Budget heralds radical new approach to UK medical research

Within the first few minutes of his 2006 Budget speech, Chancellor Gordon Brown made clear that science - in education and research - is central to the Government's plans for the British economy in the coming decades. One of his most radical proposals was for a single fund of more than £1 billion ring-fenced for the MRC and for Department of Health (DH) R&D, to support the full spectrum of biological and clinical research in the UK. How this new arrangement will work in practice is being determined through a consultation process chaired by Sir David Cooksey and steered by the Treasury and representatives of the DH and the Office of Science and Innovation (OSI; the new name of the OST), which will be reporting back in the autumn. The MRC is keen to hear a wide variety of views to help us develop our own contribution. Comments can be made through the MRC website (see box, page 2). But formal submissions should be made directly to Sir David's consultation.

MRC Chief Executive Colin Blakemore welcomed the Chancellor's news. Integrating the two funding streams could increase the speed and efficiency with which basic research can be translated into health benefits: "This Budget confirmed vividly Gordon Brown's commitment to research, especially medical research. It represents a real chance for substantial improvement for the funding arrangements in the UK, facilitating the interaction between basic and clinical research."

Colin Blakemore observed that the Chancellor's announcement demonstrated his confidence in British scientists; also that his thinking is underpinned by figures from the OSI showing that the UK now leads the group of the eight largest industrial nations in its biomedical and pre-clinical research productivity.

"The UK's record in supporting world-class medical research through the MRC is second to none. Developments in science can be found in every aspect of our daily lives including breakthroughs on ageing and drug research. The DTI is committed to ensuring that science and innovation are at the heart of government, and that we maintain the UK's leading position in medical research. We will build on the outstanding achievements of the MRC and ensure we are facilitating the research base in the best possible way."

Alan Johnson, Secretary of State for the Department of Trade and Industry (DTI).

The importance of preserving the independence from government enjoyed by the research councils is recognised. Science and innovation investment framework 2004-2014: next steps sets out the Government's vision for scientific research, recognising that funding must ensure "the continued delivery of world-class basic science, according to the long-standing Haldane principle which states that day-to-day decisions on research council scientific funding must be taken at arms-length from ministers. Funding would continue to be awarded on the basis of excellence across the..."
full spectrum of health research, from basic to clinical and public health. This will include continued support for investigator-led research”.

**Building on MRC success**

Colin Blakemore’s hope is that the single fund will provide the opportunity to build on the MRC’s considerable achievements: “We’re committed to supporting high-quality research across the entire spectrum of the biomedical and clinical sciences. We are proud of our international reputation for achievement – from the introduction of penicillin and discovery of the structure of DNA to the development of MRI; from the creation of blockbuster antibody drugs to vital clinical trials, such as those on statins and on vaccines in Africa.”

The Budget statement emphasises the Treasury’s recognition of the crucial link between science funding and innovation. Colin Blakemore added: “Companies, universities and the public all over the UK are reaping the benefits of breakthroughs made over by MRC-funded scientists. We are determined to expand that success even further. Combining the funding of the MRC and the DH will produce gains in efficiency and opportunities for collaboration that should benefit medical researchers throughout the UK.”

Colin Blakemore says the MRC is looking forward to exploiting its strengths in biomedical research through continued close working with all the health departments, including those of Scotland, Wales and Northern Ireland. The organisation is keen to demonstrate that it can respond quickly and effectively to clinical as well as scientific challenges.

**Developing UK science skills**

The Budget contained more good news for science in its commitment to achieve a step change in the area of science and the UK economy. The Government aims to create more science graduates and more science entrepreneurs. This chimes well with the MRC’s mission to sustain and develop the UK’s research capacity by training skilled scientists and supporting them at every stage of their careers.

The Next steps document points out the growing competition presented by China and India and emphasises “the need to adapt in order to continue to attract and retain high-value economic activities”. Anticipating this global scenario, the MRC is rapidly building its collaborations with scientists in China and south-east Asia to ensure it can meet the health priorities and medical opportunities of the future, in the UK and around the world.

**Backing new ideas in clinical research**

Experimental medicine is research that takes place at the interface of laboratory and patient-based studies. In recent years both the Government and the clinical research community have drawn attention to the relative lack of investment in this area. In 2005 the MRC responded to these concerns by making up to £15 million available for new research in experimental medicine. To help get a clear picture of how much funding was appropriate and where it was most needed, the MRC invited ‘expressions of interest’ from the research community. These took the form of brief sketches which outlined the aims and costs of the proposed studies.

Faced with almost 1,000 expressions of interest totalling £350 million, the MRC Clinical Research Overview Group honed the call. Focusing on need and the best use of resources, it invited proposals that “evaluate a novel intervention, including an entirely novel application of an already existing treatment in human participants with the aim to provide proof of concept.”

In March 2006, the MRC awarded £15 million to scientists across the medical research disciplines. The successful applications ranged from research into the use of melatonin to reduce brain damage in pre-term infants and the effect of statins on asthma, to testing a malaria vaccine by using killer T cells against the parasite in liver cells.

A huge boost for patient-based research, these awards will exploit the UK’s unique potential for such work. As the Government’s Next steps document points out, “few other countries have a health service that provides researchers with the potential to access virtually the entire population, through an integrated system of primary, secondary and tertiary care.”

**Collective commitment**

The MRC’s £15 million investment in experimental medicine is part of a national strategy involving partners in the UK Clinical Research Collaboration. Other initiatives include the funding of new clinical research infrastructure by the Wellcome Trust, The Wolfson Foundation and the Health Departments, to which the MRC will contribute a number of MRI scanners for use in experimental medicine studies.
Steps forward in stem cell science

Following the International Stem Cell Forum’s meeting in January, Network brings readers an update on its work to establish and safeguard standards in stem cell science worldwide...

In January 2006 members of the International Stem Cell Forum (ISCF) gathered in Paris for their fourth annual meeting, which was chaired by MRC Chief Executive Colin Blakemore. Topics ranged from progress in international collaboration and the Forum’s work on standardising characterisation of stem cell lines worldwide, to its new online cell registry and cooperation between stem cell banks.

Key ISCF projects
Members were updated on two key ISCF working group projects - the International Stem Cell Initiative (ISCI) and a global review of ethics and regulation of stem cell research. Led by Professor Peter Andrews of the University of Sheffield Centre for Stem Cell Biology, the ISCI aims to develop internationally-agreed protocols for the culture and characterisation of human embryonic stem cells. Seventeen laboratories from 11 countries contributed a total of 65 cell lines to its study, with the UK Stem Cell Bank playing a key role in the collection and distribution of materials. The study aims to establish whether the human embryonic stem cell lines created by different laboratories around the world show similar properties. An initial review of the data collected indicates that the different lines do exhibit broadly similar properties. The Forum members also aim to reach a consensus about a set of markers that can be used to define the traits and characteristics of human embryonic stem cells.

In August 2005, 60 scientists from the 17 laboratories met with other key participants to review the data generated so far and to discuss issues to be addressed. The ISCI hopes to be able to report the study results by early summer 2006.

All of the characterisation study data will be available in a searchable online registry that is being developed in partnership with the MRC. The registry will hold a wide range of information for each of the 65 cell lines, including the ability of each to form tumours; pictures and descriptions of any tumours formed when the cells are grafted into animals; details of culture conditions and feeder cells used; microbiological summaries, and information about immunological and genetic characteristics.

To build on the work of the ISCI, a second initiative is planned to compare the effectiveness of the various types of culture systems that have been proposed for maintaining human embryonic stem cells, and to examine the genetic stability of stem cell lines grown in different laboratories and under different conditions. A detailed proposal for this initiative will be presented to the Forum in May.

Mapping the ethical landscape
The global review of ethics and regulation is being carried out by the ISCF Ethics Working Party (EWP). Chaired by Professor Bartha Knoppers of the University of Montreal, the group includes ethicists, research scientists, clinicians and lawyers drawn from the Forum’s member organisations. Together they have undertaken the challenging task of reviewing the differing ethical and regulatory approaches of all countries that fund stem cell science, with a particular emphasis on research involving embryonic stem cells. Future work of the group will include developing a global register of clinical trials involving therapeutic use of stem cells.

The importance of ethics to stem cell research was brought into sharp focus when South Korean scientist Dr Woo-Suk Hwang admitted that he had falsified his research results. Dr Hwang published papers in Science in 2004 and 2005 claiming that he had created the world’s first cloned human embryos and 11 stem cell lines tailored to individual patients. The Forum participants agreed that this case emphasised the vital importance of oversight in science and of collaboration and open exchange between research teams worldwide to promote and maintain scientific integrity and transparency. The ISCF’s work, in areas such as the characterisation, banking, registration and exchange of stem cell lines, looks set to speed the development of best practice guidelines for stem cell research.

ISCF background
The MRC launched the International Stem Cell Forum (ISCF) in 2003 along with eight other international funding agencies with similar scientific principles, approaches and resources. These organisations all shared the MRC’s concerns about the need to create standardised worldwide criteria for creating, storing and maintaining stem cell lines. The ISCF now has 19 participants from 17 countries, with China, Italy and the Californian Institute for Regenerative Medicine the latest to join. The ISCF’s key principles and related activities include:

- Opposition to human reproductive cloning.
- Agreement with the use and sharing of both embryonic and adult somatic human stem cell lines.
- Belief that the creation of new human embryonic stem cell lines should be minimised.
- Defining specific standards for the characterisation and registration of human embryonic stem cell lines.
- Working towards international harmonisation of ethical and intellectual property issues.

Find out more online
For more information about the ISCF, its stem cell characterisation study and the findings of its Ethics Working Party, please go to www.stemcellforum.org
Halting the spread of flu

As the H5N1 flu virus spreads through bird populations across the world and the threat of a human pandemic looms, MRC scientists continue their vital work monitoring influenza viruses...

Most of us know what it’s like to have flu. But fewer people are aware that in 1933 scientists at the MRC’s National Institute for Medical Research (NIMR) were the first to identify the influenza virus. Fifteen years later the newly-formed World Health Organization (WHO) requested that the MRC set up the World Influenza Centre at the NIMR. This reflected the institute’s strength in flu science as well as the recent discovery that the virus changes over time and the introduction of a vaccine. Since then NIMR scientists have been working tirelessly to increase understanding of how the virus works and what can be done to combat it.

Today the World Influenza Centre is one of four global WHO Collaborating Centres responsible for early detection of flu viruses with the potential to cause a human pandemic. These centres work alongside 112 institutions in 83 countries which collect specimens and carry out initial virus isolation and characterisation work before shipping samples to the Collaborating Centres for detailed analysis. Each year the World Influenza Centre scientists at the NIMR analyse around 1,500 to 2,000 different human and animal flu viruses from about 50 countries. The outcomes of their work feed into WHO recommendations for new flu vaccines.

**Flu virus science**

Influenza is a very simple virus. Dr Alan Hay, Director of the World Influenza Centre explained to Network that there are three types of flu virus; types A and B cause major outbreaks while type C causes only mild colds.

Influenza viruses are made up of eight individual genes. There are two ways H5N1, the strain of avian flu that is currently spreading rapidly through bird populations across the globe, is an influenza type A virus. Like other type A viruses, it is defined by the haemagglutinin (H) and neuraminidase (N) proteins on its outer coat. There are 144 potential subtypes of the influenza A virus, each with one of 16 types of haemagglutinin and one of nine neuraminidases. While most of these combinations have been observed in birds, they don’t tend to affect people. “In fact, in the last century only three new subtypes of influenza A viruses mutated and spread among people – and these caused the last three flu pandemics,” said Dr Hay.

Other NIMR scientists are studying in precise detail how haemagglutinin binds to receptors on cells and fuses with the membrane of a cell it infects. They want to understand what sorts of changes would enable the virus to switch from primarily infecting birds to targeting humans. Firstly, its genes could mutate over time. Or, if the H5N1 virus infected a human cell at the same as an ordinary human flu virus, their genes could mix and give rise to a new ‘reassortant’ strain able to both transmit from person to person and cause serious disease. Scientists at the World Influenza Centre look out for both of these things, analysing samples to detect any differences between the viruses infecting people and those infecting birds. In recent months, they have been kept extremely busy urgently analysing H5N1 samples from human cases in Turkey, Iraq, Egypt and Azerbaijan, as well as other countries with suspected cases.

**From birds to people**

The haemagglutinin protein has two key roles: it binds the influenza virus to cells and infects these cells by fusing with them. It is the most important part of the virus for immunity and therefore the target of flu vaccines. An important part of WHO flu virus surveillance is monitoring viruses from around the world for changes in the haemagglutinin gene that might help the virus to bind to human cells. If H5N1 does become able to transmit between people, detailed knowledge of the haemagglutinin will help scientists to quickly determine the most suitable vaccine to use to combat a pandemic.

Scientists worldwide are becoming increasingly worried that H5N1 may cause the next human pandemic. Almost 200 people have already been shown to be infected through close contact with birds. And alarmingly, the virus has a very high mortality rate, killing over half of the people with confirmed infections.

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In February 2006, MRC Chief Executive Colin Blakemore and Professor Peter Gruss, President of the Max Planck Society for the Advancement of Science in Germany, signed an agreement to promote cooperation between their two organisations. The agreement aims to further scientific collaborations by promoting the exchange of researchers, experience, expertise, information and scientific findings.

Two workshops will be held during the next year, one in Germany and one in the UK. They will focus on molecular cell biology and brain function and will aim to help young scientists set up collaborations between the two organisations. And under the agreement, exchange visits will be organised to provide opportunities for junior scientists, PhD students and administrative staff to spend time in their partner organisation’s environment.

NIMR, told Network. His laboratory is studying all 16 types of haemagglutinin that have been isolated from avian flu viruses. By binding each protein to an artificial receptor and working out its structure, they can gain vital clues as to how changes in binding affect a virus’s ability to infect birds or humans.

**Treatment targets**

The other protein by which influenza A viruses such as H5N1 are classified - neuraminidase - helps to release new copies of the virus from infected cells. Like haemagglutinin, neuraminidase is also crucial to WHO flu virus surveillance. This protein is the target of the antiviral drugs amantadine and rimantadine. While strains of H5N1 isolated in Vietnam have been resistant to these drugs, his team has found that they may be effective against strains isolated more recently in other parts of the world. Amantadine and rimantadine are less expensive than oseltamivir and so might also be important in combating a human pandemic, particularly in poorer countries.

**Continued surveillance**

So in light of current media attention about a possible flu pandemic, what does the future hold for the MRC’s World Influenza Centre scientists? As part of their vital work monitoring flu viruses, they remain on alert for the further spread of H5N1. And as they work around the clock to detect and combat any virus with the potential to cause a human pandemic, it seems that we are in good hands.

**MRC support for flu science**

The MRC spends £1.6 million each year on flu research, predominantly through the programme at the MRC National Institute for Medical Research led by Sir John Skehel and Dr Alan Hay. However, in recognition of its key role in combating the threat of pandemic influenza through funding further research, the Council has allocated an additional £10 million to this field over the next two years. To inform its priorities and strategies in flu research, the MRC Infections and Immunity Research Board sent a scientific mission to Vietnam and China in November 2005, and in December 2005 it hosted an international conference on “Pandemic Influenza: Maximising the contributions of research”. This was followed by a call for proposals at the end of 2005. The MRC will make the first awards in May 2006, focusing on urgent research projects which need to be in place before the next seasonal influenza months. In addition to standard research grants, funding is available for international collaborations, workshops and travel grants for researchers to and from the UK.
Significant advances have been made during the past few years in the fields of genomics, proteomics and metabolomics. These advances have led to expectations that new ‘biomarkers’ might give us clearer insights into diseases and drug responses. On 31 January, the MRC held a two-day conference entitled “Disease, drugs and patient benefit – can biomarkers deliver?” The meeting aimed to identify how the UK can best contribute to research into biomarkers by capitalising on its infrastructure and scientific strengths.

**So what is a biomarker?**

Biomarkers are biological characteristics that show what is going on inside a biological system. For instance, cholesterol and blood pressure have been used for years as biomarkers of a patient’s cardiovascular risk. Professor Meindert Dahnof from the Leiden/Amsterdam Centre for Drug Research observed that the US National Institutes of Health Biomarkers Definition Working Group defines a biomarker as “a characteristic that is measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses.” He added that “just about anything” relevant to the functioning of a biological system can be used as a biomarker.

The potential uses of biomarkers are endless. Early detection and diagnosis of illnesses, prediction of a compound’s likely toxicity, and insight into the body’s response to a drug are just a few of the possibilities. Speakers at the meeting came from many medical disciplines, the pharmaceutical, biotechnology and diagnostic industries, regulatory bodies and government. They addressed issues ranging from biomarkers in drug discovery and experimental medicine to their use in clinical trials and population sciences.

“Biomarkers research is recognised as being a promising area in clinical studies, in the development of new products, and in clinical practice in the diagnosis and monitoring of the progress of treatment,” said Chief Executive Colin Blakemore when opening the meeting. Explaining that the MRC is considering making substantial funding available for biomarkers research, he added: “We need to know what the gaps and opportunities are for the UK, where there is a niche for the MRC, how we can capitalise on the strengths of the UK, where the opportunities for partnership lie, and what the likely impacts will be on human health in the short-, medium- and long-term.”

“A biomarker is a characteristic that is measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses.”

**From leaky biomarkers to biomarker signatures**

Throughout the conference, speakers gave their perspectives on how biomarkers could be used. Founder of Biotrin International, Dr Cormac Kilty, told delegates that his company is looking for novel biomarkers to detect tissue damage. These so-called ‘leaky’ biomarkers are released from cells during the early stages of damage to organs such as the kidneys or pancreas. Dr Kilty explained: “A biomarker must be highly specific to the tissue in question, it must be detectable, which means it must be accessible and it needs to be responsive. In other words it needs to go up and down in response to damage and treatment.”

Professor Paul Elliot of Imperial College London spoke about the promise biomarkers hold for monitoring disease progression and response to treatment in epidemiological studies. “Classical epidemiology is focused on factors such as social class and lifestyle and how these relate to diseases such as heart disease and cancer – without necessarily providing any information about mechanisms,” he said. Technologies such as genomics and proteomics are now providing information about mechanisms.

Dr David Armstrong, chair of the MRC’s Health Services and Public Health Research Board, suggested that biomarkers could be used as ‘surrogate outcomes’ in phase II clinical trials. This would make it possible to reduce the number of patients and to get answers more quickly than could be done by using clinical endpoints. “It seems to me that biomarkers can be construed as another group of risk factors to join other things like lifestyle, signs and symptoms that need adding to this risk paradigm. And if we think about them in that way, the kaleidoscope changes and we see them in a slightly different light,” he said.

Since 2000 there has been a 10-fold increase in the number of published papers relating to the analysis of genes, proteins and metabolic processes, illustrating the rapid advances being made in these areas. Dr George Orphanides of Syngenta told
participants that DNA chips can assess the action of 10,000 genes at once. For example, they have been used to diagnose and characterise diseases such as leukaemia and predict patients’ risk of relapse. Similarly, proteomics technologies can differentiate the way certain proteins are expressed in patients and healthy individuals. Dr Orphanides therefore suggested that the “real power” lies in biomarker signatures – assessing groups of biomarkers together and finding links with particular diseases.

Biomarker challenges

However, there are obstacles to overcome before patients and clinicians can reap the benefits of further biomarkers research. Dr Steven Williams from Pfizer Global Research pointed out that there is a lack of funding for research in the middle of the field, between the innovative basic science leading to the discovery of biomarkers and industry-funded development and product delivery. He outlined the high cost of biomarker development and validation, the “rather hap hazard” regulatory approval process and a lack of standardisation of markers that hinders their use in clinical trials. “Implementation is difficult because standardisation does not seem to be anybody’s business,” he said. Professor Ian Humphrey-Smith, from the Biosystems Informatics Institute, said that the quest for validated biomarkers involves enormous quantities of data and complex mathematical analysis. There are 20 billion potential binding sites for proteins in the human body and 30,000 proteins. This means that there is huge variance between patients, who must be studied in enormous numbers to validate or qualify new biomarkers. “Numerically the challenge is quite daunting and the biomedical sciences must be increasingly mathematically driven,” Professor Humphrey-Smith observed.

Joining forces

Virtually all the speakers saw collaborations as crucial for taking biomarkers research to the next level. These could be across government departments, research councils, different branches of medicine, academia and industry. Dr Sandy Kennedy from GlaxoSmithKline observed that companies could benefit from banding knowledge and resources together in the search for and validation of biomarkers.

Dr Lana Skirboll from the US National Institutes of Health (NIH) agreed: “Strong partnerships and operational synergy between government, academia and industry will be required.” The NIH has recently initiated an extensive biomarkers research programme and has formed strong collaborations with many public and private sector partners. All of these partners are expected to bring different things to the table, from funding and ideas to access to patients for clinical trials, and lobbying power.

Talking points

To round off the conference, participants discussed gaps and opportunities for biomarker development and came up with ideas about how the MRC could contribute and what the UK’s niche might be. Dr Armstrong then summarised the main themes of the meeting. The need for partnerships was again emphasised, as was the potential role of the MRC as an ‘impartial broker’ in such collaborations. Also recognised was the need for interdisciplinary training across molecular biology, bioinformatics, mathematics and physical sciences.

Dr Armstrong pointed out that one of the UK’s major strengths is its large patient populations, including the National Health Service and several large population-based study groups. He emphasised that biomarkers research could capitalise on these valuable resources, and that a coordinated approach to sample collection, and access to central databases, would be helpful. At the end of the conference there was a consensus among delegates that the gap in the supply chain between the discovery and application of biomarkers needed to be addressed and that a potential MRC initiative could focus on the validation of biomarkers.
There is currently much excitement in the scientific community about the Diamond synchrotron being built at Harwell, which is due to open in 2007. So that UK structural biology researchers can continue to access beamlines in the meantime, the MRC and the Biotechnology and Biological Sciences Research Council (BBSRC) have allocated £1.7 million of renewed funding for the BM14 beamline at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France. ESRF is currently the brightest x-ray light source in Europe, with 40 beamlines including BM14.

Synchrotron radiation allows scientists to probe the structure and properties of any substance, shedding light on areas as diverse as medicine, materials science, chemistry, geology, environmental science, structural genomics and archaeology. A powerful magnet inside the synchrotron bends high energy electrons that are accelerated around a synchrotron ring – this generates extremely bright light that can be used by BM14 to probe the structure of proteins, using a technique known as MAD – multiwavelength anomalous diffraction. The MRC, the BBSRC and the Engineering and Physical Sciences Research Council purchased BM14 in 2001 to provide the UK science community with a dedicated MAD-capable beamline. Recent steps forward include automating data collection from the beamline, automated sample loading, sample tracking through the use of barcodes and management of the experiment by an intelligent and interactive database known as a Laboratory Information Management System.

Today, UK structural biologists are tackling ever more complex biological questions. For instance, BM14 has enabled scientists to determine the structure of viruses, mammalian enzymes and an array of other proteins important in human diseases. Investigators interested in using BM14 must apply for beamtime – proposals are assessed by an independent review board, based on the quality of the science proposed.

In December 2005, 26 new research projects aimed at preventing cancer, heart disease and diabetes were funded by the National Prevention Research Initiative (NPRI). The initiative is managed by the MRC and draws together a broad range of funding organisations from the public and charity sectors (see box for details). These organisations are working together to support high-quality multidisciplinary preventative research. Launched in October 2004, the NPRI has an initial budget of around £12 million over five years. Its committee includes scientific experts as well as members of the public; the opinions of all committee members are taken into account when deciding which projects to fund.

Cancer, diabetes and heart disease are part of a worldwide epidemic in chronic disease that can often be prevented through healthier lifestyles. To address this urgent global problem, the World Health Organization has set a goal of saving 36 million lives through prevention research and intervention over the next decade.

The NPRI's first projects include research into discouraging alcohol misuse and smoking and promoting physical activity and a healthy diet. This work will take place in diverse settings including schools, homes, workplaces and doctors' surgeries. Exploring a range of approaches to encourage positive health behaviour, the projects involve geographers, clinicians, dieticians, exercise scientists, statisticians, psychologists, economists and epidemiologists. A second call for proposals has been agreed. This will have a very specific focus and more details will be published on the MRC website in due course.
New faces

At the beginning of 2006 the MRC Corporate Affairs Group appointed four regional communications managers to provide support to units, centres and grant holders for their public engagement activities. The regional managers will be working closely with our scientists on a number of different fronts including promotion of their research through the media, working with schools, advising on print communications and influencing local opinion formers.

Adrian Penrose is the Regional Communications Manager for Cambridge and the Midlands. He has 25 years of experience as a communications and public relations professional. Now based at the MRC Epidemiology Unit at the Elsie Widdowson Laboratory in Cambridge, Adrian was the communications manager at MRC Human Nutrition Research from 2001 to 2004.

The Regional Communications Manager for Scotland is Pauline Mullin. Pauline has spent 10 years with the Edinburgh International Science Festival and worked in communications at the Edinburgh Zoo and the Scottish Society for the Prevention of Cruelty to Animals. Most recently, she worked with a group of Scottish universities to set up and secure funding for business-academic projects.

Jude Eades, Regional Communications Manager for the Oxford region, Southampton and Bristol, comes from the National Blood Service (NBS), where she was responsible for all aspects of public relations work, media management and communication strategy for five NBS blood centres. Jude began her career at the London Evening Standard.

Sarah Hornby is the Regional Communications Manager for London. Before joining the MRC Sarah spent four years as project manager in the Wellcome Trust’s Public Engagement Development Group. Prior to that, she worked on the Young People’s Programme at the British Association for the Advancement of Science, with specific responsibility for Science Year activities.

Another new face in the Corporate Affairs Group is Public Affairs and External Communications Manager Simon Wilde. Simon’s role involves increasing engagement between researchers and politicians, public and patient involvement in research, and exhibitions and events. He comes from the Hammersmith Hospitals NHS Trust, where he was the press and communications manager for research and development. Simon previously worked in external relations at the Biotechnology and Biological Sciences Research Council.

The MRC has also appointed two new members of staff to work on clinical research strategy at head office. In addition to bringing a valuable academic clinical perspective to MRC decision-making, they will advise on ethics and governance issues relating to medical research.

Catherine Elliot completed her clinical training in obstetrics and gynaecology in Edinburgh and London before becoming a clinical lecturer at Imperial College London. She then went on to complete a Masters degree in Medical Law and Ethics and worked in medico-legal work and research ethics and governance at the MRC Prion Unit before joining MRC head office.

Joining Catherine is Helen Cope, who trained in medicine at the University of Edinburgh and pursued a career in academic psychiatry, specialising in neuropsychiatry. Before joining the MRC, Helen spent six years in research management at the Wellcome Trust, latterly as head of the careers and clinical initiatives department.

Opportunities

All applications must be costed on a full economic basis.

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<th>Full Application</th>
<th>Peer Review</th>
<th>Board Meeting*</th>
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<td>Infections and Immunity</td>
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<td>28.09.06</td>
<td>Nov 2006-Jan 2007</td>
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* Normal decision point

MRC studentships - closing dates

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Phosphorylation is now recognised as being one of the major ways in which cells coordinate their response to a wide range of agents, such as hormones, growth factors, nutrients, cell damage and even pathogens. Irregularities in phosphorylation can cause, or be the result of, major diseases including cancer, diabetes, heart attack, hypertension and rheumatoid arthritis. This makes protein kinases and protein phosphatases of enormous importance as potential drug targets. A generation ago, the world of science knew very little of protein phosphorylation. The idea that protein kinases and protein phosphatases might be valid drug targets was remote, and the suggestion that this area of science would become a major focus for investment would have been considered laughable. Yet today, it commands 27 per cent of the pharmaceutical industry’s annual R&D spending.

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I worked for 25 years on protein phosphorylation without any pharmaceutical company having the slightest interest in my research. The situation today could not be more different. This shows yet again the importance of supporting fundamental research in new fields for a long period, given the length of time that may be needed to tell whether it has therapeutic application.”

Sir Philip Cohen, Director, Protein Phosphorylation Unit

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In response to growing awareness of the importance of phosphorylation, the MRC set up the Protein Phosphorylation Unit (PPU) in Dundee in October 1990, under the directorship of Sir Philip, who is a Royal Society Research Professor. The unit employs over 100 people organised into eight groups, covering a wide range of research into this rapidly developing area.

Watching the signals
For the last three years, Philip’s own research group has been focusing on the study of inflammation. Infection by a pathogen triggers the activation of networks of protein kinases, which leads to the production of pro-inflammatory cytokines (PICs). When released into the blood, PICs stimulate other cells into action, which helps to mount an innate immune response to destroy the invading pathogen. Inflammation, however, is a double-edged sword: an over-reaction in the inflammation response can be as dangerous as no response at all, and this is a major cause of chronic inflammatory diseases such as rheumatoid arthritis and septic shock. Currently, the front line treatments available are drugs which inhibit PICs, but they are expensive, require repeated injections and only about a third of patients respond to them. A more effective treatment that can be taken orally is urgently needed. However, researchers must first understand the signaling pathways that control the production of PICs before they can identify the protein kinases in these pathways that are the best targets for new interventions.

Achieving a balance
Members of Dr Simon Arthur’s group are also exploring the inflammatory process, specifically the role of MAPKs, a particular class of protein kinases. They have recently discovered that the protein kinase MSK plays a critical role in controlling the production of substances called anti-inflammatory proteins. As Simon explains: “Fine-tuning is all important. In the immune response, the balance between inflammatory and anti-inflammatory proteins is crucial. If they are out of balance, diseases such as Crohn’s disease and psoriasis can occur.” This work could eventually lead to the development of drugs which activate specific kinases to trigger an increase in anti-inflammatory proteins, but without increasing inflammatory ones.

Protein kinases that are mutated in inherited diseases
Professor Dario Alessi’s pioneering research has provided “exciting new insights into conditions such as cancer, diabetes and hypertension.” So said the judges when he...
Important field of protein phosphorylation. Network goes north of the border to take a eutical industry ...

The MRC Protein Phosphorylation Unit's home in the Centre for Interdisciplinary Research at the University of Dundee.

was awarded the European Molecular Biology Organisation Gold Medal 2005, widely regarded as the most prestigious research prize in Europe for a life scientist under the age of 40.

Helped along by scientific serendipity, one remarkable discovery made by Dario’s group was a breakthrough in understanding how cells manage their energy ‘budget’. The team was investigating an enzyme, LKB1, which is implicated in an inherited cancer syndrome. Their aim was to work out which protein it phosphorylated, in the hope that this would lead to an understanding of how mutations in the gene encoding LKB1 cause cancer. Meanwhile, Professor Grahame Hardie, a colleague working in diabetes research at Dundee University, was investigating a different protein kinase, AMPK. Important in the control of energy levels in cells, AMPK switches off energy-hungry activities and switches on energy-generating processes when the supply is low. Grahame was struggling to identify the protein kinase that activates AMPK.

The breakthrough came when one day both teams compared notes and realised that the cancer-linked enzyme LKB1 might be the activator of the energy-controlling kinase AMPK - a theory they went on to verify. The next step for Dario Alessi was to explore whether metformin, a drug used to treat type 2 diabetes by switching on AMPK, might also help to treat cancer because it mimics one of the actions of the tumour-suppressor LKB1. A preliminary epidemiological analysis carried out with clinical colleagues at the University of Dundee Medical School indicated that this idea was likely to be correct. This has encouraged Dario to begin further trials on specific cancers in collaboration with his clinical colleagues. “The connection between AMPK and cell growth could lead to some interesting follow-up work,” he says. “If we can trick a cancer cell into thinking that it doesn’t have enough energy to divide, we may be able to stop it growing.”

Dario has recently made an important discovery about how mutations in the protein kinases WNK1 and WNK4 cause Gordon’s disease, an inherited hypertension syndrome. He has revealed that they switch on two other protein kinases, SPAK and O SRL, that play a critical role in regulating salt balance. These findings suggest that compounds which damp down the activities of WNK, SPAK and O SRL could lead to new drug treatments for hypertension. Dario and his team are now looking at how mutation of the genes encoding the protein kinases PINK and LRRK1 cause early-onset Parkinson’s disease.

**Protein phosphatases in diabetes and cancer**

Professor Tricia Cohen’s group is focusing on protein phosphatases, which remove rather than add phosphate from proteins. This is still a relatively unexplored area of signal transduction compared to protein kinases. They use a multidisciplinary approach, including gene disruption in mammals and RNA interference techniques in fruit flies. By expanding their investigation of the roles of protein phosphatase complexes that are critical for human health, Tricia and her team hope to identify targets for new drug treatments for cancer and diabetes. In diabetes, they recently showed that the disruption of a mouse gene encoding a glycogen-targeted form of a specific protein phosphatase can result in obesity and insulin resistance in later life.

As Tricia said: “Understanding the regulation of the phosphatase which is targeted to glycogen is very important. A drug capable of altering its regulation may have potential for the treatment of diabetes, a disorder that affects 150 million people worldwide.”

**Cellular secrets of flora and fauna**

Professor Carol MacIntosh and her group study plant and animal cells side by side, as they have much in common at a molecular level. For example, the team found that C-shaped proteins called 14-3-3s prevent plants from suffering metabolic collapse in the dark. “I called it ‘cuddle and...”

>> page 12
to survive the night,” Carol explained. The 3-D structure of PDK1, a protein kinase discovered by Dario Alessi, which has become an important target for developing anti-cancer drugs. Diagram: Daan van Alten and Dario Alessi, PPU.

squeeze’ because that’s what the C-shaped proteins seemed to be doing. They bind to enzymes of sugar metabolism inside leaf cells when the sun goes down, and through these actions help the plant to survive the night,” Carol explained.

Following clues from their plant studies, the group looked at 14-3-3s in human cells and discovered that these help drive cancer cells to scavenge for nutrients and regulate how glucose is used to generate cellular energy and growth. 14-3-3s have also given an unexpected insight into how viruses, for example HIV, hijack the internal machinery of a cell. The next step will be to develop drugs that antagonise or enhance the functions of 14-3-3s inside cells.

Protein kinases and DNA damage
The PPU’s most recent arrival is Dr John Rouse, who came from the Gurdon Institute at Cambridge three years ago. His group is looking at how cells deal with damage to DNA. Genetic material is unstable and chemically reactive. If DNA damage is left unchecked, the sequence and the structure of the genome changes and part of the instruction set is lost. This type of genome instability is seen in a large number of tumours. To prevent it, healthy cells are able to recognise and repair DNA damage. “Cells can launch a series of events to ensure rapid DNA repair, and to ensure that damaged chromosomes aren’t replicated or segregated until they’re repaired,” John explained. “And here’s the crunch – these responses to DNA damage are regulated by protein kinases.”

The protein kinases in question bind to the damaged DNA and this activates other kinases which, in turn, phosphorylate proteins that protect genome stability and control repair. The challenge lies in pinpointing exactly how this control mechanism works. If the group can unravel it, they may be able to develop an understanding of the mechanisms that are deregulated in cancer cells.

Working with industry
In addition to excellent science, another of the PPU’s great successes is its collaboration with several of the world’s leading pharmaceutical companies, including AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck & Co Inc, Merck KGaA and Pfizer. Set up in 1998, this is probably the largest partnership ever undertaken between the pharmaceutical industry and a UK research institution. It allows the companies to share the unit’s unpublished information, reagents, technology and know-how and to have the first right to licence the intellectual property generated.

Over the past five years, income from the venture totalling £15 million has been ploughed back into MRC research at the unit. But the collaboration doesn’t steer the research – it is in fact the other way round. And the benefits aren’t just financial, as Philip Cohen explains: “For example, we gain access to company compounds that are valuable reagents for our own research and our post-doctoral researchers and PhD students get a great insight into the pharmaceutical industry; many more go into industry as a result,” he explained. “The collaboration happened almost by chance, but now it’s established I can see what a good idea it is and well worth expanding further.” The unit also has interactions with other companies. For example, its long-standing collaboration with USA company Upstate Inc led to the setting up of a new division of Upstate in Dundee in 1999, which now employs over 100 people.

All for one and one for all
The PPU aims for a unified approach across its activities. It has a shared services division – with teams for DNA cloning, DNA sequencing, antibody and protein production and cell culture – and pools its funding from all sources so that the money can be used strategically to yield maximum benefit for the unit as a whole. For example, it has invested a large sum of money in state-of-the-art mass spectrometers to identify phosphorylated sites in proteins – an area in which Dr Nick Morrice of the PPU is a world expert – and in mouse genetics. “The unit is a pioneer in its field, and has developed a very efficient way of operating,” Philip Cohen says. “Central budgets will never be able to fund everything we would like to do, and collaboration with industry helps to provide the additional funding needed. As a result, we’re working hard for both the health and wealth of the nation.”

Future challenges
Thanks to the work of the PPU and its colleagues worldwide, the importance of phosphorylation to the body’s processes is now widely recognised. But this fascinating area of medical science will continue to challenge scientists for many years to come, as Philip is quick to point out: “The identification of the major substrates of each protein kinase and phosphatase is a major undertaking – and one that will take several decades to solve – but it’s at the heart of what we need to know in the twenty-first century.”

The PPU’s Mission
- To advance understanding of the role of protein phosphorylation and cell regulation in human disease.
- To facilitate the development of drugs to treat diseases caused by abnormalities in this process.
- To generate the reagents and improve the technologies on which more rapid progress in this area depends.
- To train the next generation of scientists who will advance our understanding of the subject.
Administrative Efficiency Project on track

It is just one month before the launch of the Shared Service Centre (SSC), which is an integral part of the MRC’s radical restructuring of the way it provides administrative support to its head office, institutes and units.

The build-up to the June launch is gathering pace. Director Phil Lambert has recruited nearly all of his senior management team as well as many of the key staff who will run the different functions within HR and finance. All of the main finance team are on board and HR is close behind.

Fitting out the new offices in Swindon was completed on schedule by mid-April. At the same time, the team has been working with MRC units to draw up standard operating procedures and best practice guides which set out the optimum way for finance and HR to work once the SSC is operational. A comprehensive training programme has been designed for staff at the SSC and at the MRC’s units to make sure that these processes are clearly understood and properly implemented. Training begins in Swindon in May.

To allow adequate time for the new processes to become established, the SSC programme will be rolled out to the various MRC units over a nine-month period. Head office will be the SSC’s first client, followed by the London Centre in July and the five Scottish units in August. All units will be working with the SSC by spring 2007.

Providing an effective, responsive service with consistent processes, improved management information and cost savings is an evolutionary process. Responding to feedback from everyone within the MRC on the steps being taken is an important part of the project. Phil Lambert and his team are developing a variety of communication routes to keep people up to speed and ensure they know where to go for information, including planning a newsletter and poster campaign. Opening the new office is an important milestone in the development of efficient common processes for finance, HR and procurement across the MRC.

A determination to provide highly professional, efficient and effective support for directors lies at the heart of the SSC programme. It will help ensure that the MRC’s support processes and systems meet 21st century requirements and help it to meet government targets for the Lyons and Gershon Reviews on administrative expenditure and regional relocation. And, together with cost savings generated by the new procurement processes, the new centre will ensure that an even greater proportion of the MRC’s financial resources are focused on research.

The SSC is building a platform that can be scaled up to meet the needs of other business both in and outside the MRC. The MRC is playing a full part in the discussions all the research councils are having about the most effective way to provide joint shared services by the end of 2009.

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New Sheffield stem cell lab

In January 2006 the University of Sheffield opened a new MRC-supported laboratory capable of producing embryonic stem cell lines that can be used in medical treatments. The cutting-edge facility is part of the university’s Centre for Stem Cell Biology. It brings researchers a step closer to new treatments for degenerative and chronic conditions such as diabetes and Parkinson’s disease and to repairing tissues after accidents or cancer. At the opening, Professor Harry Moore said: “Stem cell research is paving the way for a healthcare revolution and our new laboratory facility here in Sheffield will allow the Centre for Stem Cell Biology to be among the first in the world to develop stem cells for eventual use in medical treatments.” The laboratory is currently undergoing testing before it is granted Good Manufacturing Practice accreditation—a requirement for stem cells that will be used to treat patients.

Good news for endoscopy research

A new suite with the latest endoscopy equipment to diagnose and treat cancer, infection and inflammation of the lungs, colon, oesophagus and stomach was opened at the Addenbrooke’s Centre for Clinical Investigation in February. The Research Endoscopy Suite is a joint venture between the MRC, Addenbrooke’s hospital and GlaxoSmithKline and is only the third of its kind in the UK. It will provide the clinical infrastructure needed for collection and storage of clinical specimens with linked, high-quality data.

Cambridge brain institute opens

The MRC and the Wellcome Trust have awarded Professors Trevor Robbins and Ed Bullmore a five-year grant of £4.8 million to set up the Cambridge Behavioural and Clinical Neuroscience Institute (BCNI). The award includes a significant contribution towards the purchase of a state-of-the-art 3T-MRI machine. The BCNI aims to increase understanding of the functions of brain systems and networks and how they malfunction in neuropsychiatric or neurological disorders, which will enable clinicians to define patients’ illnesses more accurately. The institute integrates research carried out by scientists at Cambridge University, the MRC Cognition and Brain Sciences Unit, the Wellcome Trust Imaging Centre and the Cambridge Centre for Brain Repair.
Mind the gender gap

Although more than half of the UK’s bioscience PhD students are female, only one in ten network reports on the MRC’s ‘Women in Science’ initiative and how this is helping to rig

The UK’s thriving science, engineering and technology (SET) industries have a reputation for creativity, innovation and productivity. But to maintain our international competitiveness, the UK needs to increase the number of women being recruited to, remaining in and returning to SET occupations. Throughout the biological sciences a huge number of women leave between completing their doctorates and moving into senior positions. This picture is similar across Europe, the UK and within the MRC. The reported reasons for this ‘leaky pipe’ include indirect discrimination in the workplace, lack of confidence or self-esteem among female scientists, and the perception that the science environment does not offer the flexibility women need to balance a successful career with bringing up children.

The UK Government has shown its support for minimising the gender gap in science. In its Science and innovation investment framework for 2004–2014 it set out key objectives of improving the under-representation of women in science, technology, engineering and mathematics education and the workforce, as well as increasing opportunities for professional women working in SET.

First steps
It’s important that the MRC plays its part in bridging the gender gap. So in 2003 it launched an initiative to address under-representation of women in science. The first step was to establish a Women in Science Steering Subcommittee. Chaired by Professor Ann Prentice, director of the MRC Human Nutrition Research centre in Cambridge, the subcommittee is finding ways to identify and address the key issues affecting women working in science. The subcommittee is made up of both female and male MRC scientists spanning all career stages. In addition to exploring and developing strategies to address the problem of the gender gap and retention of early-career female researchers, it aims to improve opportunities for women to achieve their full potential as scientists. The group is also charged with promoting change both by the scientists themselves and also in the way in which research is organised and carried out.

Taking action
At this point the MRC Women in Science initiative is focusing on piloting initiatives among postdoctoral scientists within units and institutes, after which the subcommittee’s remit will be expanded to include other female research staff.

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‘The under-representation of women in science, engineering and technology threatens, above all, our global competitiveness.’
make it to senior positions. To help close the gender imbalance...

**Using our ASSETs**
Subcommittee member Dr Helen Sweeting, from the MRC Social and Public Health Sciences Unit in Glasgow, presented MRC findings from the 2004 Athena Survey of SET (ASSET). The survey explored the factors that influence male and female scientists’ career progression, aspirations and expectations, as well as their ideas about what may obstruct women’s advancement in scientific careers. The findings highlighted differences between men and women in career aspirations, perceptions of equality in pay, promotions and space at work, networking and wider career development activities and guidance or support for career transitions. And the survey made clear that many of the issues that the MRC faces affect other research councils and universities, so it can learn from these generic SET trends.

**Future plans**
To help the MRC move forward with its Women in Science initiative, the subcommittee recommended a combination of approaches – ‘top down’ to enable its findings to influence MRC policies and processes, and ‘bottom-up’ to increase awareness of the issue among staff, particularly those most affected. The subcommittee is now identifying further steps that need to be taken. It realises that although there isn’t a ‘one-size-fits-all’ solution, gradual improvement in MRC policies and practices will go a long way towards increasing the number and enhancing the experience of women working in science.

**Introducing the Get SET Women Database**
The UKRC Get SET Women Database is designed to help increase awareness of women in science, by providing access to women working in SET industries who can be approached for promotional and work-related opportunities. These activities could include speaking at events, acting as role models, providing comment in scientific news coverage or sitting on public boards and committees.

**Interested in getting involved?**
To ensure the ongoing development of the database, the UKRC is keen to recruit female scientists from all fields. New members are welcome whatever their career stage, from graduate to professor or director level. If you would like to get involved, please register now at www.setwomenresource.org.uk.

**A tribute to Helen Muir (1920–2005)**
The first female member of the Medical Research Council, Professor Helen Muir died in November 2005. Network pays tribute to this talented scientist, who spent her life unveiling the secrets of osteoarthritis...

Born in India in August 1920, Helen Muir was schooled in Montreux, Switzerland and Newbury, England. She went on to study chemistry and biochemistry at Somerville College in Oxford under the renowned scientist Dorothy Hodgkin, before beginning her career in 1948 at the MRC's National Institute for Medical Research, then in Hampstead. In the institute's Division of Biochemistry, Helen studied porphyrins under Albert Nieuwerger and Sir Stanley Peart. In 1954 she went to St Mary's Hospital as Pearl Assurance Arthritis Fellow, and there began her in-depth investigation of osteoarthritis. A keen hunter, Helen studied osteoarthritis in the legs of her hounds during and after their working lives. She also replicated the condition in laboratory beagles and studied it in humans. In 1966 she moved to the Kennedy Institute of Rheumatology where she served as director from 1977 until retiring in 1990.

Helen Muir's pioneering work established that osteoarthritis is not caused solely by age-related wear and tear of the cartilage in joints, but involves an active chemical process with both environmental and genetic triggers. The MRC welcomed her onto the Council in 1973. She went on to serve on MRC committees in a number of areas, including finance, management of laboratory animals, and the selection of candidates for the Pneumoconiosis and Toxicology Unit.

Many other honours followed. In 1977 Helen Muir became one of the first women to be made a Fellow of the Royal Society, and in 1981 she was awarded a CBE. A feisty redhead, Helen had a great love of horse riding. But ironically, this caused her to suffer badly from spinal stenosis – a form of the osteoarthritis she spent her life studying.

**Find out more online**
UK Resource Centre for women in SET: www2.shu.ac.uk/nrc/index.cfm
Athena Survey of SET: www.uea.ac.uk/cesd/resnet/crs_survey.htm

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**Athena Survey of SET**
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IQ and health inequalities

Many government programmes aim to reduce health differences between rich and poor. But for such interventions to be effective, it is crucial that policymakers first understand the causes of health inequalities. A study by MRC scientists at the Social and Public Health Sciences Research Unit in Glasgow has shown that IQ may explain some, but not all, socioeconomic inequalities in health.

To test whether the relationship between health and socioeconomic position would disappear if IQ was taken into account, Dr David Batty and colleagues tested the IQ of over 1,300 Scottish men and women in their 50s in 1987. Each participant's socioeconomic status was assessed by a questionnaire and their health was tracked over the next 17 years. As expected, the poorest socioeconomic groups were at the greatest risk of suffering ill health and dying early. Taking account of IQ reduced this effect, yet the risk among poorer people was still at least twice that of ‘advantaged’ people in half of the associations studied. The scientists concluded that IQ may not completely explain health inequalities between different socioeconomic groups, but does contribute to them.

British Medical Journal 332: 521-525

Human energy mystery solved

MRC scientists have unravelled one of the final puzzles in explaining how the body produces energy, with implications for understanding the ageing process and treating diseases such as Parkinson’s. Mitochondria are the ‘power stations’ inside cells that generate energy. The team, from the Dunn Human Nutrition Unit in Cambridge, has identified the structure of complex I – the fifth, most complicated member of the group of enzymes in the mitochondrial membrane that are crucial to this process. They found that the enzyme is assembled from many smaller proteins, which act as ‘building blocks’ and fit together as perfectly as pieces of a jigsaw puzzle. “One of the many new revelations from the structure is related to ageing,” said lead researcher Dr Leonid Sazanov. “We now know how elegantly different elements of the complex are arranged, so that electrons can be transferred through the complex with maximum effectiveness and minimal ‘leak’ into surroundings. If this leak were greater, more oxygen radicals would be produced, which can damage DNA and may lead to accelerated ageing.” Dr Sazanov and his colleagues believe that their findings may lead to ways to minimise further the production of damaging radicals, with implications for dealing with ageing.

Science 311: 1430–1436

Acting on impulse

Many neuropsychiatric patients, particularly those with attention deficit hyperactivity disorder (ADHD), have problems refraining from inappropriate actions such as blurt out impulsive comments or rushing in front of cars. A team of Cambridge University scientists has now shown that the ability to inhibit such actions is controlled by the brain chemical noradrenaline. Their work, jointly funded by the MRC and the Wellcome Trust, has implications for the development of new treatments for conditions such as ADHD. The participants were asked to press a left or right key as quickly as possible in response to arrows on a computer screen. When a beep sounded, this signalled that they should cease doing so – a simplified form of stopping that can be related to everyday behaviour such as being able to stop at red lights. When participants were given atomoxetine, a drug that increases levels of noradrenaline, they were more successful at inhibiting their actions. Lead researcher Dr Samuel Chamberlain, of the University of Cambridge School of Clinical Medicine, said: “These results are important because difficulties in stopping inappropriate behaviour cause some of the greatest problems for patients with ADHD and their families.”

Science 311: 861–863

Work stress and the metabolic syndrome

Stress at work has long been thought to increase the risk of heart disease, although the mechanisms for this have been unclear. MRC-funded researchers have now found that a person’s level of stress at work is directly linked to their risk of the metabolic syndrome – a cluster of risk factors that puts people at danger of heart disease and type 2 diabetes. As part of the ongoing Whitehall II study, Dr Tarani Chandola and colleagues from University College London examined the relationship between work stress and the metabolic syndrome in over 10,000 British civil servants aged between 35 and 55. They assessed the participants’ stress at work on four occasions between 1985 and 1999 and measured components of the syndrome, including obesity, high blood pressure and raised cholesterol, between 1997 and 1999. The results showed that job stress was linked to the metabolic syndrome, with a stronger association among men than women. The team suggest that prolonged exposure to work stress may reduce biological resilience, thus disturbing the body’s physiological balance.

British Medical Journal 332: 521-525
A mammoth task

Scientists at the MRC Laboratory of Molecular Biology in Cambridge have helped to invent a technique that has cracked the ancient DNA code of the woolly mammoth and established its evolutionary link with modern-day elephants. The work was carried out in collaboration with scientists from the Max Plank Institute in Leipzig, Germany, University College London, the University of California in Berkeley, USA, and the Heinrich Heine Universität in Dusseldorf, Germany. The researchers are the first to have deciphered the complete DNA sequence of the mammoth's mitochondria. Mitochondria are the power houses of cells – tiny structures which process oxygen and turn food into energy. It is hoped that the technique will be of widespread use in analysing other ancient samples of DNA. Dr Paul Dear, whose group at the MRC Laboratory of Molecular Biology is working to develop ways to analyse minuscule DNA samples, said: “When you have tools that let you look at single DNA molecules in this way, whole new horizons open up.”

Nature 439: 724–727

A risky business

Risk-taking behaviour may be linked to a lower likelihood of developing Parkinson’s disease. This was the finding of a collaborative study by researchers at the MRC’s Cognition and Brain Sciences Unit in Cambridge and their colleagues in London, Australia and the Netherlands. The scientists found that people who develop Parkinson’s disease are less likely than people without the disease to smoke, drink a lot of alcohol or have a high caffeine intake. To explore whether this link is due to personality characteristics, the researchers compared 106 patients with Parkinson’s disease with 106 healthy people. Both groups filled in questionnaires about their personality traits and behaviour, as well as their smoking and drinking habits and caffeine consumption. The Parkinson’s patients had lower levels of risk-taking and ‘sensation-seeking’ behaviour and higher levels of anxiety and depression. They tended to spurn openly hedonistic activities and be scrupulous, socially withdrawn, inflexible, disinclined to take risks and relatively passive. The scientists suggest that the apparent protective effect of smoking and high caffeine and alcohol intake against Parkinson’s disease may be because people who are more likely to take risks may also be more likely to have these habits.


Diabetes gene uncovered

Diabetes occurs when the insulin-releasing cells in the pancreas stop working and levels of glucose in the blood rise. Scientists have now discovered a gene called Nnt that is involved in insulin secretion and may prove key to treating diabetes. The team, led by Professor Roger D. Cox from the MRC Mammalian Genetics Unit at Harwell and Professor Frances Ashcroft from Oxford University, found that the gene may play a role in removing free radicals – highly reactive molecules with an unpaired electron that can damage living cells. Funded by the MRC, the Wellcome Trust and Diabetes UK, the researchers studied mice that lacked the Nnt protein and found that they had reduced insulin secretion and glucose intolerance – early symptoms of type 2 diabetes in humans. This led the scientists to think that a deficiency in Nnt protein may result in an increase in damage to the insulin-releasing pancreatic cells by free radicals and, consequently, reduced insulin secretion. “It seems very likely that Nnt is important for insulin secretion in humans,” said Professor Cox. “That would open up exciting possibilities for treating type 2 diabetes. It may even turn out that defects in Nnt can cause human type 2 diabetes.” Professor Ashcroft added: “If we understand how insulin secretion is controlled, then we may be able to intervene to restore secretion in patients with diabetes.”

Cell Metabolism 3: 35–45
Science for all

Each March, National Science Week celebrates science, engineering and technology and their impact on our everyday lives. Network reports on MRC activities during this year’s event...

National Science Week enables people of all ages to find out more about science and to meet some of those responsible for making the UK a world leader. And because the approach is informal and interactive, the experience is fun. This year there were MRC events for all ages, from schoolchildren to local radio listeners and parliamentarians. At the National Institute for Medical Research (NIMR) in north London, researcher Clare Davy organised an afternoon of workshops for sixth-formers, including arts students. Participants explored the science and issues behind the current development of a cervical cancer vaccine, moving around different stations where they could interview scientists, listen to presentations, or discuss ideas. “As well as looking at the science of virology and immunology, the event also focused on communication of science and the wider ethical and social issues of research,” explains Clare. “Interestingly, it was the non-biologists who unanimously agreed that the best part of the workshop was interviewing the science experts!”

Science in Parliament

Meanwhile the Royal Society and the Office of Science and Innovation held a morning event celebrating British science for parliamentarians and policymakers. With Alan Johnson, Secretary of State for Trade and Industry and UK Science and Innovation Minister Lord Sainsbury present, the audience heard five “outstanding young researchers” talk about their work. These speakers included Dr Danielle Turner, an MRC-funded postdoctoral researcher in the University of Cambridge’s Department of Psychiatry, who spoke about the science of cognitive enhancement. “I really enjoyed the challenge of communicating the excitement and relevance of my work,” commented Danielle.

At Westminster Dr Chris Mee (MRC Functional Genetics Unit) and Richard Page (University of Cambridge) won first prize and the Westminster Medal in a competition of 160 posters at the annual Science, Engineering and Technology for Britain reception at the Houses of Parliament. Their presentation was on “The Alzheimer’s fly: A model organism for the study of Alzheimer’s disease.”

Science across the airwaves

Broadcasting across Oxfordshire and adjoining counties, BBC Radio Oxford attracts tens of thousands of listeners each day. During National Science Week the station launched the Oxford region’s “MRC scientists on the air” project, which brought MRC scientists into the BBC studios to talk on research-related topics in the Oxford area. Chief Executive Colin Blakemore was first up, talking to afternoon presenter Bill Heine about the value of the week in helping to promote science, and the MRC’s mission to communicate its work to the public.

Dr Lizzie Burns visited BBC Radio Berkshire to talk about a series of art-science workshops she was running on behalf of the MRC in Reading. Held at the city’s Museum of Rural England, the workshops had the theme of ‘Bringing colour to life.’ Over four days, Lizzie took Reading school students and local residents on a microscopic journey through the body. After showing them colourful molecular and cellular images,

Students carrying out DNA experiments at Villiers Park.

‘Bringing colour to life’ workshop at the Reading Museum of Rural England.
she encouraged them to create their own artworks inspired by what they'd seen. She was supported by MRC scientists from the Mammalian Genetics Unit at Harwell, including Paul Denny, group leader of Infection Genetics, and Charlotte Dean, programme leader in Developmental Genetics.

Open days and visits
Also from the Mammalian Genetics Unit, Cathryn Tambini ran a workshop at St Amand’s Primary School in East Hendred, Oxfordshire. Entitled “How clean are our hands?”, the event was part of the school’s Health and Fitness Week. Professor Doug Higgs, Director of the Molecular Haematology Unit in Oxford, gave a talk on the DNA revolution to sixth formers at Sutton High School for Girls, while colleague Dr Marella De Bruijn spoke about ‘Haemopoietic stem cells in biology and disease’ as part of an evening of free public lectures in Oxford. The Weatherall Institute of Molecular Medicine hosted a knowledge-sharing day including lectures and a poster exhibition, and scientists at the MRC Anatomical Neuropharmacology Unit welcomed secondary school students from around the country to its open day. Pupils aged between 14 and 18 toured the unit’s laboratories, met scientists and helped to carry out experiments such as ‘patch-clamping’ a brain cell.

In Cambridge, the Hutchison MRC Research Centre/Cancer Cell Unit hosted an open day on the theme of ‘Making a world of difference’. This explored cancer’s impact worldwide and how lifestyle influences our risk of developing cancer. And at the Laboratory of Molecular Biology, Dr Samantha Wynne and colleagues teamed up with Dr Nicola Powles-Glover from MRC Harwell to host a working visit by 22 students at Villiers Park Educational Trust. The students spent a day carrying out DNA experiments – using computer graphics, microscopy and protein crystallization – and experiencing work in a lab first-hand. Everyone involved had a busy and thoroughly enjoyable day, which received top marks from students and teaching staff! To round off the MRC’s Cambridge activities, early-career scientists from the MRC Cognition and Brain Sciences Unit showcased their research in ‘Exploring mind and brain’ to a ‘sell-out’ audience. All the scientists involved felt this year’s Cambridge events were very worthwhile and are already talking about activities for 2007.

Hungry for knowledge
The Cambridge Science Festival also takes place in March – the week after National Science Week – and this year drew huge crowds of all ages. Researchers from the MRC Dunn Human Nutrition Unit and the MRC Biostatistics Unit hosted ‘Inner space’, an interactive exhibition which described the magic of metabolism from mitochondria to muscles. The star attraction was an exercise bike with a difference, created by scientists and built by technicians in the MRC workshop. Hundreds of visitors used the bike to ‘work out’ for themselves the relationship between food intake and energy expenditure, and a full-length model gut allowed younger visitors to get to grips with digestion. Later that day, a packed audience at the Michael House Café in the centre of Cambridge posed their diet and nutrition questions to a panel of scientists from the MRC Collaborative Centre for Human Nutrition Research.

Events diary
Cheltenham Science Festival
The MRC will once again be presenting a series of events at the annual Cheltenham Science Festival: a hands-on interactive family exhibition in the festival’s Discover Zone, based on MRC science and manned by MRC researchers; a science-art event run by Dr Lizzie Burns, and principal sponsorship of an event on ageing with Professor Raymond Tallis.

The festival takes place from 7 to 11 June 2006 in various locations across Cheltenham. More information is available at www.cheltenhamfestivals.com.

MRC Open Public Council Meeting
As part of the MRC’s commitment to openness, transparency and dialogue with our stakeholders, the MRC’s Council will be holding its second open meeting on 27 July in London. This a great opportunity for members of the public and other stakeholders to find out more about the MRC, including a recent MRC/BBSRC public consultation into research priorities in ageing.

For more information, visit www.mrc.ac.uk.

Launch of BBSRC/MRC ageing consultation report
Since March the MRC and the Biotechnology and Biological Sciences Research Council have been running a public consultation on priorities in ageing research. The MRC will be announcing the results and next steps at its open council meeting on 27 July.

More information will be available nearer the time at www.mrc.ac.uk.

BA Festival of Science
The MRC will once again take part in the BA Festival of Science, which will be held this year in Norwich from 2 to 9 September.

More details are available from www.the-ba.net/festivalofscience.
MRC people

Professor Veronica van Heyningen has been awarded the 2006 European Society of Human Genetics Prize for contributions to international human genetics research. At the award ceremony in Amsterdam in May 2006, she gave a lecture entitled “Making eyes: lessons from genetic ocular malformations”. Professor van Heyningen joined the MRC Human Genetics Unit in 1977 (then called the Clinical and Population Cytogenetics Unit), where she now heads the Medical Genetics section.

Dr Christopher Mee has been hailed as one of the UK’s top young scientists after being awarded the Westminster Medal for his work on “The Alzheimer’s Fly: A model organism for the study of Alzheimer’s disease”. Dr Mee, of the MRC Functional Genetics Unit in Oxford, was awarded the prize at the annual Science Week reception at the House of Commons in March.

Two MRC-funded studies were among 2005’s top achievements in prestigious science magazines. Professor David Porteous and colleagues at the University of Edinburgh worked with scientists at the University of Glasgow and the pharmaceutical company Merck, Sharp and Dohme Ltd to identify a gene interaction that increases the risk of mental illness. The team’s paper was ranked by Discover in its top 100 achievements of 2005. By measuring the IQs and reaction times of 898 people in their 50s in 1988 and recording which of them had died by 2002, the scientists revealed a relationship between lower IQ and early death.

In March 2006, two MRC scientists received Wolfson Research Merit Awards. Professor Avshalom Caspi, of the Institute of Psychiatry at Kings College London was awarded the prize for his research into genetics and stress, while Professor Jane McKeating of the University of Birmingham was recognised for her research into how the hepatitis C virus infects the liver.

Martin Wood has recently retired after 30 years’ service with the MRC and MRC Technology. During that time, he has been instrumental in intellectual property and licensing activities around humanised monoclonal antibodies, which have generated around £200 million in royalties for the MRC. Martin has also contributed to the foundation of many spin-out companies. We would like to take this opportunity to thank him for all his efforts and wish him a long and happy retirement.

Your feedback please

MRC Network is for anyone who has an interest in the work of the MRC, including scientists, doctors and health professionals involved in medical research, government departments and parliamentarians, and university staff and students. The aim is to provide a quick, easy-to-read summary of activities across the MRC, from research news through to funding, grant schemes and policy issues, with pointers to more in-depth information on websites and in other publications.

We are very keen to receive feedback on Network and suggestions for new features from our readers. So if you have any comments, please let us know. Just mail: newsletter@headoffice.mrc.ac.uk

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Infowatch

Testing Treatments: better research for better health care

How do we know whether a particular drug, therapy or operation really works? How reliable is the clinical evidence? Is current research fully focused on the real needs of patients? These and other thought-provoking questions are dealt with in this probing inquiry into modern clinical research. Testing Treatments was written by Sir Iain Chalmers, coordinator of the James Lind Initiative, Imogen Evans, Clinical Research and Ethics Liaison Manager at the MRC from 1996 to 2005, and Hazel Thornton, advocate for public involvement in medical research.

Cerebrum: The Dana Forum on Brain Science is billed as “the journal of opinion about brain science that can change your mind.” It focuses on issues raised by brain research, their impact, and their implications, such as how brain science affects our health and the choices we make every day. From January 2006, Cerebrum became a free web-only publication with monthly articles, features, letters to the editor and a complete searchable archive of all print issues from 1998 to 2005.

www.dana.org/cerebrum