The Medical Research Council is set to increase funding of research into influenza and other emerging infections by £10m. In late November 2005, it put out a call for proposals to enhance research to tackle emerging infections with a pandemic potential. The extra money comes on top of the £1.6m that the MRC had already spent on influenza research in 2005.

This recognition that extra funds for flu research were needed was prompted by a mission of MRC experts to Vietnam and China last October, led by Professor Andrew McMichael, chair of the MRC’s Infections and Immunity Board. The team wanted to discover more about the spread of the avian flu virus and to discuss how collaboration between the UK, China and Vietnam could be improved in the future. It also included Sir John Skehel – whose work at the MRC National Institute for Medical Research has explained how the 1918 flu virus kept its avian flu characteristics but was able to transmit between humans – Professor Anne Johnson, epidemiologist and deputy chair of the Infections and Immunity Board, and Dr Xiao-Ning Xu, an expert in SARS at the MRC Human Immunology Unit.

Opportunities for collaboration
Vietnam has the highest recorded number of cases of human infection by the H5N1 avian virus. The MRC scientists visited five Vietnamese institutions and were encouraged more about the spread of the avian flu virus and to discuss how collaboration between the UK, China and Vietnam could be improved in the future. It also included Sir John Skehel – whose work at the MRC National Institute for Medical Research has explained how the 1918 flu virus kept its avian flu characteristics but was able to transmit between humans – Professor Anne Johnson, epidemiologist and deputy chair of the Infections and Immunity Board, and Dr Xiao-Ning Xu, an expert in SARS at the MRC Human Immunology Unit.

Preparing for rapid response
Looking ahead to the result of the call for proposals, Professor McMichael said: “Some of the research can begin as early as spring 2006. But we also want to fund research which can only start if and when influenza becomes an epidemic or pandemic.”

MRC Chief Executive Professor Colin Blakemore added: “The strategy we’ve been developing here shows that we can move quickly when a health crisis emerges.”
Ensuring scientific excellence through the College of Experts

Network reports on the group of expert scientists who peer review more than 1,500 applications each year for the MRC...

As the UK’s leading public funder of medical research, the MRC must ensure that the taxpayer’s money is spent on the highest quality science with a real potential to improve human health. To achieve this, each research proposal received from scientists must be scrutinised by at least three independent experts before the MRC’s Research Boards decide whether or not to fund it. But with applications now running at 1,500 per year across the MRC’s wide and diverse portfolio, sourcing the required number of reviewers presents a considerable challenge.

To meet this need for expert senior scientists who can provide consistently high-quality reviews and who understand the MRC’s work and strategic objectives, the Council set up a College of Experts in 2005. The College is made up of more than 1,000 scientists who meet these demanding requirements, and who have agreed to review at least six research proposals per year. Each member is affiliated to one of the MRC’s five Research Boards, so that the College’s collective expertise spans the entire range of the Council’s scientific portfolio.

Colin Blakemore, Chief Executive of the MRC, says: “The MRC’s reputation is built on the quality of science that it supports. We are very grateful to the members of the College of Experts for their central role in peer review, which underpins the decisions we make. The College also provides an essential link between the Boards of the MRC and the research community they serve. We look to the College to help us to develop our strategic plans in ways that reflect the strengths and needs of UK medical research.”

Involvement in the bigger picture
What makes the College unusual is that the members’ role does not begin and end with reviewing funding applications – they also have the opportunity to help the Council to develop its scientific strategy. Members are able to influence and contribute to the MRC’s work through a range of activities, from annual workshops and participation in scientific showcases to frequent consultations on key issues. All of which means that experience as a College member is an excellent grounding for scientists who are interested in becoming a member of a Research Board or a Training and Career Development Panel, or one of the MRC’s other expert advisory groups.

“I look forward to being part of a thriving College of Experts, rather than simply one of many reviewers working separately and without being able to see or input into the bigger picture.”
Member of College of Experts

A key relationship
It goes without saying that building up a strong relationship with the new College of Experts and facilitating communication with and between its members is a key priority for the MRC. One way that the MRC has been stimulating such dialogue and synergy was through a series of introductory workshops for new members in summer 2005. Held in Edinburgh, Birmingham, Bristol and London and attended by more than 300 members, the workshops gave them the opportunity to meet Chief Executive Colin Blakemore, other MRC staff, and one another. The format was a mixture of briefings, question-and-answer sessions and informal group discussions.

After the participants had learnt more about the MRC and what their membership involved, Colin Blakemore asked for their views on current issues and in particular, the MRC’s policies on supporting clinical research and early-career scientists. Clearly welcoming this opportunity for dialogue, they asked many interesting and challenging questions, and offered some very useful suggestions. As a result, the members’ feedback has informed both the MRC’s plans for developing the College and its scientific strategy.

The workshop participants were particularly enthusiastic about learning more about their Research Boards’ scientific portfolios and contributing to development of the Boards’ scientific strategies. So the next step for the MRC will be five workshops in 2006, each involving College members, their individual MRC Research Board and the Board’s Strategy and Portfolio Overview Group. The aim is for College members to be able to hear more about their Board’s work, and to gain an insight into the work of the MRC’s Strategy Overview Groups for clinical, public health and basic research. Another key theme of the day – to which members will be encouraged to contribute – will be the MRC’s priorities for funding from the Science Budget in the Government’s 2007 Comprehensive Spending Review. To complement these strategically focussed workshops, individual members will be offered the opportunity to observe their Research Board in action at a funding meeting.

Impact of Freedom of Information Act
Another topic of interest at the introductory workshops was the Freedom of Information Act, which came into force on 1 January 2005. The Act gives individuals a legal right to obtain information held by public authorities and
universities, which raises serious questions about the anonymity and confidentiality of peer review reports. College members will be reassured to learn that the MRC and the other UK research councils have now agreed a common Freedom of Information peer review policy. It details what information the research councils will release, when, and to whom, throughout each stage of the peer review process. As Jerry Folkson, MRC Business Development Manager, confirmed, “The MRC, along with the other research councils, is improving the transparency of its peer review process. However, we will continue to preserve reviewers’ anonymity, and will not release any identifying details about reviewers in response to information requests under the Act.”

**Full economic costing**

Many College members have asked whether the introduction of full economic costing of applications is likely to lead to any changes in what is required when reviewing an application. The answer is no – the reviewer’s role remains first and foremost to comment on the scientific quality and importance of a proposal, and then to assess its ‘value for money’ on the basis of whether the level of resources are justified – or in some cases, sufficient – to carry out the research effectively.

**Easing the load**

In 2004 the MRC made major changes to its funding schemes to give researchers fewer, simpler and more flexible options. This has led to a dramatic increase in the number of applications, which has increased the pressure on both the MRC and its reviewers. To help manage the problem, the MRC has reduced the number of reviewers per application to between three and five, and publishes a wider range of award statistics to help applicants assess the likelihood of success before submitting an application. Applicants can now view online overall funds available, numbers of applications already submitted, average size of grant, award rates by MRC Research Board and university, etc. The aim is to discourage low-quality or speculative applications – which waste valuable reviewing resources – and encourage internationally competitive, appropriately costed applications, with a balance between short-term and long-term programmes.

To help College members schedule their reviewing commitments into their overall workload, the Research Management Group will be highlighting peer review ‘hot-spots’ on the MRC website alongside deadlines for receiving applications.

**Interested in joining the College?**

Are you a biomedical scientist at reader or equivalent level, who is willing to review at least six research proposals a year and to spare the time to become involved in helping to develop the MRC’s scientific strategy? If so, the MRC would be pleased to hear from you. Please contact Anne-Marie Philp of the MRC Research Management Group at recruitment.board@headoffice.mrc.ac.uk.

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**Training**

All new members have received a basic CD-format induction into the MRC and their crucial role in the Council’s work. Feedback from the 2005 workshops revealed that many members would find it helpful to receive further training and mentoring, and peer review guidelines. The MRC will therefore be holding training sessions during its 2006 College workshops and is looking at ways of developing the content of the induction CD. It will also be providing more web-based guidance about reviewing, including use of the MRC’s online reviewing system.
Basic thinking

Although 2005 brought increased support for clinical research, basic research remains the bedrock of biomedical science, underpinning the treatments and diagnostics of the future...

As Network readers will have noticed, over the last year the MRC has been a leading voice in discussions about taking forward translational and clinical research in the UK, building on the knowledge gained in the past 50 years of fundamental research. With all this enthusiasm for translation, it is important to remember that the clinical applications of the future will depend on the fundamental research of today and tomorrow. The MRC, with hundreds of its scientists engaged in world-class basic research, remains as committed as ever to ‘blue skies’ investigations. And the Council envisages that the new efforts in clinical research – from experimental medicine to the UK Biobank – will provide valuable information to guide the next steps in fundamental research. Basic and applied research rely on each other for success – both are vital steps in the journey towards improved health and economic prosperity in the UK. This is why the work of scientists such as Dr Matthew Freeman of the MRC Laboratory of Molecular Biology (LMB) in Cambridge and Dr Steve Gamblin of the MRC National Institute of Medical Research (NIMR) in north London is as important to the MRC’s future plans as that of clinical and public health researchers.

Meanwhile, at the LMB, Dr Matthew Freeman’s research into the mechanisms of growth-factor receptor signalling has led to the discovery of a family of intramembrane proteases, called rhomboids, which are turning out to have many and varied functions in both animal cells and bacteria. Most excitingly, Dr Freeman’s work has suggested that rhomboids play a part in a number of medical conditions, including parasitic infections, such as malaria, and bacterial pathogenicity.

Discoveries like these are, of course, exciting in their own right. But, as with all the best of the MRC’s innovative basic research, they do more than simply push back the frontiers of intellectual endeavour. Basic research feeds a pool of ever-increasing knowledge about cells and physiological systems, which in turn generates opportunities for translational work and eventual clinical application.

A history of translational benefits

The MRC’s history is rich with examples of basic research that has subsequently been exploited to yield improvements in human health. One notable example from the LMB started with the development of monoclonal antibodies by César Milstein and Georges Köhler in the 1970s. In the late 1980s, Professor Sir Gregory Winter began applying protein engineering technologies to the long-standing problem of creating ‘humanised’ monoclonal antibodies. His success created a revolution in the pharmaceutical industry, spawning a new and continually expanding range of antibody-based treatments. Sir Gregory’s discoveries have been used to create therapies for cancer, asthma, psoriasis, multiple sclerosis and arthritis, and for prevention of kidney transplant rejection.

Professor Mark Pepys has been studying amyloidosis since the late 1970s, moving from basic understanding to treatment. This serious condition occurs when normally soluble proteins are deposited as abnormal insoluble fibres around and between cells, damaging the structure and function of the affected organs. Amyloidosis is responsible for one per thousand of all deaths in the UK. Professor Pepys’ MRC-supported research, into both the basic mechanisms of the condition and its clinical diagnosis and treatment, led to the establishment of the UK NHS National Amyloidosis Centre at the Royal Free Hospital and University College London in 1999. The centre investigates the largest, most diverse cohort of amyloidosis patients in the world and advises about their treatment.
under the clinical directorship of Professor Philip Hawkins, and has greatly improved their diagnosis, management and survival. Professors Pepys and Hawkins have developed a new drug, CPHPC, that specifically targets serum amyloid P component, a protein universally present in amyloid deposits. CPHPC is being developed for large-scale clinical testing and may find application in Alzheimer’s disease as well as systemic amyloidosis.

**Long-term approaches**

Recognising that it can sometimes take many years for the translational benefits of basic research to become apparent, the MRC believes that long-term funding of basic research is essential. For example, the MRC’s support for research into synaptic plasticity reaches back to the 1970s, when Professor Tim Bliss of the MRC National Institute for Medical Research, together with Terje Lømo of the University of Oslo, published the first detailed account of long-term potentiation (LTP) – the rapid and sustained increase in the efficiency of synapses in a brain structure called the hippocampus. In 1986, the link between such synaptic ‘plasticity’ and behaviour was established by another MRC-supported scientist, Professor Richard Morris of the University of Edinburgh, who discovered that interference with LTP disturbs spatial learning in rodents. The field received a further boost in 1999 when the MRC Centre for Synaptic Plasticity was established at the University of Bristol, with Professor Graham Collingridge as Director. Graham has made a major contribution to our understanding of the complex molecular mechanisms that underlie LTP and other forms of synaptic plasticity. Dysfunction of synaptic plasticity is now believed to be involved in various psychiatric and neurological disorders, including Alzheimer’s disease, epilepsy and ischaemic brain injury. The efforts of Professors Bliss, Morris, Collingridge and colleagues could prove key to the development of new treatments and preventive measures for these devastating conditions.

**Strategic perspectives**

No-one can foresee where the next major discoveries and technical developments in basic research will come from, or their possible impacts in diverse and apparently unrelated fields. So, in addition to its long-term strategic vision for the funding of basic research, the MRC must also be able to recognise opportunities and to take risks in curiosity-driven science, for these can hold the key to significant improvements in treatments. The MRC focuses on funding a broad portfolio of innovative and high-quality research that underpins key translational areas and takes advantage of expertise in both the biological and physical sciences. Developing research talent is also vital.

“We recognise the vital need to safeguard the interests of fundamental bioscience and we are continuing actively to develop our basic research portfolio. Maintaining world-class research that extends from the most basic to the most applied puts the MRC in a strong position to fulfil its mission to improve the health and wealth of the nation.”

**Professor Colin Blakemore, Chief Executive of the MRC**

To maintain the existing community and nurture the next generation of skilled researchers, the MRC provides career development training schemes, along with increasing investment in state-of-the-art facilities and equipment.

**The Basic Research Overview Group:**

The MRC is actively developing its basic research portfolio and in October 2005 set up a new advisory body – the Basic Research Overview Group – to help achieve this aim. The group is responsible for cross-research board oversight of the MRC’s basic portfolio, and sits alongside two other overview groups – for clinical research and public health research. It is chaired by Professor Kay Davies, MRC Council member and Honorary Director of the MRC Functional Genetics Unit in Oxford.

The Basic Research Overview Group will monitor trends in research and funding patterns and advise the Council about the balance of scientific areas within the basic portfolio. To ensure a coherent approach, it will foster links with the clinical research and public health research overview groups and its discussions will incorporate views that emerge from the individual research board strategy groups. The group is also responsible for identifying opportunities for increasing the effectiveness of the MRC’s links with the biotech and pharmaceutical industries, with overseas research partners and with other UK funders of basic biomedical research.

To support the work of the Basic Research Overview Group, the MRC regularly looks at the range of expertise on its Research Boards to ensure a balance between basic and more applied disciplines. For example, the Physiological Systems and Clinical Sciences Board is currently recruiting an additional member with expertise in basic cell biology and its application to physiological systems and the maintenance of health. For further details, see “Opportunities” on page 7.

“Biomedical science is evolving very rapidly. The work of the Basic Research Overview Group will ensure that the MRC continually reviews its basic research portfolio, and so remains at the international forefront of bioscience and a leading player in innovations in healthcare.”

Professor Kay Davies, Chair of the MRC Basic Research Overview Group
MRC visit shows time is right for collaboration with China

Chief Executive Colin Blakemore recently led an MRC delegation to China to explore opportunities for research partnerships. 

As mentioned in our front page story, in October 2005 a team of scientific experts from the MRC visited China to meet with their Chinese counterparts. The aim of the two-week mission was to raise the MRC’s profile in China and to assess the potential for scientific collaboration in research into cancer, neuroscience, infectious diseases and biotechnology.

On visits to Beijing, Shanghai, Guangzhou and Shantou, MRC delegates were struck by the intensive investment being targeted at new buildings and state-of-the-art equipment – currently running at around 1.4 per cent of China’s GDP. It is clear that China’s strategy is to attract back expatriates to help develop a knowledge-based economy.

After a second Memorandum of Understanding had been signed – this time with the Chinese Academy of Sciences (CAS) in Beijing – an MRC delegation visited several CAS institutes in Shanghai. Professor Brian Anderton, who led the group, said about the Academy’s neuroscience activities: “There is considerable complementarity of science between the UK and China… establishing stronger links has the potential to enhance the international position of both countries.”

Public engagement was another important strand of the MRC visit. Freelance artist Judith Devons held workshops in two Beijing high schools, inspired by research at the MRC Toxicology Unit in Leicester. More than 50 pupils and teachers explored the interface between science and art through screen-printing – with Colin Blakemore joining in with gusto to produce his own souvenir print. The pupils’ group artwork, a brightly coloured wallhanging displaying their individual screen-prints, was exhibited in the British Ambassador’s residence during a reception in honour of the MRC mission.

Commenting on the MRC’s visit and the signing of the Memoranda of Understanding, the Ambassador, Sir Charles Hum, said: “We have seen some impressive developments in science during our visit, and there are great opportunities for collaboration with UK scientists.

During 2006, the MRC will be developing a series of initiatives with key agencies such as NNSFC and CAS to foster new science programmes between our two countries.”

The group’s visit began with the signing of a Memorandum of Understanding with the National Natural Science Foundation of China (NNSFC), during which Colin Blakemore told the MRC’s hosts that “The UK is watching with admiration the impressive growth in China’s economy and its increasing investment in science.”

Professor Chen Zhu, Vice-President of the Chinese Academy of Sciences, and Professor Colin Blakemore with the Memorandum of Understanding

The mission was part of the UK-China Partners in Science 2005 initiative, a year-long event supported by the Chinese and UK Governments. Led by MRC Chief Executive Colin Blakemore, the 20 delegates included directors of UK research centres, research programme leaders, clinicians and MRC head office staff. The fortnight’s activities ranged from scientific workshops on cancer and neuroscience and fact-finding site visits, to public engagement events with schools and the public.

As the MRC mission prepared to return to the UK after two fascinating weeks, Colin Blakemore summed up the group’s experience in China: “We have seen some impressive developments in science during our visit, and there are great opportunities for collaboration with UK scientists.

During 2006, the MRC will be developing a series of initiatives with key agencies such as NNSFC and CAS to foster new science programmes between our two countries.”
Opportunities

Research Board applications – October/November 2006

All applications must be costed on a full economic basis.

Molecular and Cellular Medicine

Full application: 4.5.06
Peer Review: May–July 2006
Board meeting*: 12–13.10.06

Infections and immunity

Full application: 11.5.06
Peer Review: June–August 2006
Board meeting*: 19–20.10.06

Physiological Systems and Clinical Sciences

Full application: 18.5.06
Peer Review: June–August 2006
Board meeting*: 24–25.10.06

Neurosciences and Mental Health

Full application: 25.5.06
Peer Review: June–August 2006
Board meeting*: 6–7.11.06

Health Services and Public Health Research

Full application: 1.6.06
Peer Review: June–August 2006
Board meeting*: 8–9.11.06

* Normal decision point

MRC Research Board vacancy

The Physiological Systems and Clinical Sciences Board has a vacancy for a senior scientist with expertise in basic cell biology and its application to physiological systems and maintenance of health, and research interests in one or more of the following areas:

- The regulation of cellular function
- Cell signalling and signalling pathways
- Ion channel regulation
- Cellular and molecular imaging

For further details see http://www.mrc.ac.uk/about-board_recruitment

Closing date for applications: 9 February 2006.

Calls for proposals

Influenza research

Intentions to apply: n/a
Deadline for full applications: 20.2.06

Methodology and implementation

The aim of this call is to pump-prime and strengthen the Health Services and Public Health Research Board portfolio of methodological research. The budget for the call is £4m and the Board anticipates that between 10 and 20 proposals will be funded.

Intentions to apply: 27.1.06
Deadline for full applications: 1.3.06

For further information visit www.mrc.ac.uk/funding

Milstein Fund

The Milstein Fund aims to provide support for innovative research with potential for high payback. A budget of £3m has been allocated and it is hoped that up to 10 awards will be made. The initiative is being piloted in 2006/07, although the MRC intends to continue to make funds available for this type of research in subsequent years.

Full details of the call and eligibility to apply will be announced on the MRC website in early March with an application deadline of 21 April 2006.

Good news for those seeking funding

Traditionally, if a scientist works in a research institute that receives support from a funding organisation, they are prevented from applying to another funder for response-mode funding.

The good news is that this barrier to funding is beginning to disappear – the MRC, the Biotechnology and Biological Sciences Research Council and the Wellcome Trust have finalised agreements with one another to extend eligibility for response-mode support to researchers based in institutes supported by these funders.

We hope that other organisations will soon be following our lead in removing obstacles to funding.
Body fat – there’s more to it than meets the eye

Few of us would question the health risks of obesity. But there is another side to the body fat issue, as researchers at the MRC Clinical Sciences Centre are showing…

Nowadays, virtually all of us are aware of the relationship between obesity and ill health. An increased risk of insulin resistance, heart disease, type 2 diabetes, stroke, high blood pressure and osteoarthritis are just some of the proven hazards of obesity. But scientists still don’t fully understand the mechanisms underlying this association, which is limiting their ability to develop new, more effective treatments. Nor have they fully indentified the equally important benefits of body fat. To help throw light on these issues, the MRC Clinical Sciences Centre (CSC) and Imperial College London have brought together researchers from a range of disciplines – basic scientists Dr Jimmy Bell and Dr Louise Thomas, clinical researchers Professor Gary Frost and Professor Neena Modi, and physicist Professor Jo Hajnal. Using MRI and PET imaging techniques, molecular genomic investigation and clinical research, the team aims to uncover the role of adipose tissue in health and disease.

Moving beyond the body mass index

During the last 10 years or so, there has been a growing awareness that there is more to body fat than meets the eye. In other words, the health risks of body fat can be as much to do with where it is distributed in a person’s body as with the amount of fat that they show externally. The body deposits fat in at least eight different places, within adipose tissue depots or ectopic fat depots. Adipose tissue depots include external subcutaneous fat, fat within the abdominal cavity, popliteal fat and that between muscle fibres, while ectopic depots are fat within muscle, liver, pancreatic and heart cells. Each of these depots appears to contribute differently to the body’s homeostasis. To find out more about them, including their role in the development of insulin sensitivity and type 2 diabetes, the team has pioneered a new application of MRI scanning. The new technique enables them to create whole-body-fat maps of volunteers and patients in a matter of minutes, including for neonates and premature infants. It is giving the researchers a unique insight into the environmental and genetic factors that contribute to how a person’s body deposits and mobilises fat.

Thin on the outside, fat on the inside

As a result of their investigations, the team has found themselves faced with a surprising new body type, one which reveals the limitations of the traditional body mass index (BMI) as a tool for understanding the relationship between body fat and disease. They have identified the ‘thin on the outside, fat on the inside’ individual, who has a normal BMI and low external body fat content, but disproportionately high levels of intra-abdominal fat and ectopic fat deposition. These people have been shown to have an increased risk of developing insulin resistance and type 2 diabetes, compared to subjects who have similar levels of body fat but have deposited most of it externally. And, as Dr Jimmy Bell told Network, “Through a series of interventional studies we are beginning to find that different life-style modifications can impact differently on different fat depots and hence on health and disease.”

This is leading to new treatment strategies that focus on achieving the optimum benefits for health – such as combining changes in diet and in physical activity – rather than concentrating on maximum weight loss.”

The good, the bad and the ‘ugly’

The team now believes that adipose tissue is much more than a simple storage organ for excess energy. They see it as a highly refined, physiologically tuned organ that has significant effects on many of the body’s functions, including total energy homeostasis, appetite, satiety, fertility, immune
response, growth and a sense of well-being. For example, popliteal depots include fat cells surrounding the lymph glands shown to be essential in the process of immune response in inflammation and disease. And if adipose tissue malfunctions or is absent – as happens in some environmental or genetic conditions – this can lead to severe health complications by causing excess internal (ectopic) fat to be deposited. “Through the use of MRI techniques we have recently reported that nearly 40 per cent of the UK population shows mild to severe fat deposits in the liver,” said Dr Bell, “while human subjects with newly identified genetic mutations, with little or no external adipose tissue, show significant deposits in the liver, pancreas and muscle.”

This scientific appreciation of the value of adipose tissue contrasts strikingly with the western world’s current aversion to body fat. While scientists such as the team at CSC marvel at the hidden ‘beauty’ of adipose tissue, the increase in obesity in the general population and our constant bombardment with unrealistically slim role-models by the media has made external body fat a public enemy number one for both sexes.

Restoring a sense of balance
The flip-side of this increasing obsession with obesity is the ‘ideal’ of low/zero body-fat, a paradoxical state of affairs through which our society is in danger of losing a sense of the self and the human body as a fully functioning whole.

One all too graphic illustration of this is that liposuction, one of the most extreme (and increasingly popular) forms of body fat reduction, is now so common that in some countries the waste fat from these operations is becoming an environmental hazard! So it is heartening to know that, through the use of cutting-edge imaging and molecular methodology, scientists at the Clinical Sciences Centre are helping to redress this worrying imbalance, by revealing the importance of body-fat and its true relationship to our health and well-being.

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**Researchers and public join forces over autism**

In September 2005 the MRC and the National Autistic Society hosted their second Autism Forum in London. More than 120 parents and others with an interest in autism spectrum disorder (ASD) came to meet MRC-funded autism researchers and discuss where their needs fitted into the research agenda.

**Background to the event**
Dialogue between MRC-funded scientists and the public began in 2001, when the MRC’s Review into the Causes and Epidemiology of Autism sought expertise and opinion from outside the scientific community. The Department of Health and the Scottish Executive provided £2.75m to take forward the review’s recommendations. The MRC then set up an Autism Steering Group, chaired by Professor Carol Dezateux of London’s Institute of Child Health, to encourage the spread of research networks and multidisciplinary approaches in order to stimulate new thinking in autism research. By summer 2005 the MRC had funded six high-quality research proposals, covering: environmental risk factors, cognition and behaviour, brain imaging, language and communication, memory and Asperger’s syndrome, and a clinical trial investigating the effects of enhanced parental communication on preschool children with autism. These grants totalled £3.1m, almost doubling the MRC’s investment in ASD research.

**Forum activities**
During the day MRC-funded researchers introduced their early-stage work. The audience ranged from patient group representatives to parents of recently diagnosed children, with differing levels of knowledge about ASD. They were eager to make contact with others in similar situations and to quiz the researchers. As one parent said, “Ever since my child was diagnosed with ASD we have been looking for interventions. We are here, as parents, to learn more about autism and influence the scientists. They need to marry parents’ priorities with science and take it forward from there.”

**Research highlights**
The research highlighted included several of the newly-funded studies. The Pre-school Autism Communications Trial, led by Dr Jonathan Green of Manchester University, is the largest randomised controlled trial of a non-drug treatment for autism yet undertaken. Professor Declan Murphy of the Institute of Psychiatry in London outlined approaches to brain imaging to identify differences in neural networks between individuals with autism and those with Asperger’s syndrome. Professor Jean Golding of Bristol University described how data from the “Children of the Nineties” study, which looked at how environment, experiences and genes influence children’s health, behaviour and development, is being used to explore environmental-genetic interaction in children with ASD. Dr Francesca Happe of the MRC Social and Genetic Developmental Psychiatry Centre at the Institute of Psychiatry, discussed her research exploring how the autistic mind functions. The overall context for these studies was provided by Dr Tony Charman of the Institute of Child Health, who reviewed the UK scene for autism research, and by Dr Rob Buckle of the MRC and Angie Lee Foster of the National Autistic Society, who discussed the national policy context for research priorities and reported on current efforts to enhance collaboration between funding agencies. The breadth and depth of the research presented illustrated the challenges faced by autism researchers. Nevertheless, most participants thought that progress was being made, and that the MRC is making a significant contribution to autism research and is helping to promote communication between families and researchers.
Centre profile: MRC Human Immunology Unit

The increasing globalisation of infectious disease is a major challenge to human health. The MRC Human Immunology Unit is a key player in international efforts to combat this threat, and in research into diseases involving the immune system...

The immune system is crucial to human health. Our ability to identify and destroy invading pathogens involves complex networks of interacting cells and molecules. Understanding precisely how the system works at the cellular, genetic and molecular levels will help in the development of new therapies for diseases such as AIDS, avian flu, multiple sclerosis, arthritis and eczema. This is the business of the MRC Human Immunology Unit (HIU) based at the John Radcliffe Hospital in Oxford.

It is no coincidence that the unit sits only a few yards from the bustling entrance of one of the world’s most famous teaching hospitals: the work of the unit lies squarely at the intersection of fundamental molecular science and clinical research.

Creating the big picture

The HIU, located in the Weatherall Institute of Molecular Medicine, was founded in 1998 under the directorship of Professor Andrew McMichael as a merger of two MRC programme grants, involving three senior MRC clinical fellows, a Wellcome Trust senior fellow, and a scientist recruited from Denmark, Lars Fugger.

“The unit’s initial interest was on how the immune response deals with viruses, with a big but not exclusive focus on HIV,” says Professor McMichael. “We subsequently broadened it to cancer immunology and studies on autoimmunity, with a strong core of basic immunity work.”

The HIU now has eleven research groups and employs about 100 staff in total and has an annual budget of between £3.5m and £4m, which includes funding from both the MRC and external sources. While each of the groups carries out its own research, often into diverse aspects of the human immune system, all the research is contributing to a single ‘big picture’ of human immunology, and much of the work is complementary.

The human immune system

The human immune system consists of a remarkably elaborate series of defence mechanisms against potentially harmful agents that continuously threaten the body’s health. The body takes a multifaceted approach to defending itself, from presenting straightforward physical barriers to using highly complex adaptive systems by which specialised cells recognise the presence of pathogens and mobilise other cells to destroy them.

A key element of the human immune response involves T cells. There are different types of T cell involved in recognising and destroying infected cells. T cells become activated when receptor proteins on their surface are presented with antigens — small protein fragments of invading pathogens — by other specialised cells of the immune system.

HIV, influenza and the immune response

Four HIU research groups — led by Professor McMichael, Tao Dong, Tomas Hanke and Xiao-Ning Xu — study the human immune response to HIV.

“A lot of the work is trying to understand why patients who are infected with HIV can progress to disease very differently,” says Professor McMichael. “In some people disease progresses very rapidly, while others can survive for 15 to 20 years.” One promising line of research has been into a protein produced by the virus called Nef, which subtly alters the surface of infected cells. This ‘camouflages’ the cells, so that the immune system does not recognise them as being infected and the virus survives and replicates.

The HIU has been involved in the development of a number of candidate vaccines for HIV that are currently in various stages of clinical trials. It is also part of a large international programme that was recently launched with funding from the USA National Institutes of Health to look at how the immune system responds during the very early stages of infection. In some people the virus gains a foothold early on and is present at relatively high levels, whereas in others the initial levels are much lower. “We think the immune response is playing an important role in setting these initial levels, which can have a significant influence on the subsequent progression of disease,” Professor McMichael says. “If we can identify the features of a good immune response as against a poor one, we can use this knowledge to help us design more effective vaccines.”

“The extensive work on HIV has yielded important insights into viral infections generally, including avian flu and the virus that causes SARS (severe acute respiratory syndrome). One important question with these diseases is whether it...”

“It could be that the (HIV) virus is sitting harmlessly in the body’s cells, but that the immune system over-reacts in some way.”

Professor Andrew McMichael, Director, Human Immunology Unit
Researchers in the unit have recently started a collaboration with colleagues in Vietnam, where techniques developed in the HIV work will be applied to the avian flu virus (see page 1).

Professor John Bell’s group, meanwhile, is making significant advances in understanding the immune response to the influenza virus. When a virus invades the body, fragments of its protein coat are presented as antigens to the immune system. In influenza there appears to be a common response by T cells in most individuals, suggesting that certain antigens are crucial, or “immunodominant”. Antigens are the central component of vaccines, and the development of effective vaccines relies on the identification and isolation of key antigens.

**T cell biology group**
The group led by Professor Simon Davis and Dr Ed Evans is investigating the mechanisms by which T cells are initially activated – a central event in the immune response. When the antigen – a protein fragment from a virus, for example – is presented to a T cell receptor, a biochemical trigger is pulled. Professor Davis and his colleagues believe that the status of the receptor is determined by a delicate balance between two antagonistic chemical processes occurring at the receptor protein called phosphorylation and dephosphorylation. These processes are carried out by enzymes called phosphatases and kinases, which normally have equal access to the receptor. When the antigen is presented, however, it effectively barges the phosphatase out of the way. “We believe that this exclusion of the phosphatase upsets the balance of phosphorylation and dephosphorylation, which acts as the trigger for the activation, kicking off the proliferation of T cells,” Professor Davis says. “What this suggests is that we might be able to use other ways to cause the segregation of the phosphatase from the receptor – with antibodies, for example – and thereby manipulate the signalling process to either increase or decrease T cell proliferation.”

**Immunological origin of arthritis**
Dr Paul Bowness’s team is studying the immunological origin of certain forms of arthritis, and in particular ankylosing spondylitis, which usually occurs in young men and results in swollen joints and a painful back. More than 95 per cent of sufferers have an unusual type of HLA molecule on the surface of their cells. HLA is a protein that occurs on cells in the body, enabling them to communicate with the immune system. The team is trying to understand why the presence of this particular variant of HLA, called HLA B27, hugely increases the chances of getting the disease. “These molecules are important in helping the body fight off viruses, and this particular one is especially good,” Dr Bowness says. “We think that the abnormal form of the molecule stimulates the immune system in an abnormal way, resulting in the production of molecules that cause damage and inflammation. If we can identify the form of the molecule that is causing the problem and then block it, we might be able to ‘switch off’ the arthritis.”

**Cutaneous immunology**
Dr Graham Ogg is interested in the immunology of the skin and his group has made a potentially significant breakthrough in the understanding of what causes eczema. “We believe that the root cause could be because some people have increased populations of a common bacterium, Staphylococcus aureus, on their skin, ” Dr Ogg says. Most of us have this organism present on our skin, but people with eczema appear to be partially deficient in the natural antimicrobial defences, which allows the bacterium to proliferate. The presence of so many of these bacteria stimulates skin cells called keratinocytes to produce so-called HLA class II molecules on their surface, which are otherwise not present. The HLA molecules in turn grab on to fragments of proteins from house dust mites, dog and cat fur, and pollen, and present them to the immune system as harmful foreign invaders. “T cells then release substances to react to what are apparently infected cells, causing inflammation,” says Dr Ogg. “If our ideas are correct, this has clear implications for the treatment of patients, by reducing the bacterium population on the skin and the amount of allergens such as dust mites.” The team hopes to begin a clinical trial shortly.

**Immune-cell trafficking**
A key aspect of the human immune system is the constant movement of immune cells between the blood and tissues, and between tissues and the lymphatic system, a network of vessels running throughout the body that carries...
infection-fighting cells. “These events are pivotal to the inflammatory process and are fundamental to generating an immune response,” says Professor David Jackson, who leads the group that studies this type of cellular trafficking. Understanding the processes involved at the molecular level could lead to new ways of controlling inflammation, for example, or help in the generation of vaccines.

Migration of immune cells across the lining of blood vessels and into tissue involves a protein receptor on the surface of the cells called CD44, which binds to a large carbohydrate molecule called hyaluronan, or HA. In pioneering work, Professor Jackson’s group, together with Professor Martin Noble at the Laboratory for Molecular Biophysics, University of Oxford, has crystallised CD44 and determined its three-dimensional structure. The group has also bound together CD44 and HA, crystallised the resulting structure and elucidated its 3-D characteristics. “In this way we have shown exactly where the interaction between the two molecules occurs and we understand what kind of interaction is involved,” Professor Jackson says. “This allows us to design small molecules that could interfere with the process.” The group has also made important discoveries that have allowed lymphatic vessels to be extracted from tissues and reconstituted in the laboratory.

Tumour immunology
Professor Enzo Cerundolo’s laboratory studies how the immune system recognises cancer cells, with the ultimate aim of developing vaccines against cancer. The idea behind a cancer vaccine is to present the immune system with antigens specific to different types of tumour so that the body can arm itself in advance and recognise and destroy rogue cells before they become established.

“‘There are three main issues,’” says Professor Cerundolo. “‘We need to learn how to immunise, we need to be able to monitor the immune response, and we need to identify the antigens.’ The team has achieved the latter two, and the big challenge is to learn how to package the antigen in such a way that it can get into the body and stimulate the immune system correctly.

The team is adopting a ‘prime-boost’ approach, where synthetic antigen proteins are first presented to the body in a special mixture of chemicals to ensure a powerful initial response, followed by a ‘boost’ in which the antigen is wrapped within a harmless virus. The team has worked extensively on melanoma and is now looking at colon and prostate cancer.

Mechanisms of autoimmunity
Professor Lars Fugger’s team is trying to understand why the body’s immune system sometimes fails to differentiate between an invading pathogen and the body’s own cells in autoimmune diseases such as multiple sclerosis (MS). By the very nature of their job, T-cells must be highly adaptable in order to recognise many different antigens, but this also makes the system inherently prone to mistakes. It appears that multiple sclerosis occurs when a variety of genetic and environmental factors combine in a particular way. “The only identified genetic risk factor associated with MS relates to certain HLA genes,” says Professor Fugger. “We are trying to identify the function of the individual genes. Overall there appears to be an interplay between a certain T-cell repertoire, environmental factors such as viruses, HLA genes and other, unidentified genes.”

The work of the HIU demonstrates just how complex the human immune system is, involving precise interactions between cells, molecules and genes. Slowly but surely its researchers are beginning to piece together this immensely detailed jigsaw, constantly improving our ability to treat debilitating diseases and combat life-threatening infections.

“If we can understand how the immune response controls viruses we are in a much stronger position to design effective vaccines.”

Professor Andrew McMichael (left), Director, Human Immunology Unit

Continued from page 1

Professor Blakemore went on to say, “The Vietnamese and Chinese authorities are well aware of the threat and are keen for their best scientists to work with ours.”

He also played down the suggestion that the MRC had reacted to panic and hype in the media over H5N1: “We’ve been planning this strategy for months – it was an unexpected coincidence that our work became news just as bird flu reached Europe.”

The MRC’s mission to China helped to shape an international workshop held in London in December 2005. At the event, experts looked at how the virus is transmitted from birds to people, its virulence and strategies for effective vaccines and antivirals. Their discussions helped to determine a subsequent call for research proposals by the MRC.
Translational research set to benefit from shared DNA resource

As the UK DNA Banking Network sends its first samples for testing, Network takes a look at this pioneering service...

In 2000 – three years before the final human genome sequence was completed – the MRC recognised that once this groundbreaking knowledge was published, genetic epidemiology would be needed to translate it into human health benefits. Very soon afterwards the MRC announced its plan to meet this need by creating a national DNA banking network.

Six years – and a lot of effort – later, the UK DNA Banking Network has just shipped the first set of samples to the Wellcome Trust Sanger Institute in Hinxton, Cambridge, where they will undergo extensive genetic testing. The aim is to identify genes that are risk factors for coronary heart disease – one of the 13 serious human diseases being studied in the UK DNA Banking Network (see box).

Developing the Network

The first stage of developing the network involved collecting 40,000 blood samples from volunteer patients and from unaffected individuals. This work began in 2000 was supported by £8m MRC funding. It has involved 13 collections led by clinicians throughout the UK, to enable study of the genetic causes of diseases of major public health importance. The funding provided the opportunity to extend well-established studies – for example, the Acute Coronary DNA Event Library project, which already had support from the British Heart Foundation. Other collections were completely new, for example the breast cancer collection.

Next, the MRC provided £2m funding for the development of an archiving infrastructure to support the management of the samples and data. The European Collection of Cell Cultures in Porton Down handles the blood, peripheral blood lymphocytes and EBV-transformed cell lines, and the Centre for Integrated Genomic Medical Research at Manchester University handles the DNA, with security back-up in a nearby UK Biobank facility.

Both centres have ISO9001 certification, which gives assurance that procedures for consistent quality and continuous quality improvement are followed. Their state-of-the-art facilities include automated tube, plate and liquid handling to eliminate error arising from manual processing and retrieval, which can run as high as 10 per cent in conventional labs. And because the samples are all managed in the same way, the archive has harmonised the 13 collections.

The third step was setting up the DNA Network itself. Initially the network was a forum for the sample custodians and sample managers to exchange experiences, but the focus now is on integration and making scientists aware of the benefits of using the resource, including opportunities for collaborative research.

“We delivered our first large set of samples for testing ahead of time and to specification,” said Archive Director Dr Martin Yuille. “This has strengthened the collaboration – via the Wellcome Trust Case Control Consortium – between one of the collectors and a major genotyping centre, the Wellcome Trust Sanger Institute.”

Researcher-collector collaboration

The resource clearly reduces the costs of research by providing a central facility. To fulfil its scientific potential, it attracts researchers who want to collaborate with the sample custodians. To achieve this, the DNA Network has now launched a secure website where researchers can examine data and jointly initiate project design with custodians through the network’s collaboration support service – the most advanced scheme yet for sharing materials and data in genetic epidemiology.

How to apply for access

Researchers who would like to use the collaboration support service should first register with the UK DNA Network website at www.dna-network.ac.uk. They will be sent a username and password that will allow access to data and then to the service. Data on coronary heart disease are available now, and other data sets will be rolled out in due course.
New hope for TB treatment?

Tuberculosis kills two million people each year. BCG, the only vaccination currently licensed, is not effective in the developing world; conventional treatments involve a lengthy period of combined antibiotics with significant side effects and multi-drug-resistant TB is on the increase. All of which means that new interventions are urgently needed. A potential immunomodulatory approach is in the offing now that researchers have found that high dose intravenous immunoglobulin (IVIg – human antibodies purified from plasma) has a greater effect in reducing the number of TB organisms than the bacille Calmette-Guerin vaccination. Their work showed that in mice high dose IVIg enhanced the immune response and produced a long-lasting 100-fold reduction in the numbers of TB organisms, in both the early and late stages of infection.

This reduction in TB organisms occurred after a single treatment cycle. However, it was lost in mice lacking T cells – the white blood cells critical to the immune response against TB – which suggests that T cells mediate the immune-enhancing effect of IVIg. The study, which took place at the MRC National Institute for Medical Research, was led by Dr Stephen Jolles of the University Hospital of Wales and funded by the MRC Technology Development Gap Fund. Further research in a clinical setting is now possible, as IVIg is already used for a range of autoimmune and inflammatory conditions and has an excellent safety record.

Infection and Immunity 73: 6101–6109

Memories are made of this

Until now scientists believed that structures in the brain’s medial temporal lobe (MTL) make up a single functional system that supports learning of new memories, and is independent of other cognitive functions such as language and perception. However, a recent finding from the MRC Cognition and Brain Sciences Unit in Cambridge has shown that not all parts of the MTL support the same type of memory and some may have a role in perception as well. This could lead to improvements in tests for early diagnosis of different types of dementia and in rehabilitation of memory.

The research was carried out with people who had suffered damage to different parts of the MTL. Those with damage to the perirhinal cortex had extreme difficulty in memorising objects with several features in common, but showed normal learning with objects that looked distinct from one another. As the amount of information to be remembered was the same, this result implies a difficulty with perception of the objects. However, individuals with damage limited to the hippocampus performed normally. This suggests that the hippocampus, long thought to be the neural basis for memory, is not critical for memory of objects, but may play an important role in spatial memory and perception.

Journal of Neuroscience 25: 10239–10246

Down syndrome mouse model

In a major step forward in stem cell technology, researchers have produced the first mouse model for human Down syndrome. Funded by the MRC and the Wellcome Trust, the research was led by Dr Victor Tybulewicz of the MRC National Institute for Medical Research and Professor Elizabeth Fisher of the Institute of Neurology, University College London. Down syndrome occurs in around one in every 750 births. It is caused by having three copies of chromosome 21 instead of the normal two, but scientists do not yet understand how the extra chromosome results in this complex syndrome. To model the disorder, the team manipulated mouse embryonic stem cells, by placing almost the whole of human chromosome 21 into the cells. They then used these cells to generate a strain of mouse with the additional human chromosome. The researchers have shown, in collaboration with colleagues from the Institute of Cell and Molecular Science of Queen Mary’s School of Medicine in London, the University of Newcastle, King’s College London and the MRC Prion Unit in London, that the new mouse strain has problems with memory, brain function and the formation of the heart. These changes are very similar to those that occur in people with Down syndrome. “Aneuploidy is seen in at least five per cent of all pregnancies,” said Dr Tybulewicz, “This technology will be a crucial genetic tool for investigating Down syndrome and other aneuploidic disorders, in which individuals have the wrong number of chromosomes.”

Science 309: 2033–7
Youngsters go against the grain

Youth in Britain are eating significantly lower amounts of whole-grain foods than recommended, according to scientists at the MRC Human Nutrition Research Centre. This study provides the first insight into the amount of whole-grain eaten by young people – particularly pertinent given increasing awareness of the impact of childhood diet on health in later life. Intake of a wide range of whole-grain foods was estimated, using seven-day weighed dietary records from a national random sample of 1,583 young people aged 4 to 18 years who participated in the most recent National Diet and Nutrition Survey in 1997.

Although there is currently no UK Dietary Reference Value for whole-grains, the US Department of Health and Human Services recommends three 16g servings per day. Average intake among the young people studied was 7g of whole grain per day, with no difference between boys and girls. Less than a third consumed as much as 16g per day. The main sources were breakfast cereals (56 per cent) and bread (25 per cent). A quarter of the young people studied were not eating any whole-grain foods at all. Those whose parents had a manual occupation were significantly less likely to consume any.

British Journal of Nutrition 94: 925–831

Breathless excitement

Around one in 10 asthmatics has the severe form of the disease, which often requires progressively high doses of steroids and is associated with a much higher risk of illness and death than milder forms. Research led by Professor Stephen Holgate at Southampton General Hospital has now uncovered a potential new approach to treatment, by blocking a powerful immune system chemical present in large amounts in patients with severe asthma.

The team looked at the levels of tumour necrosis factor alpha (TNF alpha) in bronchial fluid and lung tissues samples from 26 people without asthma, 67 mild asthmatics and 51 severe asthmatics. Levels were significantly higher in those with severe asthma, and mostly concentrated in mast cells, the immune cells that play a part in the inflammatory reaction in asthma. In those with mild asthma or no asthma, levels were low. “This suggests that high levels of TNF alpha are characteristic of the more chronic form of asthma that is resistant to steroid treatment, rather than a feature of the disease itself,” says Professor Holgate. When 15 severe asthmatics completed a 12-week course of Etanercept, a drug that blocks TNF alpha’s actions, all experienced a significant improvement in their symptoms.

Thorax 60: 1012–1018

Extending the benefits of statins

Statins could benefit more people if targeted at all patients with diseased arteries, regardless of their cholesterol level. This was the finding of a collaborative study by scientists from the Clinical Trial Service Unit at the University of Oxford and the National Health Medical Research Council Clinical Trials Centre at the University of Sydney. Statins help to prevent heart attacks and strokes in high-risk patients, but most doctors prescribe them only when the blood cholesterol level is above a certain threshold, even in patients with narrowed blood vessels.

This new study, involving more than 90,000 participants in 14 previously completed trials, showed that many people with lower cholesterol levels could also benefit from statin treatment. The biggest benefits occurred in those with the greatest reductions in cholesterol after statin treatment, irrespective of their presenting cholesterol level. Lead researcher Dr Colin Baigent said: “Doctors need to identify all patients at risk of a heart attack or stroke, regardless of their blood cholesterol level, and then prescribe a statin at a daily dose that reduces their cholesterol substantially, which would reduce the risk of a heart attack or stroke by at least one third.”

Lancet 366: 1267–1278

HIV drug resistance high in UK

A study coordinated by the MRC Clinical Trials Unit has found that people infected with HIV in the UK have one of the world’s highest rates of transmitted drug resistance. In 2,357 patients with the HIV virus who had never received antiretroviral therapy before, 335 were resistant to one or more antiretroviral drugs. Of this group, 257 patients were resistant to one drug class only, 44 cases showed resistance to two drug classes and 34 showed resistance to all three commonly used drug classes. Overall, there was a 14 per cent rate of resistance in the UK. The estimate is seven per cent for the USA, six per cent for France and 10 per cent elsewhere in Europe. Direct comparisons should be treated with caution, however, as different studies have used different definitions of resistance. Nevertheless, this spread of resistance may begin to compromise the enormous benefits of combination antiretroviral therapy. It also highlights the importance of early diagnosis and of health education messages about safe sex.

BMJ 331:1368–71
Inspiring the scientists of tomorrow

Young people need to experience the excitement of science before stereotypical thinking about eccentric boffins starts to take hold. This is what MRC schools initiatives are helping to achieve...

Easily overlooked in the serious business of science, young people are in fact a very important audience for the MRC. They represent the future generation of medical scientists. Not only do we need to make them aware of the importance of medical science in everyday life, we also need to inspire them with the possibilities it offers for a future career. To help reach young people and their families, the MRC has become a familiar presence at the Edinburgh and Cheltenham science festivals. And during National Science week in March, many MRC researchers present activities designed to appeal to young people, often through hands-on involvement.

Back to school

Another very effective way in which scientists can communicate their research to young people is through working in schools. This can be as simple as a researcher approaching his or her child’s school with an offer to hold an informal workshop in the science lab. Such an encounter gives children a real insight into the world of the scientist and often helps to inspire teachers with new ideas for bringing science to life. It can also be a valuable opportunity to convey important general messages, such as why girls should think seriously about science as a possible career and why animals need to be used in some areas of medical research.

The Science and Engineering Ambassadors scheme offers a slightly more formal way for researchers to get involved in communicating with schoolchildren. Run by SETNET, a UK-wide charity, the scheme aims to promote awareness of science, technology, engineering and maths among young people by providing enthusiastic volunteers to work with pupils and teachers in schools. MRC-funded PhD students may be interested in the Researchers in Residence scheme funded by Research Councils UK and the Wellcome Trust – it’s ideal for those who would like intensive, short-term involvement with schools. After a briefing day that includes ideas for activities with staff and pupils, participants spend an average of a week working in a secondary school.

MRC scientists can also provide valuable input into teachers’ understanding of medical science, through the professional development programmes for teachers provided by nine regional Science Learning Centres coordinated by the DfES and the Wellcome Trust. Three new MRC Regional Communication Managers, and the existing

The MRC National Institute for Medical Research runs an active schools engagement programme - Network takes a look at key activities

Each year the NIMR holds two school days, during which 320 to 360 Year 12 students from around forty local schools visit the Institute to hear talks on current research and see demonstrations. Younger NIMR staff then lead discussion sessions during which the students can ask questions about science, careers and ethical issues.

Another highly successful annual event is the NIMR’s research summer school for Nuffield Foundation bursary students, attended this year by 16 students aged 17–18 from 11 schools. After a half-day induction course introducing molecular biology, lab skills and record keeping, they work with staff on projects for four to six weeks. Each student then produces a poster and report of their work and receives a Gold or Platinum BA Crest award for their achievements. The posters are later exhibited at Nuffield Foundation events. In 2004, the Foundation selected two students to present their work, one at the Intel Science and Engineering Fair in Phoenix, Arizona and the other at the British Association Science Fair.

The NIMR’s work within schools ranges from occasional talks to involvement in the SETNET Science and Engineering Ambassadors scheme. The level of complexity can range from a presentation on infections during a primary school assembly to an NIMR scientist spending a week in a secondary school taking lessons.

Staff also give talks about their research to sixth-formers, often as a result of volunteering through the Biology4all website. One NIMR researcher is a regular guest lecturer in Imperial College London’s scheme aimed at ‘gifted and talented’ London children, which involves video-conferencing across a number of schools.

The Institute also holds an annual human biology essay competition for schools. It’s hugely popular. The number of entries has doubled since 2003 – in 2005 there were 127 from 17 schools. In addition to receiving a financial prize, the winner and two runners-up spend a day at the NIMR visiting the labs and talking to scientists.

Nuffield Bursary recipient Alice Firebrace on her experience at the MRC Cancer Cell Unit:

“I found the work fascinating and everyone was amazingly supportive and kind especially as it was entirely different from anything I had done at school. I contributed to sequencing the p53 gene. I learned a lot about the theory behind the project, which as well as helping my understanding of A-level genetics showed me how broad the subject of biology really is. I also learnt to use the equipment for all the experiments, the methods and techniques to grow the cells, extract and replicate their DNA and finally to sequence it.”

Mr Jonathan Rees of the MRC Cancer Cell Unit with Nuffield Bursary student Alice Firebrace
Cambridge-based Manager, will strengthen these links between MRC researchers and the Science Learning Centres.

**Investing in young people**

The MRC contributes just over £35,000 to Nuffield’s investment in three main schools programmes. The first of these, the Nuffield Science Bursary scheme, provides the funding for talented sixth formers to work with professional scientists on projects in MRC laboratories. For example, Alice Firebrace of Ipswich High School, who worked with Dr Rebecca Fitzgerald at the MRC Cancer Cell Unit in Cambridge on research into oesophageal cancer (see box on page 16). The BA Crest (Celebrating Creativity in Science and Technology) Awards encourage students aged 12 and over to develop their scientific curiosity, problem-solving and communication skills by undertaking science projects in school, some of which involve mentoring from industry or higher education institutions. The third scheme, Researchers in Residence, enables around fifty MRC PhD students per year to take their science into schools through week-long placements (see page 16 and box).

**Future focus**

Over the past few years the MRC has focused on secondary schools, where it was thought there was the greatest need to stimulate interest and literacy in science. But a recent OST report and a review by the Wellcome Trust has revealed that children are being turned off science even earlier, during their primary school years. The MRC already makes efforts to bring science projects in school, some of which involve mentoring from industry or higher education institutions. The third scheme, Researchers in Residence, enables around fifty MRC PhD students per year to take their science into schools through week-long placements (see page 16 and box).

I have previously been involved in a youth exchange project between Ghana and the UK, in which our group devised and ran an HIV education programme with Ghanaian primary and secondary schools. I was therefore able to adapt this approach, which involved a presentation of the key ideas, followed by a playground/classroom game and a question-and-answer session. I used a similar format when discussing current research and brought in equipment and consumables for the pupils to touch and talk about.

I spent 20–30 minutes in each lesson, so that I could work with two classes per school lesson time. In general the response from the children was brilliant – lively, enquiring and very involved. One lesson on prevention and transmission of HIV with Year 10 pupils went so well it was thought there was the greatest need to stimulate interest and literacy in science. But a recent OST report and a review by the Wellcome Trust has revealed that children are being turned off science even earlier, during their primary school years. The MRC already makes efforts to reach and enthuse younger children, through interactive presentations at science festivals and projects such as Dr Lizzie Burns’ very successful art-science workshops. It will now be focusing even more on imaginative, inspiring ways of engaging all its young audiences, including developing further partnerships to add value and scope to this important work.

**Activities north of the border**

In October 2005 scientists at the MRC Virology Unit, in partnership with Glasgow Science Centre, ran a week of one-day DNA workshops aimed at Scotland’s Advanced Higher biology students. Ninety students from schools throughout Scotland took part. The aim was to give them hands-on experience of state-of-the-art molecular biology techniques and the opportunity to talk with MRC scientists about their research and careers in biomedical research. Participants conducted a diagnostic experiment to detect virus DNA in mock patient samples using the polymerase chain reaction and gel electrophoresis. They also looked at DNA sequencing, interpreting the results of a sequencing experiment on a viral gene and submitting the sequence to the NCBI blast server; to identify the virus and gene it came from. A lively debate on the ethical aspects of the human genome project rounded off each day, giving everyone food for thought. Teaching aids, reagents and the experimental protocols were devised by unit staff in close collaboration with the Science Centre education programmes team, and the laboratory equipment was funded by the Scottish Executive.

**Find out more online**

- Science & Engineering Ambassadors Scheme: www.setnet.org.uk
- Researchers in Residence: http://extra.shu.ac.uk/rirn/site
- Science Learning Centres: www.sciencelearningcentres.org
- Nuffield Science Bursary Scheme: www.nuffieldfoundation.org/go/grants/scibs
- BA Crest Awards: www.the-ba.net/ResourcesforLearning
In November 2005 the Edward Jenner Institute for Vaccine Research entered a new era by merging with the vaccine programmes of Oxford University and the Institute for Animal Health (IAH). The Institute's headquarters will now be in Oxford, under the directorship of Professor Adrian Hill of Oxford University. There will be a focus on human vaccine development at Oxford and on veterinary vaccines at the IAH and at the existing Jenner building in Compton in Berkshire.

The Jenner Institute was established in 1995 as the national vaccine research institute in a public-private partnership between the MRC, the Biotechnology and Biological Sciences Research Council, the Department of Health and GlaxoSmithKline. Its scientific programmes, led by Professor Peter Beverley, have made important contributions to many fundamental aspects of vaccinology and the immune response to infection.

The new partnership links this basic science with leading translational research and vaccinology development programmes at Oxford University and at the IAH. The Institute will cover the full range of vaccinology research, from basic science to vaccine manufacture, clinical trials and field efficacy studies. Linking research programmes in veterinary and human vaccinology, for example in tuberculosis or influenza, is an innovative approach that should accelerate new vaccine development in both areas.

"This provides a unique opportunity to bring together a range of expertise in both human and veterinary vaccine research and development to tackle some of the greatest challenges to global health," said Professor Hill. "With new recognition of the broader impact of poverty-related diseases, the threat of bioterrorism and recent veterinary and human disease epidemics, vaccine development has never been more important."

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**Why IP is important to the MRC**

The potential health benefits of findings in basic science lie hidden until complex development work has been carried out. The concept of IP is vital to this translational process...

**What is IP and why does it matter?**

An individual's intellectual property (IP) can be an invention, trade mark, original design, or secret knowledge used in the practical application of a good idea. Intellectual property rights (IPR) are rights granted through law, in the form of patents or copyrights, which allow ideas to be formally transferred, sold or licensed. The generation and protection of IP allows the research that the MRC carries out in its institutes and units to be used to benefit society.

**How does the MRC use its IP?**

Translating the MRC's findings into tangible healthcare improvements often requires a massive investment. The MRC owns the IP on findings ('inventions') by its scientific staff, which enables the Council to restrict who has access to these inventions, allowing it to entice one or more companies or public private partnerships (PPPs) to commit funds to the further development of products. Society benefits through new therapies, companies benefit by getting a fair return on their investment and the MRC often benefits through sharing in the revenues generated by product sales. Any income the MRC receives goes back into funding new research, so the more it can earn through scientific findings, the more that can be ploughed back into research.

If research is published without the MRC securing IP protection on an invention, then the research may be exploited without benefit to the UK or revenue going back to the MRC for further research. More importantly, for most IP (which is usually at a very early stage in any future product development), the incentive for a company to invest in product development is greatly diminished or lost if the IP has not been protected.

**The role of MRC Technology**

In 2000 the MRC set up an affiliated company, MRC Technology (MRCT), as its sole agent acting to facilitate the transfer of technology between the MRC and the biotech and pharmaceutical industries and to protect and exploit the MRC's IP. The MRC uses MRCT to bring academic research to the market through a process known as "technology transfer", and has been leading biomedical technology transfer in the UK for many years. Patents are filed and licence agreements are negotiated by MRCT on behalf of the MRC, with the primary aim of promoting the development of new and improved products in healthcare. The commercial exploitation of new IP can involve exclusive or non-exclusive licensing to an existing company, or to a new start-up company. Start-up companies may be created to develop new MRC technologies and inventions where appropriate.

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**Vaccine institute expands**

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"This provides a unique opportunity to bring together a range of expertise in both human and veterinary vaccine research and development to tackle some of the greatest challenges to global health," said Professor Hill. "With new recognition of the broader impact of poverty-related diseases, the threat of bioterrorism and recent veterinary and human disease epidemics, vaccine development has never been more important."
Administrative Efficiency Project

In the last issue of Network we reported that the MRC’s Council had approved the business case for setting up a shared services centre (SSC), to carry out a range of administrative processes for the MRC’s institutes, units and head office. The SSC project has passed some exciting milestones since then: the MRC has appointed the Director and in late November 2005 took possession of the SSC offices in North Star House in central Swindon.

Phil Lambert, Director of the SSC, arrived in December 2005 to take up his key role in establishing the centre and recruiting his team. During the last three years Phil was Director of the shared services centre for the TetraPak Group serving 65 businesses across Europe and Africa.

When arriving at the MRC, Phil said: “Establishing a shared services centre is an enormous change programme for any business and will impact on all of us in some way or other. I am very much looking forward to meeting everyone in the MRC and working with them to ensure that the programme is an unqualified success and that together we create a service function of which we can all be justifiably proud.”

Preparation for arrival of staff
Refurbishment work and installation of IT equipment is well under way and should take three to four months to complete.

The target date for the SSC to open its doors to staff is early April 2006. A schedule for the migration of services and staff to the centre is being developed and agreed with MRC units. MRC staff can access the project plan through the MRC portal.

The Finance and Human Resources work groups have completed the process designs and validated these with MRC units through a series of workshops. This process information will be an essential part of SSC staff training and will also inform the units as to the balance of responsibilities between them, MRC head office and the new SSC.

Joint grant processing
The MRC and the other research councils have now agreed to launch a project that would lead to establishing a joint processing unit for grants and fellowship applications. This is part of the research councils’ policy of converging their processes wherever possible and introducing systems aimed at simplifying the interfaces between research organisations and applicants.

Events diary

The BA Crest Science Fair 2006
This annual event brings together winners of the BA Crest Award regional finals and 15–19 year-old self-nominated students, all of whom have carried out outstanding science, engineering and technology projects. For each of 13 regions throughout the UK, three Crest projects (Bronze, Silver and Gold) are selected to come to the BA CREST Science Fair. Judges select the best projects and young scientists for a range of prestigious prizes, including cash and international trips.

The BA Crest Science Fair in on 20 February 2006 at the Royal Society, London SW1.

For further details, visit www.the-ba.net/ResourcesforLearning/BACRESTScienceFair

FameLab 2006
This RCUK-sponsored national competition aims to help scientists to develop their skills as communicators. Famelab is searching for the new faces of UK science who will be able to develop their ideas and presentation skills for a TV audience. Regional auditions are being held in March and April 2006 in Newcastle, Swansea, Edinburgh, London and Belfast. Ten finalists will win a weekend masterclass in science communication, after which the final winner will be chosen at the Famelab final at the Cheltenham Science Festival in June 2006. The winner will receive £2,000 and a development agreement with Channel 4 TV.

For further details, including audition dates, visit www.famelab.org

MRC units at the Cambridge Science Festival
During National Science Week, MRC units will be holding a range of events at the Cambridge Science Festival. On 18 March there will be an ‘Ask a nutritionist’ question-and-answer session with MRC Human Nutrition Research at Michael House Café at 5.00pm. The Hutchison/Cancer Cell Unit is holding an open day and the MRC Cognition and Brain Sciences Unit will once again welcome the public to an afternoon of presentations and practical demonstrations. Meanwhile, a new MRC event, Inner Space – The Human Body, will explore the magic of metabolism at a central Cambridge venue.

Further details will be available on the MRC website by late January 2006.
In September 2005 Professor Sir Edwin Southern (top) and Professor Sir Alec Jeffreys were awarded the Lasker Award for Clinical Medical Research at a ceremony in New York, in recognition of their pioneering work in human genetic analysis. The Lasker Awards are often referred to as “America’s Nobel Prizes”. Seventy Lasker Award-winners have gone on to receive the Nobel Prize, including 19 in the last 15 years.

Professor Southern invented the seminal ‘Southern blot’ technique for identifying DNA sequences in the human genome while working at the MRC Mammalian Genome Unit in Edinburgh in the 1980s. Professor Jeffreys’ MRC-funded work at Leicester University includes inventing genetic fingerprinting, which has revolutionised forensic diagnostics.

The USA’s Society for Neuroscience presented MRC Chief Executive Professor Colin Blakemore with its Science Educator Award in September 2005, at the Society’s annual neuroscience conference in Washington DC. This annual prize is given to outstanding scientists who have made a significant contribution to public engagement and communication about science.

Two MRC research teams won the Queen’s Anniversary Prizes for Higher and Further Education, at a ceremony at St James’s Palace in November 2005. One prize went to Dundee University’s Division of Signal Transduction Therapy – a unique consortium of 12 research teams from the School of Life Sciences and the MRC Protein Phosphorylation Unit and six leading pharmaceutical companies, to drive the development of new drugs to combat major diseases including cancer and diabetes. The other prize was won by the Centre for Brain Function and Development at Birkbeck, University of London, for its work on brain function and cognitive development in the very young. The team includes MRC-funded scientists Professor Mark Johnson, Professor Martin Eimer, Dr Gergely Csibra, Dr Michael Thomas and Dr Fred Dick.

In recognition of her contribution to cancer research, MRC-funded scientist Dr Kaye Williams has been awarded the British Association for Cancer Research/AstraZeneca Frank Rose Young Scientist Award for 2005. Kaye works in the Experimental Oncology division of the Drug Action and Design Group at Manchester University’s School of Pharmacy and Pharmaceutical Sciences.

In November 2005 Professor Cyrus Cooper and his team at the MRC Epidemiology Resource Centre, Southampton, were Rheumatology Team of the Year in the Hospital Doctor 2005 Awards celebrating clinical excellence and innovation in medicine.

Infowatch

Wellcome Witnesses to Twentieth Century Medicine

This recent addition to the Wellcome Witnesses series looks at the development of short-course chemotherapy for TB, including work at Professor Denny Mitchison’s unit at the Hammersmith Hospital, the advent of rifampicin and reappraisal of pyrazinamide, and MRC-funded large-scale trials in Africa, India, Singapore, Hong Kong and elsewhere. It includes transcripts of a seminar of experts involved in these advances, organised by the Wellcome Trust Centre for the History of Medicine.

Short-course Chemotherapy for Tuberculosis
The Wellcome Trust Centre for the History of Medicine £6 ISBN 0854841040