Discoveries of the century
Well-known figures give us their thoughts on the biggest medical advances, past and future.

The great coffee breakthrough
How ideas exchanged in the canteen can lead to research discoveries.
A phenomenal legacy begins

Universities and Science Minister David Willetts has officially opened the MRC-NIHR Phenome Centre at Imperial College London, which will re-purpose some of the sophisticated technology from the London 2012 Olympics Anti-Doping Centre.

Unlike our genome, which collectively describes a person’s genetic material, the phenome describes all the other chemistry of our body. It is the product of how our genes and environment interact throughout development and life, and is analysed by linking our chemical, metabolic and physiological features and responses. By measuring phenome patterns throughout life, researchers at the centre aim to identify the patterns which separate those who develop particular diseases from those who don’t.

The Centre’s first three pilot studies are now underway. One study will carry out detailed analysis of samples and data taken from people at various attitudes on an expedition to Mount Everest. Oxygen levels decrease at higher altitudes, so the study will serve as a model for studying why some intensive care patients who have been starved of oxygen recover while others don’t survive.

Another of the pilot studies will aim to pinpoint what makes Europeans of Indian Asian descent more prone to type 2 diabetes than their native European counterparts—a risk that can’t be explained by differences in obesity, diet, physical inactivity or known genetic variants.

The launch of four e-health informatics research centres (eHiRCs) and the UK informatics research network by the Science Minister in May (see opposite), marked part of a £60m total investment in so-called big data or medical bioinformatics—something we excel at here in the UK.

We’re about to invest another £20m into the eHiRCs to improve access to patient records for research, extend partnerships between the NHS, industry and academia and build the necessary digital infrastructure for this research.

The four E-Health Informatics Research Centres (eHiRCs), jointly funded by the MRC and the NHS, were established with £19m joint funding from 10 government and charity partners, in an initiative co-ordinated by the MRC. Capitalising on the UK’s unique wealth of so-called ‘cradle to grave’ NHS patient data, they’ll support research linking patient records and research data and build capacity and skills in this burgeoning field.

The eHiRCs are linked with 15 UK universities, which were announced by Universities and Science Minister David Willetts in May, following investment of £19m from 10 government and charity funding organisations coordinated by the MRC.

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The aim of the eHiRCs, based in London, Manchester, Swansea and Dundee, is to capitalise on the wealth of patient data in the NHS for research. The UK is the only country in the world to have such a rich source of information on the health of its people from cradle to grave. Research using NHS patient records will help develop more effective treatments, improvements in health services delivery and drug safety and advances in understanding the causes of diseases on a scale which was not previously possible.

The eHiRCs are linked with 15 UK universities, three MRC units and include several major pharmaceutical and technology company partners. They will carry out research linking e-health records with other forms of research and routinely collected data.

The network and eHiRCs will offer interdisciplinary career development and training opportunities working with biomedical, social and computer sciences across the UK and provide a gateway for collaboration with industry, the NHS and the public.
MRC Centenary festival celebrates a healthy life

To share our 100th birthday with the widest possible audience, we're teaming up with London’s Science Museum on 15 and 16 June to create a weekend festival of MRC science.

Activities and talks will bring scientists and the public together to create an exciting hands-on exhibition called Strictly Science, keeping one step ahead – masterminded by the MRC Clinical Sciences Centre to mark the MRC’s Centenary – was visited by more than 5,000 people. Visitors were treated to lively debates, re-enactments of 100-year-old experiments and got to try out interactive digital tools used by neuroscientists such as eye-trackers and balance boards.

In the ‘tomorrow lab’, younger visitors made short videos on their visions of the future of medical research, forming part of a growing archive of ‘digital futures’ which can be found on Youtube. You can add your own ideas at www.youtube.com/strictlyscience and find out more about the exhibition at www.strictlyscience.mrc.ac.uk

Activities will include a giant nose that children can crawl inside to discover the allergens that accumulate there, target games to show the how antibiotics work and a live fruit fly experiment to demonstrate how our brains and bodies are wired together.

More details will be available on the Science Museum website:
www.centenary.mrc.ac.uk/open_days

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Strictly Science
‘Amazing’ and ‘Excellent - especially the turnip juice and eye pong’, were among the reactions of visitors to a free public exhibition on the past, present and future of medical research hosted by Imperial College London in April.

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Diabetes screening study scoops BMJ award

Research led by Professor Simon Griffin and Dr Rebecca Simmons at the MRC Epidemiology Unit has won the BMJ’s award for Research Paper of the Year. Their trial was the first robust evaluation of diabetes screening in the world. It showed that screening those in the UK population at increased risk of developing type 2 diabetes to pick up undiagnosed cases may not be as effective at preventing deaths as previously thought.

Read more about the study at www.mrc.ac.uk/ Newspublications/News/ MRC08883

Max Perutz Science Writing Award 2013

Calling all MRC-funded students and fellows! Tell us why your research matters.

First prize: £1,500 and promotion in Times Higher Education

Write an 800 word article for a non-scientific audience describing your research and explaining why it matters

Shortlisted entrants invited to a writing masterclass and an awards ceremony at the Science Museum, London on 25 September.

For more information and the entry form:
www.mrc.ac.uk/Sciencesociety/Awards

Max Perutz Science Writing Award 2013

Prizes and honours

Our Centenary year has already seen several MRC scientists receive honours, prizes and medals.

The MRC Laboratory of Molecular Biology’s Professor Michael Neuberger has been elected a Foreign Associate of the US National Academy of Sciences.

Professor Jim Smith, Director of the National Institute for Medical Research (NIMR) and Director of Research at the Francis Crick Institute, was awarded the Waddington Medal by the British Society for Developmental Biology in March, marking his significant contribution to UK developmental biology.

The NIMR’s Professor Gitta Stockinger and Professor Graham Collingridge of the University of Bristol, have been awarded the 2013 and 2014 Feldberg Foundation prizes for Anglo-German scientific exchange. Professor Stockinger has also been elected as a Fellow of the Royal Society, along with MRC Chief Executive Professor Sir John Savill, the NIBR’s Dr Jean-Paul Vincent and Professor Andrew Wilkie of the Weatherall Institute for Molecular Medicine.

Speeder access to brain tissue for research

A new online database will save brain researchers time in tracking down human tissue samples for their work.

Researchers can use the database to browse through details of all tissue samples held by the 10 brain banks which form the UK Brain Banks Network.

Funded by the MRC, NHS and five brain charities, the network holds healthy and diseased tissue from over 7,000 brains. Researchers will also be able to order samples through the database, and because all the banks now have ethics approval as research tissue banks, tissue can be provided to researchers without the need for them to apply for ethics approval first.

Find out more at: www.mrc.ac.uk/Ourresearch/Resourceservices/ UKBrainBanksNetwork/database

Royal opening for new LMB building

Her Majesty the Queen officially opened the new MRC Laboratory of Molecular Biology building in Cambridge on 23 May.

A decade in the planning, the X-shaped glass and steel edifice houses 600 scientists, providing the 21st century facilities needed to allow this prestigious MRC institute – often dubbed the ‘Nobel Prize factory’ – to take its research forward.

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Tea rooms and canteens have long been popular places for scientists to mingle and swap ideas. Katherine Nightingale explores how a chat over a coffee can lead to unexpected discoveries.

In the bright and airy canteen of the MRC Laboratory of Molecular Biology’s new building, Dr Richard Henderson is demonstrating his habit of drawing on saucers, taking a – water soluble – pen from his pocket and sketching a neat blue graph on a saucer’s rim.

It’s not a new concept. The tea room in the Physics Department at the Cavendish Laboratory in Cambridge inspired Max Perutz to persuade the MRC to build a canteen open to everyone when the MRC unit moved to the old LMB building in 1962. As the LMB’s chairman, he was keen to create a space where people from different disciplines and career stages could get together.

Perutz’s son Robin, a Professor at the University of York, says: “He just led by example. Creating a pleasant environment where people could talk informally – a place where you’d want to spend time, with good, cheap food and drink.”

It’s this informal atmosphere that many people say has played an important role in the LMB’s success, with 13 researchers sharing nine Nobel prizes in its history.

The LMB has three allotted refreshment slots – coffee in the morning, lunch, and tea in the afternoon – where researchers and support staff are encouraged to get together. While the LMB could be seen as one of the most successful places for ‘coffee culture’, many research organisations encourage researchers to spend time together, even if less frequently.

Professor Marcus Munafò, an MRC-funded researcher in the School of Experimental Psychology at the University of Bristol, sees informal time as crucial to the process of research.

“Some researchers plan their day around opportunities to interact with colleagues. I remember, during my PhD at NIMR, I planned all your experiments so you could go to all the coffee breaks”, says Dario.

“I remember during my PhD at NIMR, I planned all your experiments so you could go to all the coffee breaks,” says Dario.

Professor Dario Alessi, Director of the MRC Protein Phosphorylation and Ubiquitylation Unit in Dundee, has his own example of a coffee-room realisation.

Informal discussions with his colleague Professor Graham Hardie made both men realise they were working on two halves of the same problem. Dario’s team were looking for the target of an enzyme called LKB1, while Graham’s wanted to know what activated their enzyme of interest, AMPK. It turned out they had each other’s answers.

“Once Marcus’s research came directly from a Friday night in the pub. He researches tobacco and alcohol use and was chatting to Dr Nick Scott-Samuel, another researcher in the department who works in visual perception. We got to talking about whether the shape of your glass influences the rate at which you drink. We did the research and it turned out it was harder to accurately judge the halfway point on a curved glass than on a straight glass, making you drink faster, which has implications for public health.”

Professor Michael Neuberger cuts the LMB’s 50th birthday cake in the laboratory’s old tea room.

“Tell me about your Enzyme”, says Dario’s team to Graham’s team, and they were able to work out what was going on. It was a kind of eureka moment. Graham's lab had spent 20 years trying to find the enzyme that activated AMPK, and it was the thing that we were working on,” says Dario.

Dario’s enzyme was known to be involved in cancer, and Graham’s to be targeted by a cheap diabetes drug called metformin. Their chats led to the proposal that metformin might treat cancer, and there are now almost 60 trials investigating it for cancer prevention or treatment.

“We have quite a tradition of everyone from undergraduates to senior faculty intermingling in lots of different contexts, including coffee time and going to the pub on Friday nights,” says Dario.

“It’s not luck who you end up talking to. Talking to people in different areas can sometimes generate a new direction for your research that you wouldn’t have thought of alone. It’s important to recognise the creative aspect of talking with colleagues – and science has a strong creative dimension to it.”

One example of Marcus’s research came directly from a Friday night in the pub. He researches tobacco and alcohol use and was chatting to Dr Nick Scott-Samuel, another researcher in the department who works in visual perception. “We got to talking about whether the shape of your glass influences the rate at which you drink. We did the research and it turned out it was harder to accurately judge the halfway point on a curved glass than on a straight glass, making you drink faster, which has implications for public health.”

Nobel prizes in its history.

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Discoveries of the century

To mark our 100th birthday we asked some well-known figures what they think the biggest medical advance of the past century has been and what advance they’d like to see over the next 100 years.

**Stephen Fry; Actor, Writer and Presenter**

Past: “Antibiotics. When you think of the deaths by septicaemia and other infections I cannot think of any other more powerfully effective medical advance. Of course, whether they’ll continue to be as instrumental in the saving of lives over the next 100 years is a moot point as resistance and bacterial mutations continue apace.”

Future: “I think the realisation that cancers are not abnormal growths but essentially immune deficiencies or disruptions will result in materials and treatments that allow the body to repair cancerous cells. This should apply to retroviral cancers like leukaemia and AIDS as well as to other kinds.”

**Melanie C; Spice Girl and Diabetes UK Supporter**

Past: “For me, the most significant medical advance in the last 100 years has been the discovery of insulin to treat diabetes. Without this medical breakthrough, millions of people who are kept alive with daily insulin injections would not be here, including my brother Paul, who has type 1 diabetes.”

Future: “I would love to see a cure found for diabetes in the next 100 years. Both Paul and I are supporters of Diabetes UK, the charity which funds pioneering research into the cause of the condition and how to prevent it, improve care and treatment, and find a cure. There is some really interesting work going on, for example in developing an ‘artificial pancreas’, which will hopefully change so many lives for the better.”

**Prime Minister David Cameron**

Past: “Britain is a world-leader in terms of scientific breakthroughs and medical innovations and I congratulate the Medical Research Council for the remarkable contribution it has made to this work over the last one hundred years. From the discovery of the influenza virus and development of penicillin as a drug through to unravelling DNA and the invention of the MRI scan, the Council’s work has helped revolutionise the world of modern medicine. The number of Nobel prizes awarded for projects it has backed is testament to that achievement.”

Future: “Science moves on quickly and we must look to the next breakthrough or discovery if we are to keep Britain at the forefront of global research. Science and technology are the key to improving the lives of people across the world.

**Professor Jim Al-Khalili OBE; Theoretical Physicist, Author and Broadcaster**

Past: “Probably antibiotics, starting with Fleming and Penicillin in 1928.”

Future: “Without doubt I would say that we will have a final cure for all cancers. I envisage us understanding the molecular mechanisms underlying the mutations that take place within DNA that lead to a cell becoming cancerous. I strongly suspect this will only come about through interdisciplinary research involving biologists, chemists and physicists working together.”

**Professor Dame Sally C. Davies; Chief Medical Officer and Chief Scientific Adviser at the Department of Health**

Past: “In the past 100 years, undoubtedly vaccines. Polio vaccination in particular, as the disease has now been eradicated from all but seven countries in the world.”

Future: “In the next 100 years genomics advances will create a step change at an unprecedented level for targeted treatments for individual patients. Genomics has the potential to unlock our understanding of diseases and focus research developments on both treatment and targeted cures for diseases like cancer and dementia. The benefits to patients of genomics will improve their outcomes from treatments increase the quality of life and survival.”

**Dr Harpal Kumar; Chief Executive of Cancer Research UK**

Past: “in the past 100 years, undoubtedly, vaccines. Polio vaccination in particular, as the disease has now been eradicated from all but seven countries in the world.”

Future: “By the same token, my answer to your second question is: a solution to climate change, which is the biggest current threat to human life and engineering one with profound implications for public health, and an innovation that has still yet to reach large numbers of people around the world.”

**Fiona Godlee; Editor, British Medical Journal**

Past: “When we asked BMJ readers your first question back in 2007, they voted for sanitation, so I will say the same. Not a medical advance but an engineering one with profound implications for public health and an innovation that has still yet to reach large numbers of people around the world.”

Future: “By the same token, my answer to your second question is: a solution to climate change, which is the biggest current threat to human life and health, though I don’t think we have 100 years to achieve this breakthrough.”

Read the full list of responses and let us know your opinion on the biggest medical advances of the past and future at: www.centenary.mrc.ac.uk/centenary-poll. The general public poll results will be announced at Cheltenham Science Festival on 8 June and published in The Times newspaper.
Gout drug offers hope for heart disease patients

MRC research has discovered that an inexpensive drug called Allopurinol, used for treating gout for over 40 years, also holds promise for preventing heart disease and stroke.

In the study, carried out by researchers at the University of Dundee, half of a group of 66 heart disease patients were given Allopurinol and the other half a placebo. Results showed that Allopurinol reduces thickening of the heart muscle wall, known as left ventricular hypertrophy (LVH), a known risk factor for cardiovascular problems.

The drug is thought to work by reducing production of damaging particles called oxidative free radicals, which cause LVH, and by improving blood vessel health, meaning there is less resistance for the heart wall to pump against. The next step is for a large-scale trial in thousands of patients to prove that Allopurinol improves survival rates.

Lead author Professor Allan Struthers commented: “What we’ve shown in this, and previous studies, is that Allopurinol has properties which improve vascular health, reduce pain for angina patients, reduce oxidative stress and heart thickening and potentially prevent sudden death, heart failure, stroke and possibly heart attacks. We live in an age of austerity and finding new uses for old drugs that are cheap and safe is exactly what we need at this time.”

Journal of the American College of Cardiology 61 (9), p 926–932

Ditching lab tests gives more children access to HIV therapy

Results from a five-year clinical trial in Uganda and Zimbabwe have shown that replacing routine lab tests with ongoing clinical assessments could help more children with HIV get treatment.

The ability of children in Africa to access antiretroviral therapy (ART) is lagging behind that of adults – by the end of 2011, only 28 per cent of the two million children who needed treatment were receiving it, compared with 51 per cent of adults.

The ARROW trial, funded by the MRC and the Department for International Development, studied 1,266 children with HIV aged between three months and 17 years. It looked at whether replacing expensive routine lab tests to monitor ART with careful clinical care and follow-up could be done safely. By showing conclusively that it can, the trial supports the argument that resources are best spent extending access to life-saving treatment rather than doing routine lab tests which add little benefit.

Professor Di Gibb at the MRC Clinical Trials Unit who led the trial from the UK, explains: “The results of ARROW show that clinically-driven monitoring of children on ART is safe and can increase treatment access at lower level health facilities near to where people live, thus ensuring that as many children receive treatment as possible.”

The Lancet 381 (9875), p1391-1403

Evolutionary glitch may be culprit behind glue ear

A discovery about how the human ear is formed has shed light on why some children are prone to ‘glue ear’ – an infection which affects one in five children around the age of two.

In glue ear, fluid builds up in the middle ear chamber. This prevents the three tiny bones that carry sound vibrations to the inner ear from moving freely, causing temporary hearing loss.

Studying mouse embryos, the MRC-funded researchers at King’s College London discovered that the cells that line the middle ear cavity originate from two different tissue types – endoderm and neural crest cells. The endoderm-derived lining is covered in a lawn of cilia (tiny hairs) that help to clear debris from the ear, but the lining that comes from neural crest cells does not have cilia. This makes that part of the middle ear less efficient at cleaning itself, leaving it susceptible to infection. Previously it was thought that the lining was purely derived from endoderm.

Dr Abigail Tucker from King’s College London, said: “The process of developing the lining that covers the middle ear is flawed as these cells are not capable of clearing the ear effectively. While this process may have evolved in order to create space in the ear for the three tiny bones essential for hearing, the same process has left mammals prone to infection – it’s an evolutionary glitch.”

Published online at www.sciencemag.org, March 2013

Genetics study sheds light on heart rhythm disorders

A major international study involving 268 researchers and co-led by the MRC Epidemiology Unit in Cambridge studied genetic data from 181,171 participants over three years, which revealed 14 new genetic variations that are associated with heart rate.

The study also showed that a genetic susceptibility for higher heart rate is linked with altered electrical activity in the heart and a reduced risk of sick sinus syndrome, a type of rhythm disorder which is treated with implantation of an artificial pacemaker.

The study was led by Dr Ruth Loos, Director of the Genetics of Obesity and Related Metabolic Traits Program at the Charles Bronfman Institute for Personalized Medicine at Mount Sinai, New York, and an Honorary investigator at the MRC Epidemiology Unit. She said: “Our study tripled the number of genetic variations that are known to be associated with heart rate. These discoveries are just the beginning of something new and exciting and can hopefully be used to identify new drugs for the treatment of heart rhythm disorders.”

Published online at www.nature.com, April 2013
MRC Mitochondrial Biology Unit group leader Dr Edmund Kunji showed Sarah Harrop around his room at Trinity Hall, Cambridge, where he thinks, writes, teaches - and paints - when he’s away from the lab.

Chinese painting
I attended art academy in the evenings while I was studying for my undergraduate degrees in biology and chemistry, and that passion and interest has continued throughout my career. I have always been attracted to Chinese painting. Like science, it has a great amount of abstraction about it and both require an enormous amount of concentration.

Orchids
One of the things you have to learn to paint in order to master Chinese art techniques are Chinese orchids, and that’s how I came to start growing them — and now I have many. Really this room contains a series of my obsessions that got out of hand! They are very temperamental to grow — they don’t like water on their leaves and if you saturate the roots it kills them. They’re quite ridiculous.

Duck
Someone gave me this as a joke when I was doing my post-doctoral studies at the MRC Laboratory of Molecular Biology (LMB). In X-ray crystallography, duck pictures are often used as a way of showing symmetry in crystals, how molecules or complexes within the smallest repeating unit of a crystal relate to each other. I really don’t know why they use ducks.

Wooden model
I made this myself. It’s a structural model of the proteins that we work on: mitochondrial transporters. Our cells have compartments called mitochondria, where energy conversion takes place. Chemical compounds from food we eat come into mitochondria through these transporter proteins and then energy stored in the compounds is converted into the fuel our cells use, called ATP. Every day we move roughly our own body weight in ATP out of the mitochondria through these transporters, and the spent fuel is brought back in to be recycled. This process is crucial for life — if you were to interrupt it for even one second you would die. One potential application of our work could be the development of inhibitors that block these transporters in, for example, the malaria parasite or the amoeba that causes amoebic dysentery.

Drawing
This is my daughter Leonie’s impression of Trinity Hall — the faces you can see are the students that live here. I work full time at the MRC Mitochondrial Biology Unit but I have a room here because I’m also Director of Studies in Biology for this college, which allows me to do some teaching; something I was missing as a lab group leader.

Brushes
These are made from cockerel feathers or goat, wolf, badger or horse hair — they all have different textures and resistances. They can hold a lot of water and with one brush you can do both thin and broad lines in one stroke — it’s very expressive. Chinese paintings are done very quickly, mostly they are over within a minute or so and they have an atrocious failure rate!

Seals
The seal is an integral part of the composition of Chinese paintings. They can represent a name, a nick name, a studio name or just a little saying. I carved some of them myself. For example, one of them means ‘Singing Uninhibitedly’ — such as what you’d do when you’re drunk or as an expression of joy.

Bubble excluder prototype
These are prototypes of the Bubble Excluder, a simple device that my colleague Dr Palmer and I invented. In our line of work, studying the structures of tiny proteins inside membranes, it’s hard to get enough material, so you need to grow huge volumes of cells in large tanks called fermenters. If anything goes wrong, you end up wasting the whole fermenter, which is very costly. We came up with a fibre-optical system to monitor the growth of cells, but we found that air bubbles, which are required for their growth, would run through the measuring window and interfere with our measurements. So we invented this small, inexpensive device to keep bubbles away from the measuring window — it’s saved us lots of money. It’s been patented by MRC Technology and now we’re trying to sell it via a spin-out company we’ve set up called Cytoprom.
Each year the MRC commits over £40m to neurodegeneration research and in 2010/11 we spent nearly £18.5m on dementia research alone. The increasing burden that this devastating group of diseases is placing on families and on societies worldwide is widely recognised. According to Alzheimer’s Society figures there are 800,000 people with dementia in the UK, with numbers set to rise to over one million by 2021.

Along with the National Institute for Health Research (NIHR) and the Economic and Social Research Council we are committed to doubling funding for research into dementia from £26.6m in 2009/10 to an estimated £66.3m in 2014/15. Furthermore in 2012, Prime Minister David Cameron announced wide-ranging plans for action to address the ‘crisis’ of dementia which included accelerating research programmes on neurodegenerative diseases around a new ‘Dementias Research Platform’ to be set up in early 2014. Through this, researchers will look not just at the brain but all body organs/systems to get a fuller picture of the disease and its causes.

The Catalyst, to which the MRC and TSB have committed £180m, supports the translation of an idea from concept to commercialisation. Some of the projects include a novel drug for treating multiple sclerosis, the world’s first clinical trial of a stem cell-based voice box transplant, and an innovative low-cost implantable blood pump for advanced heart failure.

A key part of the Government’s Strategy for UK Life Sciences, the latest awards were announced at InnovateUK, the country’s largest innovation event, by Minister for Universities and Science David Willetts.

He said, “The Biomedical Catalyst is making a real impact by making sure that our innovative businesses in the UK are able to develop new products for the healthcare industry. Many great innovations often fall into the ‘valley of death’ between the creation of an idea and the market place. The Catalyst is helping the UK to bridge that gap, so that the best new ideas in healthcare can be transformed into innovative products and services.”

The next round of funding will take place this summer.

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

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

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