

Enhancing UK’s clinical research infrastructure: summary of new investments

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Medical imaging

Introduction

7T MRI

The majority of magnetic resonance imaging (MRI) used at biomedical research centres and hospitals employs either a 1.5 tesla (1.5T) or 3T electromagnetic field. 7 Tesla “ultrahigh-field” MRI, now offers increased resolution of anatomical features by increasing signal to noise ratio. Most applications of 7T MRI to date have been in neuroscience and vascular imaging (where some big advances have been made), however, this technology also offers great potential for visualising other areas such as joints and abdominal organs, which are much harder to see in detail using conventional MRI. 7T MRI is not yet approved for routine clinical use though and is likely to remain as a research tool for a number of years.

There are around 40 7T MRI machines worldwide but only 2 of these are in the UK (Oxford and Nottingham). Over the last 30-40 years the UK has played a major role in pioneering medical use of MRI technology and is home to many of the leading experts in the field. So it is important now to expand the UK’s current capability in this area to maintain its position at the forefront of MRI technology development. The Clinical Research Infrastructure Initiative has provided funds for two brand new 7T instruments and an upgrade to the existing scanner at Nottingham. Both existing and newly awarded 7T centres will be expected to operate as a network to help accelerate progress and maximise the opportunities and impacts of this area.

Hyperpolarised MRI

The technique of “spin hyperpolarised” Magnetic Resonance (MR) has the potential to provide a safe and uniquely versatile high-sensitivity tool for medical research, drug discovery and clinical diagnostics. This is a radically innovative method of molecular imaging which could potentially allow detection of labelled molecules by MRI, without exposing patients to the risks of radioactivity and without the need for ultrahigh magnetic fields. There are different ways to hyperpolarise molecules for MRI studies. These include dynamic nuclear polarisation (DNP), and Signal Amplification by Reversible Exchange (SABRE) - a novel and unique method developed at the University of York.

Hyperpolarised MRI is not yet clinically validated and, in many cases, significant work remains to successfully apply the technique in patients. Furthest advanced is the use of inert gases for respiratory studies. Funding provided by the initiative aims to accelerate progression of these technologies into clinical use.

1. Prof Richard Wise, Cardiff University (£6.7M, including £3.4M from the Welsh Government)

Cardiff University will install a new 7 Tesla MRI system within the newly rebuilt and expanded Cardiff University Brain Research Imaging Centre (CUBRIC). This system will sit alongside other imaging systems tailored to revealing the brain’s microscopic tissue structure and electrical activity, making the combination of equipment within the new CUBRIC unique in Europe. CUBRIC will also have a clinic where new treatments can be tested in patients and the way that their brains respond can be measured using the brain scanners. Using the 7T MRI system researchers will investigate the causes and treatments of brain conditions including schizophrenia, dementia, Parkinson's disease, Huntington's disease, multiple sclerosis and conditions that can cause damage to the brain such as hypertension (high blood pressure). The proposed research will also link the discovery of genetic factors associated with brain disease to

detailed assessments of brain structure and function made with the 7T MRI system. This will give a clearer picture of underlying disease mechanisms that will in turn suggest new treatments.

2. Prof Peter Morris, Sir Peter Mansfield Imaging Centre (SPMIC), University of Nottingham (£7.7M)

Nottingham has considerable expertise and a long track record of success in the development of MRI. It also has strong research programmes in gastroenterology, liver disease, metabolism, sports medicine, orthopaedics, respiratory medicine, mental health, hearing and radiological sciences. The group were the first in the UK to install and develop a 7T MR scanner, and their work and that of others has proven the capabilities of 7T MR in the brain, for example identifying markers of Parkinson's Disease. The new investment at the SPMIC will allow the capability of their 7T scanner to be expanded beyond just the brain. This technology will then be applied to a much broader set of research programmes at Nottingham. They will also be able to share their experience gained in pioneering MR studies at 7T with the other newly awarded UK centres.

Beyond 7T MRI, Nottingham has also developed strong technical expertise relating to two recently-developed methods for increasing the sensitivity of MR: hyperpolarized inert gases and dynamic nuclear polarization (DNP). Both of these techniques have the potential to produce a step change in the way MRI is used clinically. They will exploit the increased sensitivity of HP inert gases in the study of lung disease and will also undertake completely novel studies that involve using DNP to study metabolism in muscles and in the brain.

3. Prof James Wild and Prof Paul Giffiths, University of Sheffield (£7.5M, including co-funding from British Heart Foundation)

The University of Sheffield is internationally leading in research and development of the methodology for clinical lung imaging with hyperpolarised gases and proton MRI. Using these techniques they have created highly detailed functional images of lungs affected by conditions such as smoking, cystic fibrosis, emphysema, pulmonary hypertension and asthma. However, several technical barriers, such as ease of polarisation of the gases used and the additional hardware required for the MRI scanners, still need to be overcome before this technology can become a more routinely used clinical method.

The expansion of the gas polarisation facilities enabled by this grant will have many benefits for both Sheffield and collaborating centres, by creation of a national hyperpolarised gas imaging facility for collaborating institutions that don't have access to this technology. The continuing methodological research in to MRI scanner hardware and image acquisition, clinical evaluations and work with drug companies evaluating new respiratory therapies on the new 1.5T scanner will ensure that the UK becomes the leading nation in this important area of diagnostic pulmonary medicine. The award will also allow expansion of the image processing facilities in Sheffield to provide large volumes of digital data for phenotyping pulmonary diseases with computational modelling approaches being pioneered at the Insigneo Institute for In Silico Medicine in Sheffield.

4. Prof Sven Plein and Prof Gary Green, University of Leeds & University of York (£7.6M, including co-funding from British Heart Foundation and Arthritis Research UK)

Researchers at the Universities of York and Leeds are developing a new imaging method (SABRE) that has the potential to increase the signal in a MRI image by up to 100,000 fold.

Ultimately this method is expected to work with any hospital MRI scanner. The method achieves the magnetic labelling of specific molecules so that they can be visualised as they pass through the body without changing their role. With this technique it is possible to label both drugs and substances that occur naturally in the body, making the method widely applicable. Through previously and currently funded work, the York group has been developing the technical aspects of this method. We now seek to translate this progress into studies on healthy subjects in Leeds. This grant, we will create the infrastructure needed to apply this to patients with heart disease, cancer and joint disease within 5 years. The new method has however the potential to improve diagnosis through MRI imaging of a very wide range of diseases and will help speed up the development of new drugs.

Stratified medicine

Introduction

Disease development and progression, and responses to treatment, are not identical for every patient. The strategy defined as 'stratified medicine' is based on grouping patients with distinct mechanisms of disease, or particular responses to treatments, in order to identify and apply treatments that are effective for particular groups of patients (often termed 'personalised medicine'). This provides the opportunity to rapidly define or alter patient management and treatments early, 'tailoring' these towards the individual. To achieve this, researchers must be able to combine data on the molecular composition of cells and biofluids like urine, images from scans, and data related to age, gender and other characteristics to provide information on how best to diagnose a disease, quickly identify the correct treatment, and monitor patients.

5. Prof Mark Caulfield, Genomics England (Queen Mary University of London and partners) (£24M)

The UK 100,000 Genomes Project will accelerate the application of whole genome sequencing (WGS) into routine care for the National Health Service. WGS provides the most comprehensive inventory of an individual's genetic variation. By incorporating this into routine care it will transform the health services people receive, changing the processes of diagnosis and management. The UK 100,000 Genomes Project seeks to drive this change by sequencing 100,000 genomes of individuals affected by rare diseases and cancer (and their families) and infectious disease pathogens.

The UK Infrastructure for Large-scale Clinical Genomics Research will provide the infrastructure which, using the information from the 100,000 Genomes project, will develop the UK as an international centre of excellences for the analysis of very large and complex biomedical datasets. As a national resource for the development of new knowledge it will provide transformative advances in the speed and range of research into the causes and consequences, prevention and treatment of disease.

6. Prof David Adams, West Midlands Stratified Medicine Innovation & Translation Facility (University of Birmingham) (£7.2M, including co-funding from Arthritis Research UK)

Research at this new facility will focus on immune-mediated inflammatory diseases (e.g. arthritis and liver disease) and blood cancers (e.g. leukaemia), which are increasing in prevalence in the UK, partly as a consequence of an aging population. Their interdisciplinary research programme will focus on the molecular study and characterisation of different cell types within each disease and the associated molecular changes in the patient. They will

develop and test the integration of multiple diagnostic methods, including mass cytometry, metabolic phenotyping and analysis of single cells. Through this, they will obtain new insight into the mechanisms of how diseases develop and progress, and their responsiveness to treatment, with the aim to drive innovative discoveries into clinical practice through the establishment of stratified diagnostics and targeted therapies.

7. Prof Anthony Whetton, Clinical Proteomics Centre for Stratified Medicine (University of Manchester) (£12.8M)

This new facility will use new developments in mass spectrometry, such as SWATH-MS and related techniques, that support the measurement of many proteins within a single sample (such as blood, urine, or from tissue such as a tumour biopsy) within a much shorter time than has ever been possible before. Such approaches will be of huge benefit to clinical researchers as it will allow them to see the differences between samples from, for example, healthy people and people with a specific disease - this will give insights into how that disease develops and, importantly, how it might be treated. In addition, by examining the differences in the levels of particular marker proteins from patients who respond to a drug compared to those who don't respond, doctors will be able to identify which drug is the best treatment for individual patients.

8. Prof Patrick Maxwell, University of Cambridge (£14.6M)

A new scientific and computing infrastructure will be built in the School of Clinical Medicine at the University of Cambridge that will allow i) development of new technologies for measuring and imaging molecules in humans, and ii) application of these technologies directly and immediately to major research programmes for understanding and treatment of cancer, metabolic disorders, and many other therapeutic areas. Three new high-tech facilities will be created; a Stratified Medicine Core Laboratory (SMCL), a Molecular Imaging Centre (MIC), and a High Performance Hub for Informatics (HPHI). The SMCL will allow measurement of a large number of peptides and other molecules in blood or other tissue samples with enhanced accuracy and sensitivity. The MIC will allow measurement of molecules by imaging patients, rather than by lab analysis of tissue samples. The HPHI will provide the computational resources required to store and analyse the very large volumes of data produced by the SMCL and the MIC, whilst enabling linkage of the data to individual patient records and sharing with the wider scientific community.

9. Prof Munir Pirmohamed, University of Liverpool (£5M)

All drugs are associated with variability in response: that is some patients do not respond to drugs, while others develop side effects or adverse drug reactions (ADRs). The internationally recognised MRC Centre for Drug Safety Science (CDSS) allows pre-clinical and clinical scientists to work side-by-side using cutting-edge technologies to analyse well-defined clinical samples. New state-of-the-art technologies funded through this initiative will build upon this infrastructure by helping to identify the best treatments for patients based on how drug responses vary, how diseases differ between individuals, and how this information relates to variation in clinical outcomes. For example, understanding why some patients who take statins develop muscle-related problems could help identify an alternative treatment strategy for these groups. This will be achieved through investigation using different "experimental" systems ranging from single cells to experimental studies in man, to careful clinical observation of patients in clinical settings. This will facilitate translation of findings in the laboratory to clinical care (bench to bedside), but importantly lessons learnt in clinical settings will also be investigated further in the laboratories (bedside to bench), so that more can be learnt about disease processes.

Experimental medicine

10. Prof Kevin Harrington, Institute of Cancer Research (£9.6M)

Radiation therapy involves delivering high-energy X-ray beams to tumours in order to kill cancer cells. For many people with cancer, radiation therapy is very effective and frequently cures their disease. Unfortunately, when treating tumours, nearby healthy tissues will inevitably receive some of the radiation and this is associated with side effects that can severely affect a patient's quality of life. Therefore, when treating patients with radiotherapy, there is a clear need for the treatment to be delivered as accurately as possible.

In most cases, radiotherapy is planned using a CT scan to show the position of the tumour; this is usually done before the treatment starts. But even with a CT scan image it can be very difficult to determine precisely where the tumour is. The problem is compounded by the fact that radiation therapy is usually given as a series of doses (called fractions) divided over a period of weeks and the tumour may be in a slightly different position each day or may shrink during the course of treatment. To make matters even more difficult, tumours often occur in tissues that move, such as lungs.

The Institute of Cancer Research, London, aims to revolutionise radiation therapy by developing a new type of machine called an MR-Linac (to be installed at The Royal Marsden NHS Foundation Trust). This machine combines a state-of-the-art radiation machine (called a linear accelerator) with an MRI scanner. Such a machine will not only provide very accurate visualisation of the tumour, but will do so at the same time that each fraction of radiation therapy is delivered, tracking the movements of a tumour in real time within a patient during a dose of radiation. With these improvements, the margins placed around tumours can be reduced, but with confidence that the tumour will be targeted accurately. This will give both clinicians and patients greater confidence that the treatment will be effective and with fewer side-effects.

11. Prof Mark Emberton, Centre for Image Guided Therapy, University College London (£5.3M)

UCL will establish a new facility that aims to revolutionise diagnosis, risk stratification and therapy for people with cancer, based on innovations in MRI technology. They will use imaging to find out where cancer lies within the body. Whilst imaging helps to find disease, doctors don't always know whether a lesion on an image is cancer or whether it is benign. The group will therefore combine the latest imaging technologies with an understanding of the cellular and molecular environment of cancers in order to verify diseased tissues. Added to this will be the development of new technologies to deliver precise treatment to individual cancer sites. UCL have a strong track record of creating 'image-guided' therapies for prostate cancer and will seek to extend this to other cancer sites, initially lung and gastrointestinal cancers.

12. Prof Richard Trembath, Queen Mary University of London (£1.8M)

The group at QMUL plan to accelerate the use of genetics in medicine, through the study of genome in cases of parental relatedness (e.g. cousin marriage), which is common in certain UK ethnic groups including the health disadvantaged British-Bangladeshi and British-Pakistani communities. In individuals with parental relatedness, certain genes that would usually be switched on, can be completely inactivated. Finding such genetic variants and examining their consequences and benefits can lead both to an increased knowledge of how human genes work and an improved understanding of the health consequences of genetic variation in the relevant communities. A large-scale community based programme has commenced, studying as many as

25,000 apparently healthy people. Of these, individuals found to possess natural gene inactivating variants considered to be of biomedical importance, will be invited for detailed medical assessment. This may include blood or skin biopsy samples; resting and exercise blood pressure and heart rate measurements; quantification of body composition and brain and body imaging, such as MRI scans. These studies will be enabled by development of a purpose constructed clinical research facility, adjacent to the major hospital at Whitechapel, in East London. The facility will allow substantial engagement of the local East London communities and enable coordination of more highly specialised assessments, to be undertaken with and through other leading medical research centres across the UK and abroad.

13. Prof Danny McAuley, Queen's University Belfast (£1.5M, including co-funding from the Northern Ireland Department of Health, Social Services and Public Safety)

Cell-based therapies represent the cutting edge of research for new treatments for a variety of conditions. The global commercial cell therapy industry was estimated to have an annual turnover of £600M in 2011, and is estimated to grow to £12BN by 2025. Currently there is a significant gap in the UK's clinical research capabilities and infrastructure to deliver trials involving cell-based therapy, largely because cell therapies require specialised facilities to safely manage the cells for human administration.

A new cell therapy facility will be established in Belfast to enable the testing of cell therapies in clinical trials for conditions including respiratory failure in the critically ill and vision loss. This state-of-the-art facility will provide all of the capabilities required; from the storage and subsequent preparation of cell therapies for patient administration, through to the manufacturing of cell based therapies. The facility will be based in a recognised UK centre for translational research and will be available for use by external universities, hospitals and companies.

Dementias

14. Dr John Gallacher (coordinator), Dementias Platform UK (£36.8M, including co-funding from the Welsh Government)

The Dementias Platform UK is a radically new approach to dementias research. It brings together data from around 2 million study participants to try and discover the causes of dementia, and to find ways of delaying onset and slowing progression. The platform, launched in 2014, represents a growing collaboration of UK Universities and pharmaceutical companies.

This investment will increase the capability of Dementias Platform UK by enhancing the UK dementias research infrastructure in terms of facilities and science networks, putting the UK at the forefront of dementia research worldwide. The investment focuses on imaging, informatics and stem cells. For imaging, a network of new machines that can combine positron emission tomography (PET) – visualising a short-lived radioactive tracer molecule in the body to show protein deposition- with Magnetic Resonance Images that show brain structure, will be established across the UK. This will allow the molecular processes going on inside the brain that cause dementia to be studied in greater detail. For informatics, many different types of clinical data will be brought together in secure environments to make them more accessible to researchers. For stem cells, skin and blood cells from adults with and without dementia will be re-programmed to become neural cells and studied to find out how these cells change as the dementia begins and progresses.

This investment will enable better science at lower cost, delivering an integrated environment for innovative and coordinated research programmes, making the UK an internationally unique place to study dementia.

15. Prof Tarek Yousry, University College London (£1.2M)

MRI imaging has become a requisite part of the investigation of many brain disorders; but there is a need for more imaging research in dementia. The group at UCL will use innovative MRI technology in their dedicated Dementia Research Scanner Centre to maintain and enhance their position as a leader in clinically applied dementia imaging research and also to maximise their contribution to the UK Dementia Platform. The upgrade to their existing 3T MRI scanner will not only enhance the imaging capabilities locally but the related innovations will help direct the way for major multi-centre clinical trials in dementia, which are increasingly reliant on 3T infrastructure.

16. Prof James Rowe, University of Cambridge (£7M)

The new 7T MRI scanner at Cambridge will be dedicated to the challenge of dementia, supported by scientific work to understand the normal brain and develop advanced analysis techniques. It will be a major contributor to the UK Dementia Platform, a unique approach to join up medical research across the country's specialist centres and drug company partners in the fight against dementia.

The new scanner will be located on the Cambridge Biomedical Campus, next to Addenbrooke's Hospital, and will be used to detect and characterise the changes over time in major brain diseases like Alzheimer's, stroke and Parkinson's disease as well as mental health disorders and healthy ageing. The need is urgent to identify people in the earliest stages of such diseases, or even before symptoms, in order to test treatments that combat dementias. The new scanner will give much greater detail of the whole brain's structure, function and chemistry allowing researchers to understand how the brain works as a whole while still seeing detail at a sub-

millimetre scale. This detail is especially important for diseases like Alzheimer's and Parkinson's, for which small and deep parts of the brainstem are critical but difficult to see with conventional MRI.

Single cell genomics

Introduction

Single-cell technologies offer unprecedented opportunities to reveal the complex genomic, epigenomic, transcriptomic and proteomic environment in biological systems and human diseases. Research has been held back because biological insights have been drawn from groups of hundreds or thousands of cells. Variations between cells and interactions between cells in complex physiological systems were therefore lost. Application of new cutting-edge approaches will help researchers to explore differences within populations of cells and to study diseases where cells are rare (such as circulating tumour cells) to better understand disease pathology.

17. Prof Doug Higgs, University of Oxford (£5M)

The new Centre of Single Cell Biology (CSCB) at Oxford will be coordinated by the Weatherall Institute of Molecular Medicine (WIMM) which has a long-standing technical and strategic expertise in single cell research. The new investment will be used to enhance single-cell research capabilities across the campus, providing new capabilities for data analysis, new laboratories, and new equipment.

The lead programme of research in the CSCB will be focused on inherited disorders of red blood cells. These disorders are amongst the most common of all human genetic diseases worldwide with an estimated 300,000 affected babies born each year and a total number of affected UK patients of ~16,000. Currently, severely affected individuals are treated with supportive care, including lifelong blood transfusion and treatment to prevent accumulation of iron in the body, which is costly, burdensome, and gives rise to serious, long-term clinical complications. Researchers at Oxford aim to "genetically repair" the damaged genes in the patient's own blood stem cells, and single cell biology will be central to this project; identifying the blood stem cells which are the best target for this therapy, and assessing the safety and effectiveness of this approach. This programme is one example of many projects in development across the campus which will be greatly facilitated by the development of improved single cell research capabilities.

18. Prof Patrick Maxwell, University of Cambridge (£3.5M)

Examination of diseases at single cell resolution, both at diagnosis and after treatment, will transform the practice of molecular medicine by improving the quality of patient diagnosis, refining treatment options, monitoring of response to treatment, and detecting the emergence of resistance to treatment. Cambridge scientists have been at the forefront of basic research in single cell expression profiling and the analysis of circulating tumour DNA, as well as setting up local Biotech companies that develop novel single cell technologies.

A new shared core facility for single cell analysis will be created (the Cambridge Single Cell Analysis Clinical Core Facility [SCACCF]), which will serve all major molecular medicine programmes in Cambridge including cancer, neurosciences, immunity and inflammation, infectious diseases, stem cell and regenerative medicine, metabolic medicine and experimental therapeutics. The SCACCF will act as a hub for the UK and will work closely with strategic partners in the Cambridge area (Babraham Institute, Wellcome Trust Sanger Institute, the European Bioinformatics Institute, the MRC Laboratory for Molecular Biology, major pharma & biotech), to bring their different capabilities to bear on clinical research challenges.

19. Prof Cay Kielty, University of Manchester (£4.9M)

Researchers at Manchester will focus on characterising a group of rare cells (called circulating tumour cells, or CTCs) that give rise to drug-resistant cancers - such as certain lung cancers - and lead to relapse, and specific stem cells (cells with the potential to self-renew or differentiate) that can enable the regeneration of damaged tissues such as muscle, joints, skin and blood vessels. To achieve a 'step-advance' in the ability to design therapies that can specifically target such specific 'progenitor' cell populations, they will establish a ground-breaking Single Cell Research Centre (SCRC) at the University of Manchester.

Exploiting and innovating in the very latest single cell technologies, it will comprise a common integrated pipeline from receipt of clinical samples, to identification and characterisation of single target cells within each sample, to the design of treatments that target these specific cells. In this way, they will expedite progress to cell-based and 'personalised' treatments for some of the most challenging diseases and degenerative conditions of man.

20. Prof Patrick Chinnery, Newcastle University (£1.7M, including co-funding from Arthritis Research UK)

Newcastle University has a well-established track record studying the molecular basis of rare disease, underpinned by unique cohorts of patients with defined disease characteristics and biobanked tissues. Their work on rare mitochondrial, neuromuscular & musculoskeletal diseases, rare childhood cancers, rare immune deficiencies, and novel cell therapies is renowned internationally. Single cell functional genomics and proteomic approaches have the potential to advance understanding of these diseases and thus explain why patients with the same disorder develop a different clinical presentation, and respond to treatments in different ways. Researchers aim to bring together expertise and infrastructure focused on the molecular characterisation of single cells by forming the Newcastle University Single Cell Functional Genomics Unit (NUSCU).

21. Prof David Bonthron, University of Leeds (£1.1M)

The University of Leeds and Leeds Teaching Hospitals NHS Trust will establish a joint facility that will permit new biomedical research approaches, based on the sequential isolation, manipulation, observation and eventual destructive analysis (or culture and expansion) of single cells. The new Facility will be based in laboratory areas where "Next Generation Sequencing" (NGS) resources are already managed jointly by the University and Trust, delivering both clinical diagnostic services and internationally competitive genetics research.

While technically innovative, this facility will focus on delivering biological insights and capabilities that are relevant to their clinical areas of expertise and excellence; in this way these discoveries will translate quickly into patient benefit.

Specific clinical endpoints at which the Programme will be aimed include:

- improved genetic diagnosis, including identification of somatic cell mutations and application to preimplantation diagnosis
- detection of cancer-causing molecular changes in cells at low levels
- earlier and more precise classification of disease to inform therapeutic decisions (stratified medicine and molecular pathology)
- precise definition and characterization of therapeutic stem cell populations

- better understanding of the key events underlying host infection, latency and activation by major infectious pathogens, and the corresponding host immune responses.

22. Prof Tariq Enver, University College London (£3.6M)

A possible solution to identifying different cell types in cancers is to study Circulating Tumour Cells (CTCs) as surrogates of tumour tissue. CTCs are cells that are shed into the circulation and can be isolated from the blood for further analysis. CTCs are very rare cells by comparison with blood cells and highly sophisticated technology has been developed to enrich for CTCs and isolate them. In parallel there have been technological advances in genetic sequencing such that it is now possible to identify mutations and analyse gene expression in single cells. This means that, for the first time scientists can begin to understand tumour heterogeneity at the single cell level. A dedicated facility will be established with state-of-the-art equipment to enable researchers at UCL to study CTCs and improve the outcomes for patients with cancer. Initially they will establish methods to undertake complex single cell analysis and then develop and validate tests in patients who are undergoing treatment for cancer. They will also study these cells in order to understand how they are able to successfully spread through the blood stream to other organs and cause metastases. Metastasis is responsible for the death of 90% patients with cancer and it is critical to understand how this happens in order to develop more effective therapies.

23. Prof Jonathan Mill, University of Exeter (£1.6M)

The University of Exeter Medical School has been awarded £1.6 million to fund a state-of-the-art facility that will unlock some of the hidden secrets of the genome. The award will enable Exeter researchers to invest in single molecule real-time (SMRT) sequencing technology and also expand their high performance computing facilities for the analysis of complex genomic data.

The equipment will be housed in the new Wellcome Wolfson Clinical Research Facility, within the Research, Innovation, Learning and Development (RILD) building, which the Medical School shares with the Royal Devon and Exeter NHS Foundation Trust. The new technology will enable researchers to identify and analyse regions of the genome hidden from current methods for gene discovery, facilitating research into the functional mechanisms involved in disease. Only three other SMRT sequencers are currently installed in the UK, and this will be the first directly embedded within a clinical research facility.

Professor Jonathan Mill, of the University of Exeter Medical School, who led the bid for the award, said: "The last decade has seen tremendous advances in understanding about the role of genetic variation in health and disease. Despite this success, however, many regions of the genome remain hidden to contemporary DNA sequencing approaches. Our group at Exeter will acquire "third generation" DNA sequencing technology, which will enable us to fully characterise genomic complexity. We will also establish high-performance computing infrastructure needed to store and analyse this complex data.

"This important investment will enable us to make significant advances in genomics research in areas including diabetes, neurological and other medical conditions by defining genetic variation in regions where DNA does not encode proteins."

Annex 1 – Map of CRI Awards

- Theme 1: innovative technologies for stratified and experimental medicine
- Theme 2: dementias research
- Theme 3: single cell genomics

