Introduction
from the MRC Chief Executive, Sir John Savill

Welcome to the MRC Annual Review 2011/12, which gives an insight into some of our scientists’ many research achievements from the past year.

This year’s review is all about the impact that MRC-funded science makes on our health, the economy and society.

We hear from Dr Cari Free, whose Txt2stop mobile phone support programme, trialled with MRC funding and launched earlier this year, is now helping thousands of people to give up smoking.

And you can read about Professor Alasdair MacLullich’s MRC-supported invention of a device for detecting delirium, a condition which carries a high risk of dementia and death in the elderly, which is now being commercialised.

2011/12 was my first full year as Chief Executive of the MRC, and I have recently been taking stock of some of the MRC’s broader scientific and strategic achievements and impacts from the past year.

Scientifically, a key focus has been on harnessing the power of electronic NHS patient data for research to secure the UK’s future as a world leader in this field and reap benefits for human health.

Recently we jointly invested £17 million with the nine biggest government and charity funders in the UK to link electronic health records with research data to unlock its enormous research value. The impact of this is unlikely to be felt for some years, but you can read about the huge value of research involving patient data within these pages – for example, a study of samples from hospital patients has revealed a new gene variant which could help explain why flu becomes a life-threatening disease in some people while only having mild effects in others.

Strategically, working with industry has always been a priority for the MRC because commercial investment is crucial for turning our scientists’ discoveries into benefits for patients. In 2011/12 we further stepped up our collaboration with industry. We worked with the Government’s Technology Strategy Board to launch the £180m Biomedical Catalyst, which will support productive academic-industry partnerships to bring medical advances to patients faster. And we entered a landmark £10m collaboration with AstraZeneca to give MRC scientists access to 22 of the company’s compounds to advance our understanding of a broad range of diseases.

Throughout this year’s review you will see examples of how MRC research has underpinned the development of drugs, devices and diagnostics by the biotechnology and pharmaceutical industries – from successful clinical trials of a therapy for heart attack patients to early development of drugs for age-related macular degeneration.

Our discoveries are all about collaboration – not just with industry, but also with universities and charities and with the public, who volunteer for our research studies and whose taxes pay for our scientists’ world-class research. Ultimately, MRC research is about changing people’s lives. I hope you enjoy reading about some of the amazing MRC discoveries from the past year which will impact on our health, economy and society.
CONTENTS

Making an impact on health, the economy and society

Chapter 1
Leading research on the brain and mental health  Page 6

Chapter 2
Combating infection and boosting immunity  Page 12

Chapter 3
Promoting healthy lives  Page 18

Chapter 4
Fighting cancer  Page 24

Chapter 5
Targeting a healthy heart and circulation  Page 30

Chapter 6
Challenging diseases of body systems and senses  Page 36

Index:
MRC Strategic Aims  Page 42
Chapter 1
Leading research on the brain and mental health

Through increased funding for dementia research and mental illness and support for the UK Brain Bank Network, the MRC is as committed as ever to delivering excellent neuroscience and mental health research. The impact of this research covers the spectrum of neurodegenerative diseases and mental health conditions, from new treatments to social care.

With its grey plastic case and chunky buttons, the device on the table in front of Professor Alasdair MacLullich looks like something from a 1980s episode of Tomorrow’s World. Affectionately known as the ‘Delbox’, this is the first computerised test specifically designed for detecting delirium. To the uninitiated, the word delirium might sound like a Victorian malady, a disease confined to history books. But it’s a common modern-day problem and a major risk factor for dementia and death in the elderly. New ways of detecting and treating the condition are urgently needed.

Alasdair is a professor of geriatric medicine. His interest in this area was sparked during his PhD, which looked at the link between stress hormones and cognitive impairment in the elderly. More recently, an opportunity for further research came along when Alasdair was awarded an MRC Clinician Scientist Fellowship.

“That was when I really changed tack to start doing delirium research. As a clinician I’d noticed that delirium was a problem, it was very common and yet it had hardly been touched by research — and I was lucky enough to get an MRC fellowship to investigate it,” he says.

Having time away from being a busy hospital doctor allowed Alasdair the thinking space to come up with ways to understand and measure delirium, and to distinguish patients with delirium from those with dementia. He homed in on the fact that delirium sufferers cannot focus their attention for more than a few seconds, whereas a dementia patient usually can, even if brain functions such as memory are severely impaired.

Alasdair enlisted the help of a toy maker and electronic engineer to make a prototype Edinburgh Delirium Test Box, or Delbox.

The device is a simple box with two buttons (taken from a fruit machine) which flash on and off. The researcher sets the number of flashes and the timing between them and the patient is asked to count the number of flashes. Alasdair and colleagues deliberately made the design ‘retro’, in appearance so that it would feel more familiar and acceptable to the elderly patients being tested.

“It’s still got a ‘workshop in the back garden’ appearance to it,” says Alasdair. “It’s funny because I also work in the labs at the Queen’s Medical Research Institute where people do very sophisticated things like genome-wide association studies. When they see my device they’re sort of thinking so…is this it?

“But I think we have to fit our science to the problem here, not to some kind of spuriously sophisticated concept. Can delirium patients count the number of flashes or not? No they can’t. Can people with dementia do it? Generally, yes.”

Delirium affects around one in eight hospital patients, but it’s most common in older people. It can come on within hours or days after surgery or infection, or as a result of drug side-effects, and lasts for anything from hours to several months.

Alasdair explains: “Delirium’s a serious problem. That’s not just because it affects outcomes like death, institutionalisation and length of hospital stay — which obviously carry an economic burden — but also because it’s very distressing for the patient. They can have vivid, horrible hallucinations. I treated one lady who thought she was tiny and that people around her were giants. Others see blood coming out of the walls or crocodiles swimming around their beds. There’s actually evidence that people get post-traumatic stress disorder afterwards.”

Soberingly, there’s also emerging evidence that delirium is associated with an eight-fold risk of developing dementia in the future, a raised risk of losing the ability to live independently and increased risk of death.

“These patients are actually getting brain injury – which is quite a stark and alarming concept. The scale of it is so enormous that the research community is talking about this being important for secondary or even primary prevention of dementia. So if we can get a hold of what delirium is, detect it and then use this to improve patient care, we might even be able to prevent some cases of dementia.”

A critical step towards this goal will be to improve measurement of delirium, so the Delbox has attracted interest from delirium researchers worldwide. Ultimately the device could help to improve clinical detection of delirium presently only 20 per cent of cases are picked up. With the help of an MRC Development Pathway Funding Scheme grant, and support from the University of Edinburgh, Alasdair is working on further prototypes and getting them commercialised. Plans are afoot to develop a software version of the test which could be downloaded to a PC or iPad.

“I see the value of using the business route to get money in to help fund research,” says Alasdair. “I want to be involved in problem solving, getting it out there and helping people to use the device if they want to. If it makes money I’ll be happy with that — it’s good for the university and good for our country.”

PROFILE: Professor Alasdair MacLullich, University of Edinburgh
Alzheimer's genes discovery gives hope to half a million

An international consortium of researchers, led by the MRC Centre for Neuropsychiatric Genetics and Genomics at Cardiff University, has identified five new genes that increase an individual’s risk of developing Alzheimer’s disease – doubling the number of genes previously known to be associated with the disease.

The genes they identified are involved in regulating the immune system, the ways the brain processes cholesterol and fat, and a process called endocytosis, a specific cellular process that has never before linked to Alzheimer’s before. The team identified four genes that control this very precise process, which is a major indication that this plays a strong role in the development of Alzheimer’s disease.

The research, which was co-funded by the MRC, the Wellcome Trust, Alzheimer’s Research UK, and the Welsh Assembly Government, is another step forward in the quest to find a cure for this debilitating disease, which costs society more than heart disease and cancer combined.

Professor Julie Williams, who led the study, said: “The jigsaw is beginning to come together. If we can remove the bad effects of these genes through treatments, we may help reduce the number of people developing Alzheimer’s in the future. For example, if we could combat all the negative effects of the 10 genes that have now been identified in combination, we could eradicate 60 per cent of cases of the disease.”

Insights on the anxious brain

An international team of neuroscientists, including MRC researchers, have made a breakthrough in understanding how the brain responds to highly stressful and traumatic events.

Studies in mice showed that the part of the brain involved in emotions, the amygdala, reacts to stress by increasing production of a protein called neuropsin.

This triggers a series of chemical reactions which causes increased activity in the amygdala, and in turn switches on a gene which causes increased production of amyloid beta.

When mice were treated with BTC, there was a significant increase in amyloid beta levels. By analysing this and employing their new techniques, the hope is that this feedback will help bring this activity down to a lower, more manageable level.”

CID drugs could also prevent Alzheimer’s

Scientists part-funded by the MRC have identified two antibodies which could help block the onset of Alzheimer’s disease in the brain. The antibodies, ICSM-18 and ICSM-35, are already known to play a crucial role in preventing ‘protein misfolding’, the main cause of Creutzfeldt–Jakob disease (CJD, the human form of mad cow disease).

The team working at the MRC Prion Unit at University College London demonstrated, using mice, that these antibodies could block damaging effects on brain tissue caused by a toxic substance called amyloid beta. In neurodegenerative diseases like CJD and Alzheimer’s, amyloid beta becomes cumulatively attached to the surface of nerve cells in the brain, stopping them from communicating effectively and causing memory loss. The results showed that the antibodies stopped the amyloid beta proteins from taking hold and damaging the brain.

Professor John Collinge, who led the study, said: “There is an urgent need for new drugs which will help to preserve brain function and prevent memory loss. If our studies in mice are replicated further down the line, these antibodies may have a dual role in treating both CID and Alzheimer’s disease.”

Boosting brain repair

MRC scientists have discovered that a protein produced by blood vessels in the brain could be used to help the brain to repair itself after conditions such as stroke, traumatic brain injury and dementia.

The protein, called betacellulin (BTC), was found to boost brain regeneration in mice by stimulating brain stem cells to multiply and form new nerve cells (neurons).

Most neurons in the adult brain are formed while we are in the womb, but new neurons continue to be generated throughout life by stem cells. These stem cells are controlled by signals, including BTC, that dictate how fast they divide and the type of cell they become. But when the brain is injured, the stem cells stop switching from neuron production to make more of a type of cell called glial cells, leading to the formation of scar tissue.

When mice were treated with BTC, there was a significant increase in stem cells in their brains, leading to the formation of many new neurons. In contrast, when mice were given an antibody that blocks BTC activity the production of new neurons was suppressed.

Dr Robin Lovell-Badge from the MRC’s National Institute for Medical Research (NIMR), who led the research, said: “We hope that our new findings add to the arsenal of exciting approaches coming out of stem cell biology that might eventually lead to better treatments for damaged brains.”

Easing the pain

People who have spinal or nerve damage often experience pain in their limbs where there is no actual physical source of pain. This condition, known as neuropathic pain, is created by the brain.

In order to combat the effects of intense chronic pain on the body, researchers funded by the MRC have been examining whether neurofeedback training might help. Neurofeedback is a form of ‘brain training’ in which a person becomes aware of their brainwave patterns with the aid of an electroencephalogram (EEG) machine which helps them to manipulate and control the brainwaves at will.

The University of Glasgow’s Dr Aleksandra Vuckovic, who led the project, said: “Neuropathic pain usually happens because the brain is not receiving the normal sensory signals from the affected body part, so the brain over-compensates. When someone is in severe pain, EEG recordings reveal a lot of corresponding activity in the brain. By analysing this and employing our new techniques, the hope is that this feedback will help bring this activity down to a lower, more manageable level.”
Tailoring childhood anxiety treatment

MRC-funded research has led to the discovery of a genetic marker that can be used to predict whether a child suffering from anxiety disorder will benefit from cognitive behaviour therapy (CBT).

Dr Thalia Elly from the MRC Social, Genetic and Developmental Psychiatry Centre and colleagues at the Institute of Psychiatry at King’s College London collected DNA from 359 children diagnosed with anxiety disorder, which affects around one in twenty children in the UK. Those found to have a shorter version of a genetic marker called Serotonin Transporter Promoter Polymorphism (SHTPP) were 20 per cent more likely to respond to CBT and to be free of their anxiety six months after the end of their treatment.

Dr Elly said: “Childhood anxiety is beginning to be recognised as a serious health problem. CBT has been shown to help individuals think about the world around them and to experience their environment in a more healthy, positive way and hopefully stem the impact of anxiety before it gets worse in adulthood.

“Our study showed that having a short form of the gene, which can contribute to a child feeling more negative when things are stressful, may have a positive flipside, in that they are more responsive to the positive messages taught in CBT.”

The paper in which these findings were published won Macquarie University’s Excellence in Research Award 2011 for social sciences, business and humanities.

Guiding treatment of Alzheimer’s disease

Research has suggested that a drug could help many more Alzheimer’s disease patients than previously thought. Around 750,000 people in the UK and 18m worldwide have Alzheimer’s disease, a form of dementia where people suffer problems with memory, mood changes, communication and reasoning. There is no cure for Alzheimer’s but some drugs can relieve symptoms.

The drug donepezil is already widely used to treat Alzheimer’s disease in its mild to moderate stages. Doctors are currently advised to stop prescribing donepezil when the disease progresses, as there has been no clear evidence of the treatment continuing to benefit patients.

Research funded by the MRC and the Alzheimer’s Society, and led by Professor Robert Howard at the Institute of Psychiatry at King’s College, London, has now shown that donepezil can help people with moderate to severe Alzheimer’s. In fact, the benefits of treatments were greater than those previously seen in patients with less severe disease.

Professor Howard said: “As patients progress to more severe forms of Alzheimer’s disease, clinicians are faced with a difficult decision as to whether to continue or not with dementia drugs and, until now, there has been little evidence to guide that decision. For the first time, we have robust and compelling evidence that treatment with these drugs can continue to help patients at the later, more severe stages of the disease.”

“This study set a benchmark for autism research and there has been international interest in adopting the approach”

“These drugs can continue to help patients at the later, more severe stages of Alzheimer’s disease.”

Helping autistic children communicate

Children with autism find it hard to communicate socially. Parents often don’t know how to interact with an autistic baby who doesn’t make eye contact or learn to talk as healthy children do, and may be perplexed as to how to respond to their seemingly aloof behaviour. The child may become increasingly isolated from the world around them.

Professor Jonathan Green and colleagues at the University of Manchester have come up with a way of helping parents communicate effectively with their autistic child. Using video feedback, parents are taught how autistic children communicate, and then how to re-establish enjoyable interactions with their children, such as looking at things together.

As the child progresses, parents learn strategies to improve language development, for example using familiar repetitive language and action routines.

An MRC-funded trial involving 152 autistic children showed that the technique was very successful in increasing effective communication between parent and child. Because the technique requires fewer sessions with a therapist, it is cost effective compared with conventional treatment and is now being adopted by services within the NHS.

Professor Green says: “This study set a benchmark for autism research and there has been international interest in adopting the approach, with implementation now beginning in Asia. The next step will be to find ways to generalise the effect – to help autistic children’s social communication not only with their parents but also in the outside world.”

Computerised programme for ‘brain re-hab’

Cognitive Remediation Therapy (CRT) improves cognition (mental processing skills such as attention, memory and decision-making) and social functioning in patients diagnosed with schizophrenia, but because it relies on intensive interaction with a therapist, so far its use within the NHS has been limited.

CRT works by setting patients different tasks that help improve their memory, planning skills and ability to switch their response according to context (cognitive flexibility). In a project funded through the MRC’s Developmental Pathway Funding Scheme, Dr Clare Reeder at King’s College London has been studying a computerised alternative to CRT known as CIRCuiTS to see if it is a viable, effective treatment option.

Dr Reeder said: “Computerised CRT not only relieves pressure on the extremely limited access to therapists, but offers a package that is specifically designed for schizophrenia. CIRCuiTS is a new, graphically and functionally sophisticated computerised CRT programme which closely approximates ‘real life’ CRT. It’s driven by clear theoretical principles and relies on well-researched training techniques for schizophrenia. CIRCuiTS still relies on working with a therapist but it also allows patients to work independently, reducing the amount of contact they need to have with a therapist.”

The software is now complete, but it still needs to be tested for feasibility and acceptability to patients and clinicians. The study will arm clinicians, therapists and researchers with the evidence to assess how CRT can be best implemented into schizophrenia patients’ wider course of treatment.
Chapter 2
Combating infection and boosting immunity

Understanding what goes wrong when our natural defences fail is vital for developing new therapies for infections like flu and HIV, and diseases such as asthma and rheumatoid arthritis. Through investment and partnership with industry and universities, and working on the global stage, the MRC is making some exciting discoveries.

Not many MRC scientists have parachuted into icy cold oceans or researched the best way to escape from a wrecked submarine. But as a Royal Navy doctor, Chris Grainge has done both. When he’s not jumping out of planes, Chris is a respiratory medicine consultant at Southampton Hospital. Last year his MRC-funded research led to a new way of thinking about asthma which could help us use asthma drugs more effectively.

Although Chris’s medical and naval training saw him work as medical officer onboard a warship in the Caribbean and an icebreaker in Antarctica, his first love is working on the respiratory medicine wards. That’s because he gets to work with people of all ages with very different diseases. On a typical day he might see a young person with cystic fibrosis, an adult who has occupational lung disease or an older person with lung cancer or emphysema.

“I’m very fortunate in that I get to do research and clinical work,” he says. “Research is fantastically stimulating, but it can also be very frustrating. The highs are higher and the lows are lower. On the clinical side, I can work with patients from when they come in casualty, very sick with respiratory failure, right through to seeing them again in outpatients when they’re better – that’s very satisfying.”

One of the most common respiratory diseases seen by specialists like Chris is asthma. Nearly five and a half million people in the UK are currently being treated for the disease.

In asthma patients, muscle tissue around the airways contracts and makes the airways narrower, causing wheezing, shortness of breath and coughing. For most people, these symptoms are easily kept in check with inhalers. But people with chronic asthma are harder to treat. Over time the walls of the airways get thicker and produce more mucus: a process called airway remodelling. This can progress to a more serious and difficult to treat disease where there’s destruction of the lung.

It’s long been thought that this long-term decline in lung function is due to airway inflammation caused by allergies or infection. But Chris and his research team suspected that this was only half of the picture.

“What we thought was, well maybe it’s actually the airway narrowing, the fluctuation in the size of the airway that’s important. We know that lots of tissues in the body are mechanically sensitive – so for example if you lift weights your arm gets bigger, and if you jump up and down a lot your bones get stronger. So we thought if these tissues are mechanically responsive, why not the airway?” he explains.

With MRC funding, the researchers designed a study to find out. Asthma patients volunteered to be exposed to various substances to make their asthma slightly worse. Some were treated with a substance which narrows the airways but doesn’t cause inflammation. Others breathed in house dust mite allergen to cause inflammation in their lungs, and the control group breathed in harmless saline solution.

When the team studied lung tissue samples from the patients they saw no difference between the group in which the airways had been narrowed and the group in whom the airways had been inflamed.

“That was a big moment,” Chris explains. “The airway wall had thickened and the airway was producing more mucus, and was showing early signs of remodelling in both groups. So from that we concluded that airway inflammation wasn’t necessary for the remodelling we see in asthma patients, and that airway narrowing on its own can cause it.”

The impact of these findings is significant because it changes the established theory that airway remodelling over time is caused by repeated episodes of inflammation. It could explain why giving asthma sufferers high doses of anti-inflammatory drugs hasn’t been able to stop airway remodelling in the long term.

Chris says: “We know that inflammation is very important in asthma. But what people haven’t considered so much in the past is that the act of wheezing, the way that the airway narrows, can lead to long-term changes. So now we need to think about both controlling the airway narrowing and inflammation.”

Comparatively few asthma patients have chronic disease, but the cost of treating these patients is vast. So a better understanding of how to treat them could have an economic impact as well as improving their quality of life.

“Chronic asthma is a very disabling condition; sufferers find it hard to hold down a job or pick the kids up from school. So we want to try and make these lives better, but if we can find better treatments it will also help to reduce the healthcare burden on society,” says Chris.

The researchers’ next challenge will be to understand how airway narrowing leads to long-term lung damage, and then to carry out clinical trials to see if existing drugs to block airway narrowing will prevent it.

There’s unlikely to be a one-size-fits-all solution, explains Chris. “Although we lump all difficult-to-treat asthma together, they have maybe five or six very different diseases and a treatment that works in one group won’t work in another. It may be that specific drugs will one day come out of the work that we’re doing, but it also means that we’ll be able to use the drugs we already have more effectively.”
A spanner in the works for HIV?

An HIV diagnosis is no longer a death sentence for those who have access to anti-retroviral therapies – but not everyone is so lucky, and research is still working towards finding a cure or a vaccine.

Now scientists at the MRC National Institute for Medical Research (NIMR), and the University of Manchester have moved a step closer to this goal. They’ve figured out how a protein in our bodies called SAMHD1 is able to prevent HIV from replicating inside a group of immune system cells called myeloid cells.

HIV’s mode of attack is to infect immune system cells. Once inside, it converts all genetic material, RNA, into DNA, and inserts it into the cell’s own DNA. The cell reads the DNA instructions to make many copies of the viral RNA and produce new viruses. These infect and kill other cells, ultimately damaging the patient’s immune system.

The researchers have discovered that SAMHD1 is able to degrade one of the key building blocks needed for making new copies of the virus: deoxynucleoside monophosphates. This opens up the possibility of creating new drugs – or perhaps even a vaccine – which imitate this biological process and stop the virus from replicating inside myeloid cells.

The NIMR’s Dr Ian Taylor explains: “The next step will be to define more precisely, at a molecular level, how the SAMHD1 protein functions. If we can achieve this, it will pave the way for new therapeutic approaches to HIV.”

Tricking malaria-carrying mosquitoes

Each year almost 800,000 people die from malaria – a disease caused by a tiny parasite passed on through mosquito bites. One tactic being explored by malaria researchers to prevent these deaths is to genetically interfere with mosquito breeding, in the hope that controlling their numbers might limit the spread of the disease.

An MRC-funded study at Imperial College London has exposed an Achilles’ heel in mosquito mating behaviour: it seems that a female mosquito can’t tell if the male she has mated with is fertile. The research showed that females who mated with sterile male mosquitoes made no attempt to find another mate. As female mosquitoes mate only once in their lifetime, this meant they effectively missed out on the opportunity to reproduce.

This finding has stoked hopes that it might be possible to control mosquito numbers in future by introducing a genetic change that makes the males sterile, says lead scientist Dr Francesca Cattaneo. “The ability to genetically control the mosquito might offer a low-cost and effective method of preventing malaria in Africa. If this strategy is to work, we have to be sure that the insects continue to mate as normal, unaware that we have interfered with their sexual functions. This study suggests that is possible.”

Towards a universal flu vaccine

The flu virus is very good at mutating to outwit our immune system, so vaccine manufacturers are constantly playing catch-up by having to produce a new seasonal vaccine each year. Occasionally a strain will emerge for which we don’t have a vaccine and it’s impossible to predict exactly which ones might cause an epidemic. Now, MRC scientists have made a discovery which might ultimately lead to a universal vaccine capable of protecting us against all strains of the most common type of flu.

Researchers at the MRC National Institute for Medical Research (NIMR) in London, along with colleagues in Switzerland, have found an antibody called F16 which can bind to and inactivate all known types of the influenza A virus — the most common culprit behind flu in humans and animals. The antibody targets a region of the virus that does not readily mutate, suggesting that that region could be used to create a long-lasting universal vaccine.

The NIMR’s Professor Steve Gamblin, who co-led the research, explains: “As we saw with the 2009 pandemic, a comparatively mild strain of influenza can place a significant burden on emergency services. Having a universal treatment which can be given in emergency circumstances would be an invaluable asset.”

Discovery boosts fight against superbug

A breakthrough in the fight against drug-resistant infections is one step closer following the discovery of the structure of a key enzyme, NDM-1, which various forms of bacteria use to resist the most powerful antibiotics available.

MRC scientists at the Research Complex at Harwell, Oxfordshire, led by director Professor Simon Phillips, have produced a model of NDM-1, the genes for which can be passed from one strain of bacteria to another, allowing them to destroy antibiotics. The model will enable researchers and pharmaceutical companies to progress towards potential new treatments.

In recent years there has been growing concern that the usefulness of antibiotics could be coming to an end as the bacteria that cause disease become increasingly resistant to these drugs. Annually, more than 25,000 people in the EU die of bacterial infections that have been able to outmaneuver the newest antibiotics.

But, says Professor Phillips, scientists are on the case: “While there have only been around 70 cases of infection by NDM-1 bacteria recorded in the UK so far, there is no doubt of the importance of this new discovery for saving lives in the future. Knowledge of the enzyme structure is our first step in understanding how superbugs work and leads the way to the design of drugs that might prevent their action.”

Promising hepatitis C drugs in the pipeline

More than 170 million people – 3 per cent of the world’s population - are infected with the hepatitis C virus (HCV), which is a leading cause of liver-related deaths, organ transplants and liver cancer. The infection is difficult to treat effectively because the virus evolves quickly and develops resistance to drugs.

Scientists at Leeds University think they have found a way to keep the virus in check for longer. They’ve discovered details of how two prototype drugs – called p7-inhibitors – attack different parts of HCV, by targeting a protein that allows the virus to continue spreading. The study suggests these drugs could help to suppress hepatitis C when used together with other new direct acting drugs.

Dr Stephen Griffin, an MRC New Investigator Research Grant holder at the University of Leeds, who led the research, explains: “This new class of small molecule drugs, the p7 inhibitors, attack the virus directly. By learning how the hepatitis C virus reacts to these molecules, we can design drugs that are likely to be more effective for longer. We can also see how such drugs could be used together with other direct-acting drugs aimed at alternative viral targets, rather than individually or with drugs that work by boosting the immune system.”
Inflammation can heal

The discovery of a fundamentally different form of inflammation has opened up new avenues to develop drugs that aid healing and recovery from infecion.

MRC-funded researchers at the University of Edinburgh led by Professor Judith Allen have challenged existing understanding of inflammation by revealing that white blood cells already present in tissue are capable of carrying out a local response when tissue is damaged or infected. These cells can divide rapidly to build a protective layer without relying on arrival of other white blood cells from the bloodstream.

Professor Allen remarked: "Inflammation is often regarded as a 'bad thing', but by understanding how this local form works, we can improve our knowledge of how white blood cells control tissue damage. This could help in development of new drugs that either encourage local white blood cell division to help the body recover from infection or injury, or minimise it to prevent allergic reactions or scarring."

Gene map reveals MRSA weakness

Dr Ian Overton from the MRC Human Genetics Unit in Edinburgh has highlighted genes in the bacterium Methicillin-resistant Staphylococcus aureus (MRSA) that may help the superbug to survive treatment with antibiotics.

Overton and colleagues mapped 95 per cent of MRSA genes, enabling them to propose new roles for 22 genes in helping MRSA to cause disease. The gene ftnh was also singled out as a weak point for possible new drug development.

The team examined an antimicrobial agent derived from bullfrog skin, called Ranalexin, that kills MRSA. Computer analysis and laboratory tests found that Ranalexin works by weakening both the bacterial membrane and cell wall.

Dr Overton said: "Multidrug resistant Staphylococcal infections are a widespread problem. Our research could lead to a cheap, easy-to-apply treatment that eliminates the need for invasive surgery to improve the condition by fitting tiny ventilation tubes known as grommets. This is the most common operation in the UK; around 30,000 procedures are carried out each year."

Flu susceptibility gene discovered

Scientists have discovered a gene which influences how we respond to flu infection, which could help explain why flu becomes a life-threatening disease in some people while only having mild effects in others.

Those who carry a particular variant of a gene called IFITM3 are significantly more likely to be hospitalised when they fall ill with flu than those who carry other variants, the research team found.

The protein that the normal IFITM3 gene codes for plays a key role in protecting the body against flu infection. But when researchers sequenced the IFITM3 genes of 53 patients who had been hospitalised with flu, they found that some had a rare, mutated form of IFITM3. This variant gene codes for a shortened, less effective version of the IFITM3 protein, which makes cells more susceptible to viral infection.

Critical to the finding were clinical samples provided by the Mechanism of Severe Acute Influenza Consortium (MOSAIC) in England and Scotland, which is funded by the MRC, the Imperial College London National Institute for Health Research Comprehensive Biomedical Research Centre and the Wellcome Trust.

Cancer drugs could treat glue ear

Scientists from the MRC Mammalian Genetics Unit (MGU) in Oxfordshire have identified a potential new treatment for ‘glue ear’ – a common inflammatory condition in children that can cause temporary, but often prolonged, hearing loss.

The study showed that low doses of several existing drugs currently used in cancer treatment also relieve the symptoms of persistent ear inflammation in mice.

Professor Steve Brown, Director of the MGU, who led the research, said: "We found that one of the key factors in developing glue ear is a lack of oxygen reaching the middle ear. This lack of oxygen, known as hypoxia, appears to prevent the inflammation in the middle ear resolving, allowing fluid to build up, which can impair hearing."

"By using existing drugs that tackle the root causes of hypoxia, we have been able to significantly reduce hearing loss and the build-up of fluid in the middle ear of our mouse models. The fact that these drugs are already on the market means that the time and cost needed to develop them into a new treatment for glue ear could be dramatically reduced."

The research could lead to a cheap, easy-to-apply treatment that eliminates the need for invasive surgery to improve the condition by fitting tiny ventilation tubes known as grommets. This is the most common operation in the UK; around 30,000 procedures are carried out each year.

Improving TB immunisation

A new vaccine to combat tuberculosis (TB) is less effective for Gambian infants when administered at the same time as other childhood vaccines, results of a clinical trial have shown. The findings provide important evidence to guide the design of childhood immunisation schedules.

TB is a bacterial infection which kills 1.8 million people each year. The established vaccine against TB, Bacille Calmette-Guérin (BCG), offers only partial protection against the disease, so a new vaccine called MVA85A is designed to be given after the BCG to boost the body’s immune response and level of protection against TB.

But the study showed that, amongst four-month-old infants, the MVA85A vaccine is more effective when administered alone than alongside other childhood vaccines. MVA85A was safe and elicited a strong immune response in the children in the study, but results show that changes to existing immunisation schedules will maximise their effectiveness. Importantly, MVA85A had no effect on responses to other vaccines given at the same time.

Dr Martin Ota who led the study at the MRC Unit, The Gambia says: "These important results highlight that we have a real opportunity to make sure that children are protected in the future against tuberculosis by introducing effective and well-timed immunisation programmes."

“"The research could lead to a cheap, easy-to-apply treatment that eliminates the need for invasive surgery.”"
Chapter 3

Promoting healthy lives

Diet, education, genetics and lifestyle are just some of the factors that have an impact on our health and our risk of developing diseases like cancer or obesity. MRC scientists are working to understand more about how these factors come together to influence health and disease, making discoveries that can change the lives of individuals, communities and whole populations.

PROFILE: Dr Cari Free, London School of Hygiene and Tropical Medicine

In January 2012 the Department of Health launched an affordable mobile phone support programme for smokers, which has been proven to double quit rates. This programme was developed for UK patients by Dr Cari Free at the London School of Hygiene and Tropical Medicine (LSHTM) with MRC funding. Around 1,000 smokers are now signing up each month.

“Smoking cessation is one of the most cost-effective interventions you can make from a public health perspective because about half of people who smoke beyond the age of 40 will shorten their life as a result. The intervention represents a major cost saving to the NHS,” says Cari.

Txt2Stop could have an even bigger impact beyond our shores. The World Health Organization predicts that by 2030 the annual worldwide smoking death toll will have risen from six million to eight million, with the biggest rise occurring in poorer countries. With mobile phone usage widespread across the world, Txt2Stop could offer a low-cost and effective means of helping people in these countries to give up.

People particularly liked the messages where they got feedback about what they’d gained and how well they’d done. For example we sent messages saying ‘shortly after you start quitting your carbon monoxide level goes back to normal’ and then they’d receive a message at the point when their levels had returned to normal saying ‘well done’. One person said she was on the way to the shops to buy cigarettes when she got that message and then turned around and went home again.”

The research team thinks the text message support works by helping to sustain people’s motivation at times when their resolve is weaker, and through providing contact and support over a 24-hour period. For example, trial members could text the word CRAVE to receive a supportive message when they were struggling with craving.

“The peak of a cigarette craving only lasts for a minute, so part of the idea behind that message was whilst you’re texting, waiting for the message to arrive and then reading it, you’re not smoking – and by that point, the craving has usually subsided,” explains Cari.

Txt2Stop was equally effective for all age groups and across all levels of addiction and its benefits were so immediately clear that the Department of Health launched the programme on the NHS smoking website earlier this year.

“Smoking cessation is one of the most cost-effective interventions you can make from a public health perspective because about half of people who smoke beyond the age of 40 will shorten their life as a result. The intervention represents a major cost saving to the NHS,” says Cari.

Txt2Stop could have an even bigger impact beyond our shores. The World Health Organization predicts that by 2030 the annual worldwide smoking death toll will have risen from six million to eight million, with the biggest rise occurring in poorer countries. With mobile phone usage widespread across the world, Txt2Stop could offer a low-cost and effective means of helping people in these countries to give up.

People said that it was like having somebody at your side reminding you that you were going to quit and why you were doing it – and the tone of the messages was definitely set up to be supportive in that way,” says Cari.
Smoking hastens slide into dementia

Chain-smoking cigars may appear to have helped Colombo’s sleuthing skills, but research suggests that ageing male smokers lose cognitive skills such as memory earlier than non-smokers.

Scientists from University College London studied information collected across 25 years from more than 5,000 men and 2,000 women who were part of an MRC-funded study of thousands of British civil servants.

During the transition from mid-life to old age, the men in the study who smoked showed a faster decline in cognitive abilities – skills such as memory, attention and verbal fluency – than those who had never smoked. Men who carried on smoking throughout the 25-year period showed the greatest decline, but even those who had quit during the decade before the first cognitive tests declined faster than those who had always shunned cigarettes. No such link was seen in women in the study, possibly because of their tendency to smoke smaller amounts of tobacco.

Dr Séverine Sabia, who led the research, explains: “Smoking is increasingly being linked with dementia in the elderly, contributing to the burgeoning number of dementia cases as our population ages. Public health messages about smoking must continue to target all ages.”

Low-cost drug triples smoking quit rate

A drug called Tabex® whose active ingredient, cytisine, comes from the seeds of the laburnum tree, could provide a cheap and effective way to help people give up smoking.

A clinical trial funded by the National Prevention Research Initiative, a consortium managed by the MRC, found that Tabex® can more than triple the chance of someone quitting smoking for 12 months compared with a placebo. In a trial of 748 people, 8.4 per cent of those who took Tabex® abstained from smoking for a year, compared with just 2.4 per cent who were given a placebo.

What’s more, Tabex® costs the equivalent of just £1.50 for a month’s supply in countries such as Russia, where it has been available for years. The trial is the first time that researchers have gathered robust clinical evidence on the effectiveness of Tabex®.

Professor Robert West from the University College London Department of Epidemiology and Public Health, who led the study, said: “With more than a billion smokers worldwide and lung cancer still one of the top killers, we’re extremely encouraged that the benefits of Tabex are comparable with those of other smoking cessation treatments, but at a fraction of the cost.”

Weight at 18 linked to cancer decades later

Many people have ‘puppy fat’ as a teenager, but research suggests that carrying excess weight in our late teenage years poses more of a long-term health risk than we might think.

Public health researchers from the MRC/CSO Social and Public Health Sciences Unit (SPHSU) in Glasgow have discovered a link between men being overweight or obese at age 18 and death from cancer in later life. This link was apparent even if people reduced their weight during middle age.

The MRC researchers collaborated with colleagues at University College London and Harvard School of Public Health to analyse the medical records of around 20,000 male graduates who attended Harvard between 1916 and 1950.

They found that the men in the study who had the highest body mass index (BMI) at age 18 were 35 per cent more likely to die from cancer than those with lower BMIs. The associations between weight and cancer were particularly strong for lung, skin, oesophageal and urogenital (kidney, bladder, prostate and testicular) cancers.

SPHSU’s Dr Linsay Gray, lead author of the study, says: “The message here is really clear: keeping your weight healthy as a young adult can significantly reduce your chance of developing cancer. These findings point worryingly to a greater future burden of cancer.”

Caesareans on the rise among affluent

Research has shown that better off mothers in Scotland are more likely to have their babies by planned Caesarean section than mothers living in poorer circumstances. Emergency Caesarean sections, however, are equally distributed across the social spectrum.

The findings mark a sea change in practice compared with 30 years ago, when those from poorer backgrounds were more likely to have Caesarean sections, both planned and emergency.

Researchers from the MRC/Chief Scientist Office Social and Public Health Sciences Unit in Glasgow used patient records of more than 350,000 mothers in Scotland and examined who gave birth by Caesarean section in different time periods spanning 20 years. They then investigated the social class of the mothers who underwent the procedure and the level of deprivation of the area they lived in.

Lead scientist Ruth Dundas says: “The disappearance of social trends for emergency Caesarean section reflects increased equality in healthcare. However this does not explain the differences seen for elective section rates. It is important to ensure that the clinical decision-making process is the same for all women, regardless of their background.”
Breastfeeding makes for a feisty baby

‘Breast is best’ as the public health message goes, but research shows that while this advice holds true, breast-fed babies may actually be more irritable than their bottle-fed counterparts.

A study of 316 babies aged three months showed that those who were breast-fed cried more and were harder to soothe than babies who were fed formula. But the study authors believe this irritability is a natural part of communication between mothers and babies, and that formula-fed babies are unusually quiet and placid.

Lead researcher Dr Ken Ong, of the MRC Epidemiology Unit in Cambridge, says these findings should not deter mothers from breastfeeding: “Bottle-fed babies may appear more content, but research suggests that these infants are often over-nourished and gain weight too quickly.

“Rather than being put off breastfeeding, parents should be given more realistic expectations of normal infant behaviour and should receive better understanding and support to cope with difficult infant behaviours if needed.”

Pregnancy diet affects child’s future weight

A great deal of resources are being invested in tackling the rising tide of obesity and related chronic diseases worldwide. But research suggests that we might need to take action before we’re even born.

According to an international research study part-funded by the MRC, a mother’s diet during pregnancy can alter the function of her child’s DNA and lead to the child laying down more fat.

The study, published in the journal Diabetes, measured epigenetic changes in nearly 300 children at birth and showed that these strongly predicted the degree of obesity at six or nine years of age. The researchers discovered that this process, called epigenetic change, is independent of both how fat or thin the mother is, and of the child’s weight at birth.

The MRC Lifecourse Epidemiology Unit’s Professor Keith Godfrey, who led the study with colleagues at the University of Southampton, says: “We have shown for the first time that susceptibility to obesity cannot simply be attributed to the combination of our genes and our lifestyle.

“This study indicates that measures to prevent childhood obesity should be targeted on improving a mother’s nutrition and her baby’s development in the womb. Among other potential applications, epigenetic measurements might prove useful in monitoring the health of the child.”
The MRC works to improve the health of people in the UK and around the world by supporting excellent science and training the very best scientists. Our research also contributes to economic growth by creating and expanding companies, attracting investment to the UK and generating new medical advances which change people’s lives.

£900 million additional research funding has been drawn in from the private sector or international sources since 2006 thanks to MRC research.

70

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

£900 million additional research funding has been drawn in from the private sector or international sources since 2006 thanks to MRC research.

£900 million additional research funding has been drawn in from the private sector or international sources since 2006 thanks to MRC research.

In 2011/12 we spent £759.4m on research and worked with the Government’s Technology Strategy Board to launch the £180m Biomedical Catalyst which will support productive academic-industry partnerships to bring faster benefits to patients.

Our research has enhanced and influenced more than 200 international clinical guidelines, including 40 UK NICE guidelines, since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

We currently invest more than £40m each year on research into neurodegeneration. In 2011/12 we spent over £18m on dementia research alone, to help our increasingly elderly population live longer and healthier lives and reduce the economic burden that dementia places on society.

In 2011/12 we spent £759.4m on research and worked with the Government’s Technology Strategy Board to launch the £180m Biomedical Catalyst which will support productive academic-industry partnerships to bring faster benefits to patients.

We currently invest more than £40m each year on research into neurodegeneration. In 2011/12 we spent over £18m on dementia research alone, to help our increasingly elderly population live longer and healthier lives and reduce the economic burden that dementia places on society.

£900 million additional research funding has been drawn in from the private sector or international sources since 2006 thanks to MRC research.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.

More than 70 new treatments, diagnostic techniques/devices and initiatives stemming from MRC research have been launched onto the market since 2006.
Chapter 4
Fighting cancer

More than one in three people in the UK will develop some form of cancer during their lifetime. The MRC works with partners in industry, charities, the NHS and government to fund and carry out critical research aimed at preventing, understanding and fighting cancer. Better treatments are being developed, detection rates are going up and the number of people dying from the disease is decreasing year on year: our research is not only saving lives but also saving the NHS money.

With MRC funding, Wiebke and her colleagues carried out a trial of 45 patients who were known to have adrenal cancer that had spread and compared them with 100 patients who had adrenal tumours that turned out to be benign nodules.

“We ran GC/MS tests on their urine collected over 24 hours and analysed the results. This revealed that there is a specific ‘steroid fingerprint’ for adrenal cancer in the urine of some of the molecules that go on to become a steroid hormone, and these so-called precursors are not detectable in the blood. This work, funded with a biomarker grant from the MRC, has shown that the test detects the malignancy with 90 per cent sensitivity and specificity.”

This discovery will have a huge impact for patients and for the NHS because it offers the possibility of replacing expensive scans with a quick, simple urine test. A big research study is about to start to see whether the test can be transferred to a faster type of technology called high-throughput LC/MS, which could rapidly analyse urine for up to 10 steroids in less than five minutes.

“In theory, the patient could just bring the urine to the clinic and in the afternoon we would already know whether the fingerprint for malignancy is in their urine or not,” explains Wiebke. “This would also avoid the need for expensive top-to-toe CT scans to check for cancer recurrence in patients who’ve had an adrenal cancer removed, as the urine test may prove to be more sensitive than imaging. Our team are currently studying whether this is the case.”

Together with diagnostics company Bioscience Ventures, Wiebke and her team are carrying out a prospective study of the test and hope to launch it as a diagnostic product in 2013.

“The MRC biomarker grant funding was critical to the translation of my ideas to clinical application because it funded a biochemist, a mass spectrometrist who did the analysis and a computer science postdoctoral researcher who did the computational analysis. So it was absolutely key to the development of the test,” says Wiebke.

“For me, the highlight of my work is to combine clinical practice with discovery research and translational research that has lab aspects and clinical aspects to it. It’s incredibly satisfying because you can see something through from the start to the finish, such as with the adrenal tumour test, and hopefully end up helping more patients than you could ever hope to treat in your career.”

Cancer of the adrenal glands is hard to detect because the glands are hidden deep inside the body and the disease can be symptomless in its early stages — so new diagnostic tests are urgently needed. In 2011, with MRC funding, Professor Wiebke Arlt developed the first urine test for adrenal cancer which could replace expensive CT scans and avoid the need for surgery in suspected cases that turn out to be benign.

Weibke is fascinated by hormones — in fact she’s built her career around studying them. Early on in her career, as a young doctor in Germany, she was the first to establish that male hormones (androgens) affect libido and feelings of wellbeing in women. During a trial to restore these hormones in women with androgen deficiency she began to receive thank-you gifts of flowers and wine from their husbands, which she says “was an early sign of what was going on.”

She’s been hooked on endocrinology (hormone research) ever since and today she is head of the Centre for Endocrinology, Diabetes and Metabolism at the University of Birmingham. One of her particular interests is a group of hormones called steroids, which are made by the adrenal glands that sit just above our kidneys.

It was while studying rare conditions caused by under- or over-production of steroid hormones that Wiebke came up with the idea of using a technique called gas chromatography/mass spectrometry (GC/MS) to measure the individual steroid hormones in the body.

Weibke realised that this technique might also be useful for diagnosing cancer of the adrenal glands, because she had a hunch that adrenal cancer cells might lose the ability to produce normal levels of steroid hormones. She wanted to see if it was possible to distinguish adrenal cancer patients from healthy people by measuring the products of hormones broken down by the body and excreted in urine.

“In the UK a lot of imaging is done for people who complain of non-specific tummy pain, and during these procedures we often discover nodules on the adrenal glands. In a small number of cases a nodule can turn out to be cancer and needs to be taken out. But diagnosis takes multiple tests and CT scans, and that can mean huge costs,” explains Wiebke.

“Also, up to 60 per cent of surgical removals of large adrenal nodules end up revealing that the nodule is benign. So in the vast majority of these cases, a urine test would completely avoid the need for expensive surgery and the associated risks to the patient,” she adds.

“Typically, the patient could just bring the urine to the clinic and in the afternoon we would already know whether the fingerprint for malignancy is in their urine or not,” explains Wiebke. "This would also avoid the need for expensive top-to-toe CT scans to check for cancer recurrence in patients who’ve had an adrenal cancer removed, as the urine test may prove to be more sensitive than imaging. Our team are currently studying whether this is the case.”

Together with diagnostics company Bioscience Ventures, Wiebke and her team are carrying out a prospective study of the test and hope to launch it as a diagnostic product in 2013.

“The MRC biomarker grant funding was critical to the translation of my ideas to clinical application because it funded a biochemist, a mass spectrometrist who did the analysis and a computer science postdoctoral researcher who did the computational analysis. So it was absolutely key to the development of the test,” says Wiebke.

“For me, the highlight of my work is to combine clinical practice with discovery research and translational research that has lab aspects and clinical aspects to it. It’s incredibly satisfying because you can see something through from the start to the finish, such as with the adrenal tumour test, and hopefully end up helping more patients than you could ever hope to treat in your career.”
Removal of the SMG-1 gene in planarian worms caused their normal cell division to go out of control, leading to lethal, tumour-like growths. The research suggests that SMG-1 may act as a ‘brake’ on growth which, if confirmed in humans, could be exploited to develop new treatments for cancers and conditions related to ageing.

The researchers think that SMG-1 acts by suppressing a signalling pathway inside cells which is known to drive the development of many human cancers and conditions related to ageing.

Lead scientist Dr Aziz Aboobaker explained: “We’ve discovered that the SMG-1 gene and the mTOR signalling pathway, a well-known regulator of animal growth, act in harmony to exert tight control over growth and regeneration in planarians. Crucially, if this control is removed we see hyperactive cell division and the formation of tumours, which eventually kill the worms. This suggests that SMG-1 is a potential tumour suppressor gene we were previously unaware of.”

**Worming our way towards a treatment**

Scientists funded by the MRC and BBFSC at the University of Nottingham have identified a gene in a simple water-dwelling worm that might play an important role in the development of cancer.

**Leukaemia clue from bone marrow research**

Researchers have stumbled across an important clue as to why some leukaemias develop, while studying a rare bone marrow disorder.

Blood cells are made in our bone marrow, and failure of the bone marrow can increase a person’s chances of contracting some forms of leukaemia (cancers of the blood).

**A targeted drug for blood cancer**

Multiple myeloma is a blood cancer, affecting white blood cells. It carries a bleak prognosis, and patients generally only survive for around six years after diagnosis.

In the search for new treatments, researchers have long been interested in a protein called NF-κB, which activates white blood cells to fight off infections. In multiple myeloma, NF-κB goes away and helps cancerous cells to survive. But because NF-κB controls proteins that do many other important jobs in the body, scientists haven’t been able to find a way of blocking the cancer-causing aspects without also switching off other functions critical to keeping us alive.

Imperial College London’s Professor Guido Franzoso may have found the answer. He’s discovered a particular protein under NF-κB’s control which is found at much higher levels in cancer cells compared with healthy cells. With an MRC Developmental Pathway Funding Scheme grant, he’s developed a drug which blocks interaction between this protein and its cellular partner. In studies, the drug eliminated human myeloma tumour tissue transplanted into mice with zero effect on the surrounding healthy cells. The next step will be to start clinical trials in cancer patients.

Professor Franzoso is very excited about the results: “In animal models we’ve shown that this drug doubles lifespan compared with the control. And we may have also uncovered a new pathway that could help us find drugs for other diseases in which NF-κB is involved.”

**Fighting drug-resistant prostate cancer**

Prostate cancer cells depend on male hormones (androgens) to grow. So certain drugs for prostate cancer work by interfering with a protein designed to recognise androgens inside the cell—the androgen receptor.

Unfortunately, in some patients, mutations occur over time in cancer cells which change the androgen receptor and these hormone-blocking drugs no longer work.

Professor Craig Robson at the University of Newcastle has led a project co-funded by the MRC and pharmaceutical giant AstraZeneca to develop potential new prostate cancer drugs for these drug-resistant patients. Results so far have been promising—shrinking human prostate cancer tumours transplanted into mice. Now the drugs are being tested in clinical trials in cancer patients.

Professor Robson explains: “The androgen receptor protein is important in every stage of prostate cancer—all the way through to a late-stage form of the disease called castrate-resistant prostate cancer, in which patients no longer respond to anti-androgen treatments.

We are trying to develop new drugs that selectively target patients who have a mutation in their androgen receptor as a consequence of their first treatment. If the drugs we are evaluating in clinical trials are shown to be effective, we hope to be able to bring them to patients within the next two to three years.”
Extending life for ovarian cancer patients

Ovarian cancer is the sixth most common cancer in women in the UK and survival rates are poor. So it was welcome news when the first drug in 15 years to offer an improvement in survival rates for ovarian cancer was approved for use in Europe in January 2012, following promising findings from a major MRC-sponsored trial.

First results from the large-scale ICON 7 trial showed that adding the drug bevacizumab to chemotherapy for ovarian cancer can slow down the disease and may improve overall survival in women at high risk of recurrence.

More than 1,500 women took part in the study, which found that bevacizumab delayed progression of the disease by an average of two months compared with standard chemotherapy and by almost six months in women with the most aggressive cancers.

The drug, made by Roche, works by blocking the development of new blood vessels and interfering with the tumour’s ability to grow and spread to other parts of the body.

Although it won’t be known whether the drug extends the overall life expectancy of ovarian cancer patients until the final results are reported in 2013, Professor Max Parmar, director of the MRC Clinical Trials Unit in London and co-author of the study, said: “This suggests that bevacizumab could be considered as a treatment for women with an advanced form of the disease, or whose cancer has come back after chemotherapy treatment.”

“The first drug in 15 years to offer an improvement in survival rates for ovarian cancer was approved for use in Europe in January 2012.”

T-cells as cancer-fighting robots

The immune system is remarkably effective at destroying populations of virus-infected cells. Scientists at University College London are working on a way of re-programming the immune system to recognise cancer instead.

Using technology originally developed for gene-therapy, researchers can genetically modify T-cells, a special type of immune cell, to recognise particular proteins on a cancer. This marks them out for destruction but leaves healthy tissue undamaged.

An MRC Clinician Scientist Fellowship grant allowed Dr Martin Pule to set up a T-cell engineering group at the University College London Cancer Institute. “With T-cells, nature has provided us with the basis for developing remarkable cancer fighting machines,” says Dr Pule.

“This technology is still in its infancy: we are learning how to re-program T-cells with much more complex behaviours such as recognising patterns of antigens, homing to sites of disease and selectively releasing toxic payloads. This is a level of sophistication and complexity impossible with standard small molecule or protein drugs.”

Dr Pule is currently testing this new form of therapy in a clinical study of childhood leukaemia with funding secured for a study in another common childhood cancer: neuroblastoma.

Humble aspirin can protect against cancer

Twenty years of dedicated research has confirmed that a daily dose of aspirin can reduce the long-term risk of developing cancer.

The CAPP-2 trial, part-funded by the MRC, found that cancer risk can be cut by 60 per cent in people with a strong family history of the disease, but it takes at least five years for this effect to become apparent.

Evidence that aspirin protects against cancer risk has been accumulating for decades, but this was the first study to examine the suspected link using a randomised controlled trial. The key was to look at individuals with Lynch syndrome, an inherited disorder which causes cancer to develop rapidly.

Professor Sir John Burn from Newcastle University, who led the international research collaboration, said: “We’ve finally shown that aspirin has a major preventative effect on cancer because we had a lot of long-term data and because Lynch syndrome is associated with rapid development of cancer. This is a great example of how our research community and families with inherited forms of cancer can work together to answer questions important for the whole population.”

The next step for the team is to deduce the optimal dose of aspirin, which they will do by conducting another large-scale trial in around 3,000 people.

“A daily dose of aspirin can reduce the long-term risk of developing cancer.”

MRC science behind first pocket-sized DNA sequencer

A revolutionary new device that can determine the sequence of a simple genome in seconds was unveiled by UK company Oxford Nanopore Technologies in February 2012. The MinION device looks like a USB memory stick and has already sequenced a virus that contains 5,000 genetic base pairs.

Among its many uses, it’s hoped the device could be used to sequence DNA from cells in a biopsy to diagnose cancer or sequence rapidly mutating viruses and bacteria such as flu and E. coli to work out how to treat infections.

Oxford Nanopore Technologies was spun out from the University of Oxford in 2005, based on the research of Professor Hagan Bayley, an MRC programme grant holder. His research involved developing a new way of reading the sequence of DNA strands by using tiny protein pores called nanopores.

Professor Bayley explains: “The nanopores are embedded in a man-made membrane with very high electrical resistance. When a potential is applied to the membrane it causes a current carried by ions to flow only through the nanopore, the path of least resistance. Single molecules that pass through the nanopore disrupt the current, each in a different characteristic way, which allows individual molecules to be identified. In the Oxford Nanopore device, DNA is ‘unzipped’ into its two strands by an enzyme that sticks to the top of the nanopore. The DNA bases are ratched into the nanopore, and identified one at a time.”
Chapter 5
Targeting a healthy heart and circulation

Rates of heart disease and stroke are climbing the world over, making it a priority area for MRC funding. Our groundbreaking research in cardiovascular disease and stroke stretches from understanding the genetics of heart conditions and regenerative stem cell therapies to encouraging behavioural change through the use of mobile phone apps.

Every six minutes someone dies of a heart attack in the UK. Heart attack is a frightening and debilitating condition that can cause permanent damage to the heart in those who survive it, drastically altering the patient’s health. But what if there was a way to repair the heart and allow these patients to lead a normal life again?

That is one of the many quests of Professor Roger Patient at the MRC Molecular Haematology Unit (MHU) in Oxford, who is investigating the possibility of using stem cell therapy to regenerate damaged heart muscle.

Roger started his scientific career as a chemist, but soon decided that DNA was by far the most interesting chemical he’d studied and made the leap to genetics. At that time, the first experiments to transfer animal genes into bacterial cells were taking place, and Roger recalls being accosted by news reporters on his way into work who wanted to know if he was making a ‘test tube monster’.

Later he shifted gear again into developmental genetics after making the seminal discovery that embryonic and adult red blood cells are descended from entirely different cell lineages. It’s in this field that he’s worked for the past 20 years, researching how the blood and cardiovascular system forms in the developing embryo.

But these days, as a senior scientist at the MHU, Roger is more likely to be found grappling with research problems than pipettes.

“I became a lab head because for me, the exciting thing about research is the concepts and ideas. Although I loved doing the experiments, I consciously dropped being hands-on to make the lab bigger and to broaden the reach of what we were able to do,” explains Roger.

And his lab’s remit is certainly broad. Unravelling the intricacies of how cells, genes and molecules come together in the embryo to make blood, veins and heart can teach us about congenital heart defects, blood cancers and even how to repair damage inflicted by a heart attack.

In 2011, Roger’s group published research they’d carried out in zebrafish – a creature with an incredible ability to regenerate human heart tissue within five to ten years. Regenerative medicine brings to mind science fiction images of pulsating hearts growing in Petri dishes, but Roger thinks the answer will lie in stimulating the body to repair itself from within rather than transplanting tissue grown in the lab.

“If you transplant tissue into a heart, the cells have got to organise themselves if they’re growing in situ than if they are dropped in from the outside.”

It’s early days for this research, and for now the search continues for this elusive population of cells in people. But Roger’s still hopeful that we might have an idea of how to regenerate human heart tissue within five to ten years.

“It used to be that people like me working on basic research would feel a long way from research going to the clinic, but nowadays we don’t feel so far away,” he says.
A smartphone app that runs a simple test for stroke is speeding up access to medical help. Dr Will Whiteley of the University of Edinburgh used his time as an MRC Clinician Scientist Fellow to make the existing stroke test ‘FAST’ available directly to patients by creating the app.

The app asks users to check the person for three main symptoms of stroke: an inability to smile, difficulty with lifting both arms and slurred speech. If all symptoms of stroke are present, the user is told to call 999. The app also provides information about stroke, its causes and treatments and an option to speak to a specialist nurse.

Dr Whiteley said: “It has been exciting to think about how new media can be used to improve outcomes for patients. My hope is that the FAST app will enable users to recognise symptoms of stroke in an emergency situation.”

The FAST app is free on the Appstore and Android marketplace and was funded by Chest, Heart and Stroke Scotland.

Enlargement of the heart is one of the many causes of heart failure. If the muscle is weak, stiff or has been damaged, the heart can’t pump blood around the body properly.

An international research team led by the MRC Clinical Sciences Centre at Imperial College London has pinpointed a single gene – called Endog – which is associated with heart failure.

They’ve discovered that, in rats and mice, Endog influences the thickness of the muscular heart wall, how well the heart pumps and how much fat accumulates inside the organ.

Lead scientist Professor Stuart Cook explains: “Our work shows that the Endog gene plays an important role in the enlargement of the heart. It does this by interfering with the heart cells’ energy source – the mitochondria. Like any other muscle in our body, the heart needs energy to keep it pumping. If the mitochondria don’t work properly, the heart struggles to make enough energy and the cells produce toxic by-products, called reactive oxidative species, which increase thickening of the heart wall.”

“We can now start to investigate new ways to develop treatments which target the mitochondria and toxic oxidative molecules.”

A promising new drug which could encourage the heart to self-repair after a heart attack is in the pipeline, thanks to an MRC-funded discovery.

US pharmaceutical company Regenerx is gearing up to begin a phase II clinical trial of a protein called Thymosin Beta 4 (Tβ4), which is able to instruct the heart to heal itself by guiding cells from the outermost layer of the heart to move deeper inside and help to repair tissue.

The discovery that Tβ4 could mobilise these dormant cells to form new blood vessels was made by Professor Paul Riley at the University of Oxford in 2006, with support from an MRC Career Establishment Grant and the British Heart Foundation. The potential repair cells are known as epicardial progenitors, and can change into different cells depending on the signals they receive in the body.

Research in mice carried out by scientists at the University of California San Francisco has shown that Tβ4, given in combination with gene therapy, can convert non-beating heart cells (which normally form scar tissue after a heart attack), into functional, beating heart cells within one month.

Regenerx carried out a first-in-man study which has shown the treatment to be safe and are now planning a phase II study to test how effective the drug is in heart attack patients.

Professor Riley commented: “It’s exciting to see Tβ4 progress towards helping patients after our breakthrough discovery several years ago.”

Regularly putting in a long working day can dramatically raise your risk of getting heart disease, research part-funded by the MRC suggests.

Scientists from University College London (UCL) used data from the Whitehall II study, which has tracked the health of over 10,000 civil servants since 1985. The UCL research followed 7,095 men and women who worked full time and were healthy at the start of the study. Data were collected on age, blood pressure, cholesterol levels and smoking habits and the number of hours worked on an average week day.

Over the next 11 years, researchers collected information from health records and discovered that those who worked 11 hours or more a day were 67 per cent more likely to have had a heart attack than those who worked an average day of seven to eight hours.

Lead scientist Professor Mika Kivimäki says: “This new information should help improve decisions about medication for heart disease. It could also be a wake-up call for people who overwork themselves, especially if they already have other risk factors.”

A new heart ‘self-repair’ drug

A promising new drug which could encourage the heart to self-repair after a heart attack is in the pipeline, thanks to an MRC-funded discovery.

US pharmaceutical company Regenerx is gearing up to begin a phase II clinical trial of a protein called Thymosin Beta 4 (Tβ4), which is able to instruct the heart to heal itself by guiding cells from the outermost layer of the heart to move deeper inside and help to repair tissue.

The discovery that Tβ4 could mobilise these dormant cells to form new blood vessels was made by Professor Paul Riley at the University of Oxford in 2006, with support from an MRC Career Establishment Grant and the British Heart Foundation. The potential repair cells are known as epicardial progenitors, and can change into different cells depending on the signals they receive in the body.

Research in mice carried out by scientists at the University of California San Francisco has shown that Tβ4, given in combination with gene therapy, can convert non-beating heart cells (which normally form scar tissue after a heart attack), into functional, beating heart cells within one month.

Regenerx carried out a first-in-man study which has shown the treatment to be safe and are now planning a phase II study to test how effective the drug is in heart attack patients.

Professor Riley commented: “It’s exciting to see Tβ4 progress towards helping patients after our breakthrough discovery several years ago.”
Hands-free heart rate monitor for babies

One in 10 babies need help with their breathing in the first few minutes of life. During this time, doctors perform cardiopulmonary resuscitation (CPR) and monitor whether this is successful by periodically checking the baby's heart rate with a stethoscope, which can take valuable seconds.

Researchers at the University of Nottingham are developing a hands-free heart rate monitor that automatically detects a baby's heart rate. The sensor is placed in a hat — used to keep the baby warm — and detects the volume of blood, and thereby the heart rate, by shining light into the blood vessels of the baby's forehead and measuring the amount that is reflected back.

With MRC funding, the device has been tested on almost 200 babies in various settings. The researchers have shown it can measure the heart rate in days-old babies in intensive care, and newborn babies that both do and don't need resuscitation after birth.

Professor Barrie Hayes-Gill said: “Resuscitating a baby is a stressful time. Doctors are highly skilled at resuscitation, but we want to help them by offering a hands-free device to save valuable seconds.

“We are now ready to test the device in 50 to 100 babies who are receiving resuscitation. If successful, the device will be offered for routine clinical practice.”

Laying the foundations for the future of vascular imaging

In cases of stroke, every second counts and the quicker doctors can detect where the damage has taken place, the greater the chances of recovery for the patient.

In 2011 a world-leading new Acute Vascular Imaging Centre (OxAVIC) was opened next to the emergency department of the John Radcliffe Hospital in Oxford to provide patients with a faster imaging assessment of brain damage caused by stroke, and to develop pioneering techniques that will allow doctors to capture and analyse new kinds of images of the brain's circulatory system.

Several MRC-funded scientists work at the centre, and one of the research teams is led by MRC scientist Peter Jezzard, a professor of neuromaging and expert in magnetic resonance imaging.

He said: “The OxAVIC research facility is virtually unique in the world, allowing us to gain vital insights into the early progression of stroke using state-of-the-art imaging methodologies. The combination of world-class imaging science and clinical research in Oxford, alongside a strong NHS partnership, should result in some significant advances in our understanding of stroke and its treatment.”
Chapter 6
Challenging diseases of body systems and senses

MRC scientists are focused on developing new drugs, treatments, diagnostics and technologies for a wide range of diseases from macular degeneration to kidney failure. We are at the forefront of regenerative medicine – using stem cell therapies, tissue engineering and gene therapy to repair and replace organs such as the liver, to improve patients’ health and quality of life.

PROFILE: Professor Astrid Limb, Institute of Ophthalmology, London

Professor Astrid Limb partly owes her choice of research to a mistake made by a lab technician in 2002. At the time, Astrid’s lab was growing cultures of nerve cells from eyes and brains. But some of the cell culture flasks were mislabelled by the technician and a flask of nerve cells taken from the eye was grown under the wrong conditions.

“When we came to study the cells later, we found that there was one cell line that seemed to be immortal,” explains Astrid. “Then the technician went on holiday and left behind cultures of human eye cells. We discovered that a similar population of human cells, grown under the same conditions, were also becoming immortal.”

Astrid noticed that, under certain growth conditions, these cells acquired features of different nerve cells in the retina.

She’d made a striking discovery: that there was a population of stem cells in the adult human eye which was able to generate many different types of nerve cell.

Fast forward 10 years and stem cell research is a burgeoning field. Today Astrid leads research at the Institute of Ophthalmology in London which focuses on using the adult retina stem cells she discovered, known as Müller glial stem cells, to regenerate the retina in vision disorders such as glaucoma.

Glaucoma is a leading cause of irreversible blindness, with 70 million sufferers worldwide. It occurs when a build-up of pressure in the eye leads to the death of retinal ganglion cells (RGCs), which form the fibres of the optic nerve, and which transmit visual information from eye to brain. The condition can be treated in the early stages, but if diagnosis comes too late or if treatment doesn’t work, damage to the eye cannot be reversed.

“Once people with glaucoma go blind there is no cure. So our hope is that we might be able to replace some of the nerve cells in the eye using stem cells,” Astrid says.

In 2012, with funding from the MRC, Astrid’s group reported they’d successfully used Müller glial stem cells to repair nerve cells damaged in glaucoma, partially restoring vision in rats which had previously been blind.

They used chemicals to induce Müller glial stem cells to grow into precursors of RGCs, before transplanting them onto the retina of rats which had suffered retinal damage. After four weeks, the injected cells appeared to have formed new connections (synapses) with existing nerve cells, and the rats had significantly improved retinal function when their vision was tested under very low light conditions.

This technique might lead to a new way of slowing or even reversing the deterioration of sight in glaucoma and other degenerative vision conditions if it can be applied in people.

But human eyes are different to rats’ eyes because they have proportionately smaller lenses and also more liquid inside the eyeball, known as vitreous humour. If stem cells were to be injected into the vitreous humour in humans, they would disperse and fail to attach to the retina.

So the research team has recently begun seeding the stem cells onto a thin membrane of protein. They then surgically remove the vitreous humour from the eye and place the membrane on the retina to allow the cells to migrate to where they are needed.

“The surgery we’re doing in animals is actually very similar to a routine operation in humans for retinal detachment, and we have a consultant ophthalmic surgeon from Moorfields Eye Hospital and an MRC clinician scientist who are helping us with this work,” explains Astrid.

Having identified the cells, how to differentiate them, and proved that they are safe to use, Astrid is hopeful that the first clinical trials to use this technique might only be five years away. Long term though, she thinks that a different approach will be needed to restore sight permanently.

“Because Müller glial stem cells are already present in the eye, I envisage that we might ultimately be able to encourage them to differentiate in the eye using drugs,” explains Astrid.

Astrid’s career ambition is to establish a stem cell therapy for glaucoma to help a blind person to see again, and at the current rate of progress she is nearly there. She regularly speaks to glaucoma patients and says they are a source of inspiration and motivation.

“It’s a very debilitating condition, and it’s particularly upsetting to see children losing their sight from an early age and the effect that has upon them and their parents.

And for adults, who have lived a normal life to suddenly lose their sight and not being able to cross the road alone or go shopping – it’s the end of their normal daily lives.

“So if, by the end of my career I could establish a stem cell therapy for glaucoma and see just one person who has lost their sight to have their vision restored, that would be a dream – and then I can happily retire!”
Lessons from maggots

Scientists at the University of Nottingham have taken tips from greenbottle fly maggots to create a wound-healing gel that contains one of the laval’s enzymes.

Maggots are thought to help wounds heal by secreting enzymes that digest dead, bacteria-filled tissue that might otherwise cause infection. Maggots in ‘biobags’ — thin, sterile nylon bags through which they secrete the enzymes — are already used in clinical practice to treat skin ulcers, but transporting and storing live maggots can be difficult.

Professor David Pritchard and colleagues have identified a maggot enzyme called a chymotrypsin. Using MRC funding they collaborated with biotechnology company PA Therapeutics to produce the enzyme in bacteria and encapsulate it in a salt that can be dispensed inside the lab, as well as maggots, and the next step is for the gel to be tested in clinical trials.

“Most wound care products, such as dressings, are inert and simply help keep wounds clean. This enzyme can actually contribute to wound-healing. It’s important to look at organisms such as maggots to get clues about how we can find better ways to help wounds heal,” said David.

Teaching the liver to heal itself

MRC-funded scientists in Edinburgh have discovered how to boost production of key cells needed to repair damaged liver tissue. The findings open up possible new ways of healing liver damage from diseases like cirrhosis and chronic hepatitis.

In studies in mice, the scientists discovered how different types of liver cell are formed from precursor cells called liver progenitor cells. These cells either go on to form cells called hepatocytes — which are involved in clearing toxins from the body and repairing damaged liver tissue — or bile duct cells. When the liver is damaged it produces too many bile duct cells and not enough hepatocytes.

By switching certain genes on or off in liver progenitor cells in mice and in human liver tissue in the lab, the scientists were able to increase production of hepatocytes. This new understanding of how liver cells are formed could help to develop drugs to boost production of liver-regenerating hepatocytes.

Lead scientist and liver specialist Professor Stuart Forbes, of the MRC Centre for Regenerative Medicine, commented: “Increasing numbers of patients are in need of liver transplants, but the supply of donated organs is not keeping pace with the demand. If we can find ways to encourage the liver to heal itself then we could ease the pressure on waiting lists for liver transplants.”

MRC researcher Dr Nathan Davies is working with dialysis company Gambro, University College London and the Royal Veterinary College to develop a new dialysis system which will be able to help all liver patients.

A key feature is that the device will work with existing kidney dialysis machines so hospitals won’t need to purchase additional equipment.

Helping patients with liver damage

Liver disease is one of the major causes of death in the UK and is currently on the rise. A technique called liver dialysis can be used to help patients whose livers have been damaged through disease and who are unable to rid the blood of toxic or unwanted substances. Now, with MRC funding, scientists are developing a new, improved type of dialysis system.

Liver dialysis treatment is not easily accessible to all patients, and where it is available it can only help patients with very specific liver conditions including drug toxicities or symptoms such as pruritus, a disorder that leaves sufferers with uncontrollable itching.

MRC researcher Dr Nathan Davies is working with dialysis company Gambro, University College London and the Royal Veterinary College to develop a new dialysis system which will be able to help all liver patients.

A key feature is that the device will work with existing kidney dialysis machines so hospitals won’t need to purchase additional equipment.

Dr Davies commented: “Funding from the MRC is ideally suited for this project and the next step will be to test the machine in clinical trials. We ultimately hope that liver dialysis will be available to all patients that need it.”

Better drugs for blindness in the elderly

Wet age-related macular degeneration (AMD) is the leading cause of blindness in older people. It’s caused by abnormal blood vessel growth and swelling in a part of the retina called the macula. The best drugs available are called VEGF inhibitors, which interfere with blood vessel growth, but many patients are still left with poor vision and better drugs are needed.

Hope is now on the horizon. In February 2012, Glasscock and his team started a clinical trial of a new type of AMD drug and other companies have drugs in the pipeline which cause regression of the blood vessels rather than just halting their spread.

Critical to the early development of these drugs was MRC-funded work carried out by Dr David T. Shima at University College London. He’s studied genetically-modified mice which more closely mimic the disease seen in people with AMD. We’re now on the cusp of understanding the earliest changes that trigger the abnormal blood vessel growth in AMD.

Dr Shima explains: “Until recently there’s been no way of studying the earliest changes that trigger the abnormal blood vessel growth in AMD. The mouse model we’ve developed and studied has spontaneous growth of abnormal blood vessels and also the later stage retinal swelling and neural dysfunction which are seen in people with AMD. We’ve now working with multiple biopharma partners using this model to develop new drugs and results so far have been exciting.”

Alcohol damage study sheds light on rare disease

Insights into how alcohol damages DNA — and how our cells defend themselves against it — have given scientists clues on how to tackle a rare disease.

Studies in mice carried out at the MRC Laboratory of Molecular Biology in Cambridge showed that excess levels of acetaldehyde, produced when alcohol is broken down by our liver, cause irreparable damage to DNA.

Further research uncovered a two-tier defence system in cells to protect against this damage. Firstly, cells produce specialised enzymes to break down and remove acetaldehyde. If this step fails, a second mechanism kicks in to repair the damaged DNA using another set of enzymes known as the Fanconi proteins. In pregnant mice which were unable to produce either set of enzymes, alcohol consumption caused catastrophic damage to the fetus.

This suggests that people with a rare disease called Fanconi’s anaemia, who lack these DNA repair enzymes, are likely to be especially sensitive to acetaldehyde. This could explain why these individuals are susceptible to blood disorders and cancer.

Lead scientist Dr Ketan Patel said: “This new knowledge transforms our view of precisely how excess alcohol causes damage — ultimately changing our DNA. Quite apart from this, our conclusions suggest potentially simple approaches to treat Fanconi’s anaemia — currently a terminal incurable illness in humans.”
Understanding childhood listening disorders

Children diagnosed with auditory processing disorder (APD) have difficulties attending to and understanding speech, particularly when listening to someone talking against background noise.

APD is a complex disorder and there’s debate about whether it is truly a hearing problem, as the name suggests, or whether there are other causes. To gain a better understanding of APD, scientists at the MRC Institute for Hearing Research (IHR) in Nottingham have designed a new assessment of hearing ability, delivered using a computer application called STAR.

The research team used STAR to test more than 1,500 children across the UK, and the research revealed some surprising results. The IHR’s Dr Johanna Barry explains: “We concluded that APD is a disorder of higher cognitive abilities rather than an auditory problem per se. We’re now building on this research to develop a questionnaire to further understand the nature of the difficulties that these children experience every day.

“STAR can be used to test a variety of auditory abilities quickly and easily in both clinical and research settings as well as providing auditory training that may help to treat a child’s listening difficulties. STAR is currently being used in field trials by some NHS trusts and we are in discussions with industry partners to commercialise the application.”

“Eculizumab may not only prevent development of kidney failure but also enable patients on dialysis with this condition to undergo a successful kidney transplant.”

Drug to boost transplant success

Professor Stephen Wigmans and Dr Ewen Harrison at the University of Edinburgh used funding from the MRC Developmental Funding Pathway Scheme to progress development of a drug that they hope will improve organ transplant success rates.

Naturally-occurring heat shock proteins (Hsps) help to protect cells from the kind of stresses that can cause damage during transplant surgery. The new drug, AT13387, works by increasing the number of protective Hsps present in body tissues that, in turn, could boost the chances of a transplant being successful. The researchers envisage that the drug would be used to treat the organ donor before surgery, or to treat the organ outside of the body prior to transplant.

Professor Wigmans explained: “The heat shock protein therapy based on AT13387 has proven to be successful in preventing damage to cells in vitro and in a mouse model of kidney damage. The next step is to move on to a large animal study and into man where we hope enhancing the presence of heat shock proteins will make kidney and other tissue transplants even more successful for patients in the long term.”

On the trail of a rare disease

An MRC fellow has tracked down a rare, previously unidentified, kidney disease to the Troodos Mountains in Cyprus — and developed a genetic test for the disease to boot.

The kidneys of people with the disease are attacked by a part of the immune system called complement. When they have a minor infection such as a cold, this triggers complement to switch on, damaging the kidneys. Over time the kidneys scar and lose function, with 80 per cent of men with the disease showing kidney damage by age 50.

The diagnosis also means that patients can be offered treatments, such as ‘plasma exchange’ where a patient’s blood plasma — which contains complement — is swapped for donor plasma when their disease flares up.

“New drug for rare kidney disease

A new drug which could transform the lives of patients with a rare kidney disease is now available in Europe and the US, thanks to MRC-supported research.

Atypical haemolytic uraemic syndrome (aHUS) happens when a part of our immune system, called complement, malfunctions. Rather than doing its intended job of labelling invading viruses and bacteria for destruction, complement tells the immune system to attack the body’s own tissues. Left unchecked, this damages blood vessels in the kidneys and causes dangerous blood clots to form, eventually leading to kidney failure.

Until recently, the only treatment available for aHUS patients was a grueling process called plasma exchange — which involves replacing the plasma of the blood — or being hooked up to a dialysis machine, often several times a week.

With funding from the MRC and others, Professor Tim Goodship and colleagues at Newcastle University have developed an effective new and body therapy for aHUS called eculizumab. Made by Alexion Pharmaceuticals, eculizumab stops complement working, preventing it from unleashing an attack on the blood vessels. Clinical trial results show that it is very effective for treating aHUS patients. What’s more, unlike dialysis or plasma exchange — which can take several hours — eculizumab treatment takes 30 minutes and only needs to be given once a fortnight.

Professor Goodship said: “We’re delighted that treatment of aHUS with eculizumab may not only prevent the development of kidney failure but also enable patients on dialysis with this condition to undergo a successful kidney transplant.”

Drug to boost transplant success

Professor Stephen Wigmans and Dr Ewen Harrison at the University of Edinburgh used funding from the MRC Developmental Funding Pathway Scheme to progress development of a drug that they hope will improve organ transplant success rates.

Naturally-occurring heat shock proteins (Hsps) help to protect cells from the kind of stresses that can cause damage during transplant surgery. The new drug, AT13387, works by increasing the number of protective Hsps present in body tissues that, in turn, could boost the chances of a transplant being successful. The researchers envisage that the drug would be used to treat the organ donor before surgery, or to treat the organ outside of the body prior to transplant.

Professor Wigmans explained: “The heat shock protein therapy based on AT13387 has proven to be successful in preventing damage to cells in vitro and in a mouse model of kidney damage. The next step is to move on to a large animal study and into man where we hope enhancing the presence of heat shock proteins will make kidney and other tissue transplants even more successful for patients in the long term.”

On the trail of a rare disease

An MRC fellow has tracked down a rare, previously unidentified, kidney disease to the Troodos Mountains in Cyprus — and developed a genetic test for the disease to boot.

The kidneys of people with the disease are attacked by a part of the immune system called complement. When they have a minor infection such as a cold, this triggers complement to switch on, damaging the kidneys. Over time the kidneys scar and lose function, with 80 per cent of men with the disease showing kidney damage by age 50.

The diagnosis also means that patients can be offered treatments, such as ‘plasma exchange’ where a patient’s blood plasma — which contains complement — is swapped for donor plasma when their disease flares up.

“New drug for rare kidney disease

A new drug which could transform the lives of patients with a rare kidney disease is now available in Europe and the US, thanks to MRC-supported research.

Atypical haemolytic uraemic syndrome (aHUS) happens when a part of our immune system, called complement, malfunctions. Rather than doing its intended job of labelling invading viruses and bacteria for destruction, complement tells the immune system to attack the body’s own tissues. Left unchecked, this damages blood vessels in the kidneys and causes dangerous blood clots to form, eventually leading to kidney failure.

Until recently, the only treatment available for aHUS patients was a grueling process called plasma exchange — which involves replacing the plasma of the blood — or being hooked up to a dialysis machine, often several times a week.

With funding from the MRC and others, Professor Tim Goodship and colleagues at Newcastle University have developed an effective new and body therapy for aHUS called eculizumab. Made by Alexion Pharmaceuticals, eculizumab stops complement working, preventing it from unleashing an attack on the blood vessels. Clinical trial results show that it is very effective for treating aHUS patients. What’s more, unlike dialysis or plasma exchange — which can take several hours — eculizumab treatment takes 30 minutes and only needs to be given once a fortnight.

Professor Goodship said: “We’re delighted that treatment of aHUS with eculizumab may not only prevent the development of kidney failure but also enable patients on dialysis with this condition to undergo a successful kidney transplant.”

Drug to boost transplant success

Professor Stephen Wigmans and Dr Ewen Harrison at the University of Edinburgh used funding from the MRC Developmental Funding Pathway Scheme to progress development of a drug that they hope will improve organ transplant success rates.

Naturally-occurring heat shock proteins (Hsps) help to protect cells from the kind of stresses that can cause damage during transplant surgery. The new drug, AT13387, works by increasing the number of protective Hsps present in body tissues that, in turn, could boost the chances of a transplant being successful. The researchers envisage that the drug would be used to treat the organ donor before surgery, or to treat the organ outside of the body prior to transplant.

Professor Wigmans explained: “The heat shock protein therapy based on AT13387 has proven to be successful in preventing damage to cells in vitro and in a mouse model of kidney damage. The next step is to move on to a large animal study and into man where we hope enhancing the presence of heat shock proteins will make kidney and other tissue transplants even more successful for patients in the long term.”

On the trail of a rare disease

An MRC fellow has tracked down a rare, previously unidentified, kidney disease to the Troodos Mountains in Cyprus — and developed a genetic test for the disease to boot.

The kidneys of people with the disease are attacked by a part of the immune system called complement. When they have a minor infection such as a cold, this triggers complement to switch on, damaging the kidneys. Over time the kidneys scar and lose function, with 80 per cent of men with the disease showing kidney damage by age 50.

The diagnosis also means that patients can be offered treatments, such as ‘plasma exchange’ where a patient’s blood plasma — which contains complement — is swapped for donor plasma when their disease flares up.
Index: MRC Strategic Aims

The MRC Strategic Plan 2009 – 2014, Research Changes Lives, set out the direction for our research. Advancing medicine, changing lives, the MRC Annual Review 2011/12 highlights some of the research discoveries we have made over the three years since the plan was launched.

This index shows the stories of achievement selected for our 2011/12 annual review categorised by the MRC’s strategic aims.

The achievements highlighted form a fraction of the many discoveries made by our scientists, but they give a taster of how the MRC is already delivering against its objectives.

Aim 1 – Picking research that delivers: Setting research priorities which are most likely to deliver improved health outcomes

Alcohol damage sheds light on rare disease
Alzheimer’s genes discovery gives hope to half a million
Boosting brain repair
Breastfeeding makes for a feisty baby
Discovery boosts fight against superbug
Easing the pain
Gene link with heart failure found
Gene map reveals MRSA weakness
Inflammation can heal
Insights on the anxious brain
Itinerant childhood, unhealthy adulthood
Lessons from maggots
On the train of a rare disease
Pregnancy diet affects child’s future weight
Profile: Dr Chris Grainge
Profile: Professor Roger Patient
Promising hepatitis C drugs in the pipeline
Teaching the liver to heal itself
Tricking malaria-carrying mosquitoes
Worming our way towards a treatment

Aim 2 – Research to people: Bringing the benefits of excellent research to all sections of society

A new heart ‘self-repair’ drug
A targeted drug for blood cancer
Better drugs for blindness in the elderly
Cancer drugs could treat glue ear
CID drugs could also prevent Alzheimer’s
Computerised programme for ‘brain re-hab’
Drug to boost transplant success
Extending life for ovarian cancer patients
Fighting drug-resistant prostate cancer
Hands-free heart rate monitor for babies
Helping autistic children communicate
Helping patients with liver damage
Humble aspirin can protect against cancer
Low-cost drug triples smoking quit rate
MRC science behind first pocket-sized DNA sequencer
New drug for rare kidney disease
Profile: Dr Cari Free
Profile: Professor Alasdair MacLullich
Profile: Professor Astrid Limb
Profile: Professor Weeke Alft
Tailoring childhood anxiety treatment
T-cells as cancer-fighting robots
Understanding childhood listening disorders

Aim 3 – Going global: Accelerating progress in international health research

A spanner in the works for HIV?
Flu susceptibility gene discovered
Leukaemia clue from bone marrow research
Towards a universal flu vaccine

Aim 4 – Supporting scientists: Sustaining a robust and flourishing environment for world-class medical research

Caesareans on the rise among the affluent
Laying the foundations for the future of vascular imaging
Long working day boosts heart attack risk
Smoking hastens slide into dementia
Weight at 18 linked to cancer in men decades later