is therefore restricted to the eutherian lineage. A seven way comparative sequence analysis of the entire *DLK1/DIO3* region in chicken, platypus, wallaby, opossum, dog, mouse and human was performed. Results indicate that genomic signatures previously associated with imprinting clusters i.e. SINE depletion and increased GC content, were only associated with the imprinted eutherian *DLK1/DIO3* region, suggesting these features evolved in the region alongside the acquisition of imprinting. The IG-DMR, the imprinting control region for the domain, is not present in non-eutherian species. Comparative

expression and epigenetic analysis in platypus and wallaby suggest the paternal chromosome in eutherians is most similar to the ancestral *DLK1/DIO3* region.

The snoRNA and microRNA clusters in the domain were shown to be eutherian specific, causing a region of relative expansion in these species, whereas one specific eutherian region was resistant to expansion. A full length *GTL2* gene was not identified in non-eutherian species but a number of expressed evolutionary conserved regions show that this long ncRNA gene is present in non-eutherians. A region orthologous to the retrotransposon like gene, *RTL1*, was identified in both marsupials, but not in platypus or chicken. In marsupials the *RTL1* gene lacks an open reading frame and is not expressed. This indicates that, in marsupials, *RTL1* did not gain a function (or lost it) and the sequence diverged. Hence, in eutherians *RTL1* has evolved into a new gene with a function in placentation, an event that may have driven the evolution of imprinted expression within the region.



From top: Promega Representative Dr Paul Glands presents the winners with their awards:

**1st prize** Carol Ann Edwards  
(The Department of Physiology, Development and Neuroscience, University of Cambridge)

**2nd prize** Christina Marques  
(University of Porto, Portugal)

**3rd prize** Paris Veltsos  
(Queen Mary University, London)

#### References

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Edwards, C.A., Rens, W., Clark, O., Mungall, A.J., Hore, T., Marshall Graves, J.A., Dunham, I., Ferguson-Smith, A.C. & Ferguson-Smith, M.A. (2007) The evolution of imprinting: chromosomal mapping of orthologues of mammalian imprinted domains in monotreme and marsupial mammals. *BMC Evol Biol*, 7: 157.

# The Genetics Society Spring Meeting Frontiers in Epigenetics

Saturday 10 May 2008, John Innes Centre, Norwich.

Mary Byrne . John Innes Centre and Irina Stancheva, University of Edinburgh

**T**he 2008 Spring Meeting of the Society was centred on epigenetics and served to highlight the multiple and often interconnected mechanisms involved in diverse organisms. The term epigenetics refers to changes in gene expression that are stable between cell divisions, and sometimes between generations, but do not involve changes in the underlying DNA sequence of the organism. Heritable non-sequence based changes are most often thought to involve modification of DNA or chromatin and, in recent years, there has been much progress on how these modifications are established and maintained. Mechanisms of epigenetic inheritance also involve RNA either indirectly through chromatin modification and have also been proposed as heritable units potentially directly imparting cellular memory.

The meeting started with a presentation by David Baulcombe (University of Cambridge) on small RNA pathways in plants and the role these regulatory elements have in defence against virus infection. Suppression of

viruses and potentially harmful transposons is possibly an evolutionarily ancient role of gene silencing pathways. While plants have evolved silencing mechanisms for defence, viruses correspondingly encode proteins that inactivate key components of plant silencing pathways. One of these virus proteins is an F-box protein, which mediates degradation of the key small RNA effector ARGONAUTE1 protein. The precise protein degradation mechanism remains to be elucidated, but clearly differs from the typical proteasome pathway conferred by many F-box proteins. On the plant side, one mechanism of defence against systemic virus infection is exclusion from the shoot apex or meristem, which harbours the stem cell population essential for continued generation of new organs and for growth of the plant. The mechanism of this exclusion has remained elusive.

However, work on Tobacco rattle virus (TRV) provides a hint on resilience of the meristem to virus infection. TRV invades the meristem but fails to propagate in these cells due to silencing by small RNAs. This silencing potentially establishes an epigenetic state in daughter cells, thereby limiting virus spread to organs initiating from the meristem.

While small RNA pathways are an important part of pathogen and genome defence they also contribute to many developmental processes in plants and animals. Scott Poethig (University of Pennsylvania) described work on heterochronic development or phase change in *Arabidopsis*. Many targets of microRNAs encode developmental regulatory proteins so isolation of mutants affecting phase change has led to the identification and functional characterization of key

**Heritable non-sequence based changes are most often thought to involve modification of DNA or chromatin and, in recent years, there has been much progress on how these modifications are established and maintained.**

components of small RNA pathways, including small RNA binding Argonaute proteins. Phase change involves successive expression of two different microRNAs: down regulation of the corresponding target genes mediate the transition from juvenile to adult phases of growth. Targets of early expressed miR156 are the *SPL* gene family. Surprisingly, all 10 *SPL* family members vary considerably in size but all have retained miR156 target sites and individual genes from different clades still modulate phase change indicating an essential role for *SPL* genes in his process. *SPL* genes positively regulate late expressed miR172 and down regulation of AP2-like targets of miR172 are needed for transition to adult growth. Components of this pathway act in phase transition in maize indicating conservation across broad land plant lineages. By analogy, progressive maturation of *Caenorhabditis elegans* through juvenile to adult phases of growth is also regulated by successive expression of microRNAs, so possibly this is a common theme in eukaryote life cycle progression.

While we now have a handle on many genes involved in establishing epigenetic states an important question is whether epigenetic changes are of adaptive significance. Identifying epigenetic changes in natural populations and understanding the significance of these changes is a

challenging problem. Vincent Colot (CNRS) discussed a system to address these questions. A well known gene in *Arabidopsis*, *DDM1*, is required to maintain methylation states of heterochromatin but is also known to influence methylation of some euchromatin. The *ddm1* mutant is being used to generate recombinant inbred lines that enable a test for possible stable multigenerational inheritance of chromatin changes. Phenotypic variation across these lines provides a means for identifying epigenetic changes that impact on plant growth through quantitative trait analysis. Furthermore, analysis of methylation states after multiple generations following *ddm1* induced demethylation is identifying regions of heterochromatin that are remethylated and regions that are not readily remethylated suggesting distinct mechanisms act to maintain genome-wide integrity.

In animals, epigenetic mechanisms are involved in a variety of biological phenomena such as regulation gene expression, genomic imprinting, X-chromosome inactivation in placental mammals and maintenance of genome architecture. After Carol Edwards (University of Cambridge), the recipient of the Promega Young Geneticist of the Year Award, presented her work on the comparative analysis of the imprinted *Dlk-Dio3* gene cluster in eutherian,

marsupial and monotreme mammals (see the previous article). We had two further talks on genomic imprinting in mammals, focusing on basic mechanisms involved in the regulation of imprinted loci, establishment and maintenance of DNA methylation at differentially methylated control regions (DMRs) and the importance of these mechanisms in embryo development and understanding human disease. Ann Ferguson-Smith (University of Cambridge) highlighted the significance of differentially methylated imprinted regions and non-coding RNAs in regulating the monoallelic expression of genes in imprinted clusters. She focused on an exciting new discovery indicating that a KRAB family zinc-finger protein *Zfp57* is involved in maintenance of maternal and paternal DNA methylation imprints in the early cleavage mouse embryos. Although the precise mechanism of *Zfp57* function is unknown (*Zfp57* deficiency is maternal effect lethal), a hypothesis was put forward that *Zfp57* might recruit DNA methyltransferases enzymes in order to actively maintain DNA methylation at imprinted regions during the embryonic stages when most of the genome undergoes a wave of global demethylation.

Marisa Bartolomei (University of Pennsylvania) presented recent work from her lab dissecting the function of the insulator protein CTCF in oocytes and early preimplantation embryos. CTCF has an important role in regulating enhancer activity and DNA methylation at the imprinted *Igf2/H19* locus and provides a platform for binding of the cohesin complex. Ablation of the maternal pool of CTCF in oocytes, by *Zp3* promoter-driven shRNA, led to early embryonic lethality possibly caused by delay in zygotic gene activation, biallelic expression of imprinted genes and chromosome segregation defects. A more general downregulation of gene expression was observed in CTCF depleted oocytes, indicating that CTCF may have an important role in regulation of gene expression by bringing the enhancers and promoters in close proximity.

The function of CTCF as well as insulator and silencer elements dominated the talk by Rob White (University of Cambridge). His lab, in

collaboration with Steve Russell and co-workers, has recently published a high-resolution map of CTCF binding over several large regions of *Drosophila* genome, including the Hox loci. Rob highlighted the importance of CTCF enhancer blocking activity and CTCF-mediated establishment of chromatin boundaries at the *Abdominal B* locus for body patterning during *Drosophila* development. An interesting interplay between Polycomb group proteins and CTCF was also observed at these loci suggesting that in some instances Polycomb binding may be irrelevant for the activity of a nearby gene but could have an impact on a more distal one by inactivating an enhancer element. Thus long-range enhancer-promoter interactions in *Drosophila*, and probably other systems, are likely to be regulated in a complex manner by insulator proteins and Polycomb complexes.

Terry Magnuson (University of North Carolina) gave perhaps the most surprising talk of the meeting. He focused on the role of non-coding RNA *Xist* and Polycomb complexes in X-chromosome inactivation. He presented data indicating that imprinted inactivation of paternal X chromosome (Xp) initiates and proceeds normally in mouse embryos inheriting Xp devoid of Xp *Xist* RNA as well as in the absence of PRC2 complex and accumulation of histone H3K27 methylation on the inactive Xp. He proposed

that *Xist* RNA and Polycomb group proteins are dispensable for initiation but are essential for maintenance of imprinted X-inactivation in the mouse embryo. This raises the question of what is the mechanism and factors involved in the initiation of imprinted X-inactivation.

These chromosome studies were complemented by impressive genome-wide analyses of chromatin-nuclear lamina interactions in *Drosophila* and human cells presented by Bas van Steensel (Netherlands Cancer Institute). His lab is using the Dam-ID technique to map protein interaction sites on DNA. When applied to human lamin B and Emerin proteins, the mapping revealed that large, several megabase in length, regions of the genome depleted of genes and active transcription associate with the nuclear periphery. An interesting feature of these lamina-associated domains (LADs) is that their sharp boundaries are often marked with either CTCF binding sites or active gene promoters and CpG islands. It will be important to gain further understanding of how these domains are established, maintained and modified to allow transcription of LAD-resident genes.

The final talk of the meeting was the Balfour Lecture presented by Miltos Tsiantis (University of Oxford). The plant leaf is an organ specialized for light capture and



Genetics Society President Brian Charlesworth introduces the 2007 Balfour Lecture delivered by Miltos Tsiantis, Department of Plant Sciences, University of Oxford

conversion of this energy into growth through photosynthesis. A remarkable feature of these specialized organs is the variety and variation in form. Tsiantis described research aimed at understanding how this variation may arise and this is being addressed through comparisons of genetic regulation of leaf form in the simple leaf species *Arabidopsis* and the close relative *Cardamine hirsuta*, which has a compound leaf. The lobes in the compound leaf of *Cardamine* appear to originate from the marginal of the leaf, in a region long thought of as comprising a marginal meristem. One component that is required for *Cardamine* compound leaf formation involves a KNOX homeodomain protein, which is confined to the meristem in the *Arabidopsis* simple leaf but expressed in the *Cardamine* compound leaf. Since functional studies can be carried out in both species it has been possible to demonstrate the likely importance of cis-regulatory regions in species-specific expression pattern differences of one KNOX gene. Further work implicates a role for the hormone auxin together with KNOX genes in sculpting leaf shape. Tractable genetic and genomic resources in *Cardamine*, such as the isolation of novel compound leaf mutants, are providing a wealth of opportunity to further understand the molecular basis for species variation in leaf development.

# 1st Mammalian Genetics, Development and Disease Meeting

29th June 2007, School of Biosciences, Cardiff University

Rosalind John . School of Biosciences, Cardiff University

This purpose of this meeting was to promote the exchange of ideas and information between researchers working primarily, but not exclusively, on mammalian genetics, development and disease. We aimed to attract early-career researchers working on mammals from all over the UK but with a particular focus on those located in the South West of England and Wales, where no such opportunity currently existed. The format was based on the Mammalian Genetics and Development Workshop with presentations from early researchers, postdoctoral fellows and PhD students. We advertised this meeting through the Cardiff university website, by sending flyers to University head of departments and by direct emailing of colleagues.

The meeting was opened by Sir Martin Evans, Director of the School of Biosciences, Professor of Mammalian Genetics of Cardiff University and recipient of the Nobel Prize in Physiology or Medicine in 2007. In his introduction, Martin outlined the some of the fundamental developments, including the discovery and modification of mouse

embryonic stem cells, which have created new routes to experimental mammalian genetics and functional genomics. He also discussed the impact that genome sequencing projects have had on fields as diverse as cancer, neurobiology and human genetic disorders. He finished by saying that, despite huge advances in research, we still have a long way to go before unravelling the complexity of the genome and the epigenetic events that regulate its function.

The Keynote Speaker of the day was Mike Bruford whose interests encompass molecular ecology, conservation genetics and evolutionary biology. He spoke passionately about the alarming depletion of genetic resources throughout the world and the research being carried out orientated towards applying molecular genetics to preserve endangered species. He gave one compelling example of the dramatic collapse of the orangutan population in Borneo that has been linked to human activity and outlined the genetic strategies that are being undertaken to ensure that these unique animals survive and prosper. He also gave an example of

conservation programs have been successful and where DNA profiling has produced more accurate estimates of giant panda population numbers. His unique contribution to this meeting was greatly appreciated by all attendees with many individuals commenting on how his talk emphasised the global consequences of advances in modern genetics techniques.

The first talk of the day was from Vicki Marsh, a third year PhD student with Alan Clarke at Cardiff, who spoke about her work on the role of Pten in the intestine. She eloquently outlined the complex strategy that allowed her to study the consequences of conditional loss of expression of Pten in the mouse intestine in the context of Apc deficiency. This leads to the rapid development of adenocarcinoma and she proposed that Akt might be a potential therapeutic target in this process. The next talk was from Ben Colleypriest, a first MPhil/PhD research student with Vasanta Subramanian from the Department of Biology and Biochemistry at Bath University who presented his work on an in vitro model of Barrett's oesophagus and the characterisation of Cdx2

expression. Staying with the cancer theme, we heard a talk from Anthony Dallosso, a postdoctoral fellow at Bristol University with Keith Brown, who discussed the use of methylated DNA immunoprecipitation to identify targets of DNA methylation in paediatric cancer. After an unexpected interruption by a fire alarm, we then heard two talks in the stem cell theme. Susan Hunter, a long time associate of Martin Evans, presented her recent work describing the microarray analysis of the transcriptome of embryonic stem cell lines in comparison with material isolated from the inner cell mass of the developing embryo at different time points. E4.5 is a traditional time point at which stem cells are derived but she found that ES cells most resemble the E5.5 embryonic ectoderm. Alysia Battersby, a postdoctoral fellow with Nick Allen in Cardiff, then described the potential of using human ES cells in replacement therapy, with a specific focus on directed differentiation into forebrain precursors using a number of techniques including engineering transgenic hESCs to carry fluorescent reporter genes for FACs sorting. We then had a presentation from Simon Tunster, a second year PhD student in my group describing our mouse model of placental insufficiency in which foetal programming may be studied. The role of the extracellular calcium sensing receptor in lung branching was discussed by Brenda Reinhardt from

Daniela Riccardi's group in Cardiff. She presented preliminary results from the CaR knock out mouse and elegantly illustrated the use of ex-plant material in the analysis of this key developmental process.

We had a number of talks from Cardiff-based groups using mammalian systems to investigate and model neurological disorders including Alzheimer's (Mariah Lelos and Amy Reichelt from Mark Good's group), Huntington's disease (Mia Deschepper from Lesley Jones' group), Schizophrenia (Anne Kirtley from Kerrie Thomas's group), Frontotemporal Dementia (Trevor Humby) and also Amyotrophic Lateral Sclerosis (Ben Crabtree, Bath) reflecting the relative concentration of expertise in behavioural and basic neuroscience at the meeting both at the whole organism level and the molecular level.

At the beginning of the meeting Martin Evans spoke about the complexity of the mammalian genome. Although we may now know the DNA sequence, we still need to unravel the complexities of the genome. This was nicely illustrated by two talks on RNA splicing. Shane Wainwright (Cardiff) spoke about his work on an alternative splice variant of ADAMTS4 present in human patients with osteoarthritis while Dawid Nowak, a postdoctoral fellow with David Bates, University of West England and Bristol University,

spoke about a novel splice variant of VEGF which intriguingly acts as an anti-angiogenic isoform in contrast to the more commonly known variant of VEGF which is angiogenic.

The final talk of the day was from Anthony Isles, a recent recruit to the Department of Psychological Medicine at Cardiff, who discussed the evolutionary role of genomic imprinting. Although commonly thought to be involved predominantly in regulating embryonic growth, recent work suggest that many imprinted genes also play a role in post natal development including influencing risk taking behaviour.

Prizes of £75 were awarded to Brenda Meinhardt and Anthony Dallosso before the meeting ended in a wine reception kindly funded by GRI.

This first meeting in Cardiff covered the full breadth of research in Genetics from the molecular analysis of a single mRNA molecule to investigation of the genetic profile of planet Earth. We had presentations from students in the first year of their PhD to one from the Nobel Prize winner, Martin Evans. We hope, in future years, to maintain the calibre of these meetings with continued support from The Genetics Society, The Company of Biologists, Cardiff School of Bioscience, Wales Gene Park and GRI.

## A Triple Helix Meeting: Who Owns My Genome? 20th February 2008, University of Cambridge

Harsh Bhatt . The Triple Helix, Cambridge

With the ever-increasing advances in gene technology and a society with perhaps more individualism in its manner than ever before, the prospect of personal genome sequencing is one that is neither too remote, nor the easiest to ignore. Who then should have access to this information, how may it be used and what are the ethical implications? Thanks to the support of The Genetics Society, The Triple Helix Cambridge were able to debate these questions and more in - "Hands Off My Genes: The ethics and implications of personal genome sequencing", where a panel of experts attempted to address a few of these issues surrounding the subject.

The Triple Helix is an international undergraduate-run organisation that aims at promoting an open forum for students as well as the wider public to explore the interdisciplinary issues surrounding science and society.

Setting the scene by introducing what information can be obtained through these genetic tests in the first place, and how it may be applied, were Andrew Read, Professor of Human Genetics at the University of Manchester and Dr. Caroline Wright from the

PHG Foundation. Technology journalist and author, Glyn Moody, discussed how translating the genetic information from an analogue version (within our cells) to a digital one (via sequencing) could enable us to 'google' our own genome. Furthermore, with the seemingly exponential rise in information storage efficiency, a suggested view of the future included people sporting wristbands with microchips containing their personal genetic information, making it possible to do a quick check for any abnormal genotype in a potential partner. But what, as was asked, would we say is the 'right time' for such information to be exchanged - before deciding to have children, prior to marriage or indeed on the first date?

Finally, Harald Schmidt, Assistant Director at the Nuffield Council on Bioethics, brought into focus the ethical issues surrounding personal genome sequencing, amongst these being the idea of 'the right to not know' when it came to incurable diseases, and proposed how varied our own responses to such a concept might be.

With the discussion then open to the floor, a highly volatile topic emerged in the idea of insurance companies and potential employers requesting



David Summers of the Genetics Department in Cambridge (standing) chairs the Triple Helix Meeting



The audience were keen to explore issues relating to genetic confidentiality.

our genetic data to assess our candidacy. Moreover, with genomics now being sold as not just a medical tool but also a lifestyle choice in itself, some healthy scepticism about its scope and applicability is all but natural. However, the panel were unanimous in concluding that when it comes to our own personality and identity, no genome alone could map out one's sense of humour or indeed their love for science and following a query regarding the implications of tracing geographical genetic origins to explicate one's own cultural background, the evening ended with a reminder of there being "no definite test for Welshness"...

# A Taxi Driver Writes...

## The personal genome: whose DNA is it anyway?

Andrew Grierson . Academic Neurology Unit, School of Medicine and Biomedical Sciences, University of Sheffield

### What is the personal genome?

The landmark publication of the first draft of the human genome sequence in 2001 heralded a new beginning in human genetics: the post genome era. Three complete genome sequences later, in 2008 we are on the verge of the 1000 genome project and the \$1000 genome. These developments offer the most exciting opportunities for human genetics: to identify and investigate genetic variation in all of us, with the power to correlate genome-wide genotype data with human disease phenotypes. Personalised genome data is already available from a number of commercial laboratories, for around \$1000, but does this raise more questions than it is likely to answer?

The power of studying human genetics in disease risk association studies is well understood. It is exemplified by the work conducted in Iceland and other genetically isolated

populations for attributing genetic risk factors in polygenic diseases such as diabetes and heart disease. In these cases it is suggested that this balance of science and society is for the general good: there is genetic solidarity amongst the study population, and by working together they might eventually help themselves by developing preventative measures or treatments for the diseases prevalent in their societies.

The rest of the world generally lives in genetically admixed populations, so can we learn more about human diseases, our evolution and origins from studying their genetics? The answer from a number of perspectives would seem to be yes. George Church, of Harvard University, was an early adopter of DIY Genetics. He predicted that a personal genome project would be beneficial to society, and advocated a policy of openness when sharing individuals' genome sequence data. In the past 12 months a number of commercial genomics companies have emerged, but will they help realise the predicted benefits?



### Personalised healthcare or modern day snake oil?

A number of companies including Decodeme, 23andme and Navigenics offer genome-wide SNP-chip analysis for about \$1000. In addition, a host of other companies offer specific genetic risk tests,

distinct from those diagnostic tests used by hospitals and clinics for diagnostic purposes. Genome-wide analysis is currently offered without any legislative regulation, on the grounds that the service is educational not medical. However on the websites of two of these companies there are tools for ascribing an individual's genetic risk of developing a range of common diseases such as Rheumatoid Arthritis and Diabetes. These tools carry specific disclaimers such as: "While the Odds Calculator is neither a medical diagnostic nor a substitute for medical advice, it can help you confront the bewildering array of health news reported in the mass media and help you decide where you may want to focus your attention" on the 23andme webpage. Given that these may be polygenic disorders it seems unlikely that SNPs are currently sufficient to accurately predict risk in more than a subset of people. Of course a human geneticist might be able to understand the nature of an odds ratio, but without expert guidance on hand, it is clear that risk information obtained in this way could be misleading. While some may see this as little more than a genetic horoscope, others have promoted these services as an empowering lifestyle choice, where physician, scientist and participant form a virtuous circle. The novelty of this relationship is that the patient gains a personal stake in the ongoing scientific research effort. When approached on

General practitioners may be increasingly confronted by patients arriving with the results of a whole genome scan in their hand, asking what clinical intervention is on offer since they have a 10 fold increased risk of developing Alzheimer's Disease.

this issue, both 23andme and Decodeme were clear in saying that the SNP data could best be used as an indication of risk, and thus the early uptake of an established clinical diagnostic test. In many diseases the best clinical outcomes are associated with early diagnosis. It should be noted that we needn't understand the mechanistic basis for a genetic association for it to be a valid indicator of increased risk of disease.

If uptake of such personal genetics services increases, as it surely will, there is likely to be greater need for genetic counselling. General practitioners may be increasingly confronted by patients arriving with the results of a whole genome scan in their hand, asking what clinical intervention is on offer since they have a 10 fold increased risk of developing Alzheimer's Disease. This highlights one problem of marketing personalised genetics directly to the consumer, rather than via a medical practitioner. The New England Journal of Medicine outlined three more problems with these tests in a recent editorial: first the tests are not

reliable, as they are not subject to the same rigorous quality control as diagnostic tests. Second, the clinical validity of genetic associations is largely in a constant state of flux, they are active areas of research rather than diagnostic aids. Third, the use of genetic data in clinical practice, in terms of the risk or benefit to the individual, is questionable. Although there is often data supporting beneficial effects of diet or lifestyle change for disease prevention, these studies are not usually conducted in a genetically defined 'at risk' population.

Ethical issues are also raised- does the recipient of an increased or decreased risk have a duty to warn his family members of the result? How should this be approached? Will it have any effect on reproductive decision making? These questions are the domain of the genetic counsellor - but is there a safety net in place? Furthermore some people identified as having a decreased genetic risk of disease might interpret this as a justification to overindulge in a known environmental risk, such as drinking or smoking.

## Academic approaches to personal genetics

Genetic association studies are numerous in the scientific literature, but in recent years a new type of experiment has been made possible, the whole genome association study. Although these studies provide unbiased estimates of genome-wide genetic association across populations, their large size also increases the likelihood of type II error, that is failing to detect a weakly significant association after correcting for a large sample size. Interest in the predictive power of genetic variation in human disease has prompted various genome re-sequencing projects, the most ambitious of which was announced last year. The 1000 genomes project is an international collaboration that aims to generate a comprehensive catalogue of sequence variation in multiple human populations. Pilot studies are currently underway, to determine the best technical, computational and analytical approaches. Some academic studies are already of a personal nature, from the identification of genetic

founder mutations in colonial immigrant families, to the use of surnames for historical population ascertainment from the current inhabitants of Viking settlements.

These academic investigations have implications for forensic science and human evolutionary genetics. In the UK we are in the unique, and questionable, position of having a police DNA database including approximately 25% of the male population and 7% of the female population. A cost benefit analysis of this situation is beyond the scope of this article, but it seems likely that an increasing number of convictions will continue to be made on the basis of DNA evidence. Therefore a better understanding of human genetic variation will support such police investigations. Human evolutionary genetics embraces studies of the earliest fossilised remains, through pre- and early historical periods, up to the present day. Determining the genetic mutation events that underlie human evolutionary progress is essential to understand the present make-up of our genomes, and can perhaps be used to predict future evolutionary events.

## Genetic genealogists -- synergy at work

One group of amateur geneticists for whom personalised genomics has been particularly welcome are genealogists who have turned to their own DNA in the quest of identifying their ancestors. This field has been driven forward by Brian Sykes and Stephen Oppenheimer, amongst others, who have written popular science books describing their own surveys of the genetic ancestry of the Britain and Ireland. These authors are affiliated with the companies Oxford Ancestors and Ethnoancestry, which together with the US-based Family Tree DNA share the majority of the genetic genealogy market. The impact of these companies is highlighted by the fact that Oxford Ancestors turned over £1 million last year, and Family Tree DNA maintain databases containing Y chromosome haplotypes from over 124,000 customers and mitochondrial DNA records from over 65,000 customers. The general idea is that these companies market SNP and microsatellite DNA tests, the results of which can be shared amongst all customers via public databases. This aids genealogists in finding relatives when conventional paper-based genealogical research reaches a dead end. Y chromosome data alone has led to the creation of over 4,500 surname projects,

In the UK we are in the unique, and questionable, position of having a police DNA database including approximately 25% of the male population and 7% of the female population.

This community of amateur geneticists are proof of the power of genetic solidarity, and via online forums and email newsgroups, news of informative SNP markers and new branches in phylogenetic trees spreads rapidly.

which enables particularly enthusiastic genealogists to carry out phylogenetic analysis and predict shared ancestry in the distant past.

This community of amateur geneticists are proof of the power of genetic solidarity, and via online forums and email newsgroups, news of informative SNP markers and new branches in phylogenetic trees spreads rapidly. Recently for example a group of Decodeme customers interested in genealogy collaborated by sharing their data. They looked for novel SNPs that might define new branches of the Y chromosome R haplogroup, which is the most common group in Europe. They identified rs34276300 as a SNP that might indicate an early branch in the R haplogroup, and approached the DNA testing companies in order to screen themselves, and a large network of fellow enthusiasts. Within 8 weeks of the original posting on the genealogy-DNA newsgroup hundreds of customers have been tested, and many reported their rs34276300 genotype data and existing R haplogroup back to the forum, enabling these amateur geneticists to identify a new branch in the phylogenetic tree in a timescale that lays down the gauntlet to

established academic investigators.

## The future of personal genetics

Subject to government intervention, personal genetic testing is here to stay. Indeed a number of media commentators have drawn analogies to the rapid and dramatic rise in the purchase of personal computers since the mid 1970s. Although this scale of uptake seems unlikely, as the cost of personal genetic testing drops, many more people are likely to sign up. Problems exist in the area of regulation of genetic testing, particularly those that are directly marketed to consumers as 'medical lifestyle tests'. Identified SNPs will only account for a fraction of the total inherited risk, and there may be differences between population groups. We can also predict an increase in demand for genetic counselling services, that will rise in proportion to the number of people taking personal genetic tests. Furthermore it is likely that many reported genetic associations will not translate into disease mechanisms or new targets for treatment in the long term. Even if these

markers represent the best predictive tests for a disease, their uptake amongst the population is likely to be very low where there is no effective clinical treatment available. A possible benefit may be certain types of cancer where early detection is known to be a strong predictor of survival.

Positive aspects include unbiased and large-scale correlation of genotype/phenotype in humans, which may bring about advances in forensic and clinical practice. Clinical advances may or may not be facilitated by a change in the relationship between scientists, physicians and patients. Identification and classification of SNPs in the 1000 genomes project will enable academic researchers to more fully annotate the human phylogenetic tree. Increased participation and data sharing by amateur genetic genealogists may challenge academic groups in the quest to define the phylogeny of human Y chromosome markers, at least those that are common in people of European ancestry.

# Book Review

## Twelve Galton Lectures: A Centenary Selection with Commentaries

Edited by Steve Jones and Milo Keynes: The Galton Institute ISBN 978-0-9546570-1-7

Michael M Majerus . Department of Genetics, University of Cambridge.

On the improvement of our genetic future

*Twelve Galton Lectures: A Centenary Selection with Commentaries* is exactly what it says on the cover. The volume commemorates the centenary of The Galton Institute, which started life as the Eugenics Education Society in 1907, and operated under the name of the Eugenics Society from 1926-1989. There are two main elements to the content; the texts of 12 of the Galton Lectures, which have been delivered almost annually since 1914, and learned introductions to these.

I would suggest that the most instructive way to read this book is to read it twice. First, read each of the lectures alone, ignoring the introductions: simply note the lecturer and the year of delivery. Then read it again, in correct order, reading the introductions before revisiting each lecture. This way readers will consider the lectures uninfluenced by the contemporary commentaries on the lectures, which, although instructive and interesting in their own right, I found pre-emptive, somewhat distracting and occasionally overly judgmental. If you read the lectures first and only then the

commentaries, you will be able not only to judge the lectures independently of the commentaries, but also to appraise the validity of the latter.

All the lectures are concerned with the issue of eugenics, defined in 1883 by Francis Galton as “*the scientific study of the biological and social factors which improve or impair the inborn qualities of human beings and of future generations*”. In part, of course, the book is a commemoration of Francis Galton himself. Indeed, Galton was the subject of the first lecture, given in 1914 by Sir Francis Darwin. Although most remembered for his work in eugenics, Galton was a polymath. He defined meteorological anticyclones, discovered the uniqueness of fingerprints and their application to forensic science, and was a pioneer of genetic pedigree analysis and quantitative methods. He was in the forefront of the controversy between Mendelians and biometricians over continuously varying traits that was eventually resolved by Fisher (1918). Following the publication of *The Origin of Species* in 1859, he considered the action of natural selection

on humans, and in particular how it might interact with the human mind. This generated a long-term interest in human hereditary, psychology and intelligence. His work in the field of eugenics began in the late 1870s, continued until the turn of the century, and became his main preoccupation until his death in 1911.

Given the negative associations now surrounding eugenics, it is pertinent to note here that Galton himself was a proponent of positive eugenics: that is “*the augmentation of favoured stock*”. Negative eugenics – preventing reproduction in the genetically inferior – interested him little. That said, several of the lectures contained in this volume speak in favour of negative eugenics, particularly in respect of the “mentally unfit”. Over time, as a result of the 1935 negative eugenic legislation, which led to the sterilisation of 400,000 Germans, and to a lesser extent, the 60,000 court ordered sterilisations in the United States and Sweden, the word eugenics has become anathema. Yet, we now regularly practice negative eugenics in our hospitals, through screening for a variety of genetic disorders and a range of consequential practices. Indeed, through these lectures, although one can see how Galton’s original aims were to a large extent distorted and eugenics became discredited, it is interesting to note how many of the practices proposed in the early lectures are now considered more objectively and accepted by society.

In my course on evolutionary genetics in Cambridge, I have often said that many of the developments and statements in the field, and more particularly those that made them, should be viewed in the context of their age; judged in the light of what was known at that time and the prevailing academic climate. Thus, for example,

Fisher's erroneous view that the alleles of a gene would rarely, if ever, be selectively equivalent to one another, should be seen against the limited knowledge of protein chemistry and the ignorance of the chemistry of DNA of the late 1920s. Each of the lectures here should similarly be read and considered in the temporal context of its delivery. Together they give rich insights into changing social mores, views of the way that humanity is affected by selection and how artificial selection might be, and is being used to alter the natural processes that influence human evolution.

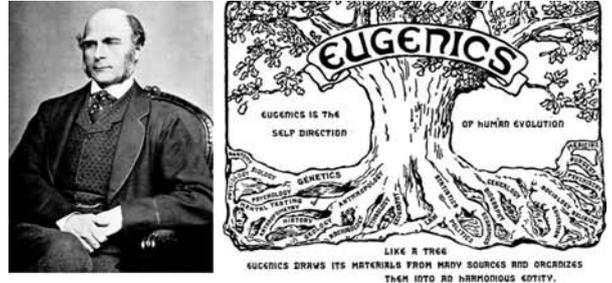
I will not give a critique of each of the lectures here. Rather, I will say that any reader is likely to find fascinating, insightful and sometimes surprising opinions in many of the lectures. The lectures provide commentaries on eugenics from the perspectives of religion, social welfare, economics, intelligence, sexuality, evolution and particularly pertinent to recent discussions in the Commons, in vitro fertilisation.

With such a wide variety of subjects, not all lectures are likely to appeal to or interest all readers equally. Thus, as an evolutionary geneticist, I found Sir Julian Huxley's 1962 lecture *Eugenics in Evolutionary Perspective* particularly stimulating. His insightful discussions of the evolutionary consequences of *Homo sapiens'* entry into the "psychosocial phase", the distribution of variance in intelligence, the

rejection of racism and the need for genetic improvement are elegantly argued and synthesised into a holistic view of the multilayered interactions between evolutionary processes and genetic change.

That said, however, all the lectures selected have something to offer. To pick just one extract, I found a passage from The Right Rev. E. W. Barnes' lecture *Some Reflections on Eugenics and Religion*, delivered in 1926, arresting. It almost perfectly describes a thesis that we would today call Intelligent Design. Here, he recognises that both fit and unfit variations arise, and proposes that it is as a result of the environment that God has created, that the fit survive and the unfit perish. He then advocates that God has given humanity the spiritual understanding to ensure that we do "not create an environment in which the feeble-minded, the criminal, and the insane can multiply rapidly". He concludes "When religious people realise that, in thus preventing the survival of the socially unfit, they are working in accordance with the plan by which God has brought humanity so far on its road, their objections to repressive action will vanish".

To conclude, I found both the lectures chosen and their commentaries instructive, rewarding and thoroughly thought provoking. The volume is a history of the evolution of both eugenics and views on eugenics. The lectures give



Sir Francis Galton, the father of the Eugenics Movement, and the logo from the 1921 International Eugenics Conference.

insights into the changing views on birth control (from the negative to the positive) eugenics (from the positive to the apparently negative), abortion, sex and artificial insemination. They deal with changes in morality, acceptability of social mores, the raise of the welfare state, and in passing, comment of the problems associated both prejudice and political correctness. Although the book is not packaged appealingly (presumably in part to keep its price to a minimum: £5.00 for a hardback book of over 350 pages), I would strongly recommend it to scholars and students of the natural and social sciences, as well as philosophers and politicians.

Our potential to "improve future generations" is increasing and will continue to increase as our understanding of the human genome and developmental genetics advances. The way that we use, or do not use, this power must be based on cogent and objective appraisal of the complex issues that touch on this sensitive subject. These Twelve Galton Lectures provide a cogent, historical context in which to consider the manipulation of our genetic future.

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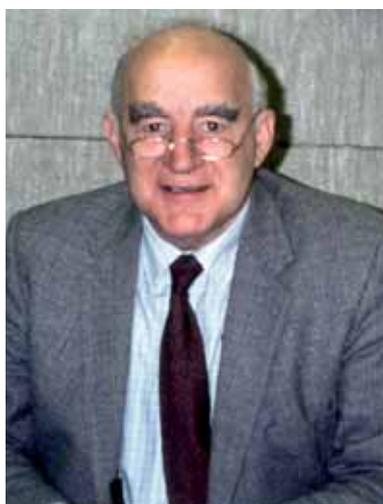
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## Professor Henry John Evans CBE PhD DSc (Hon) FRSE

24th December 1930 – 1st July 2007

Veronica van Heyningen . MRC Human Genetics Unit, Western General Hospital, Edinburgh



Last year the Genetics Society lost a most distinguished member, Professor (Henry) John Evans, who died aged 76. During his long and highly productive career he contributed hugely to the field of genetics through his work on mutagens and chromosomes and as an MRC Unit director.

Born in Llanelli, South Wales, John attended Llanelli Grammar School and went on to the University College of Wales at Aberystwyth, where he received his BSc and PhD degrees. In 1955 he joined the MRC Radiobiological Research Unit at Harwell and set to work analysing the effects of radiation and other mutagens

on chromosome structure and function in plants and fungi. He quickly made a number of significant advances – five of his first six publications were in *Nature* – and was promoted to Head of Cell Biology.

Following this early success, John was appointed at the young age of 34 to the Chair of Genetics at the University of Aberdeen where his research began to reflect a growing interest in human genetics. In 1969 he became Director of the MRC Clinical Population and Cytogenetics Unit, Edinburgh, which had opened two years earlier with the remit of monitoring chromosomal variation on a large scale in different subpopulations. Arriving after the untimely death of the inaugural director, Michael Court-Brown, John continued to support many of the large projects in progress. Work led by Patricia Jacobs, a life-long friend, continued for years after her departure. Longitudinal surveys of boys with sex chromosome anomalies revealed the detailed effects of an extra X or Y chromosome on physical health and behaviour. It is easy to forget that there was a time when there were no systematic methods for mapping and

cloning human genes. Back in the 1970s, naturally occurring chromosomal anomalies were one of the few reliable sources of information about the human genome and under John's directorship the Unit became a centre of excellence for the use of cytogenetic approaches to human genetics. Chromosome analysis of more than 10,000 consecutive newborns led to several long-term follow-up studies. One key family with a translocation segregating with severe psychiatric illness was followed with his continuing encouragement, even after his retirement, eventually leading to the identification of the now well-established gene DISC1 (Disrupted in schizophrenia 1). With colleagues he contributed to the development of early banding techniques, allowing the unambiguous identification of each human chromosome and thus helping to open up the era of gene mapping. These banding methods were used with radioactive in situ hybridisation to map satellite DNAs and with isoenzyme studies to make some of the earliest chromosomal gene assignments.

John worked tirelessly to support and encourage the staff

at CAPCU: technicians were trained in-house and through day-release to gain qualifications, while PhD students and postdocs were recruited worldwide. He was an enthusiastic and practical supporter of women scientists, making part time work possible even in the 1970s. He also nurtured emerging early-day technologies: prototype automatic karyotyping was developed under Denis Rutovitz, and homemade fluorescence-activated cell sorting equipment was available before commercial machines appeared. In 1979 the Unit hosted the Fifth International Human Gene Mapping Workshop and soon afterwards John recruited some excellent scientists to take the Unit into the molecular epoch of genome mapping and genomics, particularly Nick Hastie who eventually succeeded him as Director. I well recall the day we gathered to discuss the next big Unit project (9 June 1983 - a fateful election day) and decided to map the Wilms tumour and aniridia region on chromosome 11 using locally available deletion cases. In 1988, at John's instigation, the Unit underwent a symbolic name change, becoming the MRC Human Genetics Unit. The employment and scientific training of clinicians was always encouraged and interactions in this fertile overlap area were set up worldwide.

Throughout his time at the Unit, John continued to work

## During his career John was awarded numerous fellowships and prizes, culminating in a CBE in 1997 in recognition of his outstanding contribution to science.

on the effects of occupational and environmental exposure to mutagens. He served on numerous national and international bodies assessing the effects of radiation and setting acceptable standards for occupational exposure. He was also on the scientific advisory boards of a number of prestigious research organisations, several dealing with aspects of cancer diagnosis and therapy. In addition, he was founding governor and chair of the Caledonian Research Foundation, a charity established to support research in Scotland through fellowships and studentships.

By the time he retired in 1994, the Unit housed around 250 staff and its work was internationally renowned. Chromosome biology is still a major field of research and cytogenetics-based methods continue to be used routinely to identify disease genes. Towards the end of his Directorship, John supported the establishment of the University of Edinburgh Centre for Molecular Medicine and the Edinburgh Cancer Research Centre, both of which joined with the Human Genetics Unit last year to form the new Institute of Genetics and Molecular Medicine.

During his career John was awarded numerous fellowships and prizes, culminating in a CBE in 1997 in recognition of his outstanding contribution to science. Despite these many accolades he was always friendly and approachable, with a fine sense of humour. Social occasions, such as parties with ceilidhs, became regular fixtures on the Unit calendar.

Despite sad times, John always coped well, devotedly bringing up four teenage sons after the untimely death of his first wife from cancer. His second wife, Ros, was herself a talented cytogeneticist. Together they hosted many parties for senior and junior colleagues alike at their house with its lovely garden and fine pictures by Scottish artists collected over the years. Partly through the study of chromosomes in isolated populations, John came to love the island of Barra and spent many happy holidays there. Even quite recently he worked on the restoration of a traditional "blackhouse".

John will always be remembered by friends and colleagues and his many achievements will stand as testament to a fruitful and successful life.

## My Favourite Paper (at least one of them)

DJ De Koning . The Roslin Institute and R(D)SVS, University of Edinburgh, Roslin BioCentre, Midlothian

# Genetical genomics: the added value from segregation

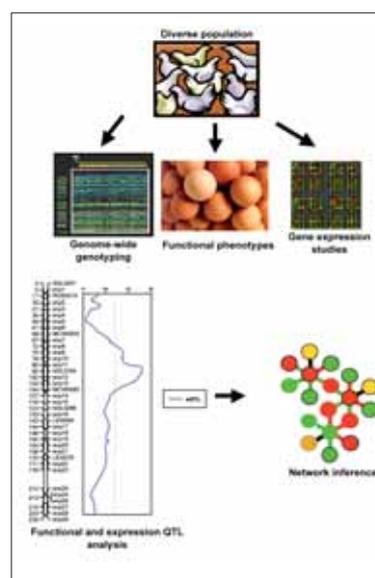
Ritsert C. Jansen and Jan-Peter Nap. (2001) *Trends Genet* 17: 388-391<sup>1</sup>

**W**hen this article appeared, gene expression microarrays or GeneChips were becoming commonplace in molecular biology. The majority of these studies were, and still are, fairly straightforward comparisons of 'treatments' (healthy vs. diseased, high vs. low, etc.) and/or studying effects over a time-course. While this was all extremely useful, it was of little help to the masses of researchers who were successfully hunting for Quantitative Trait Loci (QTL) in humans, mice, *drosophila* and many agricultural species, but far less successful at identifying functional mutations underlying these QTL.

Research groups were already supplementing their QTL studies with gene expression data in an attempt to speed up the process from QTL to gene. For example, QTL would be

mapped in an experimental cross between divergent lines, while gene expression contrasts were obtained for the founder lines. The positions of QTL would be overlaid with the positions of differentially expressed genes, suggesting positional candidate genes for the QTL<sup>2,3</sup>.

Jansen and Nap proposed to treat gene expression data like any complex trait and search the genome for QTL affecting these traits. A graphical outline of Genetical Genomics is provided in the figure below. The principal of QTL detection and Genetical Genomics is to exploit the genetic variation in a population that is genetically variable for a functional trait of interest. Such a population can be created by crossing extreme lines or breeds, followed by inter-mating of the resulting F1 generation to obtain an F2 or by backcrossing to one or both of the founder lines.



A graphical outline of Genetical Genomics. The figure was reproduced from De Koning et al<sup>14</sup>

Alternatively, a population that shows variation for the trait of interest, like a herd of livestock or a population cohort in humans, can be used directly to study the genetic variation within the

population. For QTL mapping, the segregating population is typed for molecular markers spanning the entire genome and phenotypic records for the traits of interest are collected. For Genetical Genomics, appropriate tissue samples are collected from the population for gene expression analyses. By combining pedigree data, genomic marker data and functional trait data, QTL affecting the trait of interest can be mapped to the genome. Likewise, by combining pedigree data, genotype data and gene expression data, QTL for gene expression (so called eQTL) can be mapped to the genome, and compared to the QTL for the functional traits<sup>1</sup>. By combining the location of functional QTL, eQTL, and with the locations of genes affected by the eQTL, as well as the correlation structures between the affected genes and genes in the QTL areas,

networks underlying the functional variation can be reverse-engineered<sup>4</sup>. It must be acknowledged that the publication of the first actual Genetical Genomics type studies follows closely from the Jansen and Nap paper, indicating that the ideas were already established and experiments underway at the time of publication<sup>5,6</sup>. Nonetheless, the paper is the first to formalise the concept of Genetical Genomics and, in my view, has inspired many researchers to embrace this approach as a powerful, albeit quite costly, tool for complex trait dissection.

Over the last 5 years, we have seen a large number of Genetical Genomics studies, starting from model organisms and proof-of-principle type studies, moving to general populations and doing Genetical Genomics in the

context of functional trait variation. While several reviews of the methods are available<sup>7,8</sup>, a very good example of dissecting a complex trait via Genetical Genomics is provided by Mehrabian et al<sup>9</sup>.

Ritsert Jansen is a statistician by training and initially he focussed on methodology for QTL detection; an area where he made quite some impact<sup>10,13</sup>. He has really made his mark in Genetical Genomics, co-authoring no fewer than 14 articles on the subject since the 2001 paper, addressing both methodological and design issues, as well as actual experimental studies. The strength of this article is in its simplicity and how it conveys the potential of Genetical Genomics in a very accessible manner. It certainly provided me with the direction in which I wanted to take my research.

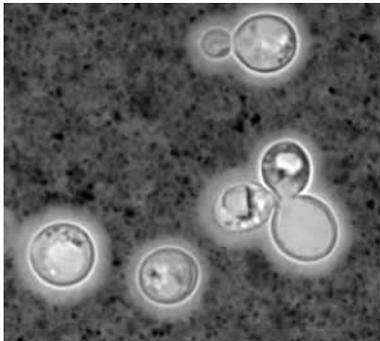
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## Genotyping a fungal pathogen, *Cryptococcus gattii*

Visit to the Centraal Bureau voor Schimmelcultuur, Institute of the Royal Netherlands Academy of Arts and Sciences.

Hansong Ma . School of Biosciences, University of Birmingham



*Cryptococcus gattii*

*Cryptococcus gattii*, the causative agent of recent cryptococcosis outbreak on Vancouver Islands in Canada, is a fatal human fungal pathogen, and unlike many other fungal pathogens, it infects immunocompetent individuals.

*Cryptococcus* has long been known to survive and proliferate inside professional phagocytes to achieve latency and long term persistent. Previous work by our group has found that strains that are good at proliferating inside macrophages seem to kill mice faster, suggesting that such intracellular parasitism is a major determinant of virulence in *Cryptococcus*. Interestingly, many of the Vancouver isolates proliferate better intracellularly than other *C. gattii* strains isolated from the rest of the world, despite the

fact that they are genetically very similar to each other. We are therefore very keen to carry out experiments to establish whether the variability in intracellular proliferation correlates with genotype (MLST and AFLP grouping), different virulence factors and isolation history (e.g. human, veterinary, environmental). Such experiments will help to reveal many complex relationships between intracellular proliferation and the factors of interest that may not be immediately obvious, and thus provide an insight into the possible causes of intracellular parasitism.

Before the visit, the intracellular proliferation rate of 65 cryptococcal strains was determined and from these data, 40 *C. gattii* strains were selected (20 are Vancouver isolates) for phenotypic (virulence trait quantification) and genotypic (AFLP) analyses in order to reveal any factors that contribute to fast intracellular proliferation. Phenotypic analysis focused on three major virulence factors, capsule size, melanin production and enzyme activity (especially proteinase and phospholipase). During the

visit, I learned how to conduct assays for all of these virulence traits, allowing us to quantify each trait across all of the cryptococcal isolates. All the measurements were done at both 25°C and 37°C in triplicate. Interestingly, this analysis revealed substantial inter-strain variation for each virulence factor measured. Intriguingly, intracellular parasitism does not seem to be determined by any single known virulence factor, although there was a significant correlation between melanin production at 37°C and intracellular proliferation rate. It is possible that the rate is also determined by other (unknown) virulence factors or by a combination of these analysed factors: we are currently undertaking statistical analysis to test for complex correlations.

For genotypic analysis, Amplified Fragment Length Polymorphism (AFLP) was carried out. AFLP is a PCR-based genetic fingerprinting technique with the capability of detecting various polymorphisms in different genomic regions simultaneously. Due to its sensitivity and reproducibility,

AFLP has become widely used for the identification of genetic variation in strains. Based on the AFLP data obtained, an intra-species phylogeny tree of chosen 40 strains was generated. The construction of the tree revealed inter-genotype variation for different traits. For example, genotype 6 isolates were found to show increased melanin production at 37°C compared to genotype 4, 5 and 7 isolates. Since genotype 6 isolates are associated with the Vancouver outbreak, it is

likely to be the case that melanin production contributes significantly towards intracellular parasitism.

CBS, as a world fungal collection centre, holds a very large number of *C. gattii* isolates covering a wide range of genotypes and isolation histories. This visit was an excellent opportunity not only to obtain valuable data and learn essential techniques (e.g. AFLP) that are not available in our institute, but also to

strengthen our collaboration with Teun Boekhout's group, who are international experts in *Cryptococcus* systematics and molecular genetics. The data obtained has made a significant contribution to our understanding of the molecular basis of macrophage intracellular parasitism by *Cryptococcus*. It will form an essential part of my PhD thesis and will be submitted as a manuscript along with recently generated microarray data within the next few months.

## Diploid males in Taiwanese *Cotesia vestalis* parasitoids

Jetske G. de Boer . Centre for Ecological and Evolutionary Studies, Groningen University.

### Heredity Field Grant awarded to Prof. L.W. Beukeboom

**C**abbage is an important vegetable crop worldwide and from personal experience I can now conclude that no meal is complete without some sort of cabbage in Taiwan. Cabbage also hosts plenty of insect pests, which in turn provide food to a wide range of natural enemies. In Taiwan, the hymenopteran parasitoid *Cotesia vestalis* is one of the most important natural enemies of diamondback moth larvae (*Plutella xylostella*), a common cabbage pest. All sexually reproducing Hymenoptera are haplo-diploid, with haploid males and diploid females

developing from unfertilized and fertilized eggs respectively. However, diploid males develop from fertilized eggs that are homozygous at a highly polymorphic sex locus under a mechanism called complementary sex determination (CSD; Whiting 1943). Diploid males represent a severe inbreeding depression because they are commonly unviable or sterile. Theoretical models predict that CSD can negatively affect population growth rate and sex ratio, and increase extinction risk. CSD may therefore play a crucial role in conservation management of economically

and ecologically important groups such as parasitoid wasps and pollinating bees, many of which have declined significantly in the Netherlands and Britain, along with insect-pollinated plants. Yet, surprisingly little is known about the frequency of diploid males in natural populations of parasitoids, with the exception of *Habrobracon hebetor*.

In February 2008, I visited the World Vegetable Center AVRDC in Taiwan to collect naturally occurring *C. vestalis* wasps with the goal of determining the frequency of

diploid males under field conditions and assessing genetic variation.

Diamondback moth larvae and parasitoid cocoons were collected from eight different fields in four locations in the lowlands of Western Taiwan. Host larvae were reared out in the laboratory to allow development of parasitoid cocoons. Cocoons were then transported back to our laboratory at Groningen University, the Netherlands, where they emerged. More than 6,000 parasitoid cocoons yielded over 4,000 adult wasps with a sex ratio between 41 and 56 % males. Flow cytometry was used to analyze male ploidy. Thus far, diploid males have been found in 5 of the 8 field sites and their frequency ranges from 0 to 3 %. The low frequency of diploid males in the native populations in Taiwan may reflect very high diversity of sex alleles and low inbreeding levels. In addition, we recently showed that CSD in *C. vestalis* is likely based on multiple complementary sex loci and this would reduce the expected frequency of diploid males dramatically (de Boer et al. 2008).

In addition to determining diploid male frequencies, I will

use the collected wasps to assess general genetic variation with microsatellite markers. Very little is known about the mating structure of parasitoid wasps under field conditions and our data set could provide more insight. In the future, I plan to collect *C. vestalis* from different parts of the world to compare diploid male frequencies and general genetic variation in native and introduced populations. *C. vestalis* is native to Eurasia and Africa and has been successfully introduced in many countries for biological control of the diamondback moth. This offers an ideal opportunity to gain insight into the potential effects of bottlenecks or founder events on the sex determination load in parasitoid wasps. I expect genetic variation to be lower and sex determination load to be higher in introduced than in native populations.

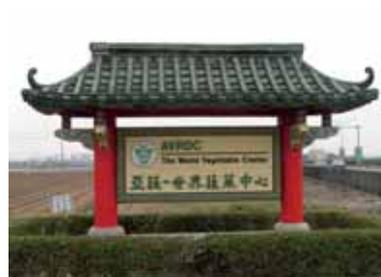
I am grateful to the Genetics Society for their help in funding this field trip and I would like to thank Dr. Ramasamy and Mrs. Lin and Mrs. Yang and the other ladies of the insectary at AVRDC for their help during the fieldwork in Taiwan.



A field owner in Taiwan anxiously inspects her crops for pest damage.



The parasitoid wasp *C. vestalis*



The Asian Vegetable Research and Development Center

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## Keystone Symposia DNA Replication and Recombination 10th - 14th February 2008 Santa Fe, New Mexico, USA

Zhenhong (Belinda) Duan . Institute of Genetics, University of Nottingham

This year Santa Fe begins a three-year commemoration of the 400<sup>th</sup> anniversary of its founding. As soon as I arrived in the city, I found the stylish local buildings along the main streets and countless museums, galleries and gift shops displaying amazing art pieces made by native Indian artists. At the far-east end of the city, mountains with snow on a background of generous sunshine and blue sky brought up a deeply pleasant feeling of excitement. Suddenly I thought that scientific research is also a kind of art. This might be the reason that the conference DNA Replication and Recombination was held in Santa Fe, a unique city in richness of history, heritage, arts and culture.

The conference opened on the evening of the 10<sup>th</sup> February with Jack D. Griffith giving a brief introduction to the meeting. He told us stories about the research and family life of Arthur Kornberg and Nancy Nosssal, two great scientists we lost recently from the field of DNA replication. E O'Donnell then gave the keynote address "Dynamic Mechanisms at the *E.coli* Replication fork". His group's work shows that *E.coli* DNA polymerase III holoenzyme

containing three DNA polIII cores can be assembled and is functional at a replication fork. Three DNA polymerases within one replisome appear to enhance functionality on the lagging strand. The third polymerase probably also helps the replisome bypass blocks on the leading and lagging blocks on either strand.

The program of the conference was well organized. Each day there were plenary sessions with four speakers in the morning and three speakers in the evening, two workshops focused on two different topics with eight speakers each in the afternoon and poster session at lunchtime or later evening. Every day was busy but still there was plenty of free time to talk with other researchers.

Stephen C. West from London Research Institute is a great speaker. His honest-style slides and smooth talking attracted me to follow his story of Aprataxin, which is a product of *APT*X gene. Aprataxin interacts with the DNA repair proteins XRCC1 and XRCC4, that in turn form complexes with DNA ligase III and DNA ligase IV. The XRCC1/DNA ligase III and XRCC4/DNA ligase IV complexes are involved in single- and double-strand

break repair, respectively, indicating that Aprataxin may be important for the repair of DNA breaks. In fact, Aprataxin acts as a proofreader for abortive ligation events in Base Excision Repair, in that it can selectively bind and remove 5'-DNA adenylates from DNA break sites. Their research suggests that oxidative damage within neuronal tissues of individuals with AOA1, a progressive neurological disorder caused by mutation of the *APT*X gene, leads to the progressive accumulation of persistent DNA nicks, and that unrepaired 5'-adenylates are the causative lesion of this neurological disease. In post-mitotic neuronal cells, which lack alternative replication-dependent mechanisms that remove 5'-adenylates, these transcription-blocking lesions accumulate over a period of years leading to disease progression.

Stephen P. Bell from Howard Hughes Medical Institute is another one of my favourite speakers. His group is interested in the strict regulation of the formation of pre-replicative complex (pre-RC). Their work shows clearly that the pre-RC kinase targets and modifies the MCMs, which bind to double strand DNA

near replication origins. Then the phosphorylated MCMs recruit DDK to pre-RC. In consequence, the modification of DDK stimulates pre-RC to open the double strand DNA near the replication origin and DNA replication is initiated.

Johannes Walter from Harvard medical School brought up their latest study on the biochemical mechanism of replication-coupled DNA interstrand cross-link (ICL) repair, a field in which I am very interested because part of my current project is also ICL repair (but using genetic methods). They use plasmids containing a single site-specific ICL and a completely soluble replication extract from *Xenopus Laevis* eggs to study the ICL repair *in vivo*. Their beautiful denaturing gels reveal that the lagging

strand of fork initially pauses at -20 nucleotides from the lesion and the leading strand advances to the site of the crosslink with a nucleotide inserted across from the DNA adduct. Lesion bypass is accompanied by dual incisions surrounding the ICL on one parental strand. Ultimately, a significant portion of the input DNA is fully repaired. They suggested a new model of ICL repair, which avoids the problem of replication fork reconstruction in the old model. However, the new model of ICL repair depends on two adjacent replication forks, which might not always be the case *in vivo*.

The conference closed very specially with a piano concert by Dr Karen Allred, a successful solo recitalist. Beautiful music brought back



Sculpture from the Museum of the Institute of American Indian Arts, Santa Fe.

nice memories of the few days in the Santa Fe. I would like to thank the Genetics Society for providing me with a travel grant for this conference. It was a fantastic trip and I return to my thesis writing with excitement and stimulation.

## Keystone Symposium on RNAi, MicroRNA and Non-Coding RNA, 25th – 30th March 2008, Whistler Resort, Canada

Rachael Nimmo . Department of Biological Sciences, Lancaster University

This was my first time at the Keystone Symposia meeting on RNAi, MicroRNA, and Non-Coding RNA and I have to say I was very impressed with the standard of the talks although it also made me a little apprehensive at the prospect of joining such a competitive, rapidly expanding field! The opening Keynote speech was given, quite appropriately, by Craig Mello. His talk set the scene for the

remainder of the meeting as he discussed his groups work on two new classes of short RNAs recently identified in *C. elegans*, the 21U and 22G RNAs, as well as the many worm AGOs. It seems that there are many different types of non-coding RNAs being identified by the multitude of profiling projects that are ongoing. It will be some time yet before we have a clear picture of all the RNAs that are produced but it seems

likely that some will be organism and even cell type specific. The 22G and 21U RNAs each seem to be associated with a different type of AGO protein: the WAGOS (worm-specific Argonautes) are required for 22G RNAs and PRG-1 for the piRNA-like 21U RNAs. These latter RNAs may be functionally analogous to piRNAs in that they interact with a Piwi family AGO, have preference for U at 5' end as well as 3' O-methylation and are localized to the germline. However they are shorter than piRNAs, 21 versus 24-30 nucleotides in length, and, rather than being transposon or repeat associated are produced from many clusters in two regions of chromosome IV. Craig

proposed that the temperature sensitive sterility associated with the *prg-1* mutant when cultured at 25°C, and the finding that mouse Piwi proteins are expressed in testes and are required for male fertility may imply a homologous heat-sensitive process involved in germline maintenance that may explain why mammalian testes are located outside of the body. Another AGO, CSR-1, one of the WAGOs, also has a striking developmental role: *csr-1* mutants are sterile and early embryos produced from *csr-1* (*RNAi*) hermaphrodites have defects in kinetochore polarity resulting in failure to correctly undergo chromosome segregation. It is not yet clear what (if any) role RNAi may be playing in this process.

Greg Hannon gave the second Keynote, describing his pioneering work on the role of piRNAs in germline genome defence against transposons, as well as more recent work on identifying endogenously generated siRNAs in the mammalian female germline. These endo-siRNAs are often generated from pseudogenes and appear to regulate gene expression. In addition, he proposed that Piwi family AGOs and piRNAs may have a role in TGS, as well as PTGS, as the founding member of the family, Piwi is localized to the nucleus in *Drosophila* nurse cells whereas other Piwi family AGOs, Ago3 and Aub are localized in the cytoplasmic perinuclear nuage in the germline, which are thought to



Snowball fights at the Keystone RNAi Symposium in British Columbia

be sites of piRNA biogenesis and RNA processing. Indeed Haifan Lin presented data that indicates that Piwi-piRNA complexes bind to chromatin at telomeric associated sites (TAS) via interaction with the chromosomal protein HP1 and activate the formation of the piRNAs encoded in the TAS.

Carlo Croce gave a very wide-ranging talk on the diverse roles of miRNAs in cancer. One nice example is the miR-29 family's role in lung cancer. miR-29 miRNAs are often down-regulated in lung cancer whereas conversely, the DNMT-3A and B methyl transferases are upregulated and are associated with poor prognosis and so the finding that there are regions of miR-29 complementarity in the 3' UTRs of these genes suggested a role for this family of miRNAs in carcinogenesis. Indeed these miRNAs were found to directly target DNMT-3A and -3B and restore normal patterns of DNA methylation when expressed in lung cancer cell lines and to inhibit tumorigenicity *in vitro* and *in vivo*.

Eric Olson presented an elegant way in which miRNAs are integrated into gene regulatory networks in cardiac muscle. There are a network of miRNAs embedded within the myosin heavy chain genes, the Myo-miR network, which control the cardiac stress response and myocyte identity through positive and negative feedback loops. This was a good example of the way in which profiling miRNAs from specific tissues in normal and diseased states using both human samples and mouse disease models can be fertile ground for yielding information on the role of miRNAs in disease, in normal development and under conditions of stress.

There were two talks describing the recently identified role for LIN-28 proteins in regulating the processing of the *let-7* family miRNAs. The *let-7* primary transcript is present throughout development in embryos, ES cells and some tumour cells but the mature miRNA is only expressed late, in differentiated cells. Both Scott Hammond and Narry Kim used a biochemical approach to show that the LIN-28 protein inhibits processing of *let-7*; however their results differed quite considerably as to which step of the processing pathway was affected. Hammond found that LIN-28 binds to the loop region of the pri-miRNA and inhibits Drosha processing whereas Kim's group found that the Dicer step was repressed by LIN-28 via the polyuridylation of the *let-7* pre-miRNA. It is not clear how these two models can be reconciled but it is possible that, despite Kim's findings that Drosha pri-miRNA processing was apparently unaffected, both steps may be negatively regulated by LIN-28. As a worm biologist I am intrigued by this new role for LIN-28, as of course this protein was first discovered as being involved in the heterochronic pathway in worms and is thought to be regulated by *let-7* as well as *lin-4* miRNAs. I wonder if this role of LIN-28 in mammals may also be conserved in worms where it would presumably act in a positive feedback loop to prevent its repression by *let-7* until the appropriate time. This kind of mechanism may also be at play in higher organisms as the *lin-4* and *let-7* binding sites in the *lin-28* 3' UTR are conserved in mammals.

Another much talked about topic was that of target prediction. It is a stumbling block in our analysis of miRNA function that we find it difficult to accurately predict biologically relevant targets of miRNAs. Although target prediction algorithms have been developed and many hundreds of targets have been predicted for each miRNA, there are still relatively few validated miRNA-target interactions. The current methods depend on conservation and the presence of a seed sequence and some recent work carried out independently by both David Bartel and Nikolaus Rajewsky, using SILAC to measure changes in the proteome in response to alterations in miRNA levels, appears to go some way to confirming that this is important in many cases. However, it also seems there are many non-conserved target sites and, in addition,

sites need not be located in the 3'UTR since some apparently functional sites are found within ORFs. This confirmed my suspicions that by only looking for target sites in the 3' UTR of genes and considering only those that are conserved as worthy of functional testing we are then creating a self-reinforcing (but possibly misleading) cycle which means that only conserved 3'UTR sites are validated! This then apparently reassures us that our models are correct and so on and so forth. It had been shown already by Joan Steitz's group that miRNA binding sites in 5'UTRs of genes are able to cause silencing but until we start looking for endogenous sites in all regions of the mRNA then we will not know how relevant this is.

There were many talks on the use of RNAi and also miRNAs in therapy and with advances in cellular delivery techniques

no doubt we will soon see these products coming to market. However in the particularly memorable final talk of the meeting on the use of LNAs to silence miRNA in primates, Morten Lindow urged us to stay single and naked – at least with regard to therapeutic short oligonucleotides! It seems that a single stranded molecule is better than a double stranded molecule at entering cells, possibly as a result of the greater exposure of hydrophobic groups.

Finally, there were an abundance of miRNA and short RNA profiling projects presented in the poster sessions: the technologies for this have advanced rapidly, especially with the advent of deep sequencing. So I am sure that in the next few years we will see an explosion in the discovery of non-coding RNA-mediated regulation in a wide variety of processes and the over-subscribed Keystone symposia on RNAi, miRNA and Non-coding RNA will no longer be viable. Instead we will see a splintering of the field as it expands. I just hope the quality of the research does not suffer because this was one of the best meetings I have been lucky enough to attend – and we had chance to do some skiing! So I guess the take home message from the meeting is that we are only just discovering the tip of the RNA iceberg. Watch this space!

## EURASNET Symposium and Workshop on Alternative Splicing and Disease

18th – 23rd February 2008, University of Montpellier, France

Prabhakar Rajan . Institute of Human Genetics, Newcastle University, UK

**A**lternative pre-mRNA splicing increases the coding capacity of the genome and proteomic diversity of eukaryotes. Global studies suggest that at least three quarters of human genes are alternatively spliced, and

many aberrant splicing events are associated with human disease. In 2006, a European Alternative Splicing Network (EURASNET) was established with funding from the European Commission Sixth Framework Programme (FP6), bringing together several

splicing research groups from different countries. Part of the EURASNET mission is to “promote understanding of the complex regulation of alternative splicing in different systems” and to “establish an active and vibrant network to share and exchange information, methods and material among the network partners” through a series of workshops and conferences.

This EURASNET workshop was held in the university town of Montpellier on the south coast of France. A plenary symposium on Alternative Splicing and Disease was held on the first day, and included invited speakers from several European EURASNET groups. The Speakers introduced concepts and presented findings from their own research into alternative splicing and disease, and also discussed the potential clinical application of aberrant splicing detection and modulation. Of particular relevance to my research in cancer biology were two talks delivered in a session entitled Splicing and Cancer: Professor Guiseppe Biamonti discussed the effect of aberrant splicing events on cancer phenotypes and epithelial to mesenchymal transition; and Professor Elmar Stickeler detailed his own translational research programme in gynaecological oncology.

The rest of the week was dedicated to a practical “hands on” workshop covering a variety of techniques for study of alternative splicing and disease. I was fortunate enough to be part of a small group of 26 students selected to take part. The workshop commenced with a series of short talks from Affymetrix on the use of their GeneChip Exon Array system for the detection of alternative splicing. Participants were able to try two software

packages (Affymetrix Expression Console and Biotique XRAY) for analysis of a publically available colon cancer dataset. Pierre de la Grange (INSERM, Paris) hosted an excellent seminar demystifying alternative splicing bioinformatics for non-specialists and explored a number of public splicing databases. He also demonstrated his own database ([www.fast-db.com](http://www.fast-db.com)), which very easy to use and can also visualise Affymetrix Exon Array data.

Other techniques covered during the workshop included the design, generation, and transfection of reporter minigenes for study of alternative splicing, RNA purification and RT-PCR, localisation of GFP fusion splicing factors by microscopy, and siRNA. Of particular interest were practical sessions using two different technologies to correct mis-splicing in disease models. In the first, we used morpholino oligonucleotides to modulate splicing of the *Ron* proto-oncogene in cancer cells and in the second, we used antisense U7 snRNA to mask a splice site mutation in the  $\beta$ -*globin* gene and correct aberrant splicing.

Despite intensive 12-hour days in the lab, we had sufficient time to explore Montpellier’s historic town centre, vibrant nightlife and even make a trip to the Mediterranean Sea! The workshop was a great opportunity to meet the experts, and try out some of

the most up-to-date molecular and cellular techniques in alternative splicing. This was an excellent introductory workshop, which I would strongly recommend to researchers in the field of alternative splicing and disease. I would like to thank the organisers for hosting the event, and the Genetics Society for sponsorship towards this worthwhile and extremely enjoyable trip.



Hands on experience at the Montpellier alternative splicing workshop (courtesy Julia Kiosz)

## SALSEA - SALMAN II (Salmon at Sea - Atlantic salmon Analysis Network)

Symposium and Workshop on Population structuring of Atlantic salmon: from within rivers to between continents & Developing a scientific framework for trans-range stock identification of Atlantic salmon. 20th – 22nd February 2008, Paris, France

Anna Finnegan . School of Biosciences, University of Exeter

**S**ALMAN is an informal network of researchers from North America and Europe undertaking microsatellite analysis of Atlantic salmon to address a wide range of population genetics subjects. Initially set up to begin to standardise a suite of microsatellite markers used range-wide, this was the second SALMAN meeting arranged to coincide with a major new international programme to identify the origins of Atlantic salmon caught at sea, SALSEA (Salmon at Sea).

The first day was dedicated to a symposium, at which leading researchers presented an overview of the most up to date literature on major themes encountered in this field. This ranged from assessing the genetic diversity between continents, through all scales, right down to assessing the diversity between tributaries within river catchments. Also included were sessions on temporal stability of populations, mixed stock analysis, optimum sampling strategies, new emerging

markers and the Atlantic Salmon Genome Project. It was incredible to attend such a focused meeting led by such prominent researchers at the cutting edge of Atlantic salmon population genetics!

Over the next two days, these themes were thrashed out in lively debates during the workshop. The various merits of new markers, sampling strategies, analytical methods and much more were explored and discussed, and it was certainly a great opportunity for me, now in my third year of my PhD, to discuss my thesis plans with the great authorities in this area of research.

Despite all this lively banter, there was still a little time to see some Parisian sites. The sponsors of the symposium, the Total Foundation, arranged a private visit to the excellent "Abysses" exhibition at the Musée d'Histoire Naturelle, and there was even sufficient time one evening to visit the Louvre! I would like to thank the Genetics Society for awarding me a Junior Scientist grant, which helped to make this trip possible.



The Atlantic salmon, *Salmo salar*.

## 49th Annual *Drosophila* Research Conference 2nd – 6th April 2008, San Diego, USA



Robin Harris . University of Manchester

The 49th Annual *Drosophila* Research Conference this year was held at the impressive 40-acre Town and Country Resort in sunny San Diego, California, and attracted well over 1000 scientists from around the world to present the most cutting edge research regarding the model organism *Drosophila*. The five day meeting sponsored by The Genetics Society of America brought together not only internationally renowned scientists from the USA, Europe and further a field, but also PIs, postdocs and postgraduates such as myself, to present and discuss our work. The assembly covered an impressive number of *Drosophila* research topics, and was organised into over 150 platform presentations, 14 subject-specific workshops and more than 1000 posters that were available 24 hours a day. Needless to say there was hardly an aspect of *Drosophila* research that was not on show at this years meeting.

The conference began with introductory talks from the meeting organisers, along with historical lectures and a touching memoriam to Seymour Benzer, the celebrated father of fly neurogenetics. Following a brief orientation, the first evening began with a reception held in the resorts enormous Golden Ballroom, where old colleagues and new

acquaintances could meet, aided somewhat by the ample supply of food and drink.

The next morning the main conference began with the first plenary session, which included a number of fascinating talks, notably a look into anti-viral immunity by Sara Cherry of the University of Pennsylvania, and a brilliant insight into the connection between cellular trafficking, polarity and growth, given by David Bilder of the University of California, Berkeley, to mention just a couple of the outstanding presentations. Following this session, the concurrent platform presentations and workshops began, which gave a (sometimes difficult!) choice between talks on four or five different areas of research. Of particular note for me were the presentations given by Mike Levine of UC Berkeley, California who described the phenomenon of paused polymerase and the extent to which this mechanism occurs in the developing embryo, and the talk given by Brenton Graveley (University of Connecticut), in collaboration with Don Rio, concerning the mechanism of alternative splicing in the Dscam gene, which is known to encode over 38,000 distinct isoforms from 95 alternative exons in this single gene alone. Each presentation stood out to

me as an example of how, simultaneously, we are able to both explore and understand the enormous complexities of a single gene performing fantastic feats of splicing, and yet still be in relatively ignorant of fundamental mechanisms underpinning basic processes such as transcription.

On each day of the conference a number of poster sessions were run, which provided an excellent chance to meet with other members of the *Drosophila* research community, and discuss their research face to face. I had an opportunity to present a poster of my work, and was delighted to find the field of stem cell differentiation, the focus of my PhD thesis, was a particularly well-represented area this year. I found that my poster was very well received, and the feedback I gathered and connections I made with fellow stem cell researchers was invaluable.

Overall the conference was an exciting experience and a great success, and has allowed me to make important decisions regarding my present and future work, as well as giving me a broader understanding in general of *Drosophila* research. I would like to thank the Genetics Society for awarding me a Junior Scientist Grant that allowed me to attend the conference.

### Genetics Society one-day meetings

Graduate students may apply for travel costs to attend these meetings. The cheapest form of travel should be used if possible and student railcards used if travel is by train. Airfares will only be refunded in exceptional circumstances. Grants for overnight accommodation are not available. Applications for travel grants should be made using the registration form, before the final deadline for the meeting.

### Meetings with Genetics Society Sponsorship

These include the annual *Arabidopsis*, *C. elegans*, *S. pombe* and Pop Group meetings. Graduate Students may apply for travel grants to attend these meetings. Applications should be sent to the Genetics Society, at least one month before the meeting. The cheapest form of travel should be used if possible and student railcards used if travel is by train. Airfares will only be refunded in exceptional circumstances.

### Genetics Society Travel Grants for Junior Scientists

PhD students and postdocs (within two years of viva) who have been members of the Genetics Society for at least one year may apply for grants of up to £300 to attend conferences in the area of Genetics that are not sponsored by the Genetics Society (Please note a maximum of one grant every three years will be awarded to any junior scientist).

Applications should be submitted by email at least one month before the meeting, to the GenSoc Office (mail@genetics.org.uk) using message subject "TGJS application" and your surname. Applications should include a brief outline of the value of the meeting to the applicant, an outline of any presentation to be made at the meeting and estimated costs. Please ask your supervisor to send a very brief email in support. Recipients of travel grants will be asked to write a short report that may be included in the newsletter.

### *Heredity* Fieldwork and Training Grants supporting field-based genetic research and training

**P**urpose: To provide grants of up to £1,000 to cover the costs of travel and accommodation associated with pursuing a field-based genetic research project or a visit to another laboratory for training (i.e. to learn a new technique). The scheme is not intended to cover the costs of salaries for those engaged in the fieldwork or the training, nor to fund attendance at conferences. The work should include a strong genetical component. Eligibility: The scheme is open to any member of the Genetics Society who has been member for at least one year engaged in field based genetic research involving plants, animals, fungi or microbes. The research field should be one in which results would typically be suitable for publication in the Society's journal *Heredity*. Only one application from any research group will be admissible in any one year. Applications should be made on the form available from the Genetics Society's web page. The application form requests a short summary of the research project for which funds are sought. This should explain the role of the proposed field research in the overall project, and indicate how the grant will be used to facilitate the field research. A detailed budget for the fieldwork will be required, as well as an outline of other possible sources of funding. Applications from PhD students or post-docs should be accompanied by a letter or e-mail of support from your supervisor. ??

Closing date: There will be one closing date of 31st January each year. Awards will be announced within one month of the closing date to allow ample time for fieldwork preparation. At the end of the grant a short report will be requested from the grant holder. This should be in a format that is suitable for publication in the Genetics Society newsletter. A maximum of one grant every three years will be awarded.

### *Genes and Development* summer studentships supporting field-based genetic research and training

**P**urpose: To provide financial support for undergraduate students in any area of genetics, to gain research experience by carrying out a research project in the long vacation, usually prior to their final year. Studentships will only be awarded for students who have yet to complete their first degree i.e. who will still be undergraduates during the long vacation when they do the studentship. There are no restrictions concerning the nationality or membership status of the student, nor do they have to be a student at a UK university.

A maximum of 40 studentships will be awarded. They will consist of an award of £150 per week for up to 10 weeks to the student plus an expenses grant of £500 to the host laboratory. The award will be made to the host institution.

Applications are invited from members of the Genetics Society who have been members on or before the deadline of March 31st, and who run a research group within a University or Research Institute or a commercial research facility. Applications must be for a named student and must include the student's CV together with a reference from their tutor (or equivalent). Undergraduate students are encouraged to seek a sponsor and develop a project application with the sponsor.

A panel of members of the Genetics Society committee will review applications. Feedback on unsuccessful applications will not be provided. The successful applicants will be required to submit a short report from the students within two months of completion of the project.

Full details and on-line application form are available at the Genetics Society website

### Sir Kenneth Mather Memorial Prize

**T**his is an annual prize of £150 to reward a BSc, MSc or PhD student of any UK University or Research Institution who has shown outstanding performance in the areas of quantitative/population genetics. Nominations should be made between July 1st and November 1st inclusive of each year through the local Head of Department or School of the nominee. Nominations should consist of no more than one page of A4, setting out the case for the nomination, including relevant comparison with other students where possible. Nominations should be sent to the Head of School, School of Biosciences, The University of Birmingham, Birmingham, B15 2TT, clearly labelled as a nomination for "The Sir Kenneth Mather Memorial Prize". Nominations will be assessed by a panel of two people with experience in the area of quantitative/population genetics, one from the University of Birmingham and the other nominated by the UK Genetics Society. Decisions will be announced in December each year.

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# the Genetics Society

## AIMS

The Genetics Society was founded in 1919 and is one of the world's first societies devoted to the study of the mechanisms of inheritance. Famous founder members included William Bateson, JBS Haldane and AW Sutton. Membership is open to anyone with an interest in genetical research or teaching, or in the practical breeding of plants and animals.

## MEETINGS

The main annual event of the Society is the Spring Meeting. This has at least one major symposium theme with invited speakers, and a number of contributed papers and/or poster sessions.

One day mini-symposia are held during the year in different regions so that members from different catchment areas and specialist groups within the society can be informed about subjects of topical, local and specialist interest. Like the spring symposia these include papers both from local members and from invited speakers. One of these meetings always takes place in London in November.

## YOUNG GENETICISTS' MEETINGS

Currently there are three meetings devoted to talks and posters by students and junior

postdocs. Promega UK is sponsoring travel to these meetings and prizes for the best contributions, plus costs for the three winners to attend the following Spring Meeting and national finals.

## INVITED LECTURES

The Mendel Lecture, in honour of the founder of modern genetics, is given usually on alternate years at a London Meeting by an internationally distinguished geneticist.

To encourage younger geneticists, the Balfour Lectureship (Named after our Founder President) recognises the contribution to genetics of an outstanding young investigator, who must normally have less than ten years postdoctoral research experience at the time of the lecture. The winner gives the lecture at the Spring Meeting.

## INTERNATIONAL LINKS

The Society has many overseas members and maintains links with genetics societies in other countries through the International Genetics Federation, the Federation of European Genetics Societies and through the International Union of Microbiological Societies.

## PUBLICATIONS

The Society publishes two major international scientific journals: *Heredity*, concerned

**The Genetics Society was founded in 1919 and is one of the world's first societies devoted to the study of the mechanisms of inheritance.**

with cytogenetics, with ecological, evolutionary and bio-metrical genetics and also with plant and animal breeding; and *Genes and Development*, which is jointly owned with Cold Spring Harbor Laboratories and which is concerned with molecular and developmental aspects of genetics.

Full and student members are entitled to reduced subscriptions both to these journals and also to *Genetical Research*, published by Cambridge University Press, to *Trends in Genetics*, a monthly journal published by Elsevier with review articles of topical interest aimed at the general reader, *Nature Genetics*, published by Nature Publishing company (MacMillan Magazines Limited), *Current Biology* journals, *BioEssays* and *Chromosome Research*.

A newsletter is sent out twice a year to inform members about meetings, symposia and other items of interest.

## SPECIALIST INTERESTS

Six specialist interest areas are covered by elected Committee Members: Gene Structure, Function and Regulation; Genomics; Cell & Developmental Genetics; Applied and Quantitative Genetics; Evolutionary, Ecological and Population Genetics; Corporate Genetics and Biotechnology. The Committee Members are responsible for ensuring that the various local and national meetings cover all organisms within the broad spectrum of our members' interests.

Please complete this form and return it, along with your payment to, The Genetics Society, Wallace Building, Roslin BioCentre, Roslin, Midlothian, EH25 9PP. Complete this section carefully. The information you provide will help us to correspond with you efficiently and ensure that your details are accurately held on our membership database.

## 1. IDENTIFICATION (as data controllers we adhere to the Data Protection Act 1998)

Title: Prof.  Dr.  Mr.  Miss.  Mrs.  Ms.

Last Name:  First Name:

Institution:

Institution Address:

Postcode:  Country:

Telephone:  Fax:

Email:

Your home address should only be given when there is no alternative Please ensure that you have included your email address

## 2. AREAS OF INTERESTS (tick as appropriate)

Gene Structure, Function and Regulation  Genomics

Cell and Developmental Genetics  Applied and Quantitative Genetics

Evolutionary, Ecological & Population Genetics  Corporate Genetics and Biotechnology

## 3. STUDENT MEMBERSHIP (if this section is not applicable please go to section 5)

As a student member of the Society you are eligible to apply for a grant to defray the cost of attendance at meetings organised by the Society. Full details regarding grants is available on registration. In addition, after one year full membership you can apply for a grant of up to £300 for overseas travel to international meetings held outwith the Society.

If you are applying for an undergraduate membership please state year of graduation:

If you are applying for a postgraduate membership please state year of starting research:

Signature of Head of Department/Supervisor

Please note: After four years' postgraduate membership you will be required to pay the full subscription fee.

mail@genetics.org.uk

#### 4. MEMBERSHIP FEES

Membership entitles you to reduced rate entry to meetings, discounts on journals, free Society newsletters plus free online access to *Heredity*. The annual subscription charges are as follows (please tick applicable box):

Full Member: \*£25.00                       Postgraduate Member: \*£15.00                       Undergraduate Member: £5.00

\* There is a reduction of £5.00 for full and postgraduate members paying by Direct Debit

#### 5. PAYMENT

Option 1: Direct Debit (UK Bank Accounts only)

Complete this membership form and send it to the address below. On receipt you will be sent a DIRECT DEBIT MANDATE to complete and return with instructions enclosed.

I wish to pay by direct debit (tick box if applicable)  **Paying by Direct Debit saves Full members and Postgraduates £5**

Direct Debit Membership subscriptions are renewed on an annual basis running from 01 June - 31 May or 01 December - 30 November depending on date of application

Option 2: Cheque

I enclose a cheque for the sum of £  payable to 'The Genetics Society'

Option 3: Card Transaction



Please note that  Visa                       MasterCard                      \* (handling charges apply raising membership fees by 3.6%)

Full Member: \*£25.90                       Postgraduate Member: \*£15.54                       Undergraduate Member: \*£5.18

Please note that  Solo                       Switch                      \* (handling charges apply raising membership fees by 00.43p)

Full Member: \*£25.43                       Postgraduate Member: \*£15.43                       Undergraduate Member: \*£5.43

Card No	Start Date:	Expiry Date:	Issue No. (if applicable)
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Cardholder Name:	Signature of Cardholder:
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#### 6. MEMBERSHIP NOMINATION

Your application for membership of the Genetics Society will not be accepted without the signature of a FULL MEMBER nominating you for membership. In instances where no full member is available you must submit a copy of your CV along with a short Academic Reference. Your application will then be considered by the Committee. Alternatively, you may contact the Society by email for a list of Society Reps in your area.

Signature of nominating FULL MEMBER (please print name in block capitals after signature)

I enclose a copy of my CV along with an Academic Reference for consideration by the Committee (Tick box if applicable)

Please return your membership application form along with any attachments to: The Genetics Society, Wallace Building, Roslin BioCentre, Roslin, Midlothian, EH25 9PP marking your envelope MEMBERSHIP APPLICATION.

Please note that the approval of new members is ratified at the Spring Meeting as part of our AGM

OFFICE USE ONLY		
Date Received	Date Processed	Membership No.
<input type="text"/>	<input type="text"/>	<input type="text"/>
DD No.	Nominal Code	Membership Pack Sent
<input type="text"/>	<input type="text"/>	<input type="text"/>

# Notification of change of address form

Note that from  my NEW ADDRESS will be:

Title: Prof.  Dr.  Mr.  Miss.  Mrs.  Ms.

(Print or Type)

Last Name:  First Name:

Institution:

Address:

Postcode:  Country:

Telephone:  Fax:

Email:

Previous address:

Please return this form to: The Genetics Society, Wallace Building, Roslin BioCentre, Roslin, Midlothian, EH25 9PP marking your envelope CHANGE OF ADDRESS NOTIFICATION.

OFFICE USE ONLY

Date Received

Date Processed



### What does *Heredity* publish?

*Heredity* publishes original research articles, reviews, and news and commentaries in ecological, population and evolutionary genetics, including:

- human population genetics
- genomics and post-genomics as applied to evolutionary questions
- biometrical and statistical genetics
- animal and plant breeding
- cytogenetics

### Who reads *Heredity*?

Researchers with an interest in population genetics, ecological genetics, evolutionary genetics, genomics, cytogenetics, applied genetics, quantitative genetics, plant and animal genetics.

### Where can I get more information?

Visit the journal online at [www.nature.com/hdy](http://www.nature.com/hdy).

### Why submit your paper to *Heredity*?

- **Online submission** allows you to submit your paper online quickly and easily, and speeds up the acceptance and review process
- **Advance Online Publication** – articles published online weekly in advance of print
- **NPG enhanced Search Tool** allows your paper to be identified with all other relevant Nature Publishing Group journals in all keyword searches, meaning your paper can be found on any online search across the NPG journal websites

**2006 Impact Factor:** 2.872\*

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\*Journal Citation Reports, Thomson, 2007

**Editor:** Richard Nichols