Tools of the trade
How biomedical research tools have evolved over 100 years

Opinion
Dementia: care today, cure tomorrow
Historic £100m charity backing for UK Dementia Research Institute

Alzheimer’s Society and Alzheimer’s Research UK have announced £100m of new partnership funding for the UK’s first Dementia Research Institute. Led by the MRC it is one of the single biggest financial commitments to dementia research in the history of both charities.

The country’s leading dementia charities have pledged £50m each towards the work of the Institute, making the total commitment a quarter of a billion pounds. Their involvement will be essential in drawing together the work of scientists and medical professionals with experience of people living with dementia, helping to create the link between research findings and delivering real changes for the diagnosis, treatment, care and prevention of dementia.

Sir John Savill, Chief Executive of the MRC said: “Together, we will lead the UK’s dementia research efforts, to search for new means to prevent and cure dementia and to transform the supportive care that people and families affected by established dementia receive. The UK Dementia Research Institute will be the research cornerstone in the fight against dementia.”

Read more at: mrc.io/uk-dementia-research-institute

See page 11 for details of the MRC UK Dementia Research Institute Momentum Awards.

Read Alzheimer’s Society Ambassador Keith Oliver’s story and his hopes for the UK Dementia Research Institute on page 22.

Win an iPad

We are keen to hear your views! For the chance to win an iPad Pro or an iPad mini help us to improve Network magazine by completing our short readership survey. Complete the survey online at: www.mrc.ac.uk/network-survey

Survey closes 31 August 2016. Terms and conditions apply.
A vision to deliver national needs

The new MRC Delivery Plan 2016-2020 was published in May. It sets out how the MRC will use our allocation from the Science and Research Budget to improve health and economic impact over the next five years.

The plan describes how the MRC will prioritise research into the most pressing health challenges worldwide, explore new scientific principles and set new paradigms, and transform health research and innovation (see more detail in triangle diagram below).

The MRC settlement includes Official Development Assistance funding from the Global Challenges Research Fund. We will therefore expand our portfolio in global health research benefiting people in low and middle income countries.

Find more details at: mrc.io/delivery-plan

Tackling global challenges

The MRC, together with four other UK research councils, have announced the first joint interdisciplinary calls from the new £1.5bn Global Challenges Research Fund (GCRF).

Worth over £40m, including an MRC contribution of up to £20m, the three calls are in non-communicable diseases, global infections, and agriculture and food systems. They aim to help provide solutions to reduce and prevent diseases in humans and farmed animals, ensure a safe, nutritious and sustainable supply of food for a growing population and improve the life-long health of billions of people in low and middle income countries.

This initial funding from the MRC and Biotechnology and Biological Sciences Research Council, with support from the Arts and Humanities Research Council, the Economic and Social Research Council and the Natural Environment Research Council, aims to enhance research and partnerships to pave the way for ambitious GCRF programmes.

Universities and Science Minister Jo Johnson said: “Our £1.5bn Global Challenges Research Fund represents the latest stage in our sustained investment in the UK’s world-leading scientists. This new £40m fund is part of our commitment to tackle global issues such as food security and life-threatening diseases like Ebola, and will help improve quality of life for people in developing nations as well as here in the UK.”

For specific call details visit: mrc.io/gcrf-foundation-awards

Embracing animal research openness

The Concordat on Openness on Animal Research – which the MRC helped to develop and was one of the first to sign back in 2014 – celebrated its second birthday in May by gaining its 100th signatory. Membership comprises institutes, councils, charities and companies who commit to:

1. Being clear about when, how and why we use animals in research.
2. Enhancing our communications with the media and the public about our research using animals.
3. Being proactive in providing opportunities for the public to find out about research using animals.
4. Reporting on progress annually and sharing our experiences.

Find out more at: www.mrc.ac.uk/animalresearch

MRC talks

Listen to news and views from across the MRC community in our quarterly MRC podcast, MRC talks. Search for MRC talks on iTunes.
Debating matters

Congratulations to all 12 competitors who have secured a place in the Institute of Ideas Debating Matters 2016 National Final in July.

Nottingham High School Sixth Form won the Debating Matters East Regional Finals which featured a debate on whether childhood vaccinations should be compulsory, against very strong competition.

Supported by the MRC for over a decade, alongside other sponsors, this national sixth form debating competition aims to offer a fresh, accessible and engaging format for debating contemporary issues.

Equality, diversity and inclusion

Research Councils UK (RCUK) has launched an action plan to promote equality, diversity and inclusion in research, recognising its leadership role in driving a change in culture.

RCUK’s Statement of Expectations for Equality and Diversity, published in 2013, outlined ambitions to lead by example in ensuring a diverse workforce; challenge bias and work towards fair and inclusive funding processes; and lead and support change in our research community. Work has already begun with the roll-out of unconscious bias training for peer reviewers and funding decision-makers.

RCUK will be engaging with the research community through a number of external events to help shape the way we implement the actions set out in this plan as well as raise awareness of the critical importance of equality, diversity and inclusion within the sector.

Read more at: mrc.io/rcuk-actionplan

Preventing pneumococcal disease

The European Medicines Agency (EMA) have approved a new multi-dose preparation of pneumococcal vaccine Prevenar 13®, sponsored by biopharmaceutical company Pfizer, based on a study conducted by the MRC Unit The Gambia.

Pneumococcal disease – including pneumonia and meningitis – mainly affects children under five and causes significant illness and death. The vaccine is a new four-dose presentation covering 13 of the more than 90 pneumococcal bacteria serotypes.

A single-dose preparation is already used in many countries, but having four doses of the vaccine in each vial, instead of one, offers a 75 per cent reduction in supply chain requirements, shipping costs and storage requirements.

Trial director Professor Beate Kampmann, Theme Leader for Vaccines and Immunity at MRC Unit The Gambia, said: “We are very pleased indeed that the high standards routinely achieved in our clinical trials have enabled the swift approval from the EMA. I thank the field team and the clinical trials group for their outstanding support.

The impact of this vaccine on affordability and therefore on prevention of serious disease in low and middle income countries will be tremendous.”

Read more about this study on the MRC Insight blog at: mrc.io/1TIFb50

Max Perutz Science Writing Award 2016

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

You could win an award of £1,500

- 800 words to describe your research to a non-scientific audience by answering:
  - why does my research matter?
  - what is it that makes my research matter?
  - what impact would your research have on increasing our understanding of health or disease?

- Open to all MRC-funded PhD students
- Submitted extracts invited to a writing masterclass and an awards ceremony in central London.

Competition open: Tuesday 24 May 2016
Closes: 9am, Wednesday 20 July 2016

For more information about this year’s competition:
mrc.ac.uk/maxperutz

Contact: maxperutz@mrc.ac.uk
@The_MRC #maxp16

“Why does my research matter?”

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UK Biobank has launched the largest body scanning project in the world involving 100,000 people. Here Professor Paul Matthews, Head of the Division of Brain Sciences at Imperial College London and one of the academic experts supporting the resource, explains how it could prove invaluable to all areas of medicine.

Building the bank
Over 10 years, the UK Biobank has recruited and gathered a wealth of high quality information from 500,000 people across the country. These people have donated blood, urine and saliva samples, provided detailed health, lifestyle and environment information and agreed to allow the biobank to follow their GP and hospital records throughout life.

Getting the whole picture
One thing making the UK Biobank so special is that it is not a ‘disease collection’ of people suffering from a specific problem. This means researchers can study people before they develop many diseases, follow them through life and understand better what factors determine their health outcomes.

Intensive investigation across multiple organs can tell us, for example, how the onset of dementia may be influenced by diet, activity levels and lifestyle, and to decode the links between diseases in organs of the body and diseases of the brain.

Understanding disease before it begins
Now that we will be adding sophisticated imaging data, the UK Biobank will help us find those changes in the brain that herald the future onset of dementia when it may still be preventable.

Many conditions such as dementia and diabetes have a complex interplay that we do not yet fully understand. We should be able to ask big questions. For example, is there a link between early dementia and excess fat around internal organs? Does this fat drive damaging, chronic inflammation in the brain?

If this were shown to be true it could lead to new ways of minimising the risk of dementia by focusing on factors we can already treat such as blood pressure, excess blood sugar and abnormal cholesterol.

Big studies to understand small factors
Large samples are an efficient way of addressing a range of public health issues and studying multiple diseases, all with investment in just one study. To understand a range of different health outcomes, our challenge is to relate changes that occur in the body – well before the onset of disease – to the risk of disease in an individual.

Large numbers are also important because the influences on disease made by lifestyle, exposures and genetics are small at a population level. Researchers need to study large numbers to be confident of the results, particularly if we’re trying to tease out the ways in which they interact.

Quality control
The resource has been developed according to rigidly-maintained standard operating procedures with regular quality-control monitoring. For the imaging study, more than 125 world experts in the US, Europe, the UK and Australia have worked together over six years to design the protocols.

A key factor in its design was future proofing the data so researchers can ask new questions in the future. Tissues and other samples from the volunteers are carefully stored, and all of the volunteers have consented to being re-contacted, so that researchers can go back to them to involve them in further studies.

The biobanking revolution
Individual health initiatives like UK Biobank are showing us the value of bringing together large amounts of different types of data. It is a powerful illustration of the value of data sharing.

I also think that it is leading towards the notion of making biobanking for data and samples part of routine healthcare. That may fundamentally transform what happens over the next decade to the extent that we may no longer need to do extra studies like UK Biobank – they may just become embedded in the way we deliver healthcare.

Find out more: www.ukbiobank.ac.uk

As told to Isabel Baker
FUNDING

MRC peer review explained

The MRC funds research across the biomedical spectrum in all major areas of healthy systems and disease. But do you know what happens to a MRC grant application when you press ‘submit’?

Understanding MRC peer review will help with navigating the selection process and learning what reviewers are looking for. We invite you to go behind the MRC scenes in our short video animation, explaining how the MRC peer review process works from application submission to decision: mrc.io/1TCB2r

Gene knockout mice awards

The MRC has launched a £1m, two-year initiative to provide pump-priming awards for UK-based research groups to undertake preliminary research using gene knockout mouse lines, developed via the International Mouse Phenotyping Consortium (IMPC).

The IMPC was established in 2011 to produce and phenotype gene knockout mice for each of their approximately 20,000 genes. So far almost 3,000 gene knockouts have been completed.

The MRC invests in the IMPC via its MRC Harwell facility (principally the Mary Lyon Centre). The centre provides the research community with validated mouse ‘models’, whose phenotype may inform critical aspects of medical research, to minimise duplication in knockout production and reduce numbers of mice used in research.

Awards of £20,000 to £40,000 are available to undertake early biological investigations that build on existing research expertise. The work should underpin longer-term research goals that are expected to be funded through standard mechanisms. The 2016 deadline for applications is 8 July.

Find more details at:
rmc.io/impc-knockout-mice-awards

Learn more about the IMPC at:
www.mousephenotype.org

To discover the Mary Lyon Centre’s world-class mouse services, see: www.har.mrc.ac.uk/services

Public health innovation

Up to £150,000 is available per application, for a maximum of 18 months, through the MRC Public Health Intervention Development scheme (PHIND), supporting early stage development of new interventions that address an important UK or global public health issue.

Projects should aim to develop interventions that target disease prevention, health promotion or a reduction in health inequalities, and encourage a new approach to intervention development. Complex, population level interventions, with a focus on non-health care settings are particularly welcome, such as transport, education, employment, leisure and the built environment.

Healthcare settings are not excluded, but projects should demonstrate potential for improved health of general, high-risk or vulnerable populations. In addition, proposals that align with the NIHR Public Health Research Programme or MRC Global Health schemes are particularly welcomed.

The next application deadline is 12 July 2016.
Find out more at: www.mrc.ac.uk/phind

Momentum awards

In preparation for the new UK Dementia Research Institute, the MRC has opened a £8m rapid action call to boost the UK research base in biomedical science.

The UK Dementia Research Institute will be the UK’s first national research institute dedicated to understanding the condition, transforming treatments and improving the lives of people living with dementia.

The MRC is inviting applications from UK universities already engaged in biomedical neurodegeneration or dementia-related research. The awards will build essential capacity, supporting the recruitment of research leaders and ‘rising stars’ from within and outside the UK, and develop new disciplinary interfaces that might exploit emerging scientific opportunities. With potential to support awards of between £0.3m and £1m for up to three years, the Momentum Awards will build capacity and connectivity in UK dementia research. Universities may only submit one application to this scheme and hold one award.

The deadline for applications is 18 July 2016.
Find out more at: mrc.io/22dlrwo

Read more about the UK Dementia Research Institute on page 3.
**Fellows of the Royal Society**

Three MRC scientists have been elected Fellows of the Royal Society in recognition of their contribution to science.

Dr Manu Hegde, Group Leader, MRC Laboratory of Molecular Biology, has been elected for his contributions to understanding how emerging secretory and membrane proteins mature to their functional state, and how quality control pathways detect and resolve mistakes during maturation.

Professor Neil Gow, Deputy Director, MRC Centre for Medical Mycology at the University of Aberdeen, has been recognised for his discoveries in fungal biology and genetics, morphogenesis and pathogenesis. His research directly impacts on the design and use of antifungal drugs, diagnostics and immunotherapies for fungal diseases.

Professor Adrian Hayday, Group Leader, the Francis Crick Institute, has been elected for his contributions to understanding how lymphocytes, a type of white blood cell, function within the epithelial tissues that line the surfaces of blood vessels and organs.

**Welcoming new MRC directors**

Dr Karen Walker-Bone has been appointed as Director of the Arthritis Research UK/MRC Centre for Musculoskeletal Health and Work. The centre, which opened in 2014, aims to find cost effective ways to reduce sickness absence and work disability from musculoskeletal disorders. The centre is co-ordinated by the University of Southampton with collaboration from 14 other UK academic institutions: [www.mrc.soton.ac.uk/cmhw](http://www.mrc.soton.ac.uk/cmhw)

Following Simon Phillips’ retirement, Professor Peter Lee has been appointed acting Director, and Dr Marisa Martin-Fernandez acting Assistant Director, of the Research Complex at Harwell (RCaH). The RCaH is a world-leading interdisciplinary centre which enables life and physical sciences researchers to access the UK’s specialist ‘Large Facilities’, such as the synchrotron light source, encouraging synergy between these areas of UK research: [www.rc-harwell.ac.uk](http://www.rc-harwell.ac.uk)

**Award for Cytosponge™ team**

Professor Rebecca Fitzgerald and her team were recognised at the BMJ Awards 2016 with a Gastroenterology Team Award for their simple diagnostic test for oesophageal cancer, called the Cytosponge™.

The upper gastrointestinal team at the MRC Cancer Unit developed the test which avoids the need for endoscopy. The Cytosponge™ is a simple pill-on-a-string swallowed by the patient which remains in place for a few minutes and is then retrieved. The cells collected are tested for the presence of a protein, Trefoil factor 3, a marker for Barrett’s oesophagus, a common precursor of cancer.

The diagnostic test was widely praised by the judging panel: “This is a novel and ingenious idea that combines a simple technology with highly advanced diagnostic techniques. We were impressed that the Cytosponge™ has the potential to be used to diagnose other oesophageal conditions”. The team are currently launching a final study in primary care (BEST3 trial). Expected to take three years to complete, it should indicate whether the test is suitable for routine clinical use.

Find out more at: [thebmjawards.bmj.com/66683](http://thebmjawards.bmj.com/66683)

Read more MRC-funded success stories at: [www.mrc.ac.uk/successes](http://www.mrc.ac.uk/successes)

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**PEOPLE**

**AMS Fellows elected**

MRC-supported scientists are among the 47 distinguished medical researchers elected as Fellows of the Academy of Medical Sciences in 2016.

Professor Gordon Brown,
Director, MRC Centre for Medical Mycology and 6th Century Chair in Immunology, University of Aberdeen

Professor Jason Chin,
Programme Leader, MRC Laboratory of Molecular Biology

Professor Stuart Forbes,
Director, MRC Centre for Regenerative Medicine, University of Edinburgh; Professor of Transplantation and Regenerative Medicine

Professor Robin Franklin,
Professor of Stem Cell Medicine, Wellcome Trust – Medical Research Council Cambridge Stem Cell Institute

Professor Graham Lord,
Professor of Medicine & Honorary Consultant in Nephrology, Transplantation and Internal Medicine, MRC Centre for Transplantation, King’s College London

Professor Timothy Maughan,
Professor of Clinical Oncology, Deputy Director of the CRUK/MRC Oxford Institute for Radiation Oncology, University of Oxford

Professor Paul Moss,
Chair, MRC Infections and Immunity Board, and Professor of Haematology, University of Birmingham

Professor Jeffrey Pollard,
Director, MRC Centre for Reproductive Health, University of Edinburgh

Professor Sylvia Richardson,
Director, MRC Biostatistics Unit, and Professor of Biostatistics, University of Cambridge

Professor Angela Roberts,
Professor of Behavioural Neuroscience, Department of Physiology, Development and Neuroscience, University of Cambridge

Professor Liam Smeeth,
Professor of Clinical Epidemiology and Head of Department, London School of Hygiene and Tropical Medicine

View the full list of new Fellows at: [www.acmedsci.ac.uk/fellows/fellowship-news/new-fellows](http://www.acmedsci.ac.uk/fellows/fellowship-news/new-fellows)
Morning flu jab more effective

Researchers from the University of Birmingham have shown that flu vaccinations are more effective when administered in the morning.

The study involved 276 adults aged over 65 between 2011 and 2013 during the annual UK influenza vaccination programme, as part of a study funded by the Lifelong Health and Wellbeing cross-council initiative.

Participants were vaccinated against three influenza virus strains either in the morning or afternoon. One month later, those vaccinated in the morning had a larger increase in the number of antibodies in their blood than those in the afternoon cohort for two of the three strains; this means they would be better prepared to fight those two strains of the virus.

Professor Anna Phillips, a co-Principal Investigator with Dr Kai Michael Toellner on the study, said: “We know that immune responses fluctuate throughout the day and wanted to examine this further. Our findings should help improve flu vaccinations, but might also provide clues to improve vaccinations more generally.” The team will now look to investigate this further in a large scale study.

Published online at stemcellstm.alphamedpress.org, 18 February 2016.

Drug promise for muscle wasting disease

A new drug to treat the muscle wasting disease ‘inclusion body myositis’ (IBM) reverses key symptoms in mice and is safe in patients, finds a study led by the MRC Centre for Neuromuscular Diseases at UCL and the University of Kansas.

IBM is the most common muscle disease in people over 45. An incurable disease, it causes progressive muscle degeneration leading to severe disability, paralysis and dependency. The precise cause is unknown and there are currently no effective treatments.

The study found that new drug Arimoclomol reversed the effects of the disease at the cellular level and improved muscle strength in mice. Arimoclomol appears to clear misfolded proteins in patients, potentially by either refolding or eliminating them. A further safety trial in 24 IBM patients found that the drug was safe in humans.

Professor Michael Hanna, co-senior author, said: “Targeting misfolding could be important for treating this disabling degenerative disease.” The team hopes to begin a full-scale clinical trial to assess the drug’s effectiveness in slowing IBM.

Published online at stm.sciencemag.org, 23 March 2016.

Treating severe paranoia with virtual reality

Researchers at the University of Oxford have shown that virtual reality has the potential to help treat severe paranoia by allowing people to face situations they fear and relearn that they are safe.

Patients with severe paranoia show extreme mistrust of other people. The research team sent 30 patients into virtual reality simulations with increasing numbers of computer characters. Participants were encouraged to test out their fears by approaching the virtual characters without using defensive behaviours like avoiding eye contact.

Patients who fully tested their fears showed substantial reductions in their paranoid delusions and were later much less distressed in a real-world situation. Further research is needed to see if the benefits go beyond the testing day.

Professor Daniel Freeman, who led the study, said: “The positive immediate results for the patients in this study show a new route forward in treatment. It’s not easy for patients – lowering defences takes courage. But as they relearned that being around other people was safe we saw their paranoia begin to melt away.”

Published online at bjp.rcpsych.org, 5 May 2016.
Conservators Rebecca Bennett and Jill Barnard are in the process of conserving 150 items from the Crick Mill Hill Laboratory (previously the MRC National Institute for Medical Research, NIMR) in preparation for the move to the Francis Crick Institute.

We are now 11 weeks into our ‘Tools of the Trade’ conservation project. So far we have treated 137 of 150 historical objects that tell the story of how research, and biomedical research tools, developed at NIMR over the course of 100 years.

The collection has been brought together by current or recently retired research and technical staff at NIMR, rescued from the various outbuildings. During the project we have met engineers who were local and had been taken on as apprentices after school, learning their technical skills on the job. Their role in collaborating with NIMR’s prize-winning researchers is celebrated in this collection, particularly as it was the engineering team who were responsible for saving so many of these objects over the years.

**Portable x-ray machine**

Looking back at the state-of-the-art research equipment brought together in 1919 the first director of NIMR Sir Henry Dale remembered it as “astonishingly few and simple… We started with an adequate supply of ordinary microscopes, desicicators and simple centrifuges, a spectroscope, a couple of kymographs and such like”. These ‘simple’ items were built upon, improved and replaced by NIMR researchers and engineers, including this 1930s portable x-ray machine, still in use in 1984.

**Insulin infusion pump prototype**

Innovations like the insulin infusion pump were built at the institute and sit in the collection, alongside more recent inventions such as Apple Mac Power Books from the mid-1990s and late 20th-century nuclear magnetic resonance probes. Later, this pump was miniaturised to a chip the size of a fingernail.

**Cell counter**

Some instruments were made by NIMR’s skilled engineers in on-site workshops; these are always beautifully designed and constructed. They are examples of collaboration between the technically-minded engineering team and the researchers to create the perfect tool for the job. Many of the objects were prototypes for instruments that are now produced commercially. This ‘cell counter’ counted infection levels of trypanosome and malaria infections. Parasitologist Neil Brown requested this innovation to speed up their work. It was developed by John Lewin and Jon Marsh in the 1950s.

**Electrophoresis apparatus**

Various pieces of electrophoresis equipment, used to separate molecules by size or charge, are very well represented in our collection. This is Frank Hawking’s electrophoresis apparatus (packaged ready for transit and storage).

**Peter Medawar’s microscope**

For us, as object conservators, this project presents an interesting challenge as we are dealing with ‘working’ objects. They arrive in our conservation lab complete with grease, soot, labels from electrical safety tests and residues from unknown chemicals, including asbestos.

**Ribosome model**

One of the final objects to be treated will be the early model of a ribosome. Designed by researcher Robert Cox and modelled by engineer Frank Doré in 1965, it was the first attempt to model its structure in detail. Cox asked leading biomedical scientists like Francis Crick to sign each of the polystyrene ‘protein spheres’. Both the fragile polystyrene and the use of light-sensitive blue biro present interesting challenges for long-term preservation – let alone cleaning headaches.

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These objects will soon be packed up and moved to the Crick. Watch this space to find out when and where you may be able to take a closer look. In the meantime, find out more about the history of the institute at:

www.historyofnimr.org.uk

Find out more about the transfer to the Francis Crick Institute in our ‘To the Crick!’ series:

www.insight.mrc.ac.uk

‘Tools of the trade’ is supported by the Preservation of Industrial and Scientific Material (PRISM) Fund:

www.artscouncil.org.uk/funding/prism
In his final report on antimicrobial resistance, economist Jim O’Neill recommended that doctors test patients to find out if their infection is bacterial before prescribing antibiotics. Here MRC-funded researcher Dr Tariq Sadiq at St George’s Institute of Infection and Immunity explains how better diagnostic tests can help combat widespread antimicrobial resistance.

Medical advances undermined

How have we been able to make so many medical advances? What’s made us so successful at treating cancer and performing heart surgery? Our ability to manage one of their most serious consequences: infection.

Antibiotic resistance undermines those advances and could mean infections that we thought we had defeated, become untreatable. Global deaths from drug-resistant infections are likely to increase over the coming years – perhaps reaching 10 million by 2050 – unless we find new ways to tackle them.

Why are tests important?

Overuse and misuse of antibiotics in agriculture and human medicine around the world has meant a growing number of infections have developed resistance to the antibiotics we have, meaning we can no longer use them. However, those drugs will still work for a proportion of cases, we just need good diagnostics to tell us when.

Treating the pathogen, not the presentation

Pathogens are anything that causes disease – including bacteria, fungi and viruses. Different pathogens can sometimes have similar ‘presentations’ or symptoms. Antibiotics only work on bacteria and for many infectious diseases it can be very difficult to know which virus, bacteria or other type of pathogen is causing the problem.

I’m working on tests that will tell doctors whether a patient has an infection such as gonorrhoea – and whether the strain they have is resistant to certain antibiotics – in 30 minutes. This is important because you have to treat patients when they come to you – you can’t wait days for the results of an antibiotic susceptibility test. In rural settings you might be prescribing many miles from a clinic.

If we can make better, faster, more portable diagnostics, we can get better at prescribing. This will help doctors choose the right antibiotic with certainty and speed and allow us to go back to using ‘old’ antibiotics with confidence that they’ll work.

Making it work at every level

At the moment we’re working on a four pathogen test to detect chlamydia, gonorrhoea, trichomoniasis and Mycoplasma genitalium, as well as a test that can detect antimicrobial resistance when the patient comes in.

But we want to do much more than just develop functional tests. We want to know what patients and doctors prefer and how effective different configurations of the test would be.

Keeping up with the bugs

Antimicrobial resistance evolves. That means the markers we use to detect antibiotic resistance will change. We have to carefully consider how we build the technology so that we can update it with new markers to keep up with the bugs. Otherwise we could end up with redundant technology in clinics that takes a long time to replace.

Tackling antimicrobial resistance will be about responsibility and action as well as innovation. That means new antibiotics but it also means making the most of what we already have through great diagnostics.

As told to Sylvie Kruiniger

“...If we can make better, faster, more portable diagnostics, we can get better at prescribing.”
**Single cell vision**

New technology is helping scientists study the secrets of single cells in more detail than ever before. **Dr Roy Drissen** at the MRC Weatherall Institute for Molecular Medicine (WIMM) tells **Sylvie Kruiniger** how single cell technology has helped them discover a new stage in blood cell development, which may have implications for the future of leukaemia treatment.

"Before Galileo invented the telescope, we could just see Jupiter. With the telescope, we saw that Jupiter had moons. That's what single cell technology is doing for biology: where we used to think there was only one type of cell, we can now see several."

That's how group leader Professor Claus Nerlov put it. Using single cell technology, the team has rewritten the step-by-step process of how mature blood cells develop from blood progenitor cells found in bone marrow. Progenitor cells, like stem cells, have the potential to develop into several different types of mature cell, a process called differentiation. Precisely mapping the different stages of this process could help us understand how different blood cell diseases, like leukaemia, develop.

**A million to one**

Before single cell technology arrived, researchers looked at populations of cells that often numbered in their thousands or millions. This meant that their characteristics had to be defined statistically by looking at the whole group and calculating their average behaviour. These profiles could hide that a sample contained distinct populations that may behave differently.

"Single cell technology allows you to look at the genes being expressed by individual cells, and that allows you to observe whether the population you're studying is all the same, or if it contains different types of cell," explains lead author, Dr Roy Drissen.

**Single cell tech in action**

The group used a fluorescence-activated cell sorting machine, known as FACS, to sort a specific cell population from mouse bone marrow thought to contain only one type of cell. This cell sample was loaded into a microfluidic chip, and inserted into a single cell, DNA-copying machine, the Fluidigm C1. The chip allows for 96 different cell samples to be individually processed at the same time.

The Fluidigm machine moves the cells into separate wells in the microfluidic chip, and circulates a mild detergent through its channels to break down the cells and release their genetic material. The machine then makes multiple copies of each cell's genetic data before ejecting the chip, with each cell carefully locked into its own chamber – along with its genetic copies. After this, the DNA from each cell type can be sequenced to reveal their unique genetic code.

The single cell technology has meant that DNA sequencing machines can work with the original cell, plus the numerous identical copies of its DNA, providing a large amount of data for analysis. In this case, when the team sequenced their cell sample, Roy found that the sample actually contained two different types of cell. They then discovered that these two different progenitor cell types each produced a different set of mature blood cells.

**Where cancers begin**

"If you look at most, if not all, blood cancers, DNA mutations in early progenitors make a cell stop differentiating. Instead of making a mature blood cell, it stays at the progenitor stage. You end up with an immature cell that just keeps multiplying," says Roy. It is this uncontrolled multiplication of cells that can cause disease.

Currently, the main treatment for leukaemia is the drastic measure of a bone marrow transplant. This replaces the patient's entire stem cell population, removing the few cells that are malfunctioning – but also destroying all the healthy stem cells at the same time. The ability of this technology to identify problem cells with greater precision opens up the potential of developing more targeted treatments for disease, with the hope of providing maximum benefit to patients and reducing the unpleasant side-effects.

Read the paper, published in Nature Immunology on 4 April 2016, at: www.nature.com/ni

Find out more about the MRC WIMM at: www.imm.ox.ac.uk
Dementia: care today, cure tomorrow

Charity partners Alzheimer’s Society and Alzheimer’s Research UK will be instrumental in involving people living with dementia in the work of the new £250m MRC-led UK Dementia Research Institute. Here Alzheimer’s Society Ambassador Keith Oliver shares his hopes for how the new institute will make life better for people with dementia, now and tomorrow.

My world changed in 2010 when I was diagnosed with early-onset Alzheimer’s disease at the age of 55. My early symptoms were falling over, an element of reduced concentration and being unable to follow things as well as I did previously.

I went to the GP thinking I’d got an ear infection and was sent for an MRI scan. When I had an appointment with a neurologist to discuss the scan he said, totally out of the blue, that it looked like the early stages of Alzheimer’s disease. After attending a memory clinic for around four months of quite intensive testing and assessments I received a diagnosis.

I see a consultant psychiatrist every four months who, coincidentally, I taught when I was a primary school teacher. I used to care for him 27 years ago and now he cares for me, which is rather nice. He’s been monitoring my medication, called galantamime, with my GP. I received a course of psychotherapy which then led to cognitive behaviour therapy to do with the double-edged sword of depression and dementia, which I’ve experienced for the first time in the last two years.

Getting involved in different groups and activities allows me to see things from other people’s perspectives. As an ex head teacher I bring to the table many years of both chairing and serving on groups, and leading big staff organisations where it wasn’t about me, it was about other people. So when it comes to things like research I come into it thinking what’s in it for people with dementia. I want to try and retain that for as long as I possibly can.

Being an ambassador for the Alzheimer’s Society gives me a sense of purpose in life and is an incredibly useful therapy. I’m very proud of the role and I feel I get as much from it as I give. As one of about 270 lay people in their research network, including carers, former carers and a few people with a diagnosis of dementia, I’m part of a panel that make recommendations to the research board of the society about what research should be funded, based on the views of the wider network. I focus my energies on the care and wellbeing aspect.

The Alzheimer’s Society uses the phrase ‘Care today, cure tomorrow’. We know a cure isn’t going to arrive tomorrow but we’re all focused on hoping to achieve one by 2025. Care projects allow people like me, and there are many hundreds of thousands of people like me, to live better today in order to still be here when tomorrow arrives. The UK Dementia Research Institute has the potential to achieve that, I hope.

I can see the parallels there with my head teacher role. You’re bringing in new talent and utilising existing talent in order to make life better for people with dementia now and tomorrow. We all want a cure, and as soon as possible. Alongside this I’m pleased to know that research into effective care for those living with, and affected by, dementia will be firmly included in the centre’s work.

It’s great to see the Government, charities, the research community and key universities about to work together to bring about this exciting venture. I’m thrilled and excited and would love to still be around to add the expression of ‘delighted’ when its potentials are realised. So at the moment I’m thrilled and excited but I’m not yet delighted, until I’m here to see the results of its success.

“I feel that this potentially very significant institute will go a long way towards attracting, recruiting, retaining and then celebrating the successes of those involved in dementia research at all levels.”
**YOUR FEEDBACK**

*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 keen to receive feedback on *Network* and suggestions for new features from our readers. To share your views complete our *Network* survey: [www.mrc.ac.uk/network-survey](http://www.mrc.ac.uk/network-survey) or email network@headoffice.mrc.ac.uk

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