

# Economic Impact Report 2012/13

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# 1.0 Introduction

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The MRC Economic Impact Report has been published each year since 2005, and is part of the research councils' performance management framework implemented by the Department for Business, Innovation and Skills (BIS). All of the MRC's reports are available on the MRC website<sup>1</sup>, and the most recent report for each research council is available on the RCUK website<sup>2</sup>.

The research councils have worked closely with BIS with the aim of streamlining the metrics that are presented in this report. The aim has also been to make reporting across the councils more consistent and to provide more informative and robust metrics.

The list of metrics agreed between BIS and the research councils can be found in Annex 1, and supporting data is presented in Annex 2. Each research council also presents a small number of additional metrics and narrative information to ensure the report reflects the full range of activities undertaken by the council. The additional metrics for the MRC are noted in Annex 1.

This report should be read in conjunction with the MRC Annual Report and Accounts 2012/13 and the MRC Annual Review 2012/13<sup>3</sup>, which provide a comprehensive summary of achievements over the period.

The MRC Economic Impact Report includes data for 2008/09, 2009/10, 2010/11, 2011/12 and 2012/13 where possible.



# 2.0 Summary and highlights

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The heart of our mission is to improve human health through world-class medical research. To achieve this, we support research across the biomedical spectrum, from fundamental laboratory-based science to clinical trials, in all major disease areas.

We work closely with key stakeholders and other research funders in the UK and internationally to deliver our mission, prioritising research that is likely to make a real difference to clinical practice and the health of the population.

Our stakeholders include the UK's health departments and other government departments and agencies, the six other research councils, the Technology Strategy Board, industry sectors such as pharmaceutical, biotechnology, nutrition, medical technology and informatics, the academic and charity sectors, and of course the public. Established in 1913 and incorporated by Royal Charter in 1920, the MRC's mission is to:

- » Encourage and support research to improve human health.
- » Produce skilled researchers.
- » Advance and disseminate knowledge and technology to improve the quality of life and economic competitiveness of the UK.
- » Promote dialogue with the public about medical research.

Our allocation for 2012/13 was agreed under the 2010 Spending Review. The MRC Delivery Plan 2011/12 – 2014/15<sup>4</sup> details the MRC's spending priorities and intended activities for the spending review period. It describes how the MRC will use its resources to achieve its mission and contribute toward the Government's objectives for the science budget. Progress in implementing the delivery plan and achievements against the milestones are monitored routinely by the MRC's Management Board. Progress is reported to Council and, via biannual meetings, to BIS. A summary of this progress is included in the subsequent annual delivery plan reporting framework document<sup>5</sup>.

In 2009, we published our five-year strategic plan, *Research Changes Lives*<sup>6</sup>, which defines our role in contributing to faster and more effective ways for medical research to flourish at all stages: from working to understand the fundamental science of how our bodies work, to tackling some of the most pressing health issues facing society.

We identified four strategic aims:

- » Picking research that delivers: setting research priorities which are most likely to deliver improved health outcomes.
- » Research to people: bringing the benefits of excellent research to all sections of society.
- » Going global: accelerating progress in international health research.
- » Supporting scientists: sustaining a robust and flourishing environment for world-class medical research.

A mid-term update, evaluating progress against the 16 objectives in *Research Changes Lives*, was published in 2012<sup>7</sup>. This report gives an overview of the MRC's activities and outcomes of MRC-funded research in addressing these objectives. It will serve as a reference point for strategic discussions to inform future research priorities for the next spending review period and the refreshed Strategic Plan, *'Research Changes Lives (2014-2019)'*.

#### 100 years of impact

2013 marks 100 years since the Medical Research Committee and Advisory Council was established in June 1913, initially to conduct research into tuberculosis and other prevalent diseases of the time. The MRC has come a long way and achieved much in the subsequent years, from discovering the structure of DNA and developing vaccines and antibiotics to identifying the causes of many diseases, such as making the link between smoking and cancer. Developments in medical research have meant that our priorities have inevitably altered in the last 100 years; however, our overriding aim has remained the same — to improve the health of people in the UK and across the world. The MRC Centenary website<sup>8</sup> includes a timeline<sup>9</sup> which maps out some of these and other landmark discoveries and impacts that have arisen from MRC-supported research during the last century.

Some of the impacts of on-going MRC investments were highlighted in the recently published RCUK timelines<sup>10</sup> which mainly focus on the Eight Great Technologies<sup>11</sup>. The timelines of particular relevance to MRC research are Sixty Years of DNA<sup>12</sup>, Regenerative Medicine<sup>13</sup> and Big Data<sup>14</sup>.

#### The MRC Centenary

During the year, the MRC publicly showcased its research successes over the past 100 years in collaboration with other major research organisations. The aim was to emphasise the impact that MRC-funded research has had, and continues to have, on UK and world health, on the economy and on society as a whole.

The Centenary aimed to engage a number of different audiences: the public to increase support for publicly-funded medical research, external stakeholders to increase a shared understanding for the benefit of collaborative research, and MRC staff, students and visiting workers to increase understanding of both the aims and strategy of the MRC, and how and where their contribution fits.

Importantly, the MRC sought to highlight the progress of medical research as a whole over the last 100 years, for example to also demonstrate the contribution of fellow research councils and other funding bodies, and not just the work of the MRC. The emphasis was largely forward-looking and focussed on cost-effective and audience-focussed activities.

During the Centenary, the MRC sought to:

- » balance scientific achievement with celebration,
- » embrace MRC life,
- » acknowledge and involve stakeholders, and
- » create a legacy

#### 2.0 Summary and highlights

The MRC Centenary also aimed to act as a platform for the MRC to show how it intends to build on the gains of the last 100 years to ensure its long-term sustainability and place at the heart of medical research worldwide. It helped the MRC maintain its support for world-class medical research through attracting and supporting the world's best scientists, and creating new, and nurturing existing, advocates - internally and externally - for medical research and the MRC worldwide.

#### Media

Centenary year got underway with three short films on BBC television as a celebration of the MRC and its achievements over the past century focussing on tuberculosis, flu and the potential of stem cell therapies. BBC 5 Live aired a two-hour live broadcast featuring the MRC chief executive and researchers past and present, including Sir Peter Mansfield, who spoke on the impact of MRI scanners in medicine.

An online MRC Centenary Poll surveyed a range of people in the public eye – scientists and non-scientists alike – and asked two important questions: 'What medical advance from the past 100 years has had the greatest impact?' And 'What will be the most important medical discovery in the next 100 years?' The poll featured in The Times with a full page spread of responses from more than 50 figures in the public eye, ranging from David Cameron and Dame Sally Davies, to Stephen Fry and former Spice Girl Mel C. According to the public, the most popular medical achievement of the past 100 years was the discovery of antibiotics, which featured on BBC Radio 4's Today Programme (13 June) looking at how the current global crisis in antibiotic resistance was being tackled by today's researchers.

#### **Centenary Awards**

To mark a century of achievements by MRC scientists, the MRC invested over £12m in MRC Centenary Awards which provided the very best MRC early-career researchers with funding to make a step change in their career, enabling the acquisition of new skills and moving their career in a new direction. The 39 individuals awarded an MRC Centenary Award were able to extend or supplement their MRC support, which offered them opportunities to explore new areas or build on existing research. In addition to individual awards, block awards were made to 27 MRC units, 23 MRC centres and 42 universities.

#### **Events**

The MRC Millennium Medal for 2013 was awarded to both Professor Sir Philip Cohen for his pioneering research into protein phosphorylation and cell regulation, and to Professor Sir Gregory Winter, whose pioneering research over many years led to the development of therapeutic monoclonal antibodies. The ceremony, the inaugural event for the MRC centenary, was held in the House of Commons and was hosted by Rt Hon Dr Vince Cable MP. Guests included members of the Houses of Parliament, academics, industry representatives and peers from the research community.

#### Public engagement

A mass public participation project, Worm Watch Lab, supported by the Medical Research Foundation, was launched as the MRC's first 'citizen science' project. It was designed to address a scientific question relevant to MRC research and was conducted in collaboration with the University of Oxford's Zooniverse team. Members of the public were invited to contribute to a neuroscience study on brain circuitry by playing a video game based on how nematode worms (*C.elegans*) lay their eggs. In the first month alone, Worm Watch Lab received 24,954 unique visits and 88,090 page views, and visitors spent an average of 3 minutes 38 seconds on the site. A second mass public participation project, A Century of Amplified Music, will also be launched during Centenary year.

#### **Science Museum**

Following a successful public exhibition at Imperial College where 5,000 people attended an interactive exhibition called Strictly Science – keeping one step ahead, a mini Centenary festival was held at the Science Museum in London. This partnership enabled the Science Museum to offer its visitors the opportunity to interact with real scientists and presented the MRC with the chance to showcase its research to a broad audience. An overarching theme of chance and choice ran through the festival and MRC scientists from nine MRC centres and units guided visitors through Life: a healthy game of chance and choice. Visitors adopted their own 'Pal' and took their character on a journey through life's ups and downs, including encounters with health-related discoveries made possible by MRC-funded research. During the two days of interactive family activities, the festival was close to capacity with over 1,200 visitors taking part, plus those who attended talks.

#### **MRC Centenary Open Week**

To commemorate the exact date on which the MRC committee first met, the MRC held its first-ever Open Week where the public at large was invited to meet and discuss medical research with MRC scientists. Over 50 separate engagement activities took place across the UK, including 16 laboratory open days, 11 public talks and debates, science workshops, art exhibitions, science café events, a Wikipedia edit-a-thon, exhibits at science festivals, four roadshows including a converted lorry used as a mobile teaching unit, and activities in the wider community such as science busking and events on mental health.

Open week tours and talks illustrated the impressive range of work undertaken by MRC scientists and received overwhelmingly positive feedback from members of the public, other stakeholders and MRC staff themselves. To date, over 12,000 people have been recorded as attending these events and activities, and this figure excludes many more people who have taken part online or via news coverage or social media.

## 2.0 Summary and highlights



3.0 Inputs: Investment in the research base

# 3.0 Inputs: investment in the research base

## 3.1 Income and expenditure

In 2012/13, the MRC's gross research expenditure was £766.9<sup>15</sup>, supporting world-class medical research to improve human health and enhance the economic competitiveness of the UK. This included:

- » £334.6m on around 1,400 grants to researchers in universities, medical schools and research institutes
- » £343.1m on around 400 programmes within the MRC's own units and institutes including £8.2m on studentships
- » £71.3m on studentships and fellowships in universities, medical schools and research institutes,
- » There were approximately 1,800 postgraduate students and 404 fellows in March 2013
- » £17.8m for international subscriptions

This is broken down in more detail at Annex 2 (Section 3.1 Income and expenditure).

## 3.2 Human capital (input)

The MRC's vision for training and careers is to train and develop the next-generation of research leaders. The MRC aims to strengthen and sustain a world-leading medical research workforce equipped with contemporary skills across a range of basic science and clinical disciplines by:

- » Supporting excellent individuals at critical points of their careers through continued investment in clinical and nonclinical research training ensuring a demanding and rewarding research experience at various career stages.
- » Investing in areas with the most potential to deliver excellence and innovation for human health, with particular attention to national strategic research skills needs.
- » Enhancing the development, support and career options for non-traditional highly-skilled technical researchers.
- » Increasing support and skills development for research leaders of tomorrow including mentorship.

The Research Career Awards spend for the financial year 2012/13 was £71.3m, with an approximate 40:60 split between studentships and fellowships: £29.2m for studentships (including Clinical Research Training Fellowships) and £41.9m for fellowships. The 2013/14 commitment for studentships and fellowships is £80m with £15m ring-fenced for medical bioinformatics.

The MRC supports more than 1,600 research leaders, either through direct employment in intramural MRC institutes and units, or funding them through university units, grants and fellowships. Further details are given at Annex 2 in Section 3.2 Human capital (input).

The MRC funds a range of fellowship award schemes for both clinical and non-clinical researchers, as well as specific fellowships schemes targeting strategically important research areas or skill-sets. There is further information on MRC schemes on our website as well as comments from researchers showing how the MRC has supported them through their careers<sup>16</sup>.

## 3.0 Inputs: Investment in the research base



## 4.1 Knowledge generation

The data on the MRC's outputs and outcomes presented in this, and subsequent sections, was collected through Researchfish (previously MRC eVal)<sup>17</sup>. This is the system used by the MRC to capture information on outputs, outcomes and impacts from MRC-funded researchers. Information in the system can be entered, amended and updated by researchers all year round, and this is then submitted to the MRC during an annual data-submission period. This means that numbers reported this year will be different to those reported last year as researchers can continue to add information retrospectively.

2012 was the fifth year that researchers used the system, and 97 per cent of the MRC scientists who had held any funding from the organisation since 2006 submitted information — more than 3,500 in total.

Analysis of the Researchfish dataset is providing a detailed picture of the progress, productivity and quality of the science we support. In particular, it is highlighting how MRC research contributes to the development of new medicines and technologies, improvements to clinical and public health policies and practices, and how MRC research encourages inward investment to the UK.

MRC-funded research carried out between 2006 and 2012 has contributed to:

- » More than 100 new products and interventions launched onto the market, including monoclonal antibody therapies for nine separate diseases.
- » Significant influence on more than 300 international clinical guideline documents, including 50 UK NICE guidelines.
- » The creation or growth of 99 companies, with 55 formed since 2006.
- » 570 patents, with discoveries from 170 (30 per cent) of these patents already licensed worldwide.
- » More than £300m in further funding for MRC groups from private sector and international funders (2006/07-2009/10).

## 4.1.1 Paper outputs

Publications are one of the most well-known types of research output; they record new knowledge, methods or insights from a synthesis of existing work, and enable these to be used in other research. The citation of publications in further peer-reviewed research articles is often used as a measure of research productivity, quality and impact.

These citation counts can be normalised by scientific field and year of publication to give a measure of normalised citation impact (nci). An nci score of 1 means that the paper is behaving as would be expected for that subject area in that year,

and this is called the world average, so an nci of above 1 means that the paper is more cited than expected. (Normalised citation impact data and analysis: Evidence, Thomson Reuters UK.) Figure 1 shows the number of unique MRC publications, by year of publication (see Annex 2 Section 4.1 Knowledge General, for actual numbers).



Figure 1: Numbers of unique publications submitted by MRC-funded researchers via Researchfish, by year of publication

The data-gathering period for Researchfish in 2011/12 closed in December 2012. The number of unique publications submitted by MRC-funded researchers (both intramural and extramural) for 2012 is therefore incomplete (partial year numbers for reviews 725, articles 5,873) and will increase; as such, a projection has been estimated.

The average normalised citation impact for MRC publications is 2.12, which is more than twice the world average<sup>18</sup>.

A further measure of the quality of publications is the number/percentage of articles that are either uncited or conversely those deemed as highly cited (i.e.  $NCI \ge 4$ )<sup>19</sup>.

For the UK in general, approximately 30 per cent of papers are never cited. This falls to eight-12 per cent in biomedical fields and for MRC-funded research this reduces further still to approximately four per cent (as shown in the Impact Profile® - figure 2).

MRC-funded research also generates a greater percentage of highly-cited papers than other UK clinical/health and medically-related research and UK biological sciences research (13 per cent compared to 5.9 and 6.7 per cent respectively).





#### **Co-authorship**

Analysis of the authors who have contributed to a research publication can be used as an indicator of collaborative working.

Analysis of these MRC-attributed papers also shows that 48.4 per cent have at least one author from outside the UK. Figure 3 shows the co-authorship of all of the MRC-funded papers reported by sector in Researchfish.



It is also useful to track the co-authorship of papers over time. Figure 4 shows the percentage of papers published by year with at least one author from either the charity sector or the private sector.



Figure 4: Percentage of papers with at least one author from either the charity or public sector, by year

#### Papers published in 2012 already exhibiting high citation impact

In this bibliometric analysis we included papers entered into the Thompson Reuters database between the years 2006 and 2011 with citation counts taken at the end of 2012, so that all papers had at least one year to accumulate citations. There are papers, however, published at the end of 2011 and 2012 that have already rapidly been cited, and are likely to feature in next year's highly cited list.

Tables 1 shows three papers published between the end of 2011 and 2012 that are already being cited at a rate that is more than 40 times the world average.

Table 1: Papers published between the end of 2011 and 2012 already being cited at a rate of more than 40 times the world average

Publication	Summary		
Galectin 8 targets damaged vesicles for autophagy to defend cells against bacterial invasion	Autophagy - cell degradation - defends the mammalian cells against bacterial infection. This study, led by <b>Dr Felix Randow at the MRC's Laboratory of Molecular Biology (LMB)</b> demonstrates that galectin-8 is a receptor for vesicle-damaging pathogens, such as Salmonella <sup>20</sup> .		
( <i>Nature</i> 2012 Jan 15; 482(7385):414-8. doi: 10.1038/nature10744)			
Short frontal lobe connections of the human brain ( <i>Cortex</i> 2012 Feb;48(2):273-91. doi: 10.1016/j.cortex.2011.12.001. Epub 2011 Dec 13)	The frontal lobe of the brain has been shown to play a role in attention and memory, executive cognition, social behaviour and consciousness. This study mapped the architecture of the short frontal lobe tracts in the human brain, the anatomy and the functional correlates of short frontal fibres being largely unknown in man. The preliminary findings can be used as a framework for understanding the anatomy of these connections in larger groups of subjects and correlate their anatomy with cognitive and behavioural performances in healthy population and brain disorders. The work was funded by Guy's and St Thomas' Charity, the Wellcome Trust, the Marie Curie Intra-European Fellowships for career development (FP7) and the Agence Nationale de la Recherche (ANR). The specimens the study relied upon were provided by the Newcastle Brain Tissue Resource, which is funded by the MRC and NIHR.	42	
Vandetanib in patients with locally advanced or metastatic medullary thyroid cancer: a randomized, double-blind phase III trial ( <i>J Clin Oncol</i> ) 2012 Jan 10;30(2):134- 41. doi: 10.1200/JCO.2011.35.5040. Epub 2011 Oct 24)	There is no effective therapy for patients with advanced medullary thyroid carcinoma (MTC). This paper presents the finding of a phase 3 clinical trial of the use of vandetanib. 331 patients were randomly assigned to receive vandetanib (231) or placebo (100). There was a significant prolongation of progression-free survival (PFS) in patients who received vandetanib compared with the placebo, with an estimated 11-month prolongation of median PFS. The secondary efficacy end points of objective response rate, disease control rate, and biochemical response also showed statistically significant benefit in the treatment group compared with the control group.	40	
	This study was predominantly funded by AstraZeneca and reported by <b>Dr</b> <b>Anderson Ryan of the MRC-CRUK Gray Institute for Radiation</b> <b>Oncology and Biology</b> , who was one of the paper's authors.		

#### Non-paper outputs

The following outputs, outcomes and impacts that have arisen either wholly or partially from MRC-funded research were all reported through Researchfish.

The data and analysis in this report represents only a small amount of what MRC does with the information collected through Researchfish. Further analysis and stories of impact can be found on the MRC website, and in particular in the Outputs, outcomes and impact of MRC research: 2012 report<sup>21</sup> and the MRC mid-term progress report<sup>22</sup>.

## 4.1.2 Collaborations

Collaborative work is of increasing importance in facilitating the delivery of all strands of the MRC's mission to improve the health of the nation through world-class medical research.

Recipients of 61 per cent of MRC awards reported that they had embarked on new collaborations as a result of their MRCfunded work. Each collaboration can include a number of partners across different sectors. These partners may be funded from multiple sectors (for example, charitable, public, and private sources) and are not confined to just the UK. Researchers reported a variety of purposes for engaging in a collaboration, including funding, access to equipment, and provision of analytical techniques and expertise.

- » Recipients of 61 per cent of awards (2,900) reported that they had been part of a collaboration between 2006 and 2012.
- » These collaborations involved a total of 15,313 partner organisations.
- » The average number of partner organisations linked via collaborations to each award was 5.28, an increase on last year's average of 4.57.
- » Seven per cent (327) of awards were highly collaborative, reporting links to more than ten partner organisations.

Researchfish data allow us to examine how researchers are engaging with partners from different sectors. Of particular interest is the extent to which researchers are actively collaborating with the private sector. The majority of collaborations reported were with academia (58 per cent), followed by the public sector (16 per cent), and then the private sector (eight per cent) and hospitals (eight per cent). This is similar to results analysed in 2010, although the categories have been revised with the introduction of the hospital/healthcare organisation category. It is noteworthy that there has been a small increase in the proportion of private sector interactions, consistent with the results from the publication data.

Figure 5 shows the proportion of MRC collaborations by sector - see Annex 2 Section 4.1 Knowledge generation for specific figures.



#### Examples of excellence through collaboration:

#### Professor Adrian Hill (University of Oxford)

#### Partnered with Okairos

Okairos is a clinical-stage biopharmaceutical company based in Switzerland. Professor Hill's research focuses on vaccine development, particularly assessing T cell-inducing vaccines against diseases such as TB and malaria. To achieve greater levels of protective efficacy, his group is currently developing more immunogenic prime-boost regimes involving recombinant adenoviruses as priming agents and Modified Vaccinia Ankara (MVA) as a boosting agent. Okairos supplied an adenoviral vaccine vector for the use in phase I and phase IIa clinical trials, adding to the evidence that a CD8-T cell-mediated vaccine can provide vaccination against disease. In 2013, it was announced that the Bill & Melinda Gates Foundation had awarded a \$2.9 million grant in support of a collaboration between the University of Oxford, Okairos and Aeras, a non-profit biotech advancing TB vaccines for the world, to develop scalable methods to enable large-scale production of multiple novel simian adenovirus vector constructs.

#### Professor I Mhairi Macrae (University of Glasgow)

Partnered with Oxygen Biotherapeutics, Inc.

Professor Macrae approached Oxygen Biotherapeutics to access the perfluorocarbon "Oxycyte" to use for further development of an MRI acute stroke diagnostic technique (previously funded by an MRC project grant). This has opened up the possibility of investigating the therapeutic potential of Oxycyte combined with hyperoxia in the treatment of stroke. The Chief Scientist Office (CSO) for Scotland awarded £225k of further funding in 2011 to take these ideas forward.

#### Professor Tracy Hussell (Imperial College)

#### Partnered with GlaxoSmithKline (GSK) and AstraZeneca (AZ)

Professor Tracy Hussell's research focus is in the field of mucosal immunology and infectious disease. She has developed a research group studying immunity, pathology and vaccination to influenza virus infection with a special interest in the secondary bacterial complications that ensue. In 2012, she was appointed director of the Manchester Collaborative Centre for Inflammation Research (MCCIR), a world-leading centre for basic and translational research in inflammation and inflammatory disease, funded through a unique partnership between academia and industry – the University of Manchester, GSK and AZ. The research generated through MRC funding forms the basis of this new centre.

#### Dr John Marshall (Queen Mary, University of London)

#### Partnered with MedImmune

MedImmune is the global biologics research and development arm of AstraZeneca. MedImmune provided access to antibody 264RAD, which Dr Marshall has demonstrated inhibits the activity of integrin alphav beta6 - a protein whose expression has been shown to be up-regulated in many types of cancer - subsequently reducing tumour growth. As a result of the work initiated on this collaboration, in 2012, Dr John Marshall was awarded a three-year grant from the charity Breast Cancer Campaign (BCC).

#### Professor Simon Gayther (University College London)

Collaborative Oncological Gene-environment Study

The Collaborative Oncological Gene-environment Study (COGS) is a pan-European consortium of investigators performing genetic and environmental risk factor studies of breast, prostate and ovarian cancers, funded by the European Commission and 7th Framework Programme. Professor Gayther's research has focused on a genome-wide association study (GWAS) to identify moderate/low penetrance ovarian cancer susceptibility alleles and have found strong evidence that multiple genetic susceptibility loci exist. In 2013, the study revealed that it had discovered more than 80 genetic 'spelling mistakes' increasing the risk of breast, prostate and ovarian cancer. For the first time, researchers also have a relatively clear picture of the total number of genetic alterations that can be linked to these cancers and ultimately hope to be able to calculate the individual risk of cancer, to better understand how these cancers develop and to be able to generate new treatments.

# Case study: MRC-funded scientists discover genetic mutation linked to Alzheimer's disease (2012)

Scientists funded by the MRC, in collaboration with Alzheimer's Research UK and the Wellcome Trust, have discovered a rare genetic mutation that increases the risk of Alzheimer's disease. The researchers analysed data from more than 25,000 people and linked a rare variant of the TREM2 gene – which is known to play a role in the immune system – to a higher risk of Alzheimer's.

The study has major implications for understanding the causes of this disease. It is thought that Alzheimer's is caused by a complex mix of genetic and environmental factors. Some genes that increase the risk of Alzheimer's have been discovered, however, these do not explain the genetic risk in its entirety. The researchers set out to uncover some of the rarer genetic variants involved in Alzheimer's, in a bid to get a clearer picture of the causes of the disease.

The researchers began by sequencing the genes of 1,092 people with Alzheimer's and a control group of 1,107 healthy people. The results showed that several mutations in the TREM2 gene occurred more frequently in people who had the disease than in those without the disease. One specific mutation, known as R47H, had a particularly strong association with the disease – appearing in 2% of people with Alzheimer's compared to 0.5% of people without the disease. The scientists then confirmed their findings in two larger independent groups, analysing data from a total of 6,675 people with Alzheimer's and 16,242 people without the disease. Again, they found that the R47H variant was more likely to appear in people affected by Alzheimer's than in people without the disease.

While this mutation is extremely rare, it increases the likelihood of developing Alzheimer's roughly three-fold – more than any of the genes that have been linked to Alzheimer's in the last 20 years. By identifying the mutation, the research provides valuable new information about the potential causes of Alzheimer's disease.

The TREM2 gene controls a protein that is involved in regulating the immune response to injury or disease, acting as an 'on/off switch' for immune cells in the brain called microglia. The R47H variant of the gene results in a partial loss of this function, with less ability to keep these cells' activity in check – potentially causing them to become hyperactive. The researchers now intend to find out more about the role of TREM2 and better understand the effects of the R47H variant.

This work was published in the New England Journal of Medicine in November 2012<sup>23</sup>.

## Case study (Regenerative Medicine): Restoration of co-ordinated limb movement in dogs with severe spinal cord injury (2012)

In a collaboration between the MRC's Regenerative Medicine Centre and University of Edinburgh Veterinary School, researchers have shown that it is possible to restore co-ordinated limb movement in dogs with severe spinal cord injury (SCI)<sup>24</sup>. The scientists have used a unique type of cell to regenerate the damaged part of the dogs' spines.

Scientists have been aware for over a decade that olfactory ensheathing cells (OEC) might be useful in treating the damaged spinal cord because of their unique ability to support nerve fibre growth maintaining a pathway between the nose and the brain.

Previous research using laboratory animals has already revealed that OECs can aid regeneration of the parts of nerve cells that transmit signals (axons) so as to form a 'bridge' between damaged and undamaged spinal cord tissue. A Phase 1 trial in human patients with SCI established that the procedure is safe.

The trial was performed on 34 pet dogs which had all suffered severe spinal cord injury. One half of the dogs had olfactory ensheathing cells from the lining of their own nose injected into the injury site. The other group of dogs were injected with just the liquid in which the cells were transplanted.

The group of dogs that had received the OEC injection showed considerable improvement that was not seen in the other group. These animals moved previously paralysed hind limbs and co-ordinated the movement with their front legs. This means that in these dogs neuronal messages were being conducted across the previously damaged part of the spinal cord.

The researchers are cautiously optimistic that the work could have a future role in the treatment of human patients with similar injuries if used alongside other treatments.

#### Case study: Division of Signal Transduction Therapy consortium (2012)

A consortium of six of the world's leading pharmaceutical companies<sup>25</sup> has invested £14.4 million in continuing research on the development of new drug treatments for major global diseases, including cancer, arthritis, lupus, hypertension and Parkinson's disease. The Division of Signal Transduction Therapy (DSTT) includes 15 research teams based at the University of Dundee. 13 of the teams are based at the MRC Protein Phosphorylation Unit and Scottish Institute for Cell Signalling (SCILLS) at the College of Life Sciences. It is thought to be the world's largest collaboration between academia and the pharmaceutical industry, and regarded as a model for how academia and industry can interact productively. The DSTT was founded in 1998, expanded in 2003 and renewed for a second time in 2008. This third renewal will secure 50 posts at Dundee until 2016.

# Case study: Professor Declan Murphy co-ordinates largest award of funding for autism research (2012)

An MRC-funded group led by Professor Declan Murphy at King's College London is co-ordinating the largest award ever made to support research into therapies for autism. EU-AIMS (European Autism Interventions - A Multicentre Study for Developing New Medications) is led by Roche and Kings College and involves 14 centres of excellence across Europe. The award was made under the EU Innovative Medicines Initiative and totals almost €30 million of funding over five years (2012-2017) from the public, private and charitable sectors

### 4.1.3 Products or interventions

Products or interventions include the development of diagnostic tools such as screening, therapeutic interventions such as drugs, vaccines, medical devices or surgery, preventive interventions, health/social care services, and several others. Researchfish also records the current stage of development that the product or intervention has reached.

Reports detailing 668 products and interventions were entered into Researchfish in 2012, from 481 awards. Note that data from 2012 is partial due to the timing of data collection, and therefore a projected total has been estimated. Figure 6 shows the products and interventions based on the year in which the most recent stage was completed, see Annex 2 Section 4.1 Knowledge generation for specific figures.



Figure 6: Number of products and interventions by year at which most recent stage was completed

Estimated Interventions

#### Products and interventions by type

The most common type of product or intervention in development was the therapeutic intervention – drug, reported by 146 awards (24 per cent of all products and interventions reported). This was closely followed by the diagnostic tool – non-imaging, reported by 124 awards (20 per cent of all products and interventions).

Figure 7 shows the percentage of each type of product or intervention reported between 2006 and 2012, see Annex 2 Section 4.1 Knowledge generation for specific figures.



Figure 7: Percentage of each type of product or intervention reported between 2006 and 2012

- Diagnostic Tool Imaging
- Dignostic Tool Non-Imaging
- Health and Social Care Services
- Management of Diseases and Conditions
- Preventative Intervention Behavioural risk modifidcation
- Preventative Intervention Nutrition and Chemoprevention
- Preventative Intervention Physical/Biological risk modification
- Products with applications outside of medicine
- Support Tool For Fundamental Research

- Support Tool For Medical Intervention
- Therapeutic Intervention Cellular and gene therapies
- Therapeutic Intervention Complementary
- Therapeutic Intervention Drug
- Therapeutic Intervention Medical Devices
- Therapeutic Intervention Physical
- Therapeutic Intervention Psychological/Behavioural
- Therapeutic Intervention Radiotherapy

#### Products and interventions by development stage

A total of 96 awards reported products and interventions as being launched onto the market since 2006, with a further 14 awards reporting products and interventions currently undergoing the process of market authorisation.

There were 145 reports of products and interventions in early- or late-stage clinical evaluation and 358 reports of products in initial or refinement stages. The inclusion of Developmental Pathway Funding Scheme (DPFS) projects in 2011 has significantly added to the number of projects in early developmental stages.

Table 2 shows the distribution of numbers of products and interventions by development stage.

	Therapeutic Intervention	Diagnostic Tool	Support Tool	Preventative Intervention	Management of Diseases and Conditions
Initial development		57	43	12	5
Refinement. Non-clinical	39	19	11	5	0
Refinement. Clinical	28	23	5	2	3
Early clinical assessment	54	29	6	19	6
Late clinical evaluation	17	4	1	3	4
Market authorisation	7	2	4	0	1
Small-scale adoption	9	23	18	2	2
Wide-scale adoption	9	14	6	2	7

Table 2: Distribution of products and interventions by development stage

In 2012, interest was raised in the number of 'investable opportunities' being produced by MRC-funded research groups. The Researchfish data shows that there are a significant number of such products and interventions at all stages of development, spanning both translational gaps identified in the 2006 Cooksey review of health research. Particular interest was raised concerning developments that faced the 'valley of death', sometimes referring to the attrition rate of projects between initial development and early clinical studies, but more commonly referring to the difficulty in obtaining commercial partners to take products into late-stage clinical evaluation and beyond. Assistance to translate discoveries such as these is available under the Biomedical Catalyst which aligns existing MRC translational research schemes with new funding for the Technology Strategy Board. The Biomedical Catalyst will support £180m of work within this spending review period.

#### Specific examples of products in development:

#### Genetic screening for heart failure gene mutation (2012)

Researchers at the MRC Clinical Sciences Centre (CSC) have discovered, using new gene sequencing technology, that defects in a protein called Titin account for 25 per cent of cases of human dilated cardiomyopathy (DCM)<sup>26</sup>, one of the principal causes of heart failure affecting more than 30,000 people in the UK. This more than doubles the number of cases for which a genetic cause can be identified and means that relatives can be effectively screened for the condition for the first time.

Titin is the largest protein in the body and so testing for mutations had previously proven difficult. The researchers were aided in their discovery of these gene mutations by ultrafast next-generation sequencing technology. The role that genetic screening plays offers the possibility of much earlier diagnosis of heart disease risk and the implementation of preventative measures, giving patients a better prognosis and reducing demand on NHS resources.

Professor Stuart Cook's team is collaborating with researchers in Europe and the US as part of a transatlantic network, supported by a \$6m Leducq award, which is using next-generation sequencing and animal models to uncover other potential causes.

#### Candidate drug for treatment of septic shock (2012)

Dr James Leiper at the MRC Clinical Sciences Centre has discovered a means of selectively reducing nitric oxide (NO), the signalling molecule responsible for dilating blood vessels, which occurs during sepsis. Sepsis is a severe whole-body inflammatory response to an infection, during which, the body makes vast quantities of NO, causing the blood vessels to completely dilate. This leads to a rapid decline in blood pressure, in turn triggering the failure of vital organs. Sepsis causes over 37,000 deaths in the UK every year, more than breast cancer and bowel cancer combined. Reducing NO in a non-selective way is unlikely to be useful, as it has both pathological and protective roles throughout the body. Dr Leiper's group has however discovered a way of reducing NO production in the vasculature system only. They have identified the gene encoding the enzyme DDAH that breaks down the molecule ADMA in blood vessels only; ADMA regulates the NO production pathway, and so by inhibiting the gene, the level of ADMA rises, subsequently blocking NO production and leading to an increase in blood pressure.

Dr Leiper has produced a DDAH inhibitor, molecule L-257, which is a candidate drug for the treatment of septic shock and plans for its first clinical trials are underway.

#### Stem cell-derived respiratory pacemaker (2011)

Together with collaborators at UCL and the University of Newcastle, Dr Ivo Lieberam at King's College London is in the initial stages of developing a new type of respiratory pacemaker device. The device will consist of embryonic stem cell-derived neural tissue (motor neurons and glia), as well as optoelectronic elements and will be used to drive respiration in patients who have lost control of their diaphragm muscle due to neurodegenerative disease, such as motor neurone disease. It is estimated that the technology will take approximately 10-15 years to develop; however, it is likely to result in a significant improvement to patients' quality of life. As a new body/machine interface, the likelihood is that it will have other applications.

#### Case study (Regenerative Medicine): RegenVOX (2013)

Professor Martin Birchall (University College London) has been awarded £2.8m from the Biomedical Catalyst to carry out the world's first clinical trial of a stem cell based larynx transplant, a project known as RegenVOX. He will seek to produce a safe and effective therapy suitable for routine NHS use, resulting in improved quality of life for patients and carers.

Over 2,000 UK patients a year lose laryngeal function due to trauma or cancer and 1,300 NHS patients a year have their larynx removed entirely. Conventional treatments for these patients leave many with substantial problems talking, swallowing and breathing.

The RegenVOX procedure involves preparing a reconstructed larynx, made from the patient's own stem cells and a donor larynx. In the lab, the team uses chemicals to remove the cells from the donor larynx leaving behind a scaffold, onto which stem cells from the recipient can be grafted. This means that the finished implant will not get rejected, like normal transplants, so patients do not need to take immunosuppressant medication.

The team is also able to turn the patient's stem cells into cartilage-producing cells to give natural strength to the transplant, and into replacement mucous membrane cells to line the inside, just like a normal larynx.

The MRC also funded the preclinical development of RegenVOX, and with this latest grant, Professor Birchall hopes to carry out the first transplant procedures in around a year. The research team will then follow ten patients for two years to test whether the procedure is safe and effective.

They will also evaluate the economics of moving treatments like this into routine healthcare, and determine the most cost-effective ways this can be managed, as well as ensuring the UK economy benefits from the potential value of this opportunity.

#### Case study: Nanopattern (2012)

MRC-funded scientists, Dr Matthew Dalby and Dr Nikolaj Gadegaard at the University of Glasgow, are set to revolutionise orthopaedic implant surgery with the use of stem cells. They are working with surgeons at Glasgow's Southern General Hospital to develop a new type of orthopaedic implant which could be considerably stronger and more long-lived than the current generation of products.

They have developed a 'nanopattern' pitted plastic that can be used to coat implant surfaces to encourage stem cells to form bone in contact with the new joint.

When traditional implants are fixed into bone marrow, the marrow's stem cells do not receive messages from the body to differentiate into bone cells, which would help create a stronger bond between the implant and the bone. Instead, they usually differentiate into a mass of soft tissue which, combined with the natural loss of bone density which occurs as people age, can weaken the bond between the implant and the body. As a person's life expectancy increases year on year, they are often outliving the durability of joint implants, which typically have a lifespan of about 15 or 20 years.

However, when stem cells are placed on the surface of the nanopattern, an array of tiny pits just 120 nanometres in diameter, they grow across the pits in such a way that they differentiate into bone cells.

An advanced implantable polymer, PEEK-OPTIMA®, is the material used for the body of the implant. In addition to being strong and not interacting with a patient's body chemistry, its key property is that it could be shaped to include the tiny pits of the bone-growing nanopattern.

#### Case study: Cytosponge (updated 2013)

Researchers at the MRC Cancer Cell Unit in Cambridge have developed a new cost-effective test called the 'Cytosponge<sup>TM</sup>' that can detect Barrett's oesophagus. Acid reflux is the primary cause of Barrett's oesophagus, a condition where the structure of the cells lining the oesophagus changes from being multiple layers of flat cells to being a single layer of rectangular cells more like the intestine. The condition affects 3-10 per cent of people in the UK with heartburn symptoms and 1-2 in 100 people with the condition will go on to develop cancer of the oesophagus over their lifetime.

Barrett's oesophagus is usually diagnosed by having a biopsy during an endoscopy. However, enduring an endoscopy can often be uncomfortable and does present some risks. It is also not practical for everyone experiencing symptoms of heartburn or indigestion to have an endoscopy. An endoscopy costs several hundreds of pounds in comparison to the CytospongeTM test which costs more in the region of tens of pounds and offers a simple yet effective method of screening for this condition. The sponge is contained within a capsule attached to a piece of string that is swallowed with water. The device then dissolves in the stomach to expand into a sponge-like mesh 3cm wide. On removal, the sponge collects cells for molecular analysis to identify the Barrett's cells and any with signs of early cancer.

Cancer Research UK has since funded a larger-scale multi-centre study to follow up these findings, which is currently on-going.

#### Case study: Optical Projection Tomography (2012)

Optical Projection Tomography (OPT) was invented in 2001 by an MRC molecular and developmental biologist, Dr James Sharpe, at the MRC Human Genetics Unit (HGU) in Edinburgh. He was trying to build 3D maps of genes and proteins in mouse embryos. The only method previously available was confocal microscopy (invented at the MRC Laboratory of Molecular Biology), which focuses a laser beam to a fine point, but cannot be used on samples larger than 1mm. To make a 3D image of this type of specimen, it was instead necessary to fit together by computer hundreds of thinly-cut serial sections; this was laborious, time-consuming and introduced distortions in the final image.

This relatively new technique produces 3D images that give unprecedented insights into the structure of tissues and the activity of genes. The method has aided research on the way genes work and may improve the accuracy of medical diagnosis using tissue biopsies.

The OPT technique has been patented and fully commercialised as a product which is used globally<sup>27</sup>, and also through an OPT Scanning Service called Bioptonics<sup>28</sup>.

A study using OPT has led to the development and publication of an interactive atlas of zebrafish craniofacial development<sup>29</sup> which illustrates the appearance, morphogenesis, and growth of the facial components during embryonic and larval development.

Reseachers at Monash University in Sydney, Australia have used the technique to study the effect of diabetes in pregnancy on the key process of kidney development<sup>30</sup>. The findings of their work showed reduced morphogenesis at a specific stage of development, and that the use of late insulin therapy had potentially irreversible effects on the developing embryo.

OPT is one of the techniques used to create images that have won Wellcome Image Awards<sup>31</sup>; these awards recognise the creation of the most informative, striking and technically excellent images. Winning OPT images have depicted a fetal mouse kidney<sup>32</sup>, the developing organs of a mouse embryo<sup>33</sup> and the nervous system of an 11.5 day old mouse embryo<sup>34</sup>.

#### Case study: MEND (updated 2013)

Mind, Exercise, Nutrition, Do it (MEND) provides healthy living programmes for children and families in local communities, including ways to make life changes in physical activity, food, self-confidence and personal development. Formally established in 2004 by UCL Institute of Child Health and Great Ormond Street, it has proven to be a model that is replicable throughout England and Wales and is now the most extensive child obesity treatment programme in the UK.

MEND is currently running more than 200 programmes per school term across the UK and is also being delivered in Denmark, the US, Canada, Australia and New Zealand. The programme is currently looking for partners to deliver the programme in the Middle East<sup>35</sup>.

A recent study on the MEND 5-7 programme demonstrated that participation was associated with beneficial changes in physical, behavioural and psychological outcomes<sup>36</sup>.

## 4.1.4 Research materials

Recipients of 46 per cent of awards (2,218) reported that their work had produced research materials for others to use; 5,226 reports detailing research materials were entered in Researchfish in 2012.

Note that data from 2012 is partial due to the timing of data collection, and therefore a projected total has been estimated. Figure 8 shows the numbers of research materials by the year in which they were realised - see Annex 2 Section 4.1 Knowledge generation for specific figures.



Figure 8: Number of research materials by year realised

Research materials include reports of databases, data analysis techniques, cell lines, models of mechanisms or symptoms, and new equipment.

Models of mechanisms or symptoms – whether in animals, human or *in vitro* - were the most common research material (32 per cent).

Figure 9 shows a breakdown of the distribution of type of research materials reported - see Annex 2 Section 4.1 Knowledge generation for specific figures.


#### Figure 9: Distribution of type of research materials reported

#### Specific examples of research materials:

#### Virtual Desktop Infrastructure - VDI (2012)

Professor Carol Dezateux and co-workers at University College London have developed a secure cloud Virtual Desktop Infrastructure (VDI) environment to be used as a service for the management of sensitive or identifiable data. The epiLab-SS (TCa) is the first of its kind in the UK, offering a scalable model of secure data processing in a private cloud, paving the way for better integration of data with the NHS and other government agencies.

#### The Plasmodium Genetic Modification Project -PlasmoGEM (2012)

Dr Oliver Bilker and colleagues at the Wellcome Trust Sanger Institute has developed the Plasmodium Genetic Modification Project (PlasmoGEM), which uses a combination of recombineering and Gateway technology to convert genomic libraries into gene targeting vectors. Significant improvements have been made to the genetic system of Plasmodium berghei, a model parasite infecting rodents. This has enabled the provision of tools for its genetic manipulation, providing the malaria research community with a freely accessible genome-wide genetic modification resource for academic research<sup>37</sup>.

#### New genetic tool for studying malaria (2013)

Dr Christine Collins and Dr Sujaan Das at the MRC National Institute of Medical Research (NIMR), in conjunction with collaborators at the University of Glasgow, have developed a new genetic tool for studying malaria<sup>38</sup>. Until now there has been no widely applicable mechanism for studying the parasite genes essential for the asexual blood stage - the stage that causes the pathology of the disease - of Plasmodium falciparum, which causes the most dangerous form of malaria. This is due in part to the short life cycle of the parasite at this stage. The researchers have however used a recombinase system to enable the efficient and rapid switch-off of its gene expression, producing Pfalciparum clones that allow the study of these genes.

#### Transgenic mice (2012)

Researchers at the MRC Prion Unit have discovered that a mutation in the CHMP2B gene causes frontotemporal dementia, the second most common type of presenile dementia after Alzheimer's. The team has demonstrated that CHMP2B is required for a process of cell degradation called autophagy. They have generated CHMP2B knockout mice and transgenic mice expressing mutant and normal forms of human CHMP2B for further study, including developing a drug screen to identify drugs to prevent disease causing changes in autophagy.

#### Enhanced Liver Fibrosis (ELF) Panel (updated 2013)

Professor Julie Parkes at Southampton University was part of a group of researchers who in 2008 developed the Enhanced Liver Fibrosis (ELF) Panel, a new method for testing for nonalcoholic fatty liver disease (NAFLD)<sup>39</sup> that may reduce the need for liver biopsies by up to 88 per cent. Liver biopsy is the undisputed best way to assess liver fibrosis or cirrhosis; however, it is an invasive procedure that can cause rare, but potentially life-threatening complications. The ELF validated the Original European Liver Fibrosis panel and removed age as a factor. The researchers also added in simple markers to the test, such as BMI, presence of diabetes/impaired fasting glucose, platelets, and albumin to improve diagnostic performance. The ELF panel is presently available for use in patients with chronic liver disease in the NHS.

### MemGold® screen for crystallisation of membrane proteins (2011)

Professor Simon Newstead at the University of Oxford has developed the MemGold® screen for the crystallisation of membrane proteins. X-ray crystallography is currently the most successful method for determining the three-dimensional structure of membrane proteins. However, growing the crystals required for this technique can be problematic. This is especially true for the -helical type membrane proteins that are of particular interest due to their medical relevance. To address this problem, Professor Newstead undertook a detailed analysis of the crystallization conditions from 121  $\alpha$ -helical membrane protein structures deposited in the Protein Data Bank. Using these data, he was able to design a more rational sparse matrix screen. MemGold® was launched in 2007 and as of 2011, was the most popular screen purchased from Molecular Dimensions, a world leading supplier of screens, reagents and instrumentation for protein structure determination by X-ray crystallography<sup>40</sup>.

#### shMOLLI method (2011)

Professor Stefan Neubauer at the University of Oxford has developed the Shortened Modified Look-Locker Inversion (shMOLLI) recovery method for T1 mapping (an magnetic resonance imaging technique) of the heart. T1 mapping allows direct in-vivo examination of microscopic changes in the myocardium, the muscular tissue of the heart, providing new diagnostic insights into cardiac disease. Existing methods require long breath holds that are demanding for many cardiac patients. The ShMOLLI method, developed in 2010, uses sequential inversion recovery measurements within a single short breathhold. Conditional interpretation of samples for reconstruction of T1-maps is used to yield accurate measurements, and this algorithm is implemented directly on the scanner. This technology has since been licensed to Siemens.

#### Case study (Synthetic Biology): 3D DNA 'origami' (2012)

Many processes in biology rely on the relative position and orientation of interacting molecules. However, because of their small size and the constant thermal fluctuations that they experience in solution, molecules are very difficult to observe and control.

In the field of nano-technology, researchers have developed a technique to construct nano-scaled 3D objects out of DNA. This technique, called 3D DNA 'origami', enables the construction of objects with a precisely designed shape by folding together many DNA strands. Therefore, DNA origami has also been likened to playing with LEGO, albeit at a molecular scale. However, whereas LEGO blocks are very rigid, researchers thought that these new DNA structures would be jelly-like, flexible structures, which would limit their use in technological applications.

However, research in Dr Sjors Scheres's group in the LMB's Structural Studies Division, and Hendrik Dietz's group at the Technische Universität München, has demonstrated for the first time that these 3D DNA origami objects are actually quite rigid. Using a powerful electron microscope, they present the first high-resolution 3D structure of a DNA origami object<sup>41</sup>. Measuring twice the size of a prokaryotic ribosome, the object comprises over 460,000 atoms and its structure provides a library of previously undescribed DNA topologies. The order in this object has been estimated to be comparable to the order in natural protein complexes, thus opening up new avenues for scientific and technological exploration.

In particular, now that it has been shown that these objects are relatively rigid and that the resulting structures can be studied using electron microscopes, it is hoped that in the future, similar methods can be used to position and orient reactive groups of molecules in scaffolds of DNA origami with enough precision to carry out complicated enzymatic or molecular recognition tasks, very much like the protein complexes in a living cell. This could then lead to a wide variety of nano-technological applications for DNA origami.

#### Case study: Genes that affect life span (2012)

MRC-funded researcher Dr Nathaniel Szewczyk, has discovered that the effect of space flight on the microscopic worm *C.elegans* could help it to live longer. Dr Szewczyk, from the MRC and Arthritis Research UK Centre for Musculoskeletal Ageing Research, was part of the ICE-FIRST project, an international consortium of scientists studying the loss of bone and muscle mass experienced by astronauts after extended flights in space.

The group discovered that spaceflight suppressed the accumulation of toxic proteins that normally collect within aging muscle. They also discovered a group of seven genes that are expressed at lower levels during spaceflight and whose inactivation under laboratory conditions extended lifespan. It is believed that these genes are involved in how the worm senses the environment and signals changes in metabolism in order to adapt to the environment.

Dr Szewczyk studies the signals that control muscle protein degradation in the human body. *C. elegans* is the perfect substitute for studying long-term changes in human physiology because they suffer from muscle atrophy under many of the same conditions that people do.

*C. elegans* was the first multi-cellular organism to have its genetic structure completely mapped and many of its 20,000 genes perform the same functions as those in humans. Two thousand of these genes have a role in promoting muscle function and 50 to 60 per cent of these have very obvious human counterparts.

Dr Szewczyk has previously shown that RNAi functions normally in spaceflight and could be used as a viable option to treat and control muscle degradation in spaceflight. This discovery is not only of interest to astronauts but will also help people who suffer from muscle wasting caused by illness and old age.

### 4.1.5 Awards and recognition

Awards, prizes, and other forms of recognition, such as being appointed to the editorial board of a journal – 'measures of esteem' – are highlighted regularly by research organisations (ROs). Measures of esteem are used internationally by some funders alongside citation analysis, peer review and research income as indicators of research quality<sup>42</sup>.

The MRC sought details of the prizes, awards and other types of recognition received by MRC researchers in order to better understand the ways in which researchers are recognised for their contributions to academia and the wider society.

In total, researchers made 11,338 reports in this section. Recipients of 50 per cent of awards reported that their work had resulted in such formal recognition for them, or for members of their MRC-funded team. The average number of reports per award (of those reporting recognition) was five (5.42). Ten or more instances of personal recognition were reported in seven per cent of all awards.

A breakdown of the number of reports of recognition by year is shown in figure 10; see Annex 2 Section 4.1 Knowledge generation for specific figures. Note that data from 2012 is partial due to the timing of data collection, and therefore a projected total has been estimated.



Figure 10: Number of reports of recognition by year

Researchfish captures information on the type of recognition reported; the most frequently reported type of recognition was being personally invited as a speaker at a conference, in 45 per cent of awards reporting personal recognition. This was followed by being appointed to a prestigious/honorary/advisory position to an external body (12 per cent). The distribution of types of recognition is shown in figure 11- see Annex 2 Section 4.1 Knowledge generation for specific figures.

#### 4.0 Outputs: Research performance

#### Figure 11: Distribution of types of recognition



- Appointment to the editorial board of, or advisor to, a journal or book series
- Attracted visiting staff or internships to laboratory
- Awarded membership, or a fellowship, of a learned sociaty
- Medal
- NIHR Senior Investigator/Clinical Excellence Award
- Order of Chivalry (e.g. OBE)
- Other Award
- Personally invited as a speaker at a conference
- Poster/abstract prize
- Prestigious/honorary/advisor position to an external body
- Research prize

#### Specific examples of awards and recognition:

#### Sir Gregory Winter (Professor of Protein and Nucleic Acid Chemistry, Laboratory of Molecular Biology)

Sir Gregory Winter FRS was awarded the 2012 Prince of Asturias Award for Scientific and Technical Research, together with Dr Richard Lerner of the Scripps Research Institute, "for their decisive contributions to the field of immunology and, in particular, for obtaining antibodies of major therapeutic value".

The Prince of Asturias Foundation bestows the Prince of Asturias Award for scientific and technical research annually for work that represents a significant contribution to the progress and welfare of mankind.

#### Professor Kathryn Maitland (Professor of Medicine, Imperial College London)

Professor Kathryn Maitland was awarded the British Medical Journal (BMJ) Research Paper of the Year 2012 for the paper 'Mortality after Fluid Bolus in African Children with Severe Infection' on the results of the Fluid Expansion as Supportive Therapy Trial (FEAST).

The BMJ awards help to celebrate those who make a valuable contribution towards improving the quality of healthcare.

### Professor Carol Dezateux (Professor of Paediatric Epidemiology, University College London)

Professor Carol Dezateux was named as the Wellchild Researcher of the Year 2012 for showing "...great passion and motivation for children's health research and... unwavering support of young researchers embarking on this career path."

#### Professor Sir Mark Pepys (Director of the Wolfson Drug Discovery Unit, University College London)

Professor Mark Pepys was knighted for Services to Biomedicine in the 2012 New Year's Honours. His most recent work has been the invention and development of new medicines for diseases which represent unmet medical need, including amyloidosis, Alzheimer's disease, heart attacks and strokes.

#### Professor Alain Filloux (Chair of Molecular Microbiology, Imperial College London)

In 2012, Professor Alain Filloux was appointed editor of the Journal of Biological Chemistry.

### 4.2 Human capital (stock)

The MRC provides most of its studentship funding to ROs, MRC institutes, units and centres as a block Doctoral Training Partnership. Some exceptions exist, including:

- » Industrial CASE awards: studentships with at least three months of relevant training with a non-academic partner.
- » MRC Clinical Research Training Fellows (CRTFs): personal awards included in the studentship portfolio due to the nature of these awards being clinicians undertaking PhD training.

Approximately 45 per cent of MRC studentships are allocated to ROs through a grant (and fellowship) income-determined Doctoral Training Partnership (DTP). The award provides ROs with significant flexibility in managing their postgraduate studentship population. Many ROs leverage additional sources of funding to further increase flexibility and critical mass of PhD cohorts.

The total number of PhD studentships across the MRC's intramural and extramural programmes at the end of 2012/13 is estimated to be approximately 1,900<sup>43</sup>.

Figure 12 shows the number of live MRC studentships as at March 2013. These are broken down by funding mechanism, showing the number and proportion of each.

#### 4.0 Outputs: Research performance



Figure 12: Number of live MRC studentships as at March 2013

In addition to PhD studentships, the MRC also invests in a limited number of research masters. In 2012, 206 Advanced Course Masters studentships were awarded in the priority areas of biomedical imaging, advanced *in vivo* sciences and mathematics, statistics and computation. Table 3 shows the awards by skills priority area.

#### Table 3: Awards by skills priority area

Priority area	No. awards	% of total 2012 award
Biomedical imaging	116	56%
Advanced in vivo sciences	48	23%
Mathematics, statistics and computation	42	21%
	206	

Further details can be seen in Annex 2 Section 4.2 Human captial (stock).

#### Industry CASE studentships

A shared vision for collaborative training has been agreed across all research councils as follows:

Research Council Collaborative Training will provide doctoral students with a first-rate, challenging research training experience, within the context of mutually beneficial research collaboration between academic and partner organisations in the private, public and civil society sectors.

Through Industrial CASE schemes, research councils promote studentships with a minimum of a three-month period of relevant training with a non-academic partner. MRC CASE studentships are awarded through an annual competition, with

approximately 35 studentships awarded per annum to a wide range of research organisations and non-academic partners. Typically, 50 per cent of awards are made to Small and Medium Enterprises (SMEs).

Research organisations have the flexibility to use their Doctoral Training Partnership to fund collaborative studentships with industrial or other partnership funders. Currently, only a few collaborative studentships are funded through this route (around 20 studentships).

The MRC encourages collaborative studentships that are truly mutually beneficial projects likely to enhance students' training. The MRC therefore does not mandate a conversion rate of Doctoral Training Partnership to collaborative studentships.

A yearly breakdown of the number of students funded under this scheme and the partner organisations is shown in section 5.1.

### 4.3 Knowledge transfer and exchange

A major focus for the MRC in recent years has been the translation of the results of basic science into improved healthcare, products and services. The MRC's translational research agenda aims to speed up the progress of discoveries in the laboratory and turn them into products and interventions that benefit the public and patients, and improve the economic productivity of the UK.

The MRC works with the NIHR and the devolved health departments to ensure that we have integrated funding schemes, infrastructure and facilities to provide a pathway for research from laboratory to standard patient use.

Supporting researchers to collaborate with industry is an integral part of our translational research strategy and at the heart of our mission to produce benefits for patients and growth in the UK economy. In 2012/13, we continued to implement innovative ways of working with pharmaceutical companies to support this goal.

In December 2011, as part of the Government's Life Sciences Strategy, we announced the MRC/AstraZeneca Mechanisms of Disease Initiative, a landmark partnership with the pharmaceutical company AstraZeneca. Under this new type of collaboration, we committed to fund UK academic researchers to use 22 de-prioritised AstraZeneca compounds to investigate disease mechanisms and explore repurposing the compounds for new disease areas. The MRC allocated £10m to fund the three-year research projects, and in October 2012 we awarded funding to 15 highly collaborative projects in areas ranging from common illnesses such as cancer and Alzheimer's disease to rarer diseases such as muscular dystrophy. Eight of the projects will use the compounds in clinical trials, while the remaining seven will focus on laboratory and animal studies.

Another initiative originally announced in the Life Sciences Strategy is the £180m TSB/MRC Biomedical Catalyst. The aim of the programme is to support academic and industry scientists to move their research more quickly from discovery to

#### 4.0 Outputs: Research performance

commercialisation, extending public sector investment further along the translational pipeline, sharing risk with industry, and linking up the activities of the MRC and TSB to provide a continuous set of support mechanisms for scientists. In August 2012, the first awards under the programme were made, with the MRC awarding £7.4m of 'Confidence in Concept' funding, which gave 14 universities grants of between £250,000 and £750,000 to help them progress promising research towards clinical testing. It should fund around 150 pilot projects. In the same round, TSB awarded £2.5m to 18 SMEs.

Later, in November 2012, the first substantial awards under the programme were made, with the MRC awarding £9.5m to ten collaborative projects led by academic institutions to carry out technical feasibility testing, establish proof-of-concept or demonstrate the clinical effectiveness of innovative technologies. The TSB provided £29.6m to 22 projects led by SMEs in the same funding round. The second substantial round of funding, made in March 2013, saw the scheme award a further £47.2m in funding. The MRC awarded £13.9m to seven universities, with the TSB awarding the remainder to 43 SMEs.

The Experimental Medicine Challenge Grants initiative supports ambitious, challenge-led programmes of research into disease mechanisms in humans. These studies will produce major new mechanistic insights into human disease, with potential application to new therapeutic approaches and opportunities for 'reverse translation' to more basic research. Six awards were supported in 2012/13 at a total value of £16m, covering infectious disease, immunity, mental health, cardiovascular disease, pregnancy and obesity.

See Annex 2 Section 4.3 Knowledge transfer and exchange for a breakdown on numbers of awards and commitment for the relevant grant schemes.

Some further strategic investments that the MRC have made during 2012/13 involve the provision of centralised resources and support for research.

#### **Biobank**

UK Biobank, a £90m project predominantly funded by the MRC, the Wellcome Trust and the Department of Health, collects and disseminates health information — physical measurements, questionnaire data and biological samples — from 500,000 UK adults between the ages of 40 and 69 at the time of recruitment. These data are available to academic and industry researchers the world over, who can use them to study how genetics, lifestyle and environment interact to cause disease in areas of public health interest. The resource will become more useful as the participants age and their data are linked to health records. UK Biobank opened to other researchers in March 2012, a significant milestone for a project which received pilot funding from the MRC in 2002.

#### e-Health research centres & the Farr Institute

In 2012 the MRC led a consortium of 10 public and charitable funding agencies to make a £19m commitment to establish four new e-Health research centres. MRC investment in this initiative was £6m. The four centres benefitted from access to patient datasets through the Clinical Practice Research Datalink, a new £60m service launched by the NIHR and MHRA in 2011<sup>45</sup>. The MRC enhanced these centres with an additional investment of £20m capital, and is following up with a further £50m support for skills, capacity and infrastructure for biomedical informatics, taking the total MRC investment in this partnership to £90m. In 2013 the partnership was launched as the Farr Institute. The Farr Institute will support the safe use of patient and research data for medical research across all diseases. The Institute's independent research will support

innovation in the public sector and industry leading to advances in preventative medicine, improvements in NHS care and better development of commercial drugs and diagnostics. It will also provide new insights into the understanding of causes of ill health which in turn will guide new biomedical research discovery. In addition to health benefits for patients and UK citizens, the Institute will help to cement the UK's reputation as a world leader in research using large electronic health data. The Farr Institute has major research centres in London, Dundee, Manchester and Swansea but also links research programmes underway across 19 UK universities.

#### Examples of outputs/impacts in this area:

#### 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 hIPSCderived 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.

#### **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<sup>46</sup>. 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.

#### **Heptares Therapeutics**

Heptares Therapeutics was formed in 2007 to develop and commercialise pioneering research involving G-protein coupled receptors (GPCRs) from the MRC's Laboratory of Molecular Biology and National Institute of Medical Research.

G-protein coupled receptors (GPCRs) provide an almost universal mechanism for transmitting signals into and out of cells. There are

800 GPCRs encoded by the human genome, which are thought to produce thousands of different receptors. The few hundred that have been studied provide key functions for the senses (for example, vision and smell), homeostasis (such as blood pressure), immune regulation, cell growth (such as abnormal cell growth in cancer), and mood/behaviour. A large proportion (around 40 per cent) of all drugs marketed across all conditions act on GPCRs, making these probably the most important drug targets known.

In 2012, Heptares granted Shire an exclusive licence to worldwide development and commercial rights to a novel small molecule adenosine A2A receptor antagonist with best-in-class potential for treating Central Nervous System disorders.

In 2013, Heptares Therapeutics published research<sup>47</sup> identifying the 3D structure of CRF1, the protein receptor in the brain which controls our response to stress. This research was achieved using the intense synchrotron light produced at the Diamond Light Source<sup>48</sup>, which is predominantly owned by the Science and Technology Facilities Council. This structural knowledge can now be applied to the determination of other GPCR structures.

To date, Heptares Therapeutics has raised over \$60 million in financing from Clarus Ventures, MVM Life Science Partners, Novartis Venture Fund, the Stanley Family Foundation and Takeda Ventures.

#### Cambridge Epigenetix

Cambridge Epigenetix is a biosciences company spun out of Cambridge University in 2012 based on oxidative bisulfite sequencing intellectual property. Bisulphite sequencing is the use of bisulphite treatment of DNA to determine its pattern of methylation, DNA methylation being the first discovered epigenetic mark. Treatment of DNA with bisulphite converts DNA base cytosine residues to 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

#### 4.0 Outputs: Research performance

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<sup>™</sup> 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 methylation pattern

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 MRC grant holder Professor Wolf Reik at the BBSRC Babraham Institute.

### 4.4 Intellectual property activity

MRC Technology (MRCT) is a key partner in our translational strategy, working to translate cutting-edge scientific discoveries from MRC units and institutes into products, and managing our intellectual property.

During 2011/12, changes were made to MRCT governance to strengthen its independence from the MRC following the adoption of new articles of association, effective from 31 January 2012. The organisation now works with the MRC under contract, and the MRC paid MRCT management fees of £4,200,000 in 2012/13 (£4,338,000 in 2011/12).

MRCT provides management of both new intellectual property and commercial opportunities arising from research by MRC staff, and the management of existing MRC intellectual property and on-going licensing arrangements. In 2012/13, 38 patents were granted, which is an increase on the 2011/12 number of 27.

In 2012/13, licensing income to the MRC from all sources was £91.7m (£78.9m in 2011/12).

### 4.4.1 Patent applications and patents granted

MRCT works with scientists from MRC-funded units and collaborating organisations to discover and protect healthcare innovations.

The data presented here and below are MRCT data and therefore represent the intramural part of the MRC portfolio only. There is a significant time lag in the process for patents to be granted, as such, there is no correlation between the number of patent applications and patents granted each year. Figure 13 shows the number of patent applications and patents granted by year.



Figure 13: Number of patent applications and patents granted by year

Patent information is also collected through Researchfish; the dataset contains details of 869 discoveries in the intellectual property section. These include 66 reports of copyrighted works, 225 reports of discoveries for which formal protection was not possible or required, and 578 reports relating to published and granted patents.

26 per cent of discoveries overall (232/869) were reported as 'licensed' by 2012. The proportion is slightly higher for patented discoveries (31 per cent, 180/579). This is similar to the proportions reported in the last two years. This calculation does not include the 10 per cent of reports where researchers indicated that details were 'commercial in confidence' and could not be provided (89/869); it would be reasonable to assume that some of these cases will translate into new licenses in due course.

### 4.4.2 Spin outs/new businesses created

MRCT has managed the creation of two new businesses in the last five years directly from the MRC's intramural programme.

The MRC also collects data on spin out companies through Researchfish. MRC funding has contributed to the set up or growth of 104 companies, 56 of which have been formed since 2006. It is estimated that these companies represent at least 500 new highly skilled jobs in the UK.

See Annex 2 Section 4.4a Intellectual Property Activity (MRCT-managed) and Section 4.4b Intellectual Property Activity (Researchfish data), for a breakdown of the data on patents and spin outs.

### 4.4.3 Income from intellectual property

Figure 14 shows the income from intellectual property, including licence income and receipts from sales of shares in MRC companies.



Figure 14: Income from intellectual property (IP)

Income from IP activity (£m)

#### Specific examples of commercialisation (reported in Researchfish):

#### Use of nanoparticles in the treatment of cancer

In 2012, Professor Sam Janes at University College London patented the use of nanoparticles in combination with mesenchymal stem cells (MSCs) in the treatment of cancer. The poor survival of both lung cancer patients and those with other forms of pulmonary metastatic disease relates partly to the inability to deliver locally targeted therapeutic agents. The ability of bone marrow-derived stem cells to migrate to areas of injury in a range of pathological conditions suggests that they may be ideal vectors for therapeutic delivery of anti-tumour factors such as tumour necrosis factor-related apoptosis-inducing ligand (TRAIL). In a clinical setting, the use of MSCs to deliver therapies for the treatment of a tumour creates a need for an imaging tool which can be used to confirm targeted delivery of the therapy to the tumour. Recently, imaging contrast agents have emerged that open up the possibility of visualising stem cell transplants in vivo using MRI and superparamagnetic iron oxide nanoparticles. This imaging technique allows for confirmation of targeted delivery of anti-tumour agents that have been transported by the MSCs as well as enabling more informed decisions to be made regarding the optimal timing of MSC therapy. The iron oxide nanoparticles contained within the MSCs can also be used to kill the cells of the tumour by thermotherapy. Tests in mice have shown that the nanoparticles vibrate when in a magnetic field, which can raise the temperature of the tumour cells by six degrees above body temperature, around the point when cancer cells start to die.

#### Styrene maleic acid lipid particle (SMALP) system

Professor Michael Overduin at the University of Birmingham has patented the SMALP system which is a revolutionary new protein stabilisation technique which could lead to 30 per cent more proteins being available as potential targets for drug development - opening up exciting possibilities in drug discovery. Understanding the structure of proteins is a vital first step in developing new drugs, but to date, drug development has been slowed because proteins are difficult to work with in lab conditions due to their instability. However, the use of SMALP nanoparticles allows the intact preservation of membrane proteins, enabling detailed analysis of their structure and molecular functions.

#### Biomineral treatment to improve renal therapy.

Dr Jonathan Powell and colleagues at the MRC Human Nutrition Research (HNR) have developed a platform technology for generating novel functionalised biominerals with many potential applications in medicine and nutrition. One of these biominerals could be a treatment for hyperphosphataemia (elevated phosphate levels) in chronic renal disease. Patients with late-stage renal disease cannot regulate phosphate levels and suffer from systemic phosphate accumulation which enhances the risk of vascular calcification. Current treatments suffer from low specificity, high pill loading, gastrointestinal side effects, calcium loading or significant toxicity concerns. The novel biomineral treatment developed by the MRC binds to phosphate in the gastrointestinal tract so it is not absorbed, acting as a 'phosphate sponge' and is expected to overcome the disadvantages of current treatments. This therapy was taken through to clinical Phase 1 trials by MRC scientists based at the MRC HNR and has now been licensed to Phosphate Therapeutics Ltd for further clinical development. Phosphate Therapeutics intends to initiate pivotal Phase II trials of this therapy in 2014 and MRC scientists continue to provide expertise into its progression.

#### DNA methylation predictor of obesity

In 2012 Professor Cyrus Cooper at the MRC Lifecourse Epidemiology Centre patented his discovery that the DNA methylation status of the coding region of selected genes, taken from a perinatal tissue sample such as umbilical cord, can be used to predict future development of diverse characteristics, such as obesity or low bone mineral content, impaired cardiovascular structure or function, ability to learn and cognitive function, neurobehavourial problems and allergies such as eczema.

#### Human milk fortifier

Professor Jimmy Bell at Imperial College London has patented a human milk fortifier with high protein and long chain poly unsaturated fatty acids that will increase capability of improving body composition and prognosis in preterm infants.

### 4.0 Outputs: Research performance



# 5.0 Outcomes

## 5.0 Outcomes

### 5.1 Human capital (flow)

Encouraging our students and fellows to establish mutually beneficial relationships with industry is key to ensuring that the UK has a skilled workforce that delivers for the UK in terms of both health benefits and economic returns.

The Higher Education Statistics Agency (HESA) DLHE (Destinations of Leavers from Higher Education) survey provides information about patterns of employment and further study or training six months after completion.

Figure 15 shows the first destination information for MRC students who completed their programmes during the academic year 2011/12 (1 August 2011 to 31 July 2012).



Figure 15: First destinations of MRC students who completed programmes during the academic year 2011/2012

The data demonstrates that six months after completing an MRC PhD, around 84 per cent of students are in employment or engaged in further study. Around 53 per cent of MRC-funded students go into research related employment, mainly in academia, and almost a quarter enter industry or research and development related employment. Further data on this is available in Annex B Section 5.1 Human capital (flow).

### 5.2 Public policy

Research in areas such as the relationship between health, diet and the choices we make, or the effect of the environment that we live in on health, are areas that often result in public health interventions and policy changes rather than commercially exploitable 'products'. These are equally important outcomes to monitor as they often have a direct impact on the public and result in significant impact. Information on influence on policy and practice is collected through Researchfish.

There were 2,879 reports of policy influences between 2006 and 2012 (plus 30 reported without a year), in 1,083 awards.

Figure 16 shows the number of reports of influence on policy by the year that it was realised. Note that three were reported without a year, see Annex 2 Section 5.2 Public policy for specific figures. Note that data from 2012 is partial due to the timing of data collection, and therefore a projected total has been estimated.



Figure 16: Number of reports of influence on policy by year

Each influence on policy is reported as a specific 'type', such as 'citation in clinical guideline' or 'participation in national consultation'. These types fall into two categories – 'influences on the policy setting process' and 'value/changes induced' and are shown in the metrics below.

There were 2,267 reports of influences on policy setting processes reported between 2006 and 2012. Figure 17 shows the breakdown by type of policy setting process with specific numbers and proportion.

#### 5.0 Outcomes





There were 610 reports of value/policy changes induced through citation in key policy documents reported between 2006 and 2012. Figure 18 shows the breakdown by type of policy document with specific numbers and proportion.



Figure 18: Breakdown of type of policy documents

#### Specific examples of influences on policy:

### MRC research identifies treatment in childhood motor neuron disease (2012)

Researchers at the MRC Centre for Neuromuscular Diseases, in conjunction with scientists at the NIH in the United States, have demonstrated that two riboflavin transporter genes are defective in children with a type of motor neuron disease called Brown-Vialetto-Van Laere (BVVL) syndrome.

Brown-Vialetto-Van Laere syndrome is a rare, neurological condition that attacks and progressively destroys motor neurons, causing paralysis of the cranial nerves. This results in the gradual deterioration of the body's functions, such as breathing, hearing, speech, movement, balance and heart function. The onset of disease is generally in infancy or adolescence. Many patients require a long term tracheostomy for ventilation and some never leave the intensive care unit.

The MRC's research, led by Professor Henry Houlden, has shown that defects in two genes coding for riboflavin transporters lead to a lack of riboflavin uptake in the cell and subsequent metabolic reduction. Treating children with high-dose riboflavin led to significant improvement in all aspects of their condition. There was evidence of stabilisation, and even reversal of degeneration, in some patients. This is the first treatable cause of a type of motor neuron disease. Prior to this finding, treatment was restricted to supportive care.

### MRC study shows that moderate drinking in pregnancy can affect a child's IQ (2012)

The MRC-funded Avon Longitudinal Study of Parents and Children (ALSPAC) has supported research resulting in a wide range of potential policy impacts. In 2012, it demonstrated that moderate drinking during pregnancy can affect a child's IQ. In contrast to previous studies where results have been conflicting due to the difficulty in separating the effects of moderate drinking from other lifestyle and social factors, ALSPAC used genetic variation to investigate the effects of drinking 1–6 units of alcohol per week among a large group of over 4,000 women. The researchers

found four genetic variants in alcohol-metabolising genes among the children that were strongly related to a lower IQ at age eight. The child's IQ was on average almost two points lower per genetic modification they possessed. The Royal College of Paediatrics and Child Health has since advised mothers to drink no alcohol at all during pregnancy.

### MRC research leads to national bowel cancer screening programme (updated 2013)

In 2010, Professor Wendy Atkin at Imperial College London published the results of an eleven-year trial funded by the MRC and Cancer Research UK (CRUK) that examined the effectiveness of a single flexible sigmoidoscopy at around age 60 in reducing colorectal cancer incidence and mortality. The trial recruited 170,000 people aged 55-64 years from 14 UK regions, and invited one third (57,000) to have the screening test, with a 70% uptake rate. Following publication of the results, the UK government announced a £60 million investment in a flexible screening programme. Alongside the main findings, Dr Atkin's research team developed a fail-safe, efficient, patient-friendly delivery system for FS screening, and a surveillance strategy following adenoma-removal. From March 2013, the NHS Bowel Screening Programme will pilot the flexible sigmoidoscopy screening test in six bowel screening centres around the country, inviting men and women at the age of 55 in for testing. It is planned to roll out the programme to everyone in the country aged 55 by 2016.

### Prevention and management of neutropenic sepsis in cancer patients (2012)

MRC-supported researcher Professor Robert Phillips at the University of York was the clinical lead for the development of the NICE guidelines on neutropenic sepsis in cancer patients which took into account his research on optimising risk predictive strategies. The new NICE guidelines provide evidence-based recommendations on the prevention, identification, riskassessment and management of this condition.

### 5.3 Public engagement

In recognition of the MRC being funded by the UK taxpayer, the MRC Strategic Plan 2009 – 2014, *Research Changes Lives*<sup>49</sup> states: "We recognise our responsibility to inform and involve the public, policy-makers and our partners about our work." The MRC's programme of public engagement is designed to build relationships with a range of audiences and to support research scientists to deliver quality activities.

The aims of the MRC's public engagement work are to increase public awareness of how medical research benefits both individuals and society, and to build public trust in the MRC and the research it funds.

#### Public engagement events by type

Researchfish collects information about public engagement and dissemination activities delivered by MRC-funded researchers. They are asked to report on their interaction with non-academic audiences. Example activities include presentation of a research talk, participation in a press conference or hosting a laboratory visit. Between 2006 and 2012, MRC-funded researchers reported 15,720 distinct dissemination activities; many recent activities relate to the MRC's Centenary Programme (please refer to section 2.0 Summary and highlights). Please refer to Annex 2 section 5.3 for a breakdown of the types of activities reported by researchers.

#### Funding for public engagement

Engagement with the public is delivered directly by MRC-funded researchers who interact with a wide range of audiences including patient groups, local communities and schools, and these activities are funded from core budgets. In addition, the MRC has a corporate budget for public engagement – £371,500 in 2012/13 – that includes small grants for researcher-led public engagement projects such as taking activities to popular music festivals and creating resources for schools. Researchers are supported in their public engagement work by a network of four MRC regional communications managers who offer help and advice and work with them to make the best use of available resource to achieve their public engagement goals. In 2012/13, the MRC delivered a variety of public engagement related training to over 300 researchers; this included writing, media, crisis communications and public engagement training. All training was delivered before a public event or media interview to improve the quality of the scientist's interaction and experience and to consolidate their learning.

#### Face-to-face engagement

In 2012/13, the MRC worked in partnership with eight of the UK's science festivals where over 200 scientists funded by the MRC spoke to the public face-to-face. They presented activities that facilitated discussion about their research and demonstrate the impact it has on health, the economy and society overall. Collectively, these festivals reached more than 149,500 people, with typical festival audiences made up of school-aged children, teachers and parents. Legacy from each of the events was delivered through take home materials; for example, 10,000 copies of *Changing Lives*, the MRC's public-facing booklet, were distributed.

#### Media engagement

Using established media channels to reach public audiences and raise awareness of the MRC and its work is an integral part of the MRC's public engagement programme. The MRC press office generated 2,234 articles, both print and broadcast, reporting the scientific achievements of researchers funded by the MRC, of which 856 featured in national media.

The MRC is encouraging and supporting scientists to use social media to share research results. In June 2012, the MRC communications team launched *Insight*, a blog-style website designed to tell the stories of research using MRC-funded scientists' own words. Between June 2012 and March 2013, *Insight* received 13,696 unique visitors. In the same time period, the @MRCcomms Twitter account more than doubled its following to 7,681 followers. A new MRC Facebook page has been

used to advertise events and spread research news. These online tools are helping the MRC to reach public audiences and be involved in online conversations about medical research. The MRC website received 871,000 visits from 500,000 unique visitors, and the MRC's magazine *Network* reached more than 6,500 readers online and 2,000 in print.

#### Specific examples of engagement activities:

#### Mapping of the gorilla genome

Dr Aylwyn Scally at the Wellcome Trust Sanger Institute was the lead author of the report "Insights into hominid evolution from the gorilla genome sequence"<sup>50</sup>, published in March 2012, detailing the mapping of the gorilla genome. This generated a large amount of media coverage, both nationally and internationally, including from the BBC, The Guardian, The Telegraph and CNN.

### The brains of people with depression respond differently to guilt

Dr Roland Zahn's research at the University of Manchester has shown that the brains of individuals with depression respond differently to feelings of guilt<sup>51</sup>. The research was published in Archives of General Psychiatry in June 2012, and generated national media coverage, which included articles in the Daily Mail, The Times, Forbes, The BBC, and USNews.

#### New prostate cancer treatment

Dr Hashim Ahmed at University College London received media coverage generated by his paper "Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study"<sup>52</sup> This paper detailed the results of a clinical trial for a new type of prostate cancer treatment, using sound waves to selectively target individual cancer sites, which could provide an alternative to traditional treatment with significantly fewer side effects. Media coverage was generated from the BBC, Sky News, and The Times of India.

#### ScienceGrrl

Dr Sarah Skeoch at the University of Liverpool is part of a network of female scientists (ScienceGrrl) whose aim it is to inspire the next generation of female scientists, technology, engineers and mathematicians. In 2012, they launched a calendar featuring a wide range of female scientists from a diverse range of backgrounds, which sold over 900 copies. The work of the network has generated media coverage from several sources, including The Guardian.

#### Using Zebrafish in research

At the Edinburgh International Science Festival in March 2013, over 1,000 children visited the MRC's Mini Scientists activity where they were introduced to the concept of using animals in medical research with two tanks of zebrafish sourced from an MRC lab. A total of 48 MRC-funded researchers, staff and PhD students talked to the children about how fish are used in cancer research in order to learn more about human growth and development. To read about the children's responses, visit the Insight blog<sup>53</sup>.

#### Involving older people in the Go Far Project

Marcus Ormerod at the University of Salford was involved in a number of public engagement activities, one of which was a talk hosted jointly by the British Society of Gerontology and the Kilburn Older Voices Exchange. After talking to the older participants and local councillors on good street design, there was a specific session on falling over outdoors during which the participants were able to input into, and inform the development of, the Go Far project. Subsequent to the event, some of the participants shared their experiences of falling over and the dramatic effect that this had had on their lives. The team will be able to use these narratives to bring forward the voices of older people in both the research and impact from the research.

#### Helping students design brain experiments

Raymond Norbury at the University of Oxford hosted two sessions for sixth form pupils from local schools. The pupils attended the University of Oxford Centre for Clinical Magnetic Resonance Research and were given a demonstration of the scanner in action, a general presentation on Magnetic Resonance Imaging (MRI) and an MRI data analysis demonstration. The pupils were also asked to work in small groups and develop their own fMRI experiment, 'Which areas of the brain process colour?' the aim of which was to encourage them to think about experimental design in general and also to think about what you can and cannot do with an MR scanner. Feedback provided by the teachers, lectures and pupils was very positive, and it is anticipated that similar presentations and workshops will continue and remain popular.

#### Students visit immunology lab

Gavin Wilkinson at Cardiff University invited school students into the lab for work experience as part of the department's on-going engagement with local schools. A total of 18 students were involved and undertook a lab research project that examined the effect of intrinsic immune defences on expression from an adenovirus carrier. The students were clearly engrossed in the work, asking many questions about the project, and formal feedback was extremely positive.

### Partnering with a local school to encourage careers in science

Researchers at the MRC Human Genetics Unit collaborated with nearby Broughton High School by sharing images and stories about research, and giving talks about life as a scientist and careers in science. Dave Cockburn, Faculty Head of Science at the school, said of the partnership: "This relationship has been extremely valuable for the staff and the students. The percentage of students taking two sciences in 2009/2010 was 16 per cent. In 2010/11, we continued with the project and the percentage is now 40 per cent. These figures speak for themselves and they would suggest the talks have helped to get more students studying two or more sciences."

#### Sharing dementia research findings

In June 2012, Professor Huw Morris, who is in receipt of MRC funding at the University of Cardiff, gave a lecture entitled 'What is dementia?' to a public audience of 400 people at the Hay Literary Festival. Professor Morris is a neurologist and geneticist at Cardiff University and the Royal Gwent Hospital, Aneurin Bevan Health Board. In his talk, he discussed the personal and social impact of dementia, how different types of dementia affect the brain and various aspects of behaviour and thinking. He described some recent new discoveries and the prospects for new treatments in dementia.



Annexes

# Annex 1: New Metrics Framework – BIS 2011/12

Key:

=to include

= optional

= remove

CATEGORY METRIC	UNITS	DEFINITION	
Total Funds Available	£m	Total funding available to the research council - Sum of Grant in Aid and Leverage	
Budget Allocation	£m	Research council Grant-in-Aid	
Leverage	£m	Funding other than Grant-in-Aid. Sum of components below	
of which Private	£m	Funding Leveraged from the Private Sector	
of which from other Research Councils	£m	Funding Leveraged from other research councils	
of which from other source	£m	Funding received from all other sources.	
of which Private	%	As a percentage of Total Funds Available	
of which Other Research Councils	%	As a percentage of Total Funds Available	
of which Other	%	As a percentage of Total Funds Available	
Total Expenditure			
of which Responsive Mode Grant	£m	Accounts Expenditure on Responsive Mode Grants	
of which Postgraduate Awards	£m	Accounts Expenditure on Postgraduate Student Support	
of which Other components	£m	Residual Expenditure on other components as Total funding minus two above	
of which Responsive Mode Grant	%	As a percentage of Total Funds Available	
of which Postgraduate Awards	%	As a percentage of Total Funds Available	
of which Other components	%	As a percentage of Total Funds Available	
Human Capital			
Principal Investigators	#	Total number of principal investigators directly supported on DATE	
Research Leaders in Sponsored Institutes	#	Total number of research leaders in sponsored institutes where applicable on DATE	
Research Fellowships	#	Total number of Research Fellowships on DATE	
Knowledge Generation			
Number of Grants assessed for reporting	#	Number of grants assessed to which the outputs reported refer	0
Refereed Publications	#	Number of papers published in peer reviewed journals	
Non Refereed Publications	#	Publications OTHER THAN those included under Refereed Publications	0
Co-authorship of refereed publications - International	#		0
Co-authorship of refereed publications - Industry	#		0
Human Capital			
Number of PhD Students Supported	#	Number of NEW PhD students supported on DATE	
Number of Masters Students Supported	#	Number of NEW Masters students supported on DATE	0
Number of Other Students Supported	#	Number of New Non PhD or Masters Students supported on DATE	

Finishing Rates	%	Percentage of PhD students submitting within 4 years of commencement of support (for example row 2007/08 refers to students who began in 2003/04)	
Student funding/training schemes			
Knowledge Transfer and Exchange			
KE Spend	£m	Total spend for relevant year across all council KTE programmes	
KE Programmes		Please State which KE programmes you support	
Commercialisation Activities			
IP Activity (discretionary)			
Patents applications	#	Patent Applications to RC investments	
Patents granted	#	Patents Granted to RC investments	
Spinouts/new businesses created	#	Number of new spinouts created from RC investments	
Income from IP activity	£m	Income from IP including areas such as licence income and receipts from sales of shares in RC funded companies.	
Human Capital			
Destinations of leavers		Total Number of leavers from Doctoral Programmes in this academic year (DLHE)	
Of which University	%		
Of which Wider Public Sector	%		
Of which Third Sector	%		
Of which Private Sector	%		
Of which Unknown or Other	%		
Of which Unemployed	%		
Placements in user organisations	#	Count instances of funded placements in user organisations	
Placements in user organisations		Examples of measured impact	
Public Policy			
Instances of influence		Examples of influence in policy	
Value/changes induced		Examples of measured impact	
Public Engagement			
PE Schemes		Examples of PE Schemes	

#### Additional MRC metrics

The MRC has also chosen to include additional metrics and/or narrative information on:

- » Non-paper outputs (part of section 4.1 Knowledge generation)
- » Translational research and knowledge exchange (section 4.2 Knowledge transfer and exchange)
- » Public engagement (section 5.3 Public engagement)

# Annex 2: MRC metrics

Sect	ion 3.1 Income and expenditure							
No.	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	
1	Budget Allocation	£m	680.8	722.2	732.0	697.5	656.2	As per Annual Report
2	Leverage (MRC definition)	£m	693.7	739.0	745.9	702.1	659.6	As per Annual Report i.e. budget
2	Leverage (BIS definition)	£m	63.4	77.1	67.6	56.5	68.3	As per BIS guidance i.e. external property (metric 2d).
2a	of which Private	£m	44.6	50.6	42.5	42.1	49.2	
2b	of which from other Research Councils	£m	5.8	9.6	11.2	9.8	15.7	
2c	of which from other source – Other Income	£m	13.0	16.9	13.9	4.6	3.4	Other income includes sales of la sales of radioisotopes etc.
2d	of which from other source - Licences and Shares	£m	64.98	66.19	61.69	78.98	91.72	Income from IP includes licence
3	Total Expenditure	£m	349.6	383.6	384.3	414.1	423.7	As per Annual Report
3a	of which Responsive Mode Grant	£m	229.5	249.3	264.5	267.6	243.1	As per Annual Report
3b	of which Postgraduate Awards	£m	67.9	78.2	78.7	86.0	71.3	As per Annual Report
3с	of which Other components - Other Research	£m	36.9	38.3	23.2	42.2	91.5	As per Annual Report
3d	of which Other components - International Subscriptions	£m	15.3	17.8	17.9	18.3	17.8	As per Annual Report

Sect	ion 3.2 Human Capital (input)							
No.	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	
4	Principal Investigators on grants	#	1006	1081	1041	958	1050	Data are expressed in terms of po (for 2012/13).
								This is the number of distinct peo been counted only once.
5	Research Leaders in Sponsored Institutes	#	349	346	289	237	239	Data are expressed in terms of po
б	MRC-funded fellows	#	368	362	387	376	351	Data are expressed in terms of po 2012/13). This figure includes Clin
								This is the number of distinct peo been counted only once.
•••••							•	

Sect	ion 4.1 Knowledge Generation						
Раре	r outputs						
No	Metric	Unit					
7	Number of grants assessed for reporting:		4,586 submitted return	ns through Researchfish.			

#### Notes

allocation (metric 1) plus other income (metric 2c).
ncome (metrics 2a, 2b & 2c), excluding that from intellectual
boratory and library services, as well as proceeds from the
income and receipts from sales of shares in MRC companies

#### Notes

oosts at December (for 2007/8 to 20011/12) or August 2013

ople, where a person holds more than one grant, they have

osts at 31 December.

hosts at December (for 2007/8 to 20011/12) or March 2013 (for nical Research Training Fellowships.

ople: where a person holds more than one grant, they have

Notes

8	Refereed Publications (publication year)	#	2006	2007	2008	2009	2010	2011	
8a	Reviews	#	395	493	647	797	680	744	
8b	Articles	#	3,298	4,157	4,789	5,440	6,125	6,242	1
8c	Total	#	3,693	4,650	5,436	6,237	6,805	6,986	6

9	Co-authorship of refereed publications - International	#		48% of MRC-funded peer reviewed papers published between 2006 and 2012 which have at least one author from outside the UK.							
10	Co-authorship of refereed publications - Industry	#		8% of all MRC-funded peer reviewed papers published between 2006 and 2012 have at least one author from the private sector.							
Non paper outputs											
No	Metric										
11	Collaboration				Num	ber of collaborations re	ported with at least one	partner in the relevant se	ector.		
				Sector				Num	ber	%	
				Academic				793	35	59%	
				Non-Profit	t			77	б	6%	
				Learned So	ociety			36	5	0%	
				Multiple				15	6	1%	
				Private				103	88	8%	
				Public				220	00	16%	
				Hospital				102	23	8%	
				Unknown				40	0	3%	
				Total				135	64 1	00%	
No	Metric	Unit	No year	2006	2007	2008	2009	2010	2011	2012	Total
12	Products or Interventions	#	5	42	25	54	125	162	122	78 (partial)	613

2012	Total	The data gathering
725	4,481	period for
5,873	35,924	Researchtish in 2012 was October and
5,598	40,405 (partial)	November, therefore
	48,405 (estimate for full year)	the figures for 2012 are partial, as such a projection has been estimated.

2011	2012	Total
122	78 (partial)	613
	85 (estimate for full year)	

		•••••••••••••••••••••••••••••••••••••••
Type of Products & Interventions	Number	%
Diagnostic Tool - Imaging	47	8%
Diagnostic Tool - Non-Imaging	124	20%
Health and Social Care Services	7	1%
Management of Diseases and Conditions	28	5%
Preventative Intervention - Behavioural risk modification	33	5%
Preventative Intervention - Nutrition and Chemoprevention	9	1%
Preventative Intervention - Physical/Biological risk modification	3	0%
Products with applications outside of medicine	5	1%
Support Tool - For Fundamental Research	62	10%
Support Tool - For Medical Intervention	32	5%
Therapeutic Intervention - Cellular and gene therapies	30	5%
Therapeutic Intervention - Complementary	4	1%
Therapeutic Intervention - Drug	146	24%
Therapeutic Intervention - Medical Devices	9	1%
Therapeutic Intervention - Physical	6	1%
Therapeutic Intervention - Psychological/Behavioural	35	6%
Therapeutic Intervention - Radiotherapy	1	0%
Therapeutic Intervention - Surgery	8	1%
Therapeutic Intervention - Vaccines	24	4%
Total	613	100%

No	Metric	Unit	No year	2006	2007	2008	2009	2010	
13	Research Materials	#	1594	481	275	399	566	537	

No	Metric	Unit	No year	2006	2007	2008	2009	2010	2011	2012	Total
13	Research Materials	#	1594	481	275	399	566	537	484	409 (partial)	4745
										475 (estimate f year)	or full
				Type of R	lesearch Material			N	ımber	%	
				Antibody					165	3%	
				Cell line					253	5%	
				Data analy	rsis technique				631	13%	
				Database/	Collection of Data/Biolog	gical Samples			917	19%	
				Improvem	ents to research infrastr	ucture			287	6%	
				Model of r	mechanisms or symptom	ns - human			118	2%	
				Model of r	mechanisms or symptom	ns - in vitro			90	2%	
				Model of r	mechanisms or symptom	ns - mammalian in vivo			1175	25%	
				Model of r	mechanisms or symptom	ns - non-mammalian in vi	/0		110	2%	
				Physiologi	cal assessment or outco	me measure			150	3%	
				Technolog	gy assay or reagent				847	18%	
				Other/Unk	nown				2	0%	
				Total					4745	100%	
No	Metric	Unit	No year	2006	2007	2008	2009	2010	2011	2012	Total

	No	Metric	Unit	No year	2006	2007	2008	2009	2010	2
--	----	--------	------	---------	------	------	------	------	------	---

14	Awards and Recognition	#	77	793	902	1314	1779	2339	2338	1796 (partial)	11338
										2256 (estimate for full year)	
				Type of Award a	& Recognition			Number		%	
				Appointed to the	editorial board of, or ad	dvisor to, a journal or b	ook series	1266	ſ	11%	
				Attracted visiting	staff or internships to l	aboratory		310		3%	
				Awarded member	rship, or a fellowship, of	a learned society		996		9%	
				Medal				283		2%	
				NIHR Senior Inves	stigator/Clinical Exceller	nce Award		119		1%	
				Order of Chivalry	(e.g.OBE)			46		0%	
				Other award				2		0%	
				Personally invited	l as speaker at a confere	ence		5131	Z	15%	
				Poster/abstract pr	rize			548		5%	
				Prestigious/honor	rary/advisory position to	o an external body		1343	1	12%	
				Research prize				1294	-	11%	
				Total				11338	1	00%	
								•		•	
				<b>_</b>				<b>_</b>			

Sect	ion 4.2 Human Capital (stock)									
No	Metric									
15	Number of PhD Students Supported	See narrative in section 4.2 of main	body of report.							
		The total number of live MRC studer	ntships as at March 2013 was 1900. Th	nese are broken down	below by funding me	chanism, showing the numbe	er and proportion of e	ach.		
		Funding mechanism			#	%				
		Doctoral Training Partnership			856	45				
		MRC Intramural Students			458	24				
		Capacity Building Students			149	8				
		Clinical Research Training Fellowshi	p		142	7				
		MRC Centre Studentships			190	10				
		Industrial Case Studentships			105	6				
		Total			1900	100				
17	Finishing Rates	Registration years 2004 to 2006* - D	ata from JeS Submission survey 2011 200	, this therefore only inc 4*	cludes students who	completed the survey.	2	006*		
		Registration year	#	%	#	%	#	%		
		Within 5 years	326	91.6	394	90.8	286	89.4		
		Greater than 5 years	9	2.5%	4	0.9	0	0.0		
		Delayed submission	6	1.7	9	2.1	25	7.8		
		Student will not submit	15	4.2	27	6.2	9	2.8		
		Unknown								
		Total number of records	356		434		320			
No	Metric	Unit	2008/09	2	2009/10	2010/11		2011/12	2012	/13
18	Student funding/training schemes	£m	3.2	2.5		3.1	3.4		3.5	
				Indu	ustry case studentshi	ps – funding by academic ye	ar.			
Cart										
Sect	ion 4.3 Knowledge Transfer and Ex	change								

No	Metric											
19	KE Spend	See narrative in section 4.3.										
20	KE Programmes	Numbers of awards and total commitment values for some of the MRC	ranslationa	l schemes.								
			200	8/09	200	9/10	201	0/11	201	11/12	201	2/13
		Scheme	#	£m	#	£m	#	£m	#	£m	#	£m
		Regenerative Medicine Research Committee*	12	6.4	13	7.3	10	7.6	7	4.5	6	3.9
		Developmental Pathway Funding Scheme (DPFS)(directly managed)	15	6.4	17	8.7	19	12.0	18	11.9	-	-
		Developmental Clinical Studies (DCS)	-	-	3	5.3	10	13.7	20	22.3	-	-
		Developmental Pathway Funding Scheme (DPFS)**	-	-	-	-	-	-	-	-	10	6.4
		Biomedical Catalyst Fund ***	-	-	-	-	-	-	-	-	41	30.7
		* Regenerative Medicine Research Committee was previously the Translational Stem Cell Research Committee, to provide support for high quality proposals aiming to develop reget ** In early 2012/13 the DPFS and DCS schemes were merged into one scheme, now known *** Biomedical Catalyst (BMC) commitment includes awards made through the DPFS Pane Confidence In Concept scheme	Research Comm enerative medi a as DPFS, one e el and Major Av	nittee (TSCRC). L cine therapies to round of which w vards Committee	Drawing on the o improve hum was funded in 1 e from Sept 20	experience and an health. May 2012. 12 onwards, aca	d expertise of the ademic costs of	he MRC's TSCRC n Early and Late	, the MRC has o stage business	established the F s-led BMC award:	Regenerative N s and awards m	ledicine nade und

Sect	ion 4.4a Intellectual Property Activi	ity (MRCT manage	ed)					
No	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	
21a	Patents applications (MRCT managed)	#	20	25	12	12	20	This data is collected through MF
22a	Patents granted (MRCT managed)	#	24	29	32	27	38	programmes.
23b	Spinouts/new businesses created (MRCT managed)	#	0	0	2	0	0	Income from IP includes licence
24	Income from IP activity (MRCT managed)	£m	64.19	66.17	61.69	78.98	91.72	

Sect	ion 4.4b Intellectual Property Activit	ty (Researchfish o	data)								
No	Metric	Unit	Unknown	2006	2007	2008	2009	2010	2011	2012	Total
21b	Numbers of patents (Researchfish data)										
	Not licensed	#	93	10	40	80	116	114	57	38	548
	Licensed	#	53	16	31	17	42	37	18	18	232
	Commercial in confidence	#	14	4	11	б	11	23	10	10	89
	Total	#	160	30	82	103	169	174	85	66 (partial)	869
										100 (estimate for full year)	
23b	Spinouts/new businesses created		Pre 2006	2006	2007	2008	2009	2010	2011	2012	Total
	(Researchfish data)	#	48	5	7	10	8	9	11	6	104

MRC funding has contributed to the set up or growth of 104 companies, 56 of which have been formed since 2006. It is estimated that these companies represent at least 500 new highly skilled jobs in the UK.

Higher Education - other

Not known or not reported

School Teaching or Teacher Training

Self Employed, Voluntary and Unpaid work

Not employed

Total

Other Employment

R & D Sector Unknown School (Education other)

Industry & Commerce - research related

Industry & Commerce - not research related

Sect	ion 5.1 Human Capital (flow)						
No	Metric						
25	Destination of leavers	The following data show the first destination of PhD stud	dents qualifying or comp	pleting their courses betw	ween 1 August 2008 and	31 July 2012.	
		Please note that this is an incomplete return and does no	ot cover the total numbe	r of students funded by	the MRC.		
		Taken from DLHE (Destination of Leavers from Higher Ed	ucation) data 2013 whic	h collects data on stude	nts who completed their	courses between 1 Aug	ust 2011 - 31 July 2012.
		Category	2007/08	2008/09	2009/10	2010/11	2011/12
		Engaged in Study	12	19	17	9	22
		Government & Public Sector - not research related	9	19	26	14	0
		Government & Public Sector - research related	6	5	б	4	34
		Higher Education - academic	3	9	7	15	6
		Higher Education - mainly research	70	100	126	125	133

Notes

RCT and therefore only represents MRC's intramural

income and receipts from sales of shares in MRC companies.

No	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13
26	Placements in user organisations	#	46	34	34	33	35
	Numbers of industrial CASE awards over the last four years, these are awarded in partnership with industry or policy making bodies						
		In 2012/13 MRC awarded 18 (out of 35)	industrial CASE studentships to SMEs. T	he industrial partners for all 35 awards i	n 2012/13 are listed below:		
			Company	SME	Awarded		
		Acuity ETS Ltd		Y	1		
		Apitope		Y	1		
		Aptamer Solutions Limited		Y	1		
		Critical Pharmaceuticals		Y	1		
		Dundee Cell Products (DCP)		Y	2		
		Eisai UK		Ν	1		
		Eli Lilly and Company Ltd		Ν	2		
		ExpreS2ion Biotechnologies		Y	1		
		GlaxoSmithKline (GSK)		Ν	1		
		Imanova Ltd		Y	1		
		Isogenica		Y	1		
		Janssen		Ν	1		
		Linguamatics & Psychologyonline		Y	1		
		Morvus Technology Ltd		Y	1		
		MRC Technology		Y	1		
		National Autistic Society		Ν	1		
		New-Food Innovation ltd		Y	1		
		NovaBiotics Ltd		Y	1		
		Novartis		Ν	3		
		Novartis Pharma AG, Basel,					
		Switzerland		Ν	1		
		Novartis/ NIBR (Novartis Institutes for	BioMedical Research)	Ν	1		
		Oxitec Ltc		Y	2		
		Pfizer		Ν	1		
		Pfizer Global Research		Ν	1		
		Pfizer Neusentis		Ν	1		
		Phicotherapeutics		Ŷ	1		
		Simcyp Limited		Y	1		
		UCB Pharma		Ν	1		
		Vertex		Ν	1		
		Waters limited		Ν	1		
		Total			35		

.....

Sect	ion 5.2 Public Policy								
No	Metric	Unit	No year or pre-2006	2006	2007	2008	2009	2010	Ĩ
27	Instances of Influence on Policy and Practice	#	30	300	250	375	487	501	
28	Instances of influence	Influences on policy s	etting processes, 2292 re	ports between 2006 an	d 2012.				
29	Value/changes induced	Citations in key policy	documents, 614 reports	between 2006 and 2012	2.				
		*please note that 3 ins	stances of influence on p	oolicy were reported with	h a category of 'other'.				<b>.</b>

No	Metric			
0	PE Activities	Below is a summary of the data by type of dissemination activity reported between	2006 and 2012.	
		To reduce the burden on researchers they are advised to report just one of any type	of activity within any given year the	erefore these figures
		Туре	Number	%
		A formal working group, expert panel or similar	1727	11%
		A magazine, newsletter or online publication	2038	13%
		A press release, press conference or response to a media enquiry.	1572	10%
		A talk or presentation	5850	37%
		Participation in an activity, workshop or similar	2627	17%
		Participation in an open day or visit at my research institution	1015	6%
		Scientific meeting (conference/symposium etc.)	891*	6%
		Total	15720	100%

2011	2012	Total
553	413 (partial) 567 (estimate for full year)	2909

ctivity.

when compared to the other 'types' in the table above.

# Endnotes

- The MRC Economic Impact Reports can be found at: http://www.mrc.ac.uk/Newspublications/Publications/ EIRF/index.htm
- RCUK Economic Impact Reporting Frameworks can be found at: http://www.rcuk.ac.uk/kei/maximising/ MeasuringImpact/Pages/EIRFs.aspx
- 3. The MRC Annual Report and Accounts and Annual Review can be found at: http://www.mrc.ac.uk/ Newspublications/Publications/index.htm
- 4. The MRC Delivery Plan can be found at: http://www.mrc.ac.uk/Newspublications/Publications/DeliveryPlan/ index.htm
- The MRC delivery plan reporting framework can be found at: http://www.mrc.ac.uk/Newspublications/ Publications/DeliveryPlan/index.htm
- 6. The MRC strategic plan, Research Changes Lives can be found at: http://www.mrc.ac.uk/Newspublications/ Publications/Strategicplan/index.htm
- 7. The mid-term update on progress against objectives can be found at: http://www.rclprogress.mrc.ac.uk/
- 8. http://www.centenary.mrc.ac.uk/
- 9. http://www.centenary.mrc.ac.uk/timeline
- 10. http://www.rcuk.ac.uk/Publications/reports/Pages/Timelines.aspx
- n. http://www.policyexchange.org.uk/publications/category/item/eight-great-technologies
- 12. http://www.rcuk.ac.uk/documents/documents/dnaTimeline.pdf
- 13. http://www.rcuk.ac.uk/documents/documents/RegenerativeMedicineTimeline.pdf
- 14. http://www.rcuk.ac.uk/documents/documents/Big%20Data%20Timeline%20WEB.pdf
- $_{15.}$  This is compared to  $\pm759.4m$  in 2011/12
- 16. MRC Fellowships: http://www.mrc.ac.uk/Fundingopportunities/Fellowships/index.htm
- 17. More information on Researchfish can be found at: www.researchfish.com and http://www.mrc.ac.uk/ Achievementsimpact/Outputsoutcomes/Researchfish/index.htm
- The normalised citation impact scores were taken at the end of 2012 for MRC publications published between 2006 and 2011 (as reported in Researchfish).
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- 21. Outputs, outcomes and impact of MRC research: 2012 report http://www.mrc.ac.uk/Achievementsimpact/ Outputsoutcomes/Researchfish2012/index.htm
- 22. MRC mid-term progress report http://www.rclprogress.mrc.ac.uk/
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- Daniel S. Herman, et al, Truncations of Titin Causing Dilated Cardiomyopathy New England Journal of Medicine 2012; 366:619-628
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- 40. http://www.fundacionbiofisicabizkaia.org/bilbaobiophysics/2011/images/pdf/Newstead\_MPcrystallisation.pdf
- 41. Cryo-EM structure of a 3D DNA-origami object PNAS (2013) http://www.pnas.org/content/ early/2012/11/14/1215713109.full.pdf+html
- 42. http://www.arc.gov.au/era/
- <sup>43.</sup> Data collected from the Je-S student data portal (CRTFs collected by MRC in house system), information on students at MRC centres has been collected directly from the centres via email correspondence.
- <sup>44.</sup> Numbers of students for the advanced course masters are notional numbers for three intakes across three years and as such, do not take into account any leveraging by the RO.
- 45. http://www.cprd.com/intro.asp
- <sup>46.</sup> 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.
- 47. Kaspar Hollenstein, James Kean, Andrea Bortolato, Robert K. Y. Cheng, Andrew S. Doré, Ali Jazayeri, Robert M. Cooke, Malcolm Weir & Fiona H. Marshall. Structure of class B GPCR corticotropin-releasing factor receptor 1, *Nature* DOI: 10.1038/nature12357
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