Outputs, outcomes and impact of MRC research: 2013/14 report

SECTION 2.4: Industry interactions and other collaborations
Industry interactions and other collaborations

The MRC supports the most promising response-mode and strategic research, with the greatest potential for long-term advances. The MRC has a unique role in funding discovery science through to early clinical studies, and the training needed to deliver this, within a complex medical research ecosystem. It is the productive interactions between researchers globally and across all sectors that are essential for this research to be translated into wider impact. It is important that the MRC creates the optimal conditions for the right interactions to flourish. An analysis of approaches to track these productive interactions with particular focus on information about reported collaborations, sources of further funding and the creation of spin out companies is available in the quantitative analysis sections 3.2, 3.3 and 3.10.

Researchers providing feedback via Researchfish identify collaborations that can be evidenced (via activities such as joint funding, joint publication, and exchange of expertise, staff and/or facilities) as being productive and supportive of achieving their research goals. Each reported collaboration can include a number of partners already supported by funding from different sources (for example, charitable, public, and private sector) and are not confined to just the UK. Researchers reported a variety of purposes for engaging in a collaboration including provision of expertise, research materials and funding. Collaboration has been shown to be a driver of research excellence. In a period of constrained public finances it is even more important to have access to a wider range of facilities and equipment through a pooling of resources and expertise. In addition to establishing and maintaining collaborations, researchers obtain funding to continue or expand their work. This “further funding” may be competitively won, at least in part, as a result of holding MRC support. Success in obtaining further funding may indicate that the research group has established a high quality track record and is therefore able to present attractive proposals for future research.

The MRC has also made an extensive contribution to the formation and growth of spin out companies. The formation of spin out companies is one route to the commercialisation of discoveries, resulting not only in improved healthcare, but also in positive economic impact, such as employment and direct investment into the UK.

A number of case studies relating to the MRC’s collaborations, impacts on the private sector and leveraging of further funding can be found throughout this chapter in the following areas:

- Cancer
- Metabolic diseases
- Obesity and nutrition
- Neurodegeneration and neurology
- Natural protection
- Infectious diseases
- Sexual development
- Rare diseases
- Global health
- Regenerative medicine
- Environmental exposures
- Musculoskeletal health
- Reproductive health
- Epigenetics

Further information on each piece of research can be found on the Research Councils UK (RCUK)’s information portal — the Gateway to Research — by entering the project reference number listed under each case study in the search field.
SECTION 2.4: Industry interactions and other collaborations

Collaborations: Developing drug-like molecules for cancer

Professor Terence Rabbitts at the University of Oxford studies small molecules and peptides that mirror the inhibitory properties of antibodies with the aim of developing drug-like molecules for therapeutic application. MedImmune, the biologics research and development arm of AstraZeneca, has provided Professor Rabbitts with proteins to test in vitro and in vivo lung cancer molecules for an ability to enter cells and produce a therapeutic effect.

Project reference number: MR/J000612/1

Collaborations: Colorectal cancer screen

As a result of a Confidence in Concept award in 2012, Professor Saul Tendler at the University of Nottingham has embarked on a collaboration with Oncimmune, a company specialising in early cancer detection to identify new autoantibody biomarkers for colorectal cancer.

Project reference number: MC_PC_12019

Impacts on the private sector: Kesios Therapeutics Ltd

Kesios Therapeutics is a spin out company formed in 2012 by Imperial Innovations, originally founded as the technology transfer office of Imperial College London. Kesios Therapeutics Ltd is focused on the development of small molecule drug candidates that are targeted at haematological malignancies, cancers of the blood, bone marrow, and lymph nodes. It builds upon the work of one of its founding directors Professor Guido Franzoso, head of the Centre for Cell Signalling and Inflammation at Imperial College London.

Project reference number: G0901436

Impacts on the private sector: Development of DNA damage assay

Chemotherapy for diseases such as cancer involves treatment with compounds designed to cause DNA damage, leading to cell death. However, resistance to these compounds and treatment failure can often occur. Repair of the DNA damage is the commonest cause of resistance.

Professor Simon Reed at Cardiff University has developed a method to detect, quantify, and localise DNA damage at high resolution throughout the human genome. He has provided use of this to GlaxoSmithKline to determine the mechanism of genetic toxicity caused by drugs and the response of the epigenome to this damage. The epigenome describes complex chemical DNA modifications which can change gene expression. Understanding these responses could allow patients that are likely to respond well to particular treatments to be identified.

Project reference number: MR/K000926/1
Collaborations: Structure and function of AMPK

AMP-activated protein kinase (AMPK) functions in the regulation of cell energy. Evidence suggests that it may therefore play a role in human diseases characterized by defects in energy metabolism. Professor David Carling’s current research at the MRC Clinical Sciences Centre focuses on the regulation of AMPK using structure/function analyses and the physiological role of AMPK using transgenic models. Professor Carling has identified the mode of action of small molecule activators of AMPK and will use this in order to determine whether there are any natural ligands that activate AMPK by a similar mechanism. As part of an industrial CASE studentship in 2013, AstraZeneca have synthesised a number of small molecular activators of AMPK. They have also produced a fluorescent analogue molecule for one of these activators that will be used as a probe to screen for natural ligands that compete with the binding.

Project reference number: MC_U120027537

Impacts on the private sector: Targeting Nrf2 in the treatment of diabetes

Professor John Hayes at the University of Dundee studies the regulation of the transcription factor Nrf2, primarily in relation to its role in cancer. Nrf2 increases the expression of antioxidant genes. In normal cells, activation of Nrf2 has strong anti-inflammatory effects and limits damage caused by oxidative stress, which results in the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Oxidative stress is thought to be involved in the development of many diseases, including cancer and diabetes. Professor Hayes has acted as a consultant for Sanofi on a project led by Dr Dieter Schmoll to target Nrf2 in the treatment of diabetes.

Project reference number: MR/J001465/1

Collaborations: Smartphone app to monitor food intake

Researchers at the University of Leeds have developed a smartphone app in conjunction with Blueberry Consultants that enables users to monitor their food intake and exercise. My Meal Mate also allows users to set a weight loss target and sends them a weekly update on progress via text message. In a pilot randomised controlled trial, the researchers, led by Professor Janet Cade, compared the app to other ways of monitoring food intake - an online food diary and a traditional paper version. Over the six months of the study, those using the app lost an average 4.6kg (10lbs), compared with the 2.9kg (6.5lbs) and 1.3kg (3lbs) lost by the paper-based and online diary users, respectively. A link to the app has been placed on the NHS Choices website. Since its launch in 2013, there have been between 10-50,000 downloads. This is the only weight loss app supported by published peer-reviewed evidence.
SECTION 2.4: Industry interactions and other collaborations

Project reference number: G0802108

Further funding: Investigation of healthy eating and lifestyle during pregnancy

Around one in five pregnant women in the UK are obese. Obesity is linked generally to poor health and also to pregnancy complications, such as gestational diabetes, high-blood pressure and pre-eclampsia, and miscarriage. Dr Sharon Simpson at Cardiff University is conducting a clinical trial to evaluate the effectiveness of a weight management intervention in pregnancy on gestational weight gain, pregnancy and birth outcomes and weight at 12 months following birth. This study has since attracted £72,000 from Slimming World to follow up on the trial results.

Project reference number: G0802038

Collaborations: Parkinson’s and antioxidant compounds

Parkinson’s disease is associated with a loss of dopamine-containing nerve cells in the mid-brain area. Dopamine is a neurotransmitter that plays a central role in motor control. Also common in a number of age-related neurodegenerative diseases is the misfolding of aggregated — or accumulated — proteins. The link between the two has so far been inconclusively proven, however, it has been suggested that misfolded insoluble proteins are toxic to nerve cells and that the aggregation may be a defensive means of alleviating the toxicity by removing the misfolded proteins. There is increasing evidence that oxidative stress plays a major role in the death of nerve cells. Researchers have shown that the abnormal protein aggregates in Parkinson’s contain oxidatively-modified α-synuclein — a protein found in the tips of nerve cells in the brain — which shows a greater propensity to aggregate compared to non-oxidised α-synuclein.

Professor Tilo Kunath at the MRC Centre for Regenerative Medicine at the University of Edinburgh is currently testing a new antioxidant compound developed by Antoxis Ltd in a cell-based model of oxidative stress and Parkinson’s disease.

Grant reference number: MR/J012831/1
Further funding: Biomarkers to study the progression of Parkinson’s and Alzheimer’s diseases

Professor David Brooks’ research at Imperial College London involves the use of positron emission tomography (PET) and magnetic resonance imaging (MRI) to diagnose and study the progression of Alzheimer’s and Parkinson’s diseases.

He was awarded £250k in 2011 to lead the UK research centre of the Parkinson’s Progression Markers Initiative (PPMI) — a major international study into the progression of Parkinson’s disease. Coordinated and part-funded by the Michael J Fox foundation, the study will involve 400 patients in Europe and the US in the earliest stages of Parkinson’s to identify key biomarkers for the disease.

Reliable and robust biomarkers to monitor the progression of Parkinson’s, which affects around 127,000 people in the UK, would improve patient care, lead to new drugs and enhance understanding of the condition.

In this study, blood, urine, and spinal fluid samples will be taken from the patients, and analysed, along with data on motor skills and brain scans to track the progression of the disease.

The programme is working closely with industry partners, and is receiving support, either financial, or in-kind, from 15 different pharmaceutical companies, including Roche, GlaxoSmithKline, GE Healthcare and Pfizer.

Project reference number: G1100810

Impacts on the private sector: Floceleris

Floceleris is a spin out from the University of Cambridge formed in 2012 by Dr Damian Crowther and colleagues. The company is developing a pre-symptomatic test to capture and measure the aggregation of amyloid beta peptides that occurs during neurodegeneration from clinical samples. The test will be used to find new drugs that inhibit disease progression and serve as a companion diagnostics tool to stratify patients and personalise treatments for Alzheimer’s patients. In 2013 Dr Crowther was awarded the Carpe Diem Life Science Award for the best start-up company for Floceleris, in the University of Cambridge’s Entrepreneurs Business Creation Competition.

Project reference number: G0700990

Collaborations: Investigating calcium regulation in Alzheimer’s disease

Alzheimer’s disease is a neurodegenerative disorder characterised by plaques — accumulated clumps — of the protein ß-amyloid and ‘tangles’ of the protein tau within nerve cells, which are associated with neuronal (nerve cell) death.

There is evidence that increased intraneuronal calcium concentration mediates neuronal toxicity. Sodium calcium exchangers (NCXs) play an important role in regulating intracellular concentration and there is some evidence that reduced NCX function may contribute to neurodegeneration.
Professor Wendy Noble at King’s College London has shown that β-amyloids mediate the cleavage of a sodium calcium exchanger (NCX3) and therefore that reduced NCX3 activity could contribute to the sustained increase in intraneuronal calcium concentrations associated with nerve cell dysfunction in Alzheimer’s disease. The University of California, San Francisco provided specific NCX antibodies enabling Professor Noble to use these to screen post-mortem neurodegenerative diseased brain.

Project reference number: G0700355

Further funding: Identification of biomarkers for disease progression in Alzheimer’s disease

Dr Stephen Newhouse is a senior bioinformatician at the MRC Social, Genetic and Developmental Psychiatry Centre. His research is focused on the biomarkers of disease, including dementia and cardiovascular disease, and in 2012 he was awarded £131k from Janssen-Cilag to identify biomarkers for progression in Alzheimer’s disease.

In an international study, he reviewed 163 previously identified candidate biomarkers for the progression of Alzheimer’s disease and conducted a replication study for 94 of these. The study found that nine of the 94 biomarkers — such as complement C6 and pancreatic prohormone — were associated with Alzheimer’s disease characteristics, suggesting that Alzheimer’s disease does affect the protein constituents of the blood and should be considered for further investigations.

Project reference number: G9817803B

Collaborations: Complement UK

Professor Steven Sacks at the MRC Centre for Transplantation at King’s College London, in partnership with Professor Paul Morgan at the University of Cardiff, set up Complement UK in 2009. Complement UK is a group of 40 UK scientists and clinicians at 20 centres whose recent work involves complement – part of the immune system. The primary goal of the partnership, which brings together expertise in structural biology, chemistry, immunology, genetics, protein therapeutics and imaging sciences, is to facilitate collaborative interdisciplinary research, particularly in rapidly growing areas where investigators need access to technical and scientific expertise and to large groups of patients. As a result of this collaboration, Alexion Pharmaceuticals Inc has funded four four-year PhD studentships in this field.

Project reference number: MR/J006742/1

Collaborations: Critical Care Alliance

Professor Paul Morgan at Cardiff University is also part of the Critical Care Alliance, a network of clinicians, mathematicians and physicists across South East Wales, South West England and West Midlands. The aim of this interdisciplinary alliance, set up in 2010, is to facilitate translational research in the area of sepsis and the critically ill patient. In 2012 the alliance was awarded two grants from the Technology Strategy Board (TSB): Sepsis I - Multi-pathogen detection and/or simple discrimination and Sepsis II - Advancing biomarker use in sepsis management.
Collaborations: Identification of a new amyloidosogenic variant of β2-microglobulin

β2-microglobulin is part of the major histocompatibility complex (MHC) proteins, present on almost every nucleated cell in the body. The function of the MHC is to bind fragments of proteins from within the cell derived from pathogens and display these to T cells – triggering cells containing foreign proteins to be attacked by the immune system. Excess β2-microglobulin is only cleared from the body through the kidneys, so patients on long-term dialysis have an abundance in their blood. This then aggregates into amyloid — a type of insoluble protein — fibres that are deposited in bones and joints, causing painful arthritis, cysts and pathological fractures.

In 2011, Dr Sophie Valleis at the Cochin Institute in Paris identified a new amyloidosis-causing variant of β2-microglobulin in patients at her clinical centre\textsuperscript{22}. The affected patients have normal kidney function; but develop rare visceral amyloidosis that leads to bowel disease. Professor Vittorio Bellotti and his research team at University College London have fully characterised the protein and identified its mechanism of amyloidosis, shedding light on the molecular mechanism of this poorly understood process\textsuperscript{23}.

Project reference number: MR/K000187/1

Impacts on the private sector: Sannox Therapeutics

Sannox Therapeutics is a spin out based on the research of Professor George Baillie at the University of Glasgow. Professor Baillie is developing novel therapeutic agents to treat a number of diseases which have an unmet clinical need. The ultimate aim is to progress potential drugs to such a stage that they would be attractive to pharmaceutical companies or investors to take forward to the marketplace. Professor Baillie’s team have developed a system in which they can interpret the interfaces of protein:protein interactions and produce peptides that disrupt specific protein complexes. The lab uses screening techniques to convert peptides into conventional small molecules that could also disrupt protein:protein interactions. It is hoped that this platform will lead to drugs with fewer side effects as the compounds target the cellular location of a particular protein or enzyme rather than its overall activity.

Project reference number: MR/J007412/1

Unexpected impacts

Collaborations: Breed identification of dogs

Dr Carri Westgarth at the University of Liverpool embarked on a collaboration with researchers at Canisius College in New York to investigate the perceptions of dog rescue centre workers on breed identification of dogs resembling pit bull terriers – restricted by breed-specific legislation in the UK. The researchers concluded that participants did not strongly agree on whether a dog was a pit bull, bringing into question the validity of determining breed identity based on appearance alone.

Project reference number: G1002402
Collaborations: Investigating the emergence of novel MRSA strains in cattle and their transmission to man

Professor Mark Holmes at the University of Cambridge has formed collaborations with the Health Protection Agency (HPA) and Statens Serum Institut (SSI) in Denmark to investigate the emergence of a new MRSA strain in cattle and humans. In 2011 MRSA strains with a MecC gene — a new form of the MecA gene, the gene present in MRSA that encodes a penicillin-binding protein — were identified to be present in cattle and humans. The strain was undetectable by current diagnostic tests, a concern when trying to identify the source and transmission of infection. Professor Holmes has exchanged Staphylococcus aureus isolates with both organisations, who have also undertaken functional analyses on the samples. Professor Holmes has conducted whole genome sequencing on the samples, which has led to the HPA implementing a diagnostic test based on this data in order to incorporate screening for MecC MRSA as part of their surveillance activity.

Project reference number: G1001787

Impacts on the private sector: Prokarium

Professor Ian Henderson at the University of Birmingham sits on the scientific board of Prokarium, a spin-out of Cobra Biologics. He is helping Prokarium develop a vaccine for Enterotoxigenic Escherichia coli (ETEC), the leading bacterial cause of diarrhoea in the developing world and which is responsible for between 300,000 and 500,000 deaths annually. In addition, every year more than 10 million travellers contract diarrhoea caused by ETEC, which costs €200m annually in medical resources within the EU, and accounts for €450m in lost productivity.

In 2013 the company received a £0.4m award from the TSB and BBSRC for the development of vaccines against ETEC and Clostridium difficile and the development of their oral vaccine platform Vaxonella.

Project reference number: G0900857

Collaborations: Determining the structure of the Plasmodium falciparum cytosolic ribosome

In 2013 Professor Sjors Scheres at the MRC Laboratory of Molecular Biology (LMB) began collaborating with the Walter and Eliza Hall Institute of Medical Research (WEHI) in Australia to determine a preliminary structure of the Plasmodium falciparum cytosolic ribosome by cryo-EM single-particle analysis. The purified ribosome samples were provided by WEHI. Malaria is caused by infection with parasites of the genus Plasmodium and affects 300 million people each year, resulting in one million deaths. The ribosome is essential for protein synthesis and details of the parasite’s specific ribosome structure may lead to the rational design of new treatments for the disease.

Project reference number: MC_UP_A025_1013
From cell biology to an MRSA vaccine

Impact summary

BBSRC and MRC-funded research contributed to the creation of spin out company Absynth Biologics by Professor Simon Foster and Dr Jorge Garcia-Lara from the University of Sheffield.

The company is developing vaccines against S. aureus and MRSA infection, and aims to enter preclinical development within three years.

The company also received further funding from the MRC and Technology Strategy Board via the Biomedical Catalyst to take forward the vaccine to a pre-clinical stage.

Fundamental research into the bacterium Staphylococcus aureus led to the creation of spinout company Absynth Biologics. The company is now working to produce a vaccine against the bacterium, including methicillin-resistant S. aureus, or MRSA.

Absynth Biologics, founded in 2007 by Professor Simon Foster and Dr Jorge Garcia-Lara from the University of Sheffield, has identified two promising protein targets for use in vaccines against S. aureus. The company aims to start preclinical development in the next few years.

“We had a finite number of targets, of which we’ve tested a number. We now have several lead targets, which are the basis of what Absynth is doing at the moment in terms of the S. aureus vaccine,” says Foster.

Much of Foster’s fundamental bioscience research, which led to the formation of Absynth Biologics, was funded by BBSRC. The MRC subsequently provided significant funding enabling Foster to study the interaction between S. aureus and humans, particularly how natural human defence mechanisms can be exploited to combat the bacterium’s drug-resistance, and to develop the vaccine. Absynth has also obtained funding from the Technology Strategy Board. Funded through the Biomedical Catalyst, these awards will help to take forward the vaccine to a pre-clinical stage.

The company is currently in a funding round with investors, which, if successful, will enable Absynth to grow and move to the next stage of product development.

The superbug

S. aureus causes a wide range of infections, including septicaemia, endocarditis and wound abscesses. It is often resistant to antibiotics and one particular strain, methicillin-resistant S. aureus (MRSA), is the ‘superbug’ responsible for many hospital deaths.

It is a commensal organism, meaning that it lives alongside us all the time, and around one third of people carry it up their noses without suffering ill effects. Infections only occur when the bacteria are able to invade the body, for instance during a surgical procedure. In 2011 S. aureus was directly linked to 638 deaths in England and Wales, and MRSA killed 364 people in the same year. MRSA was estimated to have killed over 11,400 people in the USA in 2010, and has led to many more infections and deaths around the world.

Antibiotics have been the conventional treatment for bacterial infection for 60 years. However antibiotic resistance is becoming a pressing concern. Although some new antibiotics are being developed, it is likely that over time, a similar pattern of resistance will develop and so alternative strategies will be essential. One alternative is to generate protective immunity through vaccination.

A vaccine could help protect people in situations where they are most vulnerable to S. aureus and MRSA infections, particularly during elective surgeries such as knee, hip or heart valve replacements, reducing healthcare costs. It could also be used to vaccinate some groups against the...
threat of 'community-associated' MRSA (i.e. an MRSA infection not associated with a medical setting); this includes people in care homes and prisons as well as the armed forces and hospital staff.

**Ground-breaking research**
Absynth Biologics arose from Foster’s research into S. aureus. In particular, Foster’s group had been studying genes in S. aureus that are essential to its survival, with support from BBSRC’s Exploiting Genomics initiative; Garcia-Lara was the senior researcher on the grant.

The researchers used a genomics approach to identify over 200 potential essential genes in S. aureus. Several of the proteins encoded by these genes were associated with the cell membrane, but with loops or domains predicted to be on the outside, which could make suitable vaccine targets. However, the prevailing view was that these proteins were protected by the bacteria’s impermeable cell wall so were unlikely to stimulate an immune response. Foster disagreed. “We had done a lot of work on cell wall structure and architecture over the years, and we knew the cell wall wasn’t quite as impermeable as people might have thought.”

With Follow-on funding from BBSRC in 2006, the team demonstrated that they could protect against S. aureus infection by vaccinating with a peptide derived from a loop of membrane protein, giving them a number of potential new vaccine targets. In particular, they focused on developing vaccines against proteins essential for the existence of S. aureus and its ability to cause disease. “The problem with many of the surface proteins is the bacteria alter them, or can do without them, so there is a lot of variability,” says Foster. Absynth Biologics’ initial funding enabled them to spend two years collecting more data. The researchers subsequently established a collaboration and license agreement with German company MorphoSys in 2010. Subsequent funding from the MRC in 2011 allowed Professor Foster to test combinations of the vaccine targets and identify the most effective formulation for protection against S. aureus.

In 2012, Absynth received a feasibility award through the Biomedical Catalyst, a translational research programme run by the MRC and the Technology Strategy Board to begin development of a vaccine. Following that, in 2013 Absynth received more than £2m from the Technology Strategy Board and the MRC, again through the Biomedical Catalyst and part-administered through the MRC’s Developmental Pathway Funding Scheme (DPFS), to continue this work.

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**Notes and references**

1. See: [http://www.absynthbiologics.co.uk/](http://www.absynthbiologics.co.uk/)
2. See: [http://www.shef.ac.uk/mbb/staff/foster](http://www.shef.ac.uk/mbb/staff/foster)
3. £1,552,975 to Absynth and £460,731 to University of Sheffield for “Staphylococcus aureus Infections - Development of A Novel, Effective Vaccine”
7. See: [http://www.absynthbiologics.co.uk/page/1n8x8/News.html#GRD%20award](http://www.absynthbiologics.co.uk/page/1n8x8/News.html#GRD%20award)
8. Biomedical Catalyst: [https://www.innovateuk.org/-/biomedical-catalyst#](https://www.innovateuk.org/-/biomedical-catalyst#)

Images: MRSA. Image credit: National Institute of Allergy and Infectious Diseases (NIAID)
Collaborations: Molecular genetics of sexual development

Dr Andy Greenfield at MRC Harwell studies the molecular genetics of sexual development. In 2011 he embarked on a collaboration with researchers at the Pasteur Institute in Paris to assess the role of p38 MAPK signalling in mouse testis determination. The Pasteur Institute supplied Dr Greenfield with mouse mutant material and data concerning gene mutations in patients with disorders of sexual development.

Project reference number: MC_U142684167

Collaborations: UK10K project

The UK10K project is a major collaboration among several leading academic and research institutions including the MRC, Wellcome Trust, Department of Health, Bristol University and King’s College London.

The project, which started in 2010, aims to better understand the link between rare and low-frequency gene mutations and human disease by studying the genetic code of 10,000 people in great detail.

Several MRC researchers are involved in the project, including Professor Peter Scambler at University College London who has helped identify several new genes involved in ciliopathy spectrum disorders. These are genetic diseases of the cellular cilia, slender organelles that protrude from the larger cell body, such as those lining the windpipe, where they sweep mucus and dirt out of the lungs. Results include the identification of gene mutations causing jeune asphyxiating thoracic dystrophy (JATD), a sometimes lethal disease characterised by shortened ribs and long bones, accompanied by renal, liver and retinal disease\textsuperscript{14}, Mainzer-Saldino syndrome, characterised by retinal degeneration and kidney disease\textsuperscript{15} and primary ciliary dyskinesia, that causes a defect in the action of the cilia lining the respiratory tract, fallopian tube in females, and the flagella of sperm in males, resulting in respiratory infections and infertility\textsuperscript{16}.

Project reference number: G9901217

Further funding: African partnership for chronic disease research

Professor Manjinder Sandhu at the University of Cambridge and the Wellcome Trust Sanger Institute is the lead researcher for the African partnership for chronic disease research (APCDR), funded by the MRC until 2018. The APCDR is an international partnership comprising 18 centres from 12 different countries set up to assess the burden and causes of non-communicable diseases such as diabetes and heart disease in sub-Saharan Africa. Professor Sandhu’s team is providing expertise in the genomics of chronic disease, informatics, and epidemiology, and providing access to high throughput next-generation sequencing. Expertise from the different centres ranges from the epidemiology of diabetes and cardiovascular disease in African populations to bioethics and population-based surveys and interventions. The African centres are also providing resources and infrastructure for sample collection (clinics and field stations) and analyses.
The collaboration has already attracted two further funding awards - £2.55m from the Wellcome Trust to study the burden, spectrum and cause of type 2 diabetes in sub-Saharan Africa and an additional MRC grant of £885k to assess the burden and cause of non-communicable diseases.

The partnership is also taking part in several on-going projects including the African Genome Variation project, led by the Wellcome Trust Sanger Institute, and an HIV/anti-retroviral therapy/non-communicable disease meta-analysis.

Project reference number: G0901213

**Regenerative medicine**

**Further funding: Neural stem cell transplantation as treatment for multiple sclerosis**

Dr Stefano Pluchino at the Wellcome Trust-MRC Cambridge Stem Cell Institute has previously shown that the systematic injection of adult neural stem cells protects the central nervous system (CNS) from the degeneration induced by inflammation in small rodents and non-human primates with experimental MS, ischemic stroke or spinal cord injury. He is currently studying the cellular and molecular mechanisms regulating stem cell plasticity — the ability to give rise to cell types situated in a different location to where they are found — in pre-clinical models of complex CNS diseases such as multiple sclerosis and spinal cord injury. In 2011 Dr Pluchino was awarded £171k from Banca Agricola Popolare di Ragusa (BAPR) – the agricultural cooperative bank of Ragusa for the "somatic neural stem cell transplantation as novel therapeutic approach for the treatment of multiple sclerosis."

Project reference number: G0800784

**Impacts on the private sector: DefiniGEN**

DefiniGEN is a University of Cambridge spin out formed in 2012 to supply human induced pluripotent stem cells (hiPSC)-derived liver cells to the drug discovery and regenerative medicine sectors. The company is based on the research of Dr Ludovic Vallier and his team at the Anne McLaren Laboratory of Regenerative Medicine. Dr Vallier’s team developed the technology that has the ability to produce hepatocytes in a highly reproducible and scalable manner for commercial use. This is a major breakthrough in the costly and time-consuming process of developing new therapies. Demonstrating that a new drug candidate is free from liver toxicity is a key part of the drug development process. Currently, either primary human hepatocytes or immortalised cell lines are used for toxicity testing. Primary hepatocytes have a high degree of batch-to-batch variation, are expensive and difficult to obtain in suitable quantities, while immortalised cell lines are an inferior model for toxicity testing. The hiPSC-derived cells produced by DefiniGEN, however, show many of the functional characteristics of primary cells, are highly reproducible and can be made in large quantities, making them ideal for toxicity testing. The technology has also been used to effectively model a diverse range of inherited liver diseases and has the potential to accelerate the development of new therapies for these conditions.

Project reference number: G0701448
SECTION 2.4: Industry interactions and other collaborations

Further funding: Developing biomarkers for subclinical atherosclerosis
As part of the European Commission’s Framework Programme 7 (FP7), the MRC/DH Centre for Environment and Health at Imperial College London has been awarded £641k for the study of novel tools to integrate early-life environmental exposures and child health across Europe and £2.5m to develop biomarkers for subclinical atherosclerosis, a potentially serious condition where arteries become clogged up by substances such as cholesterol.

Project reference number: G0801056

Musculoskeletal health

Further funding: Effects of musculoskeletal health on extended working lives
The current rises in life-expectancy, the subsequent increase in numbers of older people and increasing pension costs has prompted government policies to extend working lives. By 2034 the number of people aged 85 and over is projected to be 2.5 times larger than 2009, reaching 3.5 million and accounting for five per cent of the population\(^{40}\). However, working for an extended period of time may not be feasible for those with major, or chronic health problems. 58 per cent of those aged 60 and over report having a long-term condition, with 25 per cent of over 60s having two or more.

Information on the factors that influence work participation at older ages can be used to optimise government and employer policies to identify interventions to help older workers and to improve the design of work for older people.

Professor David Coggon leads a programme of epidemiological research on the inter-relation of work and health, aimed at informing policy and clinical practice, at the MRC Lifecourse Epidemiology Unit, University of Southampton. In 2012 he was awarded £180k from Arthritis UK to study the effects of musculoskeletal health on extended working lives.

Project reference number: MC_UU_12011/5

Reproductive health

Impacts on the private sector: Icthus Therapeutics
Icthus Therapeutics is a new spin out from the University of Edinburgh’s College of Medicine and Veterinary Medicine focused on women’s health, and in particular on endometriosis. The founders are academics and clinicians from the NHS’s Centre for Reproductive Health and the Royal Infirmary of Edinburgh and include Dr Andrew Horne. The company is funding ‘PURFECT’ - a pilot clinical trial to determine whether purified fatty acids are effective in the treatment of endometriosis-associated pelvic pain.

Project reference number: G0802808

Environmental exposures and child health
Impacts on the private sector: Cambridge Epigenetix

Cambridge Epigenetix is a biosciences company based on oxidative bisulfite sequencing intellectual property that was spun out of Cambridge University in 2012. Bisulfite sequencing is the use of bisulphite treatment of DNA to determine its pattern of methylation. DNA methylation, whereby a methyl group is added to a cytosine or base, is an epigenetic mechanism that cells use to control gene expression. Treatment of DNA with bisulphite converts the DNA base cytosine to the RNA base uracil, but leaves 5-methylcytosine (5-mC), the methylated form of cytosine, unaffected. Thus, bisulphite treatment introduces specific changes in the DNA sequence that depend on the methylation status of individual cytosine residues, yielding single-nucleotide resolution information about the methylation status of a segment of DNA.

Recent studies have shown that at some sites in the genome, the level of 5-Hydroxymethylcytosine (5-hmC), a new mammalian DNA modification, can be comparable to the level of 5-mC, emphasising the importance of identifying these variants accurately. However, traditional bisulfite sequencing cannot discriminate between 5-hmC and 5-mC.

In 2013, the company published the results of a successful beta trial evaluating their pioneering TrueMethyl™ oxidative bisulfite sequencing technology. TrueMethyl utilises a selective chemical oxidation that accurately distinguishes between 5-mC and 5-hmC. It enables analysis of the DNA methylome with unprecedented accuracy and opens new avenues for basic research, pharmaceutical discovery and diagnostics.

Playing a key role in the product validation process and assisting the company in the understanding of epigenetic science were 13 leading epigenetics labs around the world. These included Professor Wolf Reik at the BBSRC Babraham Institute.

Project reference number: G0801156
Endnotes

2 MRC Laboratory of Molecular Biology (LMB) spin out Cambridge Antibody Technology (CAT), formed in 1989, is still noted as the only academic spin out company that has resulted in the discovery of a blockbuster treatment, Humira®. By 2009, Humira® was being used in 80 countries in the treatment of 370,000 patients and in 2013 Humira® sales reached $9.6bn, making it the largest earning pharmaceutical in the world. CAT was acquired by AstraZeneca in 2006 for £702 million, at which time CAT employed more than 300 staff.
3 Some of the MRC’s more recent successes include Oxford Nanopore Technologies, Heptares Therapeutics, Pentraxin Therapeutics, Bicycle Therapeutics, and Thakis Ltd, an Imperial College London spin out that based on the obesity research of Professor Steve Bloom, and which was acquired by US-based Vyeth Pharmaceuticals for $100 million in 2008.
4 Imperial Innovations now invests in businesses built on intellectual property developed at or associated with the Universities of Cambridge and Oxford and University College London in addition to Imperial College.
6 Conversely, Nf2 is also activated in cancer cells, and this is associated with increased drug resistance.
9 As of May 2014, according to the Google Store.
15 http://www.ppmi-info.org/
16 In the UK, Germany and Austria.
17 www.nrhs.uk
18 http://www.gen.cam.ac.uk/news/crowther-carpe-diem-prize
26 http://www.absyntheticbiologics.co.uk/
27 £1,552,975 to Absynth and £460,731 to University of Sheffield for “Staphylococcus aureus Infections - Development of A Novel, Effective Vaccine”
29 http://www.cdc.gov/abcs/reports-findings/survreports/mrsa10.html
30 http://www.who.int/mediacentre/factsheets/fs104/en/
31 http://www.absyntheticbiologics.co.uk/page/1n8x8/News.html#GRD%20award
32 https://www.innovateuk.org/-/biomedical-catalyst#
33 As at May 2014, according to the Google Store.
41 http://www.defininger.com/
SECTION 2.4: Industry interactions and other collaborations
