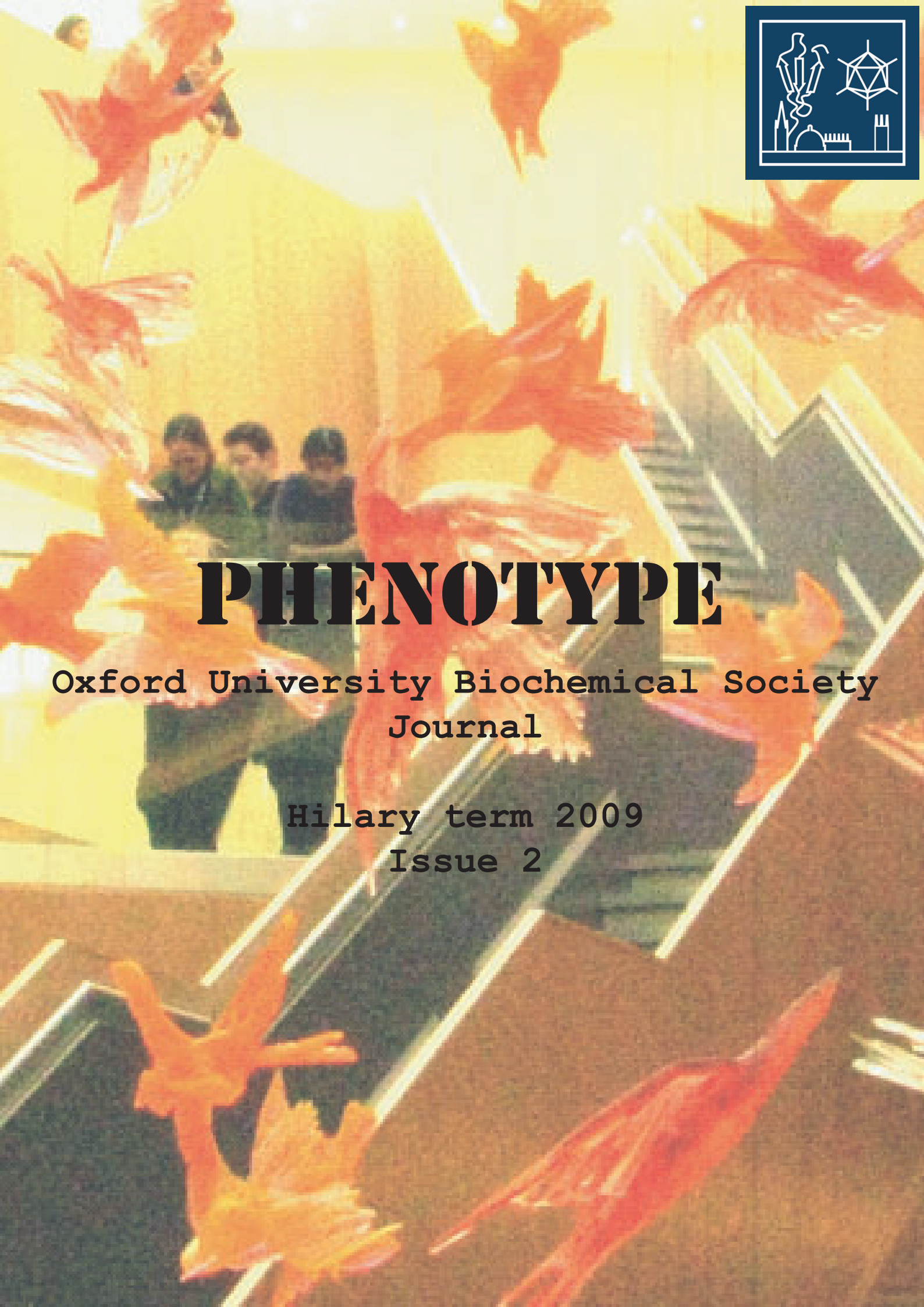

PHENOTYPE

Oxford University Biochemical Society Journal

Hilary term 2009
Issue 2



OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

Hilary Term 2009

Dear Reader,

OUBS is proud to bring to you the second issue of **PHENOTYPE**. We would like to thank all of you for your encouraging and useful feedback. We hope that you all have settled well in the new Department building and look forward to many new fruitful associations and friendships. The second issue of **PHENOTYPE** would not have been possible without the contribution of various people in this Department. Our heartfelt gratitude to Prof. Reid for sharing with us remarkable history of the MRC Immunochemistry unit based in this Department which closed last July. We would also like to thank Prof. Sherratt for contributing an enlightening article on his scientific journey so far and his research interests and Dr. Woollard for an extremely interesting interview.

'OUBS Careers Day' on 11th February promises to be an extremely useful event where we have invited eminent speakers from various fields such as patent law, medicine, publishing, finance, academia and biotechnology.

We at OUBS strive hard to bring to you something exciting and new every term and therefore really value your suggestions. We wish you a very Happy New year and a successful Hilary term.

Regards,
OUBS team

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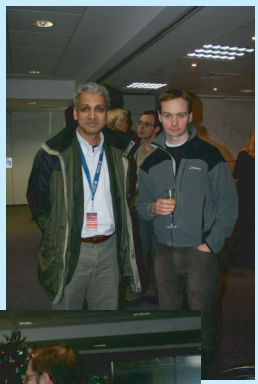
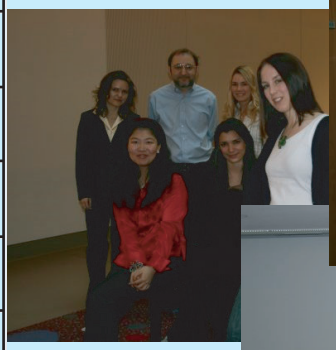

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PHENOTYPE

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OUBS EVENTS

2nd February
Dr Colin Goding
The Ludwig Institute for Cancer Research, University of Oxford
"Transcription and signalling from stem cells to cancer"

11th February
OUBS Careers Day

16th February
Dr Daniel Finley
Harvard Medical School
"Ubiquitin chain processing by the proteasome and its regulation via a novel stress response"

23rd February
Dr Margarete Heck
Queen's Medical Research Institute, University of Edinburgh
"Using Drosophila genetics to put invadolysin in its place"

2nd March
Prof Robert Konrat
Max F. Perutz Laboratories, University of Vienna, Austria

9th March
Prof Stefan Grimm
Faculty of Medicine, Imperial College London
"Screening for apoptosis genes: new insights into the respiratory chain and tumourigenesis"

4th May
Dr Fumiko Esashi
Weatherall Institute of Molecular Medicine, University of Oxford

11th May
Prof Tom Strachan FRSE FMedSci
Scientific Director, Institute of Human Genetics, Newcastle University

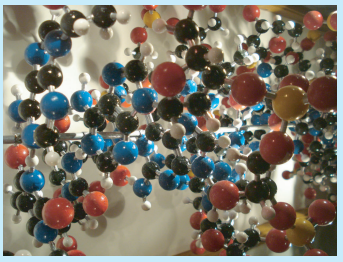
18th May
Prof Chris Abell
Department of Chemistry, University of Cambridge,
Co-founder of Astex Therapeutics

All the seminars will take place in the Seminar room of the New Biochemistry building at 4 pm.

OUBS EVENTS

The 2009 Careers Day will take place on Wednesday 11th February 2009, in the Main Meeting Room, New Biochemistry Building

Time	Speaker
9.00	**Prof Jane Mellor** Principal Investigator, Department of Biochemistry
9.30	**Ms Zoe Maunsell** Clinical Scientist, Oxford Radcliffe Hospitals NHS Trust
10.00	**Dr Philip Webber** Patent Attorney, Frank B. Dehn & Co.
10.30	COFFEE BREAK
11.00	**Dr Richard Capper** Scientist, Molecular Biology Group, Oxford Gene Technology
11.30	**Prof Chris Kirk** Chief Executive, British Biochemical Society
12.00	**Dr Jonathan Crowe** Publisher, Oxford University Press
12.30	**Dr Barry McGuinness** Healthcare Analyst, hedge fund Millennium Capital Partners LLP
13.00	**Ms Tracey Wells** Assistant Director, Oxford University Careers Service



OUBS Careers Day 2009 is sponsored by:

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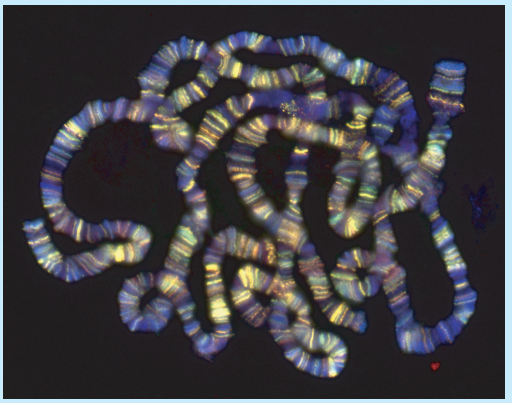
RESEARCH HIGHLIGHTS

With the new *Institute for Chromosome Biology (ICM)* opening on the third floor of the New Biochemistry building, we would like to look at some recent papers by groups from the Department on the subject of chromosome replication, repair and recombination.

Chromosome segregation is central to the passage of the genetic information from generation to generation. The mechanisms controlling this process in the budding yeast *S.cerevisiae* have been investigated in a recent manuscript from the Nasmyth lab **(Rowland B *et al, in press*)**. The authors used a suppressor screen and acetylation assays to show that acetyltransferase Eco1 acetylates the cohesin ring during the course of cohesion establishment. They followed this discovery up with protein interaction studies to find that Scc3, Pds5 and Rad61 form a complex which genetically counteracts Eco1 activity. These results allow for more refined models of cohesion establishment process to be put forward.

In contrast to eukaryotes, *E.coli* segregates its chromosome sequentially soon after replication, but prokaryotic chromosome segregation is poorly understood. FtsK translocase localizes at the forming septum and interacts with the octameric KOPS DNA sequences oriented from the origin to *ter*, where chromosome decatenation takes place by FtsK and the XerCD recombinase. To address the importance of KOPS-guided directionality of FtsK translocation, the Sherratt lab has created a KOPS-blind allele of FtsK and showed that the dimer resolution has only minor defects, probably due to the random and therefore 50% correct FtsK translocation being sufficient **(Sivanathan V *et al, Mol. Microbiol.*)**. However chromosome unlinking becomes less efficient when there are defects in chromosome organization, for example, in the absence of MukBEF.

DNA damage is an important signal for the onset of senescence. WRN helicase/exonuclease has been implicated both in DNA recombination and repair, and is mutated in the premature human aging Werner's syndrome. Having previously identified the fly orthoogue of WRN, DmWRNexo, the Cox lab has found a novel point mutation that shows mitotic recombination 20-fold higher than wild type **(Boubriak I *et al, Biogerontology*)**. To investigate the molecular basis of increased genomic instability, the authors have generated the recombinant version of mutant DmWRNexo and assayed its 3'-5' exonuclease activity *in vitro* against wildtype and nuclease-dead DmWRNexo. The mutated DmWRNexo showed little nuclease activity, which is rather unexpected given that the mutation lies away from the active site.

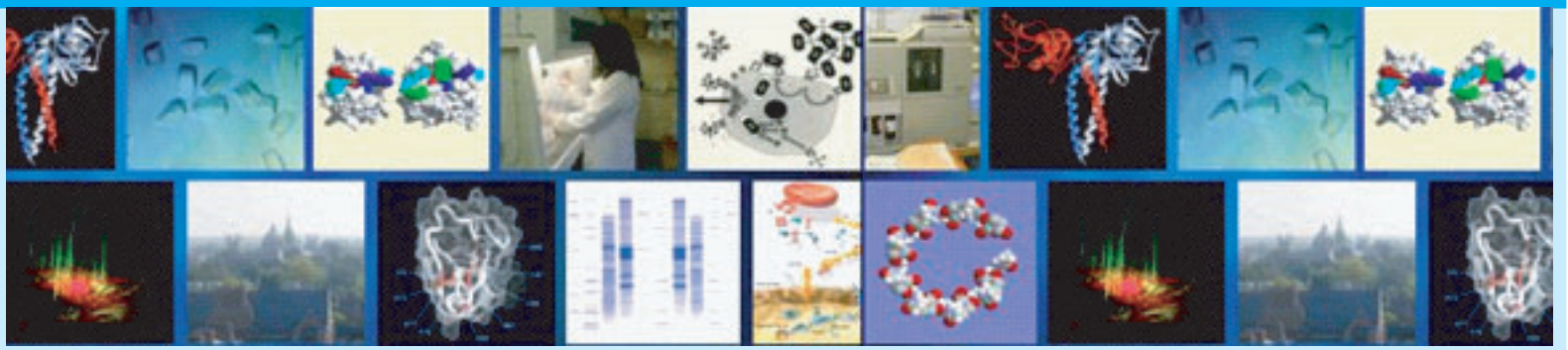


There are many players in the DNA damage signaling, most prominently ATM and ATR kinases that phosphorylate many targets following genotoxic stress. ATR is known to phosphorylate Chk1 kinase in concert with other proteins such as Rad17-RFC and the Rad9-Rad1-Hus1 (9-1-1) complex, but the mechanism of this combined action remains unclear. To this end, the Lakin group has repressed Rad17 by siRNA in HeLa cells to find a reduction in the number of cells with Rad9 foci at the DNA damage sites **(Medhurst *et al, J Cell Sci.*)**. FLIP and FRAP analyses were then employed to discover that Rad9 is immobile in DNA damage foci but is mobilized in cells with downregulated ATR. Together, these data suggest a model in which Rad17 and ATR collaborate in regulating Rad9 localisation and association at sites of DNA damage.

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

MRC Immunochemistry Unit 1967 – 2008: forty-one years of immunological research within the Biochemistry Department



The MRC Immunochemistry Unit was set up in 1967, when Professor Rodney Porter moved from St Mary's Hospital Medical School, where he carried out research on immunoglobulin structure (for which he was awarded a Nobel prize in 1972), to take up the Whitley Chair of Biochemistry at Oxford University and Honorary Directorship of the Unit. On his retirement, from the Chair of Biochemistry in 1985, Professor Porter would have continued as Unit Director – but tragically he died in a car accident that year. Ken Reid served as Director from 1985 up until the Unit closure, on his retirement, in September 2008.

Over the period 1967-1984, the Immunochemistry Unit occupied the fourth floor of the Biochemistry Tower Block before moving to the first floor of the, then newly built, Rex Richards Building in 1984.Immunoglobulin structure was the initial focus of research in the early years in the Unit, involving Betty Press (who played an important role in the structural work at St Mary's), George Stevenson and Lol Mole. However, by the early 1970's, research on the proteins of the complement system was a major focus, initiated by studies on the structural requirements for IgG to activate the classical pathway of the complement system - this led to the establishment for a model of C1q and the mechanism of activation the C1q C1r2 C1s2 complex - through studies involving Ken Reid, Bob Sim and Alister Dodds. Many other complement proteins were then characterised, utilizing the Unit's strong background in protein isolation and sequencing techniques (involving Jean Gagnon and Tony Willis), with the Unit becoming recognised as a leading international force in this area – as exemplified by the research on the covalent binding properties of C3 and C4 involving Alex Law, Alister Dodds and Bob Sim. Another successful major area of research, over the period 1970-78, was initiated by Alan Williams, whose studies on the characterisation of lymphocyte cell surface proteins, leading on to concept of the Immunoglobulin Superfamily, quickly achieved international recognition. In 1978, this research moved to the MRC Cellular Immunology Unit - upon Alan's appointment as its Director.

In early 1980s, the movement of the Unit into utilising molecular biology techniques led to Mike Carroll, Duncan Campbell and David Bentley cloning the genes for the human complement proteins C4 factor B and C2 – all located within in the MHC Class III region and this became a major initiative, with Duncan Campbell's group mapping of many other genes in this region. This research moved with Duncan, on his becoming Director at the HGMP Resource Centre at Hinxton in 1998 (Duncan is now back in Oxford – carrying out research in the Dept. of Physiology, Anatomy and Genetics. Research on hyaluronan binding proteins in inflammation, led by Tony Day, and on the roles of collectins and complement in innate immunity (involving Ken Reid, Howard Clark and Bob Sim), and on the protein engineering of cell surface inetgrins (Alex Law) were the major initiatives at the Unit's final quinquennial review, and all these highly rated research programmes have now been relocated and are continuing – with: integrin work via Alex Law, though his position as Professor at Nanyang University in Singapore: the work on hyaluronan binding proteins via Tony Day through

MRC Immunochemistry Unit 1967 – 2008: forty-one years of immunological research within the Biochemistry Department

through his Professorial position at Manchester University; the research on lung surfactant collectins SP-A and SP-D, and their possible use as therapeutics, via Howard Clark who holds the Chair of Child Health at Southampton; research on complement proteins and pathways via Bob Sim, now at the Pharmacology Department in Oxford. The Protein Characterisation Facility, which was a very successful part of the Unit's infrastructure, continues within the Department - by Tony Willis in the Glycobiology Institute. Ken Reid remains in Oxford and continues his connection with the University via his Fellowship at Green-Templeton College.

In July this year a three-day meeting was held in Oxford, which was attended by about 60 per cent of the 300 people (staff, visiting scientists and students) who had worked in the Unit, at some time during the past 41 years. Many of those at the meeting were from the 130 who obtained DPhil degrees while at the Unit and had helped contribute to the output of more than 1200 publications from the Unit staff and collaborators, over the past 40 years – and their participation at the meeting demonstrated the influence the Unit has had in the setting up of a wide range of ongoing structural and cellular immunology research programmes.

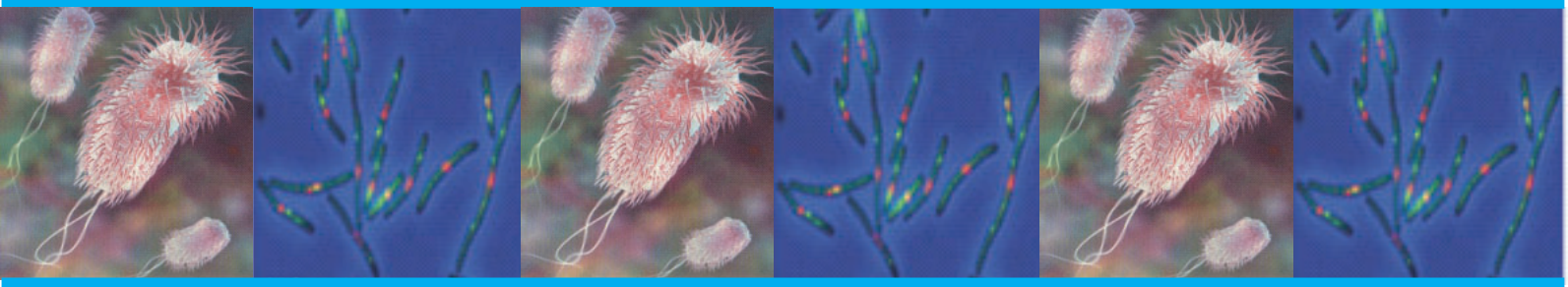
Ken Reid obtained both his BSc (1965), in Biochemistry, and his PhD (1968), for studies on insulin structure and biosynthesis, at Aberdeen University – and then was awarded an ICI Postdoctoral Fellowship (1969) to join Professor Rodney Porter's group within the MRC Immunochemistry Unit at the Department of Biochemistry in Oxford and became a member of MRC senior scientific staff in 1971. He was the Director of the MRC Immunochemistry Unit over the period 1985 – 2008. He carried out research on the structures and functions of a number of proteins of the human serum complement system throughout the period 1970-1980 and then moved on to study the group of mammalian defense proteins – known as the Collectins. The properties of the lung surfactant proteins SP-A and SP-D, and how they might be engineered to produce novel therapeutics which would provide defence against lung infection and inflammation were the main focus of his research group up to the Unit's closure on his retirement in September 2008.

Photo taken at a reception prior to the Unit's final meeting in Oxford in July 2008.
L-R - Tony Day, Marilyn Rugg, Jenny Parsons, George Stevenson, Tony Willis, Ken Reid, Bob Sim, Jean Gagnon, Jackie Shaw, Alister Dodds, Howard Clark, Alex Law

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

"BUGS AND ME!" by David Sherratt



January 1958. Age 13. In an instant my mind was made up; my future lay with DNA and chromosomes! This was the result of a series of inspirational Xmas lectures on 'DNA' at my local University by Hans Kornberg, who had recently arrived as Professor of Biochemistry there. Undergraduate biochemistry, at Manchester, was OK, but I encountered little DNA. There was much more physiology and metabolism in biochemistry courses those days! So off I went to do a PhD in the newly formed [and first] Molecular Biology Department in the UK at Edinburgh University. At that time Edinburgh was a Mecca for developmental biology and genetics; intriguingly, Kim Nasmyth, his Whitely Chair predecessor, Ed Southern, and my Iveagh Chair predecessor, Paul Nurse, all spent overlapping periods there in the 1960s-70s.

I had decided already that if one wanted to exploit the interdisciplinary power of molecular biology to study molecular mechanisms, one had to use bacteria or their viruses. So I set out to understand the molecular mechanisms of transcriptional control of an inducible antibiotic resistance gene in Bacillus [details of the lac operon were just being revealed]. This was followed by a postdoc in California working on replication and DNA processing of the recently discovered ColE1 plasmid. On returning to the UK in 1971 to set up my own research group, just as restriction endonucleases, plasmid vectors and recombinant techniques were emerging, I decided to investigate the replication, segregation, conjugation and the genetic organization of ColE1, because it appeared to be a biochemically tractable minichromosome. Then, one had to make your own enzymes. Slab gels had not yet been developed for DNA analysis, so DNA was analyzed in tube gels, one sample at a time, or by velocity sedimentation in the ultracentrifuge. DNA sequence analysis was a dream on the horizon.

Since a PhD student I had been intrigued by transposable elements [TE; jumping genes], proposed on genetic grounds by Barbara McClintock in the 1940s. The physical realization of these elements was emerging just as I was starting my own research group, and I thought that they might make powerful genetic mutagens. So in addition to standard molecular biological characterization of ColE1, we set out to develop techniques for using TE as genetic tools. This not only turned out to be very successful, but careful observation of the TE properties led us into studies of transposition mechanisms and into site-specific recombination, highly productive projects that would dominate the next 20 years of our research.

By following our noses this led us into chromosomal processing in E. coli, the topic that is the focus of our attention at present. Our journey into chromosome biology came from our demonstration that a site-specific recombination system that functions in stable plasmid segregation is used by circular bacterial chromosomes to ensure that newly replicated chromosomes are present as unlinked monomers prior to their segregation. Frustration at being unable to make this work in vitro using purified recombinases, led us to conclude that a factor was missing. Genetic and then biochemical analysis showed

segregation. A substantial amount of our recent work has focussed on a functional analysis of FtsK translocase, using biochemical, genetical, structural and single molecule studies. At the same time we developed new cell biological assays for visualizing genes and molecular machines in living cells, which have enabled us to gain important new insight into how chromosome replication-segregation shape chromosome organization. Our present mission is to explore the biology of the bacterial chromosome at single molecule resolution in close to real-time so that we can visualize in living cells the assembly, action and disassembly of molecular machines. We then perturb the natural biology using small molecules and targeted protein ablation. The era of single molecule in vivo biochemistry is here.

Although I have spent my whole career working with E. coli, I have interacted mainly with the eukaryote DNA recombination and repair community and the chromosome biology fields rather than with microbiologists. I have never felt the need to be defensive about our use of E. coli. In the past, as now, much basic mechanistic biology of DNA and chromosome behaviour-processing has come from bacteria. The resolving power of the techniques that you can apply to this organism remains unmatched. But bacteria are just not fantastic model organisms, they [and Archaea] are important in their own right; estimates suggest they comprise >50% of the Earth's biomass and are responsible for most bioconversions. They are found in diverse and extreme environments and show unrivalled metabolic and signalling flexibility. A single human individual's bacterial cells outnumber human cells by around a factor of 10. Back of envelope calculations show that the number of bacterial organism generations in a single person's gut during one year outnumber the total number of vertebrate generations that have occurred during vertebrate evolution on Earth. Therefore, bacteria have had huge evolutionary opportunities during the ~3 billion years that they have inhabited this planet. They may have adopted apparently simple, largely single cell lifestyles, but they internal metabolism, macromolecular processing and signalling potential is second to none. Furthermore, they communicate efficiently and in sophisticated ways with the outside world and with other organisms.

A reading of the November 14th 2008 issue of 'Science' illustrates just some of the emerging bacterial knowledge. The tuberculosis bacterium is shown to have a protein degradation system that uses ubiquitin-like targeting. Abundant marine cyanobacteria photosynthesize without producing oxygen [they lack photosystem 2], thereby allowing the same cells to fix nitrogen. The genome sequence of a bacterial endosymbiont reveals how it uses nitrogen and carbohydrates from its protozoan host, which inhabits the termite gut, thereby playing a key role in wood digestion by the termite. With new advances in imaging, and the applications of high throughput sequencing and genome analysis, the fascinating and important biology of bacteria is being ever more revealed.

So what of the future for biomedical research? Our knowledge and understanding has just touched the surface. Most has yet to be discovered and understood. If you are passionate about science, there are enormous opportunities to go out there and contribute to what we know and how it can be exploited. Be brave; do not be frightened by the challenges ahead. Much of the best is yet to come!

David Sherratt, FRS, has been Iveagh Professor of Microbiology at the Biochemistry Department, University of Oxford since 1994. Before that he was Professor of Genetics at Glasgow University [1980-1994] and Lecturer in Microbial Genetics in the University of Sussex [1971-1980]. He has successfully trained > 60 Ph.D/D.Phil students, has been President of the UK Genetics Society [1993-1996], and an EMBO member since 1983. He was elected FRS in 1992 and to the American Academy for Microbiology in 2003.

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

"RAISING THE DEAD" by Alice Blachford

Recent research has demonstrated successful cloning of mice from the genetic material taken from bodies frozen over 16 years ago. This raises the intriguing possibility of 'resurrecting' mammals that became extinct millions of years ago. But how practical is this view and are we likely to see Woolly Mammoths roaming the Highlands of Scotland?

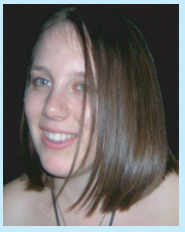
In November 2008 Teruhiko Wakayama in Japan published a paper announcing the first example of cloning a mammal from genetic material taken from a body frozen at -20°C for over 16 years without cryoprotectant. These conditions are in stark contrast to those used for normal cloning procedures, for example the cells used to create Dolly the Sheep were frozen quickly and preserved by cryoprotectant to prevent the formation of harmful ice crystals that can damage the DNA. The conditions used in this research more closely resemble the conditions experienced by tissues frozen within the permafrost tundra, where many bodies of extinct mammals have been discovered. Frozen within the permafrost cells bind tightly to each other and freeze gradually due to the large body size, additionally cells are subjected to repeated freeze-thaw cycles, causing cell rupture and DNA damage.

The cloning process used by Wakayama is similar to that used to create Dolly the Sheep but with an additional step required to obtain embryonic stem cells. The genetic material was taken from brain cells and transferred into eunucleated oocytes and made to enter the cell cycle by an applied electric current. Nuclear embryonic stem cells are obtained and undergo a second round of nuclear transfer and tetraploid aggregation, resulting in chimeric offspring. Genetic analysis of the chimeric mice demonstrates their nuclear genetic material is identical to the frozen donor mouse.

Obtaining a live clone of mice frozen 16 years ago demonstrates it is possible for some genetic material to maintain its integrity after an extended period of freezing without cryoprotectant. However, not all cells of the frozen mouse were able to be used as nuclear donors as many had significant genetic damage. Many cryoprotectant's are polysaccharides', usually containing sucroseor trehalose, and this may explain why brain tissue exhibits such good preservation during freezing and thawing. The main 'fuel' of the brain is glucose and it is possible this could act as an endogenous cryoprotectant. Additionally freeze-thaw cycles may have caused some genetic instability that rendered the brain cells more susceptible to reprogramming into embryonic stem cells.

This research raises the possibility of 'raising the dead' – at least in genetic form. It is not a realistic prospect for humans to be frozen and subsequently 'resurrected' in the future as a clone, as although genetically identical to the former self it is well known that a person is shaped by their environment, not just their genetics. This research brings us one step closer the possibility of bringing back mammals already extinct and preserving the genetic material of animals facing extinction as a form of conservation. Indeed many projects are underway to completely sequence the mammoth genome. However, even if genetic material is found from these mammals the difficulty could be in finding egg donors as species have important biological differences, such as the mitochondrial DNA, that may prevent interspecies DNA transfer. Currently the African elephant is favoured as an egg donor for the Woolly Mammoth genetic material. Additionally it is important to remember that these animals became extinct for a reason, for example environmental changes, loss of habitat and loss of genetic diversity. Is the current world able to accommodate such species if they were brought back to life or would they live out their existence within zoos?

Alice Blachford is a fourth year undergraduate student of Biochemistry.



OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

INSPIRING THE NEXT GENERATION OF BIOCHEMISTS!

Opportunities to communicate Biochemistry to the young ones

by Dr Mark Roberts

Biochemistry is not part of the school curriculum so often people have no idea how much biochemical research is impacting on their lives. Communicating our science outside these glass walls is an important part of being a scientist and over the coming year there are a number of opportunities to communicate our science to the outside world and inspire the next generation of biochemists:

National Science and Engineering Week
March 6th to 15th
Organised by the British Association this huge celebration of science occurs yearly in March. Last year there were 3,500 events with an estimated 1.4milliion people attending! Taking part can occur at many levels from organising your own event to taking part in a pre-organised event.

One easy one to take part in is the Wow!How? event which takes place at the University Museum on March 7th. This is a science fair aimed at young children with stalls relating to all areas of science. Last year members of the department did experiments ranging from DNA extraction from peas to the biochemistry of bread to lava lamps and colour chemistry!

There are two main ways to take part:
Volunteer and help run an already devised stall. There are a large number of pre-planned stalls which you can volunteer to help with eg: Biochemistry of bread / DNA extraction
Devise your own stall /display on an area of science that interests you and that you feel you can communicate to children!

Further details are available from the University Museum. For details of this and how to volunteer see: http://www.museums.ox.ac.uk/db/volunteers

This is only one of the many events happening around Oxford during national science and engineering week. For more details about other events going on in Oxford or details/ help on how to organise your own event see:http://www.the-ba.net/the-ba/Events/NSEW/index.htm, http://www.oxfordshiresciencefestival.co.uk/about-oxfordshire-science-festival/2008/

Sutton Trust Summer School
"The main objective of the Sutton Trust is to improve educational opportunities for young people from non-privileged backgrounds and increase social mobility." - Sir Peter Lampl, Chairman

As you can see from the quote the aim of this is slightly different from NSEW in that it is aiming to encourage students to go to university from backgrounds who would not normally come. This year Biochemistry is running a summer school for the first time taking 30 students for one week starting from July 12th. They will do a varied program with some lectures, practical work and tutorials designed to give them a taste of what university life is like here and also to show them what an exciting interesting and varied subject biochemistry is. To put this on we do need helpers to help run the practical and tutorial sessions so if anyone is interested in helping contact Mark Roberts on the LG floor (mark.roberts@bioch.ox.ac.uk)
Further details can be found at:
http://preview.tinyurl.com/biocss

Dr Mark Roberts is a post-doctoral fellow at the Department of Biochemistry in Systems Biology. He is Praelector in Biochemistry at Lincoln College .

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

5' WITH... Dr Alison Woollard

Dr Woollard's research group is studying the molecular mechanisms controlling cell proliferation and cell fate determination during *C. elegans* development. She is a fellow at Hertford college.

Q. When did you realize that you wanted to be a scientist?

I was a big-time collector of bugs and the like from an early age, and would enjoy doing all sorts of strange "experiments" on them like soaking them in my dad's home-brew and other acts of unspeakable cruelty. In fact my parents are very fond of reminding me of how I used to eat worms....

Q. If you were not a biochemist, what would you be...

Goodness knows. Perhaps a barrister. Prosecuting. I've always fancied the courtroom atmosphere, and being able to say "Would you really have the jury believe, Mr. Bloggs, that on the night of the 15th...."

Q. Your favourite book…

"100 Years of Solitude", by Gabriel Garcia Marquez. Full of magic. And "Enduring Love" by Iain McEwan, for the fantastic opening scene.

Q. If you are not in the lab you are...

Frantically cycling up and down the Botley Road depositing/gathering children.

Q. Worst disaster in the lab...

Ah that's a very sore point at the moment in my lab. Somehow, during the move to the new building, one of my liquid nitrogen tanks got emptied, and we lost all the strains (about 500!). There's nothing wrong with the tank now, so we've no idea how this happened, but its pretty devastating. The other event I remember vividly is setting fire to Hans Lehrach's first ever gridded S. pombe cosmid filter when I was a graduate student. I was stripping a probe off the filter (which was very specially lent to our lab) and left it in hot buffer a tad too long.... Lehrach was NOT amused.....

Q. What has been the most important moment of your career so far?

Being offered a PhD position by Paul Nurse. There was such a buzz in the lab - a really creative atmosphere that opened up my mind.

Q. In your view, what is the importance of luck in research?

Serendipity is the mother of discovery. Although I'm also a subscriber to the view that successful scientists make their own luck to a certain extent, or at least have the where-with-all to exploit luck when it comes their way.

Q. Describe your personality in five words.

Cautiously optimistic verging on cheerful

Q. One human trait you hate.

Duplicity

Q. Favourite vacation spot.

The Cumbrian fells, with a pair of stout boots and an OS map.

5' WITH... Dr Alison Woollard

Q. Best advice you ever received.

From my PhD supervisor: "If you are ever intimidated by someone, just imagine them sitting on the lavatory". Works every time.

Q. What has been your biggest mistake or regret?

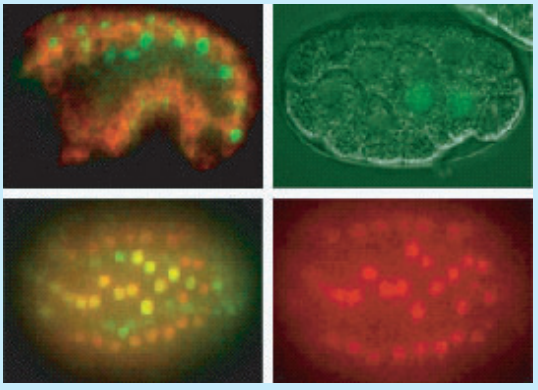
Surely I'm far too young for regrets...

Q. Favourite classical experiment?

That's a tricky one. There are so many beautiful ones to choose from, especially in molecular biology and genetics. But I guess most of these will be rather familiar to readers, so I think I'll go for a much older "natural experiment", one that underscores the nature and importance of controls, and served as one of the founding experiments in the field of epidemiology. An epidemic of cholera swept London in the 1850s. John Snow, a prominent physician (he attended Queen Victoria) became convinced that cholera was water-borne, very much against the prevailing theories at the time, which blamed miasmas, or infectious airs. Snow mapped all the cholera incidences and found a black-spot around the water pump in Broad Street (now Broadwick Street, in Soho), providing circumstantial evidence for the disease being water-borne. Then, Snow went on a big data gathering exercise. He interviewed the household of every cholera victim and the results were stunning, explaining all the presumed exceptions, and making a solid use of statistics. Victims who lived closer to other pumps, for example, seemed to have preferentially drunk from the Broad Street pump, and those who lived nearby but did not contract cholera had not drunk the pump's water. In other words, the apparent anomalies ultimately fit the pattern. In fact, Snow's conclusions were convincing enough to persuade the local authority to remove the pump's handle. Finally, as buildings acquired their own plumbing, and pipes led to each house from different water companies, Snow could very accurately trace the source of the water. In one neighbourhood affected by cholera, two water companies were competing service providers. Individual homes, standing side by side - sharing the same geographical features and socio-economic profile- had different water supplies. Here was the opportunity for the perfect controlled study: the causal effect of one variable could be isolated using tandem observations. It turned out that the incidence of cholera among Southwark and Vauxhall's users was twenty times that of Lambert's, and the Southwark and Vauxhall Water Company turned out to be taking water from sewage-polluted sections of the Thames. According to Wikipedia, the Annual Pumphandle lecture features a ceremony in which members of the John Snow Society remove and then replace a pump handle to symbolize the continuing political challenges that face public health discoveries.

Q. How do you imagine biochemistry research will change in the next twenty years?

We'll be in a tremendous muddle trying to come up with models to account for ever larger and more obscure data sets! Seriously, though, I think there are very exciting times ahead as technological revolutions drive the ever more intricate analysis of biological systems. But we must keep an eye on the big picture, and the important questions...



tbx-9::GFP and *lin-26* image
from Dr Alison Woollard's lab

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

GRADUATE MATTERS
by Dr Mary Gregoriou
Director of Graduate Studies

Q. What are the new regulations for confirmation of DPhil Status in 2009?

Two years and two terms from starting the PRS/DPhil course (i.e. 8th Term) students normally need to apply for confirmation of their DPhil status, to determine whether adequate progress towards the research goals has been made and whether there is a realistic plan and detailed timetable for timely submission of the thesis. (Most DPhil students are expected to submit their thesis within 4 years but those on the 5-year Joint PhD/DPhil Degree course within 5 years.) It is not possible to submit a thesis for examination until the D.Phil. status has been confirmed by the Board.

The procedure for confirmation of status involves submitting an application form (GSO.14) to the Board. The form requires candidates to provide either a 500 word account of the status of their thesis or an abstract of their thesis along with a timetable showing when thesis subsections will be completed.

A candidate whose first application for confirmation of his or her status is not approved shall be permitted to make one further application following the procedures laid down in this section normally within one term of the original application, and shall be granted an extension of time for one term if this is necessary for the purposes of making the application.

If a candidate's second application is not approved then depending upon the committee's recommendation the student could be transferred to MSc. Status (with the student's agreement) or if the student contests this recommendation, then the same procedure as for transfer to D.Phil. status (see (ii) above) will be followed. If the assessors also recommend transfer to MSc. status, the Committee will act upon their recommendation.

Q. How can I get more information about Research Student Funds?

The cost of a graduate student's research varies depending on the costs of the methods they use in attempting to answer their research questions. Funds are secured by a supervisor or by a programme, not normally by research students. Applications to funding bodies are made 1-2 years before admission of a student. Supervisors may also have been awarded flexible research funds which can be used to support graduate students' research within the supervisors' wider research programme. Some graduate scholarships make little or no contribution to graduate research costs, so costs must all be provided by the supervisor's funds. Others (e.g. The Wellcome Trust, CRUK, BHF studentships, etc) contribute essentially all the graduate research costs. I'm not aware of any funding body that makes research grants directly to research students. As students progress in their DPhil, their results could contribute to a research grant proposal, which if successful could generate research funds for further study. This provides an excellent opportunity to learn the skill of writing effective grant proposals. Also, close to graduation, students may apply for their own postdoctoral research fellowships, and usually this is the first time a student writes a research proposal, usually with the close guidance of the head of the host laboratory.

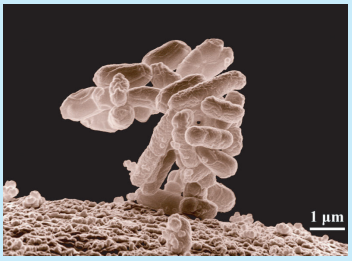
In Oxford, colleges often make a contribution to research students' expenses by way of small grants (£100-£400) to assist with academic expenses such as attending a conference.
For additional sources of conference funding please see:
http://www.bioch.ox.ac.uk/aspsite/index.asp?pageid=514?

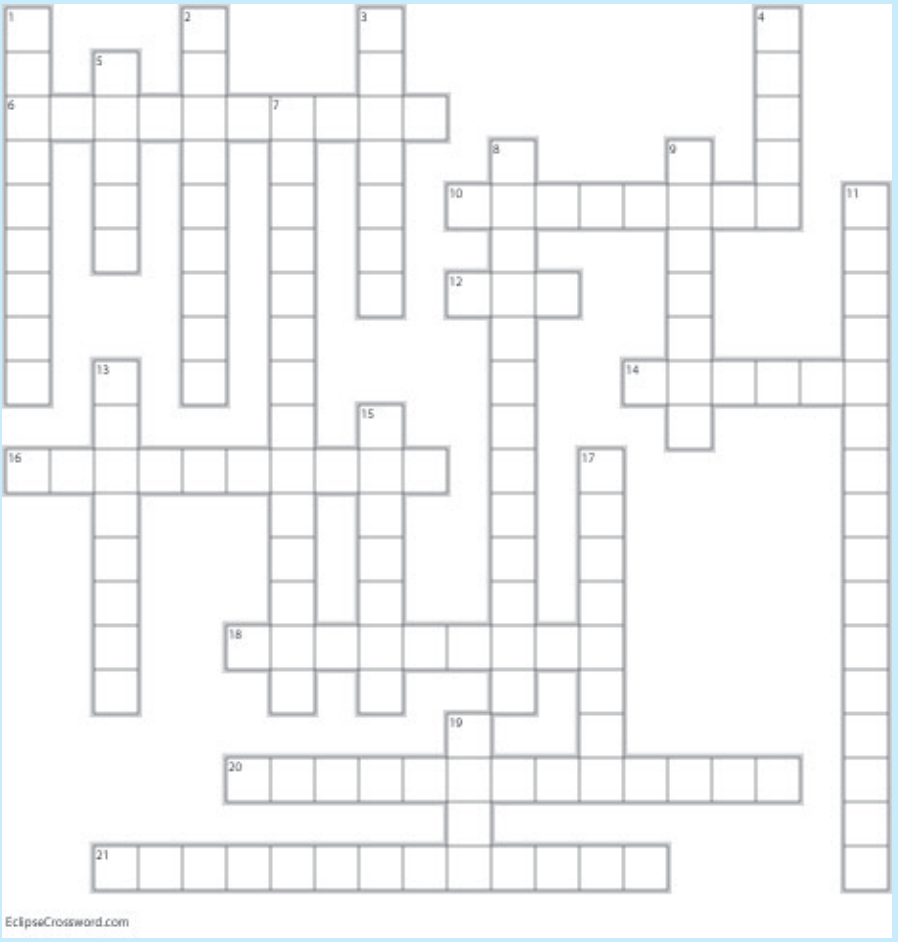
OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

CROSSWORD "Model organisms"

As in the previous issue, we offer you to try your wits at this crossword. Send your answers to oubs@bioch.ox.ac.uk by 1st March 2009. The winner will be drawn out of a hat and gets £10 worth of book vouchers!



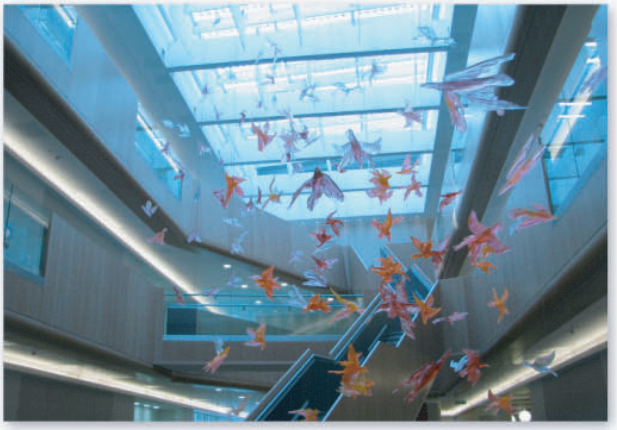


Across

6. Greek for "dew lover". (10)
10. *Escherichia coli* are a gram _____ bacteria. (8)
12. A model organism used by Ivan Pavlov to demonstrate conditioning. (3)
14. A genus of squid, whose giant axon was used by Andrew Huxley and Alan Hodgkin in their studies of nerve function. (6)
16. Species of this genus of archaea are hyperthermophiles, which greatly facilitates purification of native and recombinant proteins. (10)
18. A popular aquarium fish used for research in vertebrate development. (9)
20. A genus of soil dwelling amoeba that uses cAMP as a chemotactic agent. (13)
21. Greek for "sugar fungi". (13)

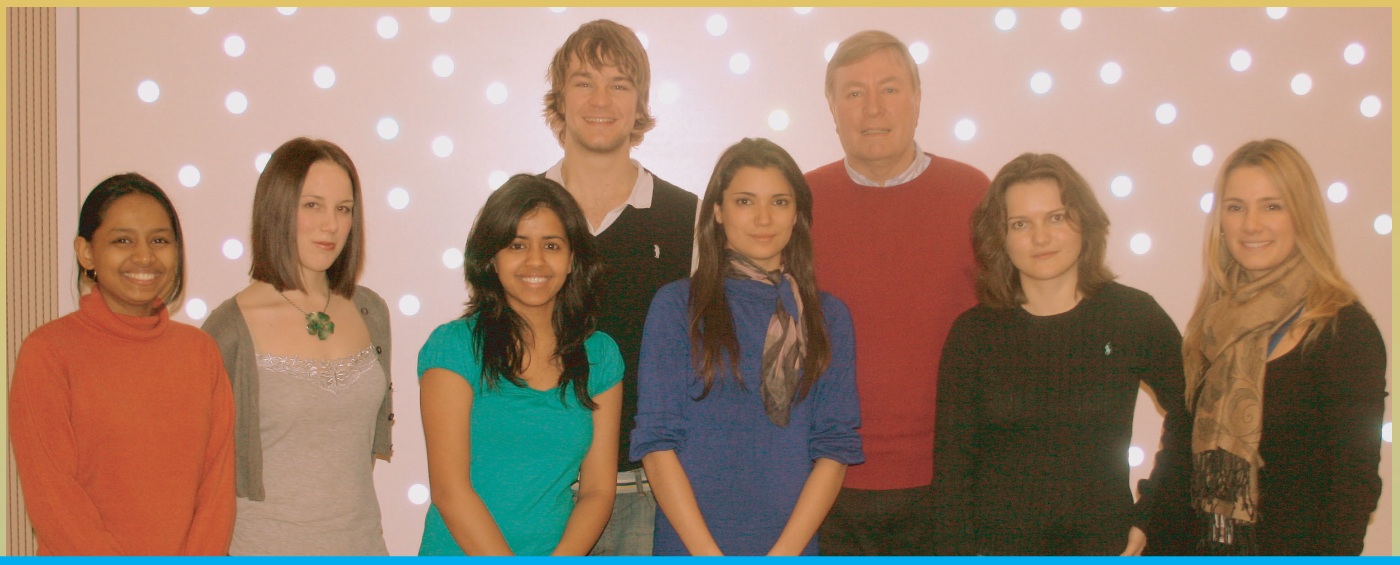
Down

1. Discovered lambda bacteriophage. (9)
2. Current method for transformation of *A.thaliana*, which involves dipping a flower into a solution containing *Agrobacterium*, DNA and a detergent. (6, 3)
3. A genus of sea hares (marine molluscs) used by Eric R Kandel for his research on the physiological basis of memory storage in neurons. (7)
4. Barbara McClintock discovered transposons while working with this model plant. (5)
5. A primary mammalian model, with a high degree of homology to humans. (5)
7. With only 0.05% males, most *C.elegans* are _____. (14)
8. This African clawed frog is tetraploid. (7, 6)
9. _____ yeast has rod-shaped cells, and was used by Paul Nurse in his research on eukaryotic cell cycle. (7)
11. Edward Tatum and George Beadle formulated the "one gene, one enzyme" hypothesis while working on this model fungus. (10, 6)
13. The famous Fly Room, where Thomas Hunt Morgan did his pioneering research on *D.melanogaster*, was located at which university? (8)
15. *Arabidopsis thaliana* is a member of which family of plants (common name) (7)?
17. Phage genome integrated in its bacterial host. (8)
19. "In the beginning was the _____" by Andrew Brown is the story of how three men won the Nobel Prize for their research on the humble nematode. (4)



OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE



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L-R Anjana Badrinarayan, Alice Blachford, Sarah Iqbal, James Halstead, Maria Caroll, Prof Tony Watts, Marina Kolesnichenko, Camilla Oxley

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