The Neuroscience Network
Cambridge | London | Oxford
In 2015, Alzheimer's disease and other dementias overtook ischaemic heart disease as the leading cause of death in England and Wales\(^1\). This statistic is a stark reminder that dementias, and neurodegeneration diseases as a whole, are a growing concern globally. As we all face a growth in the ageing population, it is more urgent than ever to accelerate efforts in translational neuroscience.

Recent advances in genetics, diagnostics and imaging have progressed scientists’ understanding of what causes a large number of neurodegenerative diseases. Many of these scientists reside within the greater south east of England, and the region has both breadth and depth in terms of neuroscience research. Turning progress in basic science into effective treatments still remains the challenge; however collaborative efforts will prove vital in ensuring scientific developments translate into improved patient care.

The ‘Golden Triangle’ is the world-leading life sciences cluster of Cambridge, London and Oxford, sitting at the heart of England’s greater south east. This cluster is home to cutting-edge scientific research and ground-breaking medical innovations, which benefit not only the surrounding communities but also has a global impact. With some of the oldest and most prestigious universities in the world and five out of the seven academic health sciences centres in the UK, this region is uniquely located to stimulate collaboration and turn discoveries into pioneering medical treatments, therapies and technological developments. New research centres in the area, such as The Francis Crick Institute, The Alan Turing Institute and the Translation & Innovation Hub at Imperial White City Campus, complement the thriving life sciences ecosystem, and aim to accelerate the translation of lab-based research into life-saving treatments.

By working closely with academic, research and NHS institutions, MedCity aims to stimulate an interconnected region for life sciences research, development, manufacturing and commercialisation, which will subsequently bring about greater economic growth and improvements to public health. Together we invite our colleagues across the globe to collaborate with industry and academia within the region to help drive forward future neuroscience innovations.

Sarah Haywood
MedCity, CEO

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\(^1\)Deaths registered in England and Wales - Office for National Statistics. 2015
Neurodegenerative disease research in the region

Dementia encompasses many diseases which result in physical changes in the brain and a decline in mental ability. Alzheimer’s disease is the most common type of dementia; however other diseases include Parkinson’s, Huntington’s and Creutzfeldt-Jakob disease. Symptoms vary across disease types but all have a common pathological mechanism - the misfolding, aggregation and accumulation of proteins in the brain. There is currently no cure for dementia and other neurodegenerative diseases. Recent clinical trial failures of therapies for Alzheimer’s have dealt a major blow for large pharmaceutical companies, such as Eli Lilly, Pfizer and Merck, and Alzheimer’s disease drug candidates have one of the highest failure rates of any disease area - 99.6%, compared with 81% for cancer⁵. In 2012, the UK Prime Minister launched a national challenge to fight dementia, improve the care of those suffering with the disease and make the UK the best place in the world to undertake research into dementia and other neurodegenerative diseases³. Since then huge strides have been made in improving diagnosis rates and social care, but the challenge remains.

A major driving force behind this mission is the network of neuroscientists at the world-class universities, pharmaceutical companies, research councils and charities in the golden triangle and greater south east of England. Four of the world’s top ten universities are located in this region, many of which have a very strong track record of breakthrough discoveries in neuroscience, including the 1936 Nobel Prize winning work of Sir Henry Dale and Otto Loewi at UCL for their investigations on the chemical transmission of nerve impulses, and Andrew Huxley and Alan Hodgkin’s 1963’s Nobel Prize for their work on the conduction of action potentials along nerve fibres at Cambridge, which they shared with Sir John Eccles at the Australian National University⁴. Key to the region’s success has been its collaborative mindset – a drive to embrace and exchange ideas with scientists and professionals from around the world. The neuroscience community has also been quick to establish cross-departmental, interdisciplinary interactions and utilise technological advances in surrounding fields. Neuroscientists regularly work alongside physicists, engineers and computer scientists in order to develop new techniques to further drug discovery and algorithms for innovative diagnostic imaging tools.

Investment for neurodegeneration disease research has also increased vastly over the last few years. Since 2010/11, the UK government has increased spending on dementia research by nearly 50 per cent, including £20 million for the world’s largest social science research programme on dementia and care and the world’s largest dementia population study, Dementias Platform UK, a 5-year £53 million public private partnership led by the Medical Research Council (MRC)⁷.

The Dementia Discovery Fund (DDF) was launched in 2015 to fund the discovery and development of novel dementia treatments. The $100 million fund was raised by investors including the UK Department of Health and Alzheimer’s Research UK alongside world-leading major pharmaceutical companies including Biogen, GlaxoSmithKline, Johnson & Johnson, Lilly, Pfizer and Takeda. The DDF works collaboratively with universities, academic institutes and the pharmaceutical industry internationally to identify novel dementia research projects and nurture these through the pre-clinical phase, enabling further development in clinical trials⁸.
Alzheimer’s Research UK (ARUK) is the leading dementia research charity in the UK. Over the past five years the charity’s strategy has led to them to increasingly look around the world for new approaches to tackle dementia by partnering with likeminded innovators. Initiatives like the Dementia Consortium and the ARUK Drug Discovery Alliance have pioneered collaborative approaches to research that unite academia, industry and biotech in a common desire to make better and swifter progress towards the next treatment.

The Dementia Consortium was launched in 2013 to close the gap between fundamental academic research and the pharmaceutical industry’s drug discovery programmes. With an initial £3 million of funding, the Consortium unites ARUK with the MRC and five pharmaceutical companies; AbbVie, Astex, Eisai, MSD and Lilly. Applications to collaborate with the Dementia Consortium are open globally to academic researchers and SMEs focussing on target validation and drug discovery projects for any neurodegenerative disease. The projects are screened and refined by MRC Technology, who help to confirm viable drug targets for further development and provide access to the pipeline compound database, as well as a wide range of resources. Dr David Reynolds, Chief Scientific Officer at ARUK says: “At the heart of Alzheimer’s Research UK’s core goal is investing in drug discovery with a clear deliverable and assisting the academic community in carrying out dementia research projects. The Consortium is currently funding projects in the UK, Florida, Luxembourg and Italy, all of which are producing promising results and will feed into our development pipeline.”

The second initiative, the Drug Discovery Alliance was launched in 2015 as one of the largest and most co-ordinated efforts to find new drugs for dementia. The Alliance consists of three Drug Discovery Institutes at the universities of Cambridge, Oxford and UCL, all focused on early stage drug discovery for neurodegenerative diseases. “The task of the Alliance is to help accelerate treatments for dementia by working closely with lead academics at each of the institutes to identify projects to partner with” – Professor Paul Whiting, Chief Scientific Officer, ARUK UCL Drug Discovery Institute. “There is a wealth of knowledge and experience across the golden triangle of Cambridge, London and Oxford and there is also a great collaborative environment, which stimulates research at all levels.”

“The Alliance is a distributed collective whereby each institute has its own portfolio and is an independent unit but shares expertise and knowledge. At Cambridge there is expertise in autophagy with Prof David Rubinsztein, a lead academic scientist. In Oxford, there is a focus on inflammation studies and structural biology of scaffold structures in brain cells. And UCL has a wealth of experience researching synaptic health and axon trafficking. In the region we are very lucky to have strong academics, strong universities and strong research.” – Dr David Reynolds.
Professor John Hardy  
Chair of Molecular Biology of Neurological Disease  
UCL Institute of Neurology

UCL is ranked number one in Europe for neuroscience research, and second in the world\(^9\). In December 2016, it was announced that UCL had been selected as the ‘hub’ of the national Dementia Research Institute, a new £250 million investment to bring together research efforts to diagnose and treat a range of neurodegenerative diseases. UCL’s well-regarded neuroscience department was a key element in the decision to lead the Institute and fundamental to these research strengths is Professor John Hardy.

Based at the UCL Institute of Neurology, Professor Hardy has led pioneering work into the genetics of Alzheimer’s and has played a pivotal role in advancing our understanding in a number of major neurodegenerative diseases. Professor Hardy discovered that a mutation in the gene for amyloid precursor protein (APP) caused deposits of amyloid to form in brain tissue. Professor Hardy and colleagues set out the influential ‘amyloid cascade hypothesis’ which places amyloid at the centre of brain changes that cause Alzheimer’s, establishing the protein as a key target for new treatments. In 2015, he was awarded the Breakthrough Prize in Life Sciences, the first to be awarded to a UK researcher, for his ground-breaking research into the genetic causes of Alzheimer’s disease, and other neurodegenerative diseases.

**Professor Hardy said:** “Of the 70-80 genes associated with neurological diseases, more than half of them were discovered at the UCL Institute of Neurology. The Institute is unique and combines neuroscientists, geneticists, cell biologists, clinicians and teaching staff, all with the sole purpose of reducing the burden of neurodegenerative diseases.”

“The National Hospital for Neurology and Neurosurgery deals with some of the most difficult neurological cases and provides the ability to directly access patient cohorts and insights, which are hugely beneficial. The focus of our research is on patient health and there is a strong link between basic research and the patients. The geography of the region aids this focus, with the facilities and expertise all within a short walk.”

Professor Hardy also played a key role in producing the winning bid to host the new national Dementia Research Institute, which will be led by Professor Bart De Strooper. “Bart will make an excellent head and he will bring his strengths in basic molecular biology of neuroscience. The institute will form a ‘hub-and-spoke model’ whereby UCL will be the hub and other centres around the UK will form the spokes, so that we are all connected.” – **Professor Hardy.**

\(^9\) Thomson Reuters Essential Science Indicators, Neuroscience.
Neurodegenerative diseases, such as Alzheimer’s, Amyotrophic Lateral Sclerosis/Motor Neuron Disease, Parkinson’s and Huntington’s disease all display very different disease states and symptoms, however, molecularly they are very similar and result from the deposition of misfolded proteins in the brain or in the peripheral nervous system. Another common feature of these diseases is that they predominately start late in life.

“Cells have evolved to survive harsh conditions, and mechanisms such as protein quality control prevent fatal damage. In diseased cells, many of these quality control systems fail to recognise misfolded protein, which lead to aggregation” said Professor Bertolotti. The work of Professor Bertolotti’s group at The MRC Laboratory of Molecular Biology (LMB) in Cambridge aims to exploit the defence systems of brain cells and find strategies to boost them in those cells who have bypassed the natural defences.

Professor Bertolotti added: “In normal cells, there is a balance between misfolded proteins and quality control mechanisms. In aging cells however, this balance is disrupted so that the quality control mechanisms slow and the build of misfolded proteins increases. Protein quality control systems are very complex and it is impossible to predict how to improve the system when it does go wrong. In my group we have created a number of unbiased approaches with the aim of finding strategies to fight cell death when a misfolded protein has been detected.”

Recent work in the group to identify compounds to selectively inhibit stress phosphatases has produced some promising results in mouse models of Charcot–Marie–Tooth disease, and Professor Bertolotti is currently involved in forming a spin-off company called CamPhos to develop targets for other phosphatases and the common neurodegenerative diseases.

The MRC LMB has a long tradition of world class research attracting world class scientists. “It is a self-propagating process: outstanding science then brings outstanding scientists from everywhere in the world and this sustains outstanding research. What brought me to the UK is a feeling that original research is possible and supported in the UK, particularly at the LMB where 5 years of funding of our research programmes allows us to explore unknown territories. This is a rare possibility.” – Professor Bertolotti.
Dr Maria Jimenez-Sanchez said: “I gained a Career Development Fellow award from the MRC which helped me set up my own research group at The Maurice Wohl Clinical Neuroscience Institute. It’s a wonderful, collaborative environment which stimulates open innovation and brings together over 250 clinicians and scientists to look at a range of neurological and mental health diseases. Some of the best neuroscientists are located in the south east of England and naturally you want to go where the best people and science are.”

Maria’s work involves investigating the role that astrocytes play in Alzheimer’s disease. In the brain, neurons are responsible for processing information, learning and memory, while other specialized brain cells called glial cells are necessary to maintain neuron health and to aid neuron function. Astrocytes are the most abundant type of glial cell and although they play a predominately protective role, their response may become deleterious when damage in the brain is prolonged, such as in Alzheimer’s disease. “The aim of my work is to investigate how astrocytes can protect neurons in Alzheimer’s disease. If we are able to identify which factors released from astrocytes are responsible for mediating neuroprotection, we will be able to design effective therapeutic tools.” – Dr Maria Jimenez-Sanchez.
Brainminer was created in April 2015 to translate the research developed by Professor Sebastein Ourselin’s group at the UCL Centre for Medical Image Computing (CMIC). Professor Ourselin is Head of the Translational Imaging Group within CMIC, aiming to bring engineering innovation in medical imaging into the clinic.

Brainminer is developing a quantitative imaging analysis and reporting solution. It’s patented platform technology automatically and intelligently analyses magnetic resonance imaging (MRI) scans. Current visual assessment methods can take significant time and may miss small but highly important changes in pathology during the early stages of disease progression. Evidence suggests that 30-40 percent of patients displaying clinical symptoms of dementia remained undiagnosed following diagnostic workup. The technology developed by Brainminer provides an automatic anatomical parcellation of MRI scans, assesses volumes of key tissue structures and then compares these to a data-set of healthy images/volumes, in order to improve accuracy and rates of diagnosis. “Although initially developed to aid the diagnosis of Alzheimer’s and other forms of dementia, the platform is extensible into a wider range of neurological disorders including multiple sclerosis and stroke, as well as vascular diseases and cancers” said Ian Harris, Brainminer CEO.

Brainminer is supported by the NIHR UCL Hospitals Biomedical Research Centre, and the technology is currently under testing within the UCL Hospital Trust. In 2016, NHS England’s Small Business Research Initiative for Healthcare awarded Brainminer £1 million to develop its dementia product towards CE marking, which will be ready to market by Q3 2017. The company plans to raise Series A funds to support the commercialisation of the initial product and complete development of its next two products by the end of 2018.

**Ian Harris added:** “Our platform and tools are based on fantastic scientific research from one of the best universities in the world. UCL is known for neuroscience, computer science and machine learning, and Brainminer is at the interface of all three. The golden triangle is locationally very strong and this benefits not only the scientific community but also the investor community.”
Gold Standard Phantoms is a UCL Institute of Neurology spinout company which is developing, marketing and selling calibration services for Quantitative Medical Imaging. The aim of the company is to provide a series of calibration devices that will enable a step change in the delivery of radiology and move beyond the subjectivity of analysing MRI scans of patients with serious slow progressing diseases such as dementia.

Quantitative Medical Imaging differs from traditional imaging in which an image is qualitatively interpreted by a trained radiologist, and instead turns the imaging system into scientific apparatus for measurement of a physical parameter or quantity. Professor Xavier Golay, Gold Standard Phantoms CEO said: “Delaying the onset of dementia using disease modifying treatments could reduce the cost of dementia by half. We are working to develop a series of MRI techniques that could provide us with an early indication that something is wrong with patients, yet closer enough to the development of the disease so that we can be sure the right people get the treatment.”

“Early changes in the function of the brain of patients with Alzheimer’s will be directly reflected by the level of blood delivered to the brain, called brain perfusion. Many research groups have been working over the last three decades to precisely measure this parameter, brain perfusion, without any possibility to calibrate any of these measurements. Therefore, we set out to build the first ever perfusion brain imaging phantom on the market.”

Gold Standard Phantoms has also developed an online platform that will provide an automatic calibration based on calculated values that the phantom should produce. The phantoms can be used to make sure that whatever measurements are collected with the MRI scanner can be done so reproducibly and in the same way across different hospitals.

Professor Golay is also Vice Dean of Enterprise for the UCL Faculty of Brain Sciences. “The region encompassing London, Oxford and Cambridge is a real research powerhouse. The expertise in neurology at Queen Square; the institutes and hospitals are world-class and are very special. We are now beginning to see a real change in the commercialisation of this research, and a few success stories, which will hopefully increase the trend further and bring about more successful medical products and treatments.” - Professor Xavier Golay
**Oxford**

- Alzheimer’s Research UK
- Oxford Drug Discovery Institute
- Chronos Therapeutics
- Nuffield Department of Clinical Neurosciences
- Oxford Cognitive Neuropsychology Centre
- Oxford Centre for Human Brain Activity (OHBA)
- Neuro-Bio

**Cambridge**

- Alzheimer’s Research UK
- Cambridge Drug Discovery Institute
- Cambridge Cognition
- Gen2 Neuroscience
- MRC Laboratory of Molecular Biology
- MRC Cognition and Brain Studies Unit
- John van Geest Centre for Brain Repair
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From drug discovery to digital health and medtech to diagnostics, we are here to support life sciences and healthcare companies large and small to do business in the golden triangle.

MedCity has partnered with other organisations to set up initiatives designed to support SMEs in the healthcare and life sciences sector, such as:

- Angels in MedCity; connecting angel investors with innovative life sciences companies;
- Digital Health.London; partnering with London’s Academic Health Science Networks and NHS England to grow the ecosystem of digital health companies and support collaboration with the NHS;
- Collaborate to Innovate; encouraging SMEs to partner with world-leading academics in the region;

**How we can work with you**

Whatever your need or the stage of your business, MedCity can help you navigate the richness of the greater south east’s life sciences ecosystem. Our support includes:

- Matching you to the right academic, clinical and industry partners
- Helping you locate facilities and work spaces
- Supporting you in setting up clinical trials
- Guiding you through regulatory and procurement processes
- Connecting you with influential networks

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Contact us

MedCity can help you navigate and access different parts of the academic, NHS and industrial life sciences and healthcare environment across the golden triangle of Cambridge, London, Oxford and the greater south east region of England.

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