MRC scientists join front line in global fight against flu outbreak

Profile: The Centre for Cognitive Ageing and Cognitive Epidemiology, Edinburgh

News from the Medical Research Council June / July 2009

MRC NETWORK
MRC scientists join front line in global fight against flu outbreak

As fears of a global flu pandemic grabbed the headlines in April and May, scientists at the MRC National Institute for Medical Research (NIMR) were working hard to analyse and monitor isolates of the virus, known as influenza A (H1N1), to help develop a vaccine. Network looks at their progress so far and reviews how the story unfolded.

Influenza virus A (H1N1) originated in Mexico and began circulating in the human population in late April. As this article went to press there were 15,510 cases worldwide in 53 countries. By 28 April, the virus had been characterised genetically by the US Centers for Disease Control and Prevention (CDC) from isolates in California and Texas. The virus was shown to be unusual because it had genes from swine influenza viruses, but it was not one that had been previously recognised.

On 29 April, the World Health Organization (WHO) raised the worldwide pandemic alert level to Phase 5 following human-to-human transmission of the virus in two countries within a WHO region. As the virus broke out, isolates of the virus were being rushed across the Atlantic from the CDC to the WHO World Influenza Centre, housed at NIMR in North London. Experts at NIMR then joined forces with the world’s leading influenza experts to begin to analyse the isolates, taken from nasal swabs from infected patients in the US and then grown in a culture dish. Their challenge is to try to understand the virus and to identify how it changed over time and from one patient to another.

Working closely with colleagues at the Health Protection Agency to coordinate their efforts, the scientists are now studying the virus in the safety of the NIMR’s High Containment Facility, which is designed to contain such dangerous pathogens securely. They hope to figure out its structure and evolution, which will feed into development of a potential influenza A (H1N1) vaccine.

Dr Alan Hay, who is leading efforts at NIMR to monitor any evolution in the virus, explained: "Our expertise and facilities allow us to characterise the virus, develop antiserum and compare different cases, looking particularly at antigenic drift – that is monitoring changes in the virus that could have an impact on its susceptibility to drugs or the suitability of different vaccines. This will be the crucial question in the coming weeks and constitutes ongoing work until the epidemic comes to an end."

At a press conference held at NIMR on 1 May, Dr Hay added: "Influenza viruses, such as the swine-like human influenza A (H1N1), can mutate rapidly. It’s therefore important that we monitor the characteristics of the virus as it may spread around the globe. We need to monitor for changes in its sensitivity to antiviral medicines and also see whether, like seasonal human influenza viruses, the virus changes such that the vaccine has to be updated. We will be analysing the virus over the next few days and weeks but it will be some months before a vaccine is available."

In the meantime, the UK is well prepared should the population start to become ill. The current indication is that the virus is susceptible to antiviral agents, and the UK recently doubled its stockpile of the antiviral drugs oseltamivir (Tamiflu™) and zanamivir (Relenza™), following agreements signed earlier this year with Roche and GlaxoSmithKline.

Speaking in April as news of the influenza A (H1N1) outbreak emerged, Sir Leszek Borysiewicz said: "The UK Government has put systems in place earlier this year to increase supplies of flu drugs, making the UK one of the most prepared countries in the world. Research from NIMR published last year ensured stockpiles of both currently available drugs were amassed."

The UK’s total capacity is currently 33 million treatment courses of the antiviral drugs – enough to provide treatment for half of the UK population.

The World Influenza Centre at NIMR is one of a handful of WHO Collaborating Centres for Reference and Research on Influenza around the globe that are working together on monitoring and analysis work. The centre at NIMR is analysing further virus samples from patients in the UK and from countries around the world to keep the virus under close surveillance.

Speaking on 8 May, Dr John McCauley, influenza virologist at NIMR said: "So far there are no unexpected changes between the samples. Although we are seeing some degree of diversity, it is of little significance. We know that viruses can mutate rapidly and possibly become resistant to antivirals so we are eager to receive more samples and continually monitor any changes in the H1N1 strain."

Watch out for updates on the MRC website at www.mrc.ac.uk

Update from the MRC Chief Executive

April saw the Government announce the budget for 2009/10, and despite challenging economic circumstances the MRC was delighted to hear that the science budget ring-fence over the spending period has been maintained.

We are confident this will allow us to honour all existing grants and contracts from our generous Comprehensive Spending Review settlement. This includes our new Strategic Plan for research over the next five years, Research Changes Lives, launched on 10 June.

As well as launching a new strategy, the MRC is also looking to improve conditions for its employees. Last year all MRC employees were asked to take part in a survey on pay, grading and careers. While overall scores were more positive than the UK national benchmark on engagement, there was a negative response to the issue of pay and reward. Clearly, we need to change this if we are to continue to be the employer of choice for the best people. To ensure our staff are rewarded for their dedication and commitment, we are reviewing pay structures and developing a new performance management process. We have also been working with the trade unions over ongoing discussions with the Government about pay arrangements, and should be able to give an update on progress this month.

As you will have read on the preceding pages, MRC scientists at the NIMR are playing a key role in global efforts to combat the influenza A (H1N1) virus which emerged in the human population in April. I am proud of their efforts and of the contribution they are making. Over the coming months they will continue to work with the WHO and the HPA to help identify how the virus is evolving and work out how it might adapt as it spreads more widely. Regular updates will be posted on the MRC website.

Sir Leszek Borysiewicz
The MRC will allow us to support and underpin world-throughput DNA sequencing. This investment from the Principal Investigator of the Scotland Hub, Mark Blaxter, from the University of Edinburgh and the Roslin Institute of the University of Edinburgh said: “DNA sequencing will enable us to address questions about diseases, and gather answers that were undreamt of only a decade ago.”

He added: “Inviting regional applications has generated innovative partnerships between academic institutions, as well as engagement with industry, the NHS and Regional Genetics Services. This initiative will engender innovative ways of working and enable new and exciting discoveries. We hope the hubs will allow scientists to ask increasingly precise questions about diseases, and gather answers that were unprecedented only a decade ago.”

The investment by the MRC was made following a review of the available HTS facilities in the UK which made recommendations to the MRC’s Strategy Board. Following an initial pilot call for addiction research proposals which existed. Details are available on the MRC website at: www.mrc.ac.uk/fundingopportunities Calls/Addictionresearch/index.htm

The three hubs have been given funds to buy HTS machines that will enable the UK to retain its world-leading standing in DNA research. They will also provide MRC-funded technical support and bioinformatics expertise that will allow academics to make the most of the equipment and expand the potential of these resources.

John Jeans, MRC Chief Operating Officer, said: “This investment is key to retaining and enhancing the UK’s competitiveness. It makes plain the MRC’s commitment to supporting high quality basic research and exemplifies the responsiveness of MRC strategic investment to the needs of the research community.”

He added: “Inviting regional applications has generated innovative partnerships between academic institutions, as well as engagement with industry, the NHS and Regional Genetics Services. This initiative will engender innovative ways of working and enable new and exciting discoveries. We hope the hubs will allow scientists to ask increasingly precise questions about diseases, and gather answers that were undreamt of only a decade ago.”

The investment by the MRC was made following a review of the available HTS facilities in the UK which made recommendations to the MRC’s Strategy Board. Following this consultation with experts in the field, Strategy Board called for proposals for regional hubs because this model builds on existing, and often fragmented resources. It also ensures that MRC funds help to create centres of excellence that provide a service to the genetics and genomics research community.

Mark Blaxter, from the University of Edinburgh and Principal Investigator of the Scotland Hub, said: “DNA sequencing lies at the heart of modern biology. Scotland has a strong record and leading expertise in high-throughput DNA sequencing. This investment from the MRC will allow us to support and underpin world-leading genetics research across Scotland and beyond, working with MRC researchers investigating issues such as familial cancers, psychiatric disease and the genomics of pathogens such as E. coli, C. difficile and malaria.”

### THE HUBS IN BRIEF

#### Scotland

GenePool, the Scottish next-generation genomics facility – University of Edinburgh, University of Dundee, MRC Human Genetics Unit (Institute of Genetics and Molecular Medicine), University of Glasgow, University of Aberdeen, The Roslin Institute of the University of Edinburgh.

- doubles local ability to deliver DNA sequencing
- will invest in technologies and bio-computing scientists to help users identify the most important genetic information in their data

#### North of England

University of Liverpool, University of Sheffield, University of Manchester, University of Lancaster.

- expands the leading Advanced Genomics Facility (AGF) in Liverpool to serve North England’s research leaders in universities and hospitals
- will offer a one-stop shop providing advice for all stages of work
- provides training and pump-prime cost-sharing programmes

#### East of England

University of Cambridge, European Bioinformatics Institute, Babraham Institute, NIHR Cambridge Biomedical Research Centre.

- will collaborate with European Bioinformatics Institute to provide researchers with access to sequence data analysis tools
- will apply HTS to routine medical diagnostic uses, such as prenatal diagnosis, and re-sequencing of disease genes (eg BRCA genes linked with breast cancer) in collaboration with the National Blood Service and NHS Regional Clinical Genetics Services

### Boosting research to beat addiction

#### Long-term use of illegal psychotropic drugs, alcohol misuse and problems caused by hazardous gambling can have devastating effects on families and individuals, especially on young people.

To address these problems, the MRC and the Economic and Social Research Council (ESRC) recently launched an initiative to fast-track research towards improving public health in the area of addiction and substance misuse.

Addiction researchers from across the UK have been invited to submit proposals to develop “research clusters”. These will comprise researchers from different groups and institutions with excellent track records in their own disciplines. The clusters must include scientists new to addiction research, to build capacity and expertise in the field.

The groups of scientists will work together across different disciplines to address addiction research themes of Cause, Harm, Alcohol and Treatment – priorities identified by consulting a cross-section of the UK addiction research community and Government at a workshop in late 2008.

Gavin Malloch, the MRC Programme Manager involved in this project, said: “Addiction and substance misuse carry a large health burden and high social and economic costs. The pathways into addiction, the harms caused by it, and novel treatments are all areas that are in urgent need of research. This initiative allows us to approach the issue from biological, psychological and social perspectives, which we hope will lead to real public health outcomes. It’s an exciting opportunity to bring together experts from different disciplines and address questions that cannot be answered by the usual routes of funding.”

The MRC and the ESRC expect to support the development of up to ten clusters, which will submit proposals to address issues such as the cause and life course of addiction; the harms caused by addictive drugs, gambling and substance misuse; and the development of new treatments and interventions to reduce harm. Alcohol was singled out as a particularly pertinent public health problem in the UK, and a special case in relation to Government strategies. The alcohol research clusters will not necessarily focus on alcoholism, but will investigate the effects of hazardous drinking and support interventions to reduce heavy alcohol consumption.

Decisions on which cluster bids to support will be made in June 2009.

The new initiative is one aspect of a wider strategy on addiction research being developed as part of the MRC’s strategic coordination of health research in the UK. In February, the MRC awarded eight grants under an initial pilot call for addiction research proposals which was designed to kick-start research in the field by taking advantage of research infrastructure that already existed. Details are available on the MRC website at: www.mrc.ac.uk/fundingopportunities Calls/Addictionresearch/index.htm
Sharing research to benefit people

Publicly-funded research data are one of the MRC’s biggest assets. MRC scientists share these assets widely with collaborators and scientists working in similar areas to benefit scientific knowledge, the economy and, most importantly, human health. But the MRC is keen to maximise the scientific potential of its data even further. To make it easier to share data in a responsible way, the MRC is working with the Science and Technology Facilities Council (STFC) to develop a Data Support Service Project over the next two years.

The project aims to find out what is needed for data sharing and preservation, how it can best be done, and what the real benefits and costs would be. One of the activities of the project will be to create a web-based gateway to a catalogue of MRC population-based datasets. This will allow bona fide researchers anywhere to easily find descriptions of the data (metadata) and compare data from different study cohorts.

Staff at MRC research institutions will continue to maintain their own datasets and to provide the highest levels of security and assurance to study participants. Rigorous governance procedures will allow the data to be accessed whilst protecting study participants.

Professor Diana Kuh is Principal Investigator of the UK’s oldest national birth cohort study, the MRC National Survey of Health and Development – one of the studies participating in the pilot project. She says: “Data sharing is a critical aspect of our work. Our external collaborators have worked closely with us on many key research findings in areas of national significance, such as mental health. A central catalogue of MRC datasets will help scientists outside the unit to see what data are held by each study, and to find out who to contact within the MRC to access the data for research projects.”

The Data Support Service Project is due to be completed in 2011. Watch out for updates in future issues of Network.

European Parliament votes on animal research

Scientists from the MRC have been meeting UK and European Parliamentarians to talk through the implications of proposed revisions to the 1986 EU Directive 86/609 on the protection of animals used for scientific purposes. The revised Directive, which if adopted would see significantly tighter restrictions on live animal experiments across the continent, went to a full European Parliament vote in May.

The European Parliament considered 397 proposed amendments to the Directive published by the commission, and passed most of those put forward by the UK Bioscience Sector. The Directive is also being considered by the Council of Ministers – it must be agreed by both this council and the parliament before it can be passed.

Sharon Bowles MEP and local MP Dr Evan Harris visited the Mary Lyon Centre at MRC Harwell at the end of 2008. They were shown the living conditions of the mice that are housed there, and saw how the current stringent animal welfare guidelines are implemented in the UK.

Sharon said: “The three principles of animal research have to be the ‘3Rs’ – reduce, refine, and replace. Ultimately we would love one day for no tests on animals to be done at all.”

Sharon Bowles MEP and Dr Evan Harris MP view living conditions of the mice at the MRC Mary Lyon Centre, Harwell.

“The Mary Lyon Centre is a fine example of the kind of good practice we’d like to see supported by the Directive.”

Evan added: “The UK’s standards of welfare for animal research subjects are among the best in the world – and we want the rest of Europe to come up to our standards. Animal research is paying immense dividends in terms of cures for diseases that afflict both humans and animals.”

Andrew Duff MEP met scientists and policy staff from the Wellcome Trust, the University of Cambridge and the MRC on a visit to the Wellcome Trust Sanger Institute in Cambridge in April. Discussions included specific examples of how parts of the Directive would run counter to animal welfare and the risk in the proposals of undermining the competitiveness of European science. Mr Duff stressed the importance of the scientific community across Europe working together to engage in discussions on the Directive. Further visits with other MEPs around the UK are planned.
INDUSTRY UPDATE

Comparing diversity in academia and industry

In April, scientists at the MRC Laboratory of Molecular Biology in Cambridge had the opportunity to hear first-hand about the skills that industry seeks in scientists from Dr Ruth McKernan, Chief Scientific Officer at Pfizer Regenerative Medicine.

Dr McKernan was invited to speak at an event focused on diversity in the workplace organised by MRC Women in Science and Cambridge AWiSE (Association for Women in Science and Engineering). Offering advice to scientists considering a move to industry, Dr McKernan said that some of the key skills and attributes industry looks for when recruiting scientists are education and ability, practical and problem-solving experience, motivation, communication skills and flexibility.

On the topic of diversity in the workplace, she said: “In my experience, the more diverse a group is when looking at a problem, the better the solution.” Evidence suggests that a balance of sexes and a diverse range of ages, cultural backgrounds and ethnicities in the workplace leads to better, more profitable companies and better colleague engagement.

She added: “At Pfizer, the biggest barrier to increasing diversity was that managers tended to hire in their own image. To tackle this, equality and diversity training is now compulsory and ‘good behaviour’ is actively monitored and rewarded.”

Megan Davies, Assistant Director of LMB, added: “While industry and academic research often seem to be different, at the heart of both activities are the people. Finding ways to harness the varied and diverse skills and talents available in the research community, and to enable individuals to prosper, is as important to the MRC as it is to industry.”

Sowing the seeds of innovation

“Stay on your toes and be alert to the possibilities”. This was the advice to researchers who could be unwittingly working on a commercial breakthrough of the future from Richard Henderson, Director of Heptares Therapeutics Ltd, speaking at MRC Technology’s Innovation Afternoon on 11 May.

The event took place at the MRC Laboratory of Molecular Biology (LMB) in Cambridge. It aimed to stimulate commercial thinking and to encourage collaboration between MRC scientists and MRC Technology (MRCT).

Heptares originated from the LMB in 2007, and Richard was one of several guest speakers at the event who outlined case studies of drug development in industry. He explained: “We set out in 1990 to learn about general principles of membrane proteins, with no thoughts of drug development. Through fortuitous developments of the research, sharing our ideas and appropriate networking with key people in research and industry combined with professional expertise in MRCT, we were able to secure seed funding.” He added that Heptares has now secured external funding to progress its ideas further.

The presentations were followed by an Innovation Competition which gave shortlisted post-doctoral and PhD students the chance to put forward their translational research ideas to a panel of experts. Anna Paterson from the MRC Cancer Cell Unit won with a presentation on a molecular assay for targeted therapy and appropriate patients in a way that maximised clinical responses. Anna won a personal prize of £500, and £5000 for her research group.

Anna said: “This event was a fantastic opportunity to apply our research in a uniquely different context”.

His advice to the Network leads was to allow sufficient time and space for the researchers to understand one another’s cultures. “Multi-disciplinary collaboration involves bringing together dramatically different working approaches – lawyers, physicists, architects and computer scientists all have totally different expertise and ways of approaching a problem, and these must be respected before collaboration can take place,” he said.

Other speakers included Professor David Hawkes, Director of the multidisciplinary Centre for Medical Image Computing at UCL; Angela Barnard who spoke about involving the public in research; and Dr Lee-Ann Coleman talked about the role of information providers in supporting research.

The day was rounded off with the official launch of the three LLHW Centres by Lord Sutherland of Houndwood, chair of an influential House of Lords select committee which produced a report on ageing research.

He said: “Demographic change is something we have to live with, and we will all age better if we understand the ageing process. That is why it is tremendously important that the research councils have thought through their priorities in this area. They are not simply approaching this from where they come from, but are dealing with where they are going.”

Clinicians, engineers, biologists, economists and others are to form new multi-disciplinary research teams under the second phase of the cross-council Lifelong Health and Wellbeing (LLHW) initiative.

The LLHW partners have jointly invested £500,000 to establish ten Collaborative Development Networks, following a call for proposals in November 2008. Each Network will build a multi-disciplinary team within one of the research areas of mental capital, mental health and wellbeing markers for the ageing process; interactions between the determinants of healthy aging; and interventions that promote healthy aging and independence in later life.

On 11 May, the MRC held a workshop on behalf of the LLHW initiative. The event brought together the leaders of the new Networks, and included talks from speakers with experience of multidisciplinary working. One speaker was Professor Nick Tyler, Director of the UCL Crucible Centre, which is one of three multi-discipline centres established last year as the first phase of the initiative.

Liking the UCL Crucible Centre to “a sort of magician’s pot, bringing together base elements to produce gold” Nick said that one of the major benefits of multi-disciplinary research was that it allowed exploration of new frontiers. “The practice of research develops and changes as the result of researchers from different backgrounds working together,” he said.

His advice to the Network leads was to allow sufficient time and space for the researchers to understand one another’s cultures. “Multi-disciplinary collaboration involves bringing together dramatically different working approaches – lawyers, physicists, architects and computer scientists...”
Growing older brings a welcome calm to the pace of life for many people, but when thinking and reasoning abilities start to slow down too it can be frightening. The personal, social and financial burden of decline in cognitive function makes it one of the mostly costly aspects of ageing.

To help establish exactly how ageing affects cognitive ability, the Centre for Cognitive Ageing and Cognitive Epidemiology (CCACE) was established at the University of Edinburgh in September 2008 with funding of £3.4 million from the cross-council Lifelong Health and Wellbeing Programme. The centre was officially launched in May (see article p9).

When Network visited the centre, Director Professor Ian Deary described the centre’s research objectives: “It’s really the lifelong interplay between thinking skills and health that we are interested in. Scientists working in the centre are trying to identify the risk factors for, and mechanisms of, individual differences in age-related cognitive decline, that is cognitive ageing. To complement this, others are looking at the relationship of mental ability in youth to disease and death in later life, the field known as cognitive epidemiology.”

There are six research groups in the centre linked through collaborations in grants, publications, and postgraduate student supervision. Each group focuses on a different aspect of ageing research: cognitive epidemiology, human cognitive ageing, neuroendocrine aspects of cognitive ageing, and models of cognitive ageing and neural health.

These are underpinned by two methodology groups: cognitive epidemiology; human development and health. Their focus is on chronic conditions including cardiovascular disease, diabetes and cancer; they also investigate links to mental illness. Part of the group’s work is to explore genetic and environmental contributions to these links. They are also interested in factors early in life that may predict cognitive ability in childhood, for example smoking and alcohol consumption by parents.

David is currently on a six-month sabbatical at the George Institute for International Health, part of the University of Sydney. He believes the creation of the centre has been crucial to help collaborations between cognitive epidemiologists succeed, he said: “Previously, my collaboration with Ian Deary and his colleagues had been successful but unfunded. The establishment of the CCACE has cemented these ties and made us even more productive. Attending meetings at the centre, informal and formal, has also brought me into contact with centre members who represent a very eclectic range of disciplines both within the University of Edinburgh and other establishments like the MRC Epidemiology Resource Centre in Southampton. Personally, I have learnt a lot and I think the quality of our work within the centre, both completed and planned, reflects this.”

His experience reflects another of the centre’s aims: to train researchers to be capable of using multiple technologies in clinical and basic science to maximise opportunities for multidisciplinary collaborations.

Dr David Batty leads the CCACE cognitive epidemiology group from the MRC Social and Public Health Sciences Unit in Glasgow. Researchers in the group use databases to examine the cause and mechanisms of associations between cognitive ability and health. Their focus is on chronic conditions including cardiovascular disease, diabetes and cancer; they also investigate links to mental illness. Part of the group’s work is to explore genetic and environmental contributions to these links. They are also interested in factors early in life that may predict cognitive ability in childhood, for example smoking and alcohol consumption by parents.

Since 2004, members of the Lothian Birth Cohort have repeated cognitive ability tests every three years. Professor Deary and his colleagues have also arranged medical tests, genetic studies and brain imaging to build as complete a picture as possible of each participant’s cognitive ability and potentially influential factors.

Professor Deary added: “What is important about the ‘Disconnected Mind’ project is that the human studies are complemented by animal and cellular studies. We have scientists looking at brain changes from imaging in the Lothian Birth Cohort and, in parallel, another team is looking at changes in white matter in rodent models of ageing.”

**Capturing the ageing brain**

Professor Joanna Wardlaw leads the brain imaging group that has been examining changes in the brain’s white matter in people in the Lothian Birth Cohort. White matter is the tissue that connects the different parts of the brain and enables thoughts to pass around it.

“One of the big focuses in the brain imaging group is changes in white and grey matter, development of..."
abnormalities in the brain and how these changes and abnormalities relate to cognitive ability in older age. We are trying to determine how these changes might be associated with cognitive ability in early life and with life events like cardiovascular problems, nutrition and other lifestyle factors,” explained Professor Wardlaw.

The team is building maps of white matter in the brain and quantifying tissue loss. They have found that typically, on a scan, an abnormality shows up as a bright spot within the white matter tissue of the brain. They don’t know yet what causes these bright spots but they have determined that the more bright spots present, the more likely a person is to go on to have a stroke or deteriorating cognitive ability. Professor Wardlaw and her team are using imaging to investigate and understand this link.

One other approach to this is to use rodent models to better understand the mechanisms involved. For example, the experimental model team, lead by Professor James McCulloch and Dr Karen Horsbrough, is currently characterising a potential model of white matter damage with ageing, and Professor Wardlaw and colleagues are working on a model of small vessel stroke as the loss of cognitive ability and dementia is often linked to stroke.

Looking ahead
By bringing together experts in epidemiology and imaging with information gleaned from the participants of the Lothian Birth Cohort, researchers in the CCACE are contributing to figuring out how and why ageing slows people down.

Reflecting on the first few months of the centre’s existence, Professor Deary is extremely positive. He says: “The formation of the centre has revolutionised our work here. It has provided infrastructure and gravitational pull. It is remarkable how quickly people have come to look to the centre as their base, and it is being used to launch new initiatives – research, teaching and outreach – in cognitive ageing and cognitive epidemiology. The researchers and their teams have welcomed this formal recognition of their community, and the fact that it affords growing numbers of new researchers in its important research areas.”

OPPORTUNITIES

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ODGT to be re-launched as MRC e-Val

Last year saw the launch of the MRC’s new online mechanism for collecting information on research outputs, the Outputs Data Gathering Tool (ODGT). The MRC now plans to re-launch the ODGT this autumn as MRC e-Val. Full details of the successes from last year, along with the plans for 2009 will be reported in the next issue of Network.
Research Complex at Harwell nears completion

Building work on the Research Complex at Harwell (RCAH) continues apace with much of the external structure now complete. The Complex, which is due to be completed by the end of September 2009, aims to provide facilities for researchers from the life and physical sciences who are conducting work at the Diamond Light Source synchrotron facility, the ISIS neutron facility and other shared facilities on the Rutherford Appleton Laboratory (RAL) site.

The RCAH will also be home to the Oxford Protein Production Facility-UK (OPPF) which is relocating from its current site at the Wellcome Trust Centre for Human Genetics in Oxford.

Professor Simon Phillips, the RCAH Director, is pleased with how the project is progressing:

“The building is still on schedule, and on budget, and remarkably light and spacious inside. The first round of grant and fellowship applications has now been received, and these are currently under review. We aim to spend October and November equipping the labs; research groups will begin to move in before the end of the year. It’s an exciting time.”

The MRC is now inviting proposals through its grant and fellowship schemes for researchers wishing to occupy space in the RCAH. There is research council space allocated in the building for 15 to 20 additional researchers, including short-term visitors and longer-term research teams. Preference will be given to researchers using Diamond or other facilities at the RAL site. Researchers in the RCAH will be encouraged to explore potential collaborations with other researchers in the complex and across the RAL site as a whole.

To apply to become one of the initial occupants of the RCAH, applications should be made to the 2009 deadlines of current MRC funding schemes, including research grants, new investigator research grants, career development awards and senior fellowships. For more information, see the MRC website at www.mrc.ac.uk/Ourresearch/Resourcesservices/RCAH/Opportunities or contact Paula Clements at paula.clements@headoffice.mrc.ac.uk

Regenerative Medicine Laboratory opens in Cambridge

May saw the official opening of the Anne McLaren Laboratory for Regenerative Medicine, which forms part of the MRC Centre for Stem Cell Biology and Regenerative Medicine, at the University of Cambridge.

The event also celebrated the official opening by Sir Leszek Borysiewicz of the West Forvie Building where the laboratory is housed.

The new laboratory is directed by Professor Roger Pedersen, and provides space for around 60 laboratory researchers. It has several tissue culture laboratories specially designed for stem cell cultures and tissue engineering, as well as specialist facilities for induced pluripotent stem cell production.

Research at the laboratory will focus on areas of human stem cell research such as regenerative neurology, haematopoietic stem cells (stem cells from blood), tissue engineering of pancreatic and liver cells, cancer stem cells, and cardiovascular medicine.

Professor Pedersen said: “The opening of the Laboratory for Regenerative Medicine provides a compelling opportunity to bring together Cambridge’s stem cell researchers.”

The MRC Centre for Stem Cell Biology and Regenerative Medicine, which comprises the Anne McLaren Laboratory and the Wellcome Trust Centre for Stem Cell Research, opened in January 2009. The Centre is part of Cambridge University’s Cambridge Stem Cell Initiative. Further information can be found at www.stemcells.cam.ac.uk

MRC Mitochondrial Biology Unit launched

The MRC Mitochondrial Biology Unit in Cambridge (formerly the Dunn Human Nutrition Unit) was officially opened on 1 April by Sir Leszek Borysiewicz, Unit Director Professor Sir John Walker, and Regius Professor of Physic Patrick Sissons.

Exhibits illustrating the unit’s activities were on display to attendees of the launch event, including a demonstration of the mitochondrial genome and how mitochondrial DNA replicates and segregates in normal and disease states. Visitors could also find out about the design of new drugs targeted against mitochondrial carriers in parasites.

A three-dimensional model has been commissioned to be displayed in the unit exploring how scientific discoveries on a molecular level can be scaled up to architectural dimensions.
Nicotine products raise concerns

Nicotine-containing tobacco replacement therapies designed to help people kick their smoking habit could potentially cause mouth cancer, new research suggests. The research was co-funded by an MRC PhD studentship and the Institute of Dentistry, Barts and the London School of Medicine and Dentistry, Queen Mary University of London. The research team investigated the influence of the gene FOXM1, a gene which is expressed at high levels in many forms of cancer, on mouth cancer and found that it was highly expressed in the progressive stages of the disease. They also studied the effects that different tobacco substances had on human mouth cells and discovered that nicotine – at the same levels as those found in tobacco replacement therapies – raised FOXM1 expression in the cells. Lead author Dr Muy-Teck Teh, said: “We’ve shown the FOXM1 gene is activated by nicotine in human mouth cells which raises the possibility that nicotine could potentially increase the risk of mouth cancer. We want to stress, however, that further research is needed to determine conclusively whether this is indeed the case. There is no doubt however about the harmful effects of smoking, so smokers should make every effort to quit.”

Published in PLoS ONE. doi:10.1371/journal.pone.0004849

Moderate obesity cuts life expectancy

A new analysis of 900,000 people from around the world has shown that obesity can take years off life expectancy – although not as many as smoking does. The analysis was funded by the MRC, the British Heart Foundation and Cancer Research UK, supporting the University of Oxford’s Clinicals Trial Service Unit. Data were collated from 57 long-term research studies mostly based in Europe or North America which followed people for an average of 10 to 15 years. During the study period 100,000 people died, making it the largest ever investigation of how obesity affects mortality. The studies used body mass index (BMI) to assess obesity. Moderate obesity, defined as having a BMI of 30 to 35, was shown to cut life expectancy by about three years. Severe obesity (a BMI of 40 to 50) shortened lives by 10 years – equal to the effects of lifelong smoking.

Mortality was lowest in those who had a BMI of 23 to 24. Oxford University’s Dr Gary Whitlock, who led the analysis, said: “In countries like Britain and America, weighing a third more than the optimum shortens lifespan by about 3 years. For most people, a third more than the optimum means carrying 20 to 30 kilograms of excess weight. If you are becoming overweight or obese, avoiding further weight gain could well add years to your life.”

Published in The Lancet, 18 March 2009

New research gives hope for breakthrough cancer treatment

New research into the interaction between normal cells and transformed cells has given hope to uncovering an effective treatment for cancer. The MRC-funded study examined the boundary between normal cells and transformed cells. Transformed cells can result in cancer. The results showed that transformed cells change their shape and are removed from the tissues when surrounded by normal cells. The researchers also identified signalling pathways which are activated in these cells when surrounded by normal cells, but not when they were surrounded by other transformed cells. The activity in the transformed cells and the cell-to-cell contact with surrounding normal cells appeared to influence the way they behaved. This was a novel approach because it focused on the interaction between normal and transformed cells, whereas past research has focused only on transformed cancer cells and overlooked the fact that mutations occur in a cell which is surrounded by normal cells. Lead author Yasuyuki Fujita, from the MRC Laboratory for Molecular Cell Biology at University College London, said: “The research could help us understand how cancer initiates and develops, and further studies into this behaviour could help find ways of treating cancer effectively.”

Published in Nature Cell Biology, April 2009

Breakthrough makes lab-produced stem cells safer for humans

Scientists from the UK and Canada have paved the way for stem cells made from skin cells to be safely transplanted into humans, which could ultimately spell an end to the need for human embryos as a source of stem cells. The research team reprogrammed human skin cells to act like embryonic stem cells without needing to use viruses to modify the cells’ DNA, overcoming the increased risk of cancer which is normally associated with using viruses. The breakthrough came when two research teams who had been working on separate cell reprogramming methods, led by Dr Kesuke Kaji from the MRC Centre for Regenerative Medicine and Dr Andras Nagy from the University of Toronto, combined their techniques. Dr Kaji had found a non-viral method to deliver four genes to the cells in a single DNA fragment, and a way to remove them after reprogramming, however they left a ‘footprint’ behind which could disrupt other genes at the site of insertion. Meanwhile Dr Nagy’s group had developed a reprogramming system that allowed the removal of inserted genes without a trace. Dr Kaji said: “I was very excited when I found stem cell-like cells in my culture dishes. Nobody, including me, thought it was really possible. This new method will advance the field of regenerative medicine, and should help understand diseases and test new drugs.”

Published online in Nature, March 2009


**Oxfordshire Science Festival**

The Oxfordshire Science Festival 2009 kicked off with an afternoon of Science in our world! – hands-on activities from many of the county’s leading science organisations.

Ten MRC scientists representing units across the region swapped pipettes for play dough in the main shopping area of Oxford, as they demonstrated how the human body works, and what happens if we don’t look after it.

This was followed by an MRC-sponsored evening debate intriguingly entitled ‘Sixty minutes of sex’. The equally-intrigued audience directed the debate by posing questions on the ethical dilemmas around the science of sex to a learned panel that included a biologist, psychiatrist, sex-therapist and the Bishop of Swindon.

Two units gamely opened their doors to teenagers from local secondary schools; hosting open days that have become increasingly popular with local science educators. The MRC Mammalian Genetics Unit at Harwell now has a bespoke teaching laboratory on site and scientists took 20 A-level biology students from King Alfred’s School, Wantage, get to grips with the new teaching lab at MRC Harwell.

**University of Cambridge Science Festival**

Around 30,000 people attended this year’s University of Cambridge Science Festival in March, which was themed ‘Centuries of science’ in honour of the university’s 800th anniversary. The MRC was an associate sponsor and over 100 enthusiastic MRC scientists and other staff from ten MRC units and centres in Cambridge took part.

Scientists from the MRC Laboratory of Molecular Biology (LMB) reconstructed their hugely popular Royal Society Summer Science Festival exhibit ‘Can worms unlock the secrets of our mind?’ Visitors viewed worms under the microscope and controlled their behaviour with light to understand the surprising similarities between ourselves and animals with just 302 nerve cells.

**Exploring mind and brain** was the theme of the MRC Cognition and Brain Sciences Unit’s look back at over 50 years of research in Cambridge. As well as interactive activities, presentations included ‘Sixty minutes of sex’. The equally-intrigued audience directed the debate by posing questions on the ethical dilemmas around the science of sex to a learned panel that included a biologist, psychiatrist, sex-therapist and the Bishop of Swindon.

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**Nutrition on the move**

With motivation levels starting to flag as the Easter holidays approached, Cambridgeshire schoolchildren received a welcome visit from the MRC Collaborative Centre for Human Nutrition Research’s Artsbus in April, which aims to help children better understand nutrition and health.

Working with the University of Cambridge Rising Stars initiative, staff from the centre organised a programme of events called ‘Nutrition on the move’ that school children could work through to learn about nutrition. The Artsbus visited three local primary schools and invited all pupils at key stage 2 level (aged 7-11 years) to come on board.

The children took part in eight activities based on the messages in the Government’s healthy eating campaign, Change4Life. Activities included fruit tasting, keeping a food diary, and measuring heart rate before and after exercise.

The Artsbus visits had an enthusiastic response from pupils. Ella, aged 8, said: “I liked the exercise on the step and the food tasting. I didn’t like the melon but I tried it and managed to eat it!”

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Profile: Tony Peatfield, the new Director of Corporate Affairs

Tony Peatfield was promoted to Director of Corporate Affairs in April, taking on overall responsibility for the MRC’s corporate governance, policy and corporate communications. Network spoke to him about his career so far and how he sees the MRC progressing in future.

Tony graduated from Bristol University in 1974 with a degree in physiology. His first job was a two-year stint of teaching in Nigeria with Voluntary Service Overseas, an experience which made a deep impression. “It taught me to recognise that a lot of other people are much worse off than I am and therefore to focus on big problems rather than the petty minutiae of life,” he says.

Next he undertook his PhD in respiratory physiology at St George’s Hospital Medical School, London. But after a couple of post-doctorate positions in the UK and abroad, he decided that working in a laboratory wasn’t for him. He explains: “I liked whole animal physiology and that really wasn’t the way the science was going at the time, so I felt maybe this was the time to do something different and try a career that would still use my science but which gave me the bigger picture of scientific endeavour.”

He joined the MRC as a Programme Manager in May 1985, at first with the Cell Biology and Disorders Board. In 1992 he was promoted to Board Programme Manager of the Health Services and Public Health Research Board. He was seconded to the Office of Science and Technology in 2001/02, working on the Cross-cutting review of Science and Research. He has been Head of Corporate Governance and Policy since March 2002.

When questioned about the highlights of his 24 years at the MRC, Tony is not short of examples. In his first job at the MRC he was involved in a large programme of research on magnetic resonance imaging. The research led to the development of an imaging technique which is now used worldwide and won a Nobel prize for the programme’s director, Sir Peter Mansfield.

He is proud to have played a role in establishing the Health Services and Public Health Research Board, transforming it into a board with the responsibility to develop health services and public health, which he says “had been rather a poor relation beforehand”. He was also heavily involved in getting government backing for the development of the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), based on the previous MRC Centre for Best Practice for Animals in Research.

“Policy is extremely important to the MRC and to maintaining its reputation. It may be underestimated by some people, partly because it’s not very visible,” says Tony. “But it provides the framework for researchers and is also important for continued public support. If policies are right then much else falls into place and scientists can get on with what they’re best at, their research.”

Tony believes the MRC can look forward to a bright future and is set to build on its reputation for success and scientific excellence. He says: “I think we have some very good biomedical scientists in this country, and excellent training programmes, so for the next generation of researchers, I think the future is very bright. We must keep an eye out on the regulatory side of things and make sure that that doesn’t become too burdensome. If we can do that then I think there will be successes for the MRC in the future just as there have been in the past.”

Professor Robin Ali of the UCL Institute of Ophthalmology and Faculty, National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital in London, has received an Ophthalmology Research Award from the Alcon Research Institute. Professor Ali received US $200,000 in unrestricted grant money to continue his research and will be recognised at the next Alcon Research Institute Symposium, at which he and previous winners will present data and discuss current research in ophthalmology. Professor Ali’s main research interest is the development of gene and stem cell therapies for the treatment of retinal disorders. Professor Ali said: “To be included as a member of the Alcon Research Institute is one of the highlights of my career.”

Dr Stanley Chang, chairman of the Alcon Research Institute, added: “The scientific contributions Professor Ali has made to the study of vision will have profound effects on future research and treatments.”

Professor Sir Philip Cohen, Director of the MRC Protein Phosphorylation Unit at Dundee University, was awarded the Society for Biomolecular Sciences (SBS) Achievement award on 29 April. Sir Philip received a commemorative plaque and a £5,000 honorarium, presented at the 15th annual conference of the Society in Lille, France. Sir Philip said: “It is a great honour to receive the really prestigious SBS Achievement Award. I am particularly pleased that it has taken place at the Lille Grand Palais, which I first visited 10 years ago when I came to watch my daughter Suzanne play for Scotland in the World Bridge Olympiad which was held at this venue.”

The award rounded off a successful week for Sir Philip; he flew to attend the SBS Symposium directly from Washington DC where he was inducted as a Foreign Associate of the US National Academy of Sciences on 25 April in recognition of his groundbreaking work in biochemistry and biology.

Dr Brian Hemmings, a postdoctoral fellow in the MRC Protein Phosphorylation Unit from 1980-1982, has been elected a Fellow of The Royal Society in recognition of his important contribution to our understanding of protein kinases and protein phosphatases. Brian was the first to identify Protein Kinase B, which is now an important target for the development of anti-cancer drugs.

Professor Peter Somogyi, Director of the MRC Anatomical Neuropharmacology Unit at Oxford University, has been awarded the Feldberg Foundation’s 2009 Feldberg Prize for his contribution to neuroscience. Professor Somogyi’s research into complex neuronal networks has bridged knowledge of the molecular, synaptic and network levels of neuronal circuit organisation. He recognised that explanations of normal and pathological events in the brain can only come from the rigorous definition of neuronal circuits, which led him to discover new principles about how neurons are organised in the brain’s basal ganglia, cerebellum, neocortex and hippocampus. Professor Somogyi will deliver the Feldberg Prize Lecture at the Max Planck Institute for Brain Research in Frankfurt am Main in June 2009.

Three MRC scientists have been recognised for excellence in medical science by being elected as Fellows of the Academy of Medical Sciences. They are: Dr Francois Guillemot of the MRC National Institute for Medical Research, Professor Matthias Merkenschlager of the MRC Clinical Sciences Centre and Professor Neil Burgess, MRC Senior non-clinical Research Fellow at University College London. The new Fellows will be formally admitted to the Academy at a ceremony on 24 June.

Professor Sir Alan Fersht, Director of the MRC Centre for Protein Engineering, has been awarded the prestigious Wilhelm Exner medal of the Austrian Academy of Sciences for his contribution to biotechnology.
John Graham Duncan 1915–2008

John Graham Duncan worked for the Medical Research Council for 33 years until he retired from his role as Administrative Secretary in 1978. He died in June 2008 at the age of 92.

After completing degrees in Economics and Law at Glasgow University in the 1930s, John worked for the Agricultural Research Council before joining the MRC in 1945. He was appointed in a newly-created post of Establishment Officer to oversee personnel administration. One of his first tasks was to unify the MRC’s employment arrangements and conditions. He worked his way up through the ranks to Principal Administrative Officer in 1960 and finally became Administrative Secretary in 1967, the equivalent of today’s Deputy Chief Executive role.

Nick Winterton, former MRC Executive Director, who retired earlier this year, said “John Duncan was Administrative Secretary when I joined the staff of Head Office in 1969. I remember John as someone hugely committed to the MRC who approached issues with great care and rigour and who set high standards for those he worked with. At a very early stage he saw the need for the Council to adopt a more pro-active policy on the commercial exploitation of research outcomes. Current cycling enthusiasts might also like to know that he was a keen cyclist having a bike at both ends of his commute to the office.”

This is a memory shared by John’s son, James, who recalls his father cycling to Walton-on-Thames station to catch the train to London. He cycled wearing a bowler hat, with his George VI R-emblazoned civil service briefcase balanced on the handlebars. “Even in the 1950s, it looked odd,” he said.

John is survived by his wife, Elizabeth, his children James, Jennifer, Janet and John, and five grandchildren.

MRC launches research plans for next five years

The MRC set out its research plans for the next five years on 10 June with the launch of its new Strategic Plan 2009-2014, Research Changes Lives.

Research Changes Lives emphasises the impact that world-class research has on the health and wellbeing of society. It sets the path for improving health by delivering new treatments for disease and maintaining excellence in the basic research that underpins this.

Sir Leszek Borysiewicz said “Research Changes Lives sets out the MRC’s vision for the future. It shows how the MRC will support medical research which speeds the transition to better health and wellbeing of individuals and populations in the UK and beyond. As we approach our centenary, we will build on our outstanding achievements to date to meet this goal – with continued commitment, enthusiasm, and leadership at the international forefront of research.”

The launch event, at BMA House in London, was attended by around 100 key stakeholders including Council members, Directors of MRC Institutes, Units and Centres, Office for the Strategic Coordination of Health Research Board members and Chief Executives of the Research Councils and major UK health charities.

Copies are available to download from the MRC website at www.mrc.ac.uk/strategicplan