UK Dementia Research Institute

Science Vision: Stimulating the pipeline to treatments

Neurodegenerative diseases are complex and to make progress in treating them we bring together expertise from many different disciplines and apply this across the different stages of research.

Stage 1: Discovery research

The core of our work is innovative discovery science, to unravel the cellular and molecular pathways that underpin the diseases that give rise to dementia. Our researchers study cells, animal models and humans using all the tools of modern biomedical science to find the earliest stages of the disease as this will be the optimal time to intervene. This work will fill the translation pipeline with fresh and innovative ideas and concepts. This is where the UK DRI will make the biggest difference and this is where we give our researchers academic freedom and flexibility to capitalise on their creativity and talent.

Stage 2: Experimental medicine

Observations emerging from our discovery science must be relevant to human biology. We are strengthening our clinical expertise so we can effectively apply our findings in proof-of-concept experiments in people and human tissues. This includes experimental medicine activity where we work closely with partners such as Dementia Platform UK and Health Data Research UK who specialise in patient groups, clinical observations and health data.

Stage 3: Translation

We ultimately aim to translate our discoveries into drugs, tests, devices and other products or services that will help people affected by dementia. This activity calls for strong partnerships with those who understand how to advance compelling proof-of-concept experiments into clinical trials. We see ourselves here as initiators, stimulators and sought-after collaborators. We have had early success in this area (including a gene therapy spin-out) and growing this activity will bring success.

Enriching collaboration

With our Centres and Group Leader programmes well established, we are focused on stimulating even more synergistic research activity. We have built and will continue to create a range of funding options and competitive resources to drive connections and innovation across our Centres. These include the UK DRI Animal Models Programme (in collaboration with MRC Harwell), Cross-Centre postdoc awards, Pilot Awards and The Directors' Strategic Initiatives programme.

Our cross-Centre 'Themes' programme is the most important mechanism by which we organise and shape our Institute-wide multidisciplinary science. It stimulates scientific debate and exchange of insights, including between Early Career Researchers. Themes are the vehicle to address major cross-disease cutting-edge scientific questions in a collaborative way. For example, the 'iPSC microglia forum' arose from the Neuroinflammation Theme and is creating a benchmark framework to assess the viability and reproducibility of iPSC-derived microglia through standardisation of protocols and the use of Institute-wide control cell lines. These discussions have also led to the IPMAR programme: an Institute-wide effort based in Cardiff to generate highly annotated iPSC cells for neurodegenerative research.

The collaborative nature of our Themes facilitates relationships between researchers at the UK DRI and stakeholders across the UK: we have over 50 external collaborators linked to the Themes, including the University of Oxford, University of Newcastle, the Francis Crick Institute, ARUK Drug Discovery Alliance, the Queen Square Brain Bank, and DPUK, and will continue to strengthen partnerships.

Deploying data science

Data underpins most of the growth trends in the life sciences sector and the UK DRI will increasingly generate a tremendous amount of research data, particularly from the data-rich single cell -'omic approaches and the real-life patient data collected by our Care Research & Technology Centre. We are establishing the infrastructure and the know-how to handle these data, to mine them and to make them FAIR (findable, accessible, interoperable and reusable) to the wider scientific community. However, our ambition goes

beyond these infrastructure essentials. We are in a unique position to link basic research data with clinical data generated by others, to arrive at integrated understanding of disease processes.

We will build on our recently launched strategic partnerships with the DEMON Network and the Alan Turing Institute, and further explore collaborative opportunities with new partners such as Health Data Research UK and EMBL-EBI.

A Director of Data Science and Informatics will lead a programme to radically transform our approach to data science and lead a small team of data experts (statisticians, software developers, data scientists, biomathematicians etc) that will support the Institute-wide implementation of *in silico* science. The Centres will recruit additional Group Leaders with expertise in data science. We will create a data-friendly culture in the UK DRI by providing the necessary resources to enable meaningful data-driven approaches, such as supporting open reproducible science, a new programme of training opportunities and by growing a cadre of dementia researchers who are familiar with data science and are equipped to share their data.

Providing the best resources

The distributed nature of the UK DRI presents an opportunity to link Centres around the application of technology. This interface of technology and research is a vital area where the Institute adds significantly to the UK's capabilities in neurodegeneration research. We cluster technology in the UK DRI into key areas:

- Experimental medicine and biomarkers
- Functional 'omics and single-cell biology
- Advanced microscopy and biophysical techniques
- Cellular manipulation technologies
- Human iPSC-based models
- Small molecule and antibody provision

To provide our researchers with access to specialist technology and expert collaborators, we are implementing a range of Technology Platforms - geographically distributed networks of expert labs active in a technology area or using a specific group of techniques. Dedicated Platform Managers have oversight of these resources, promoting new advances within the UK DRI and connecting researchers with new opportunities.

Training and capacity building

The field of dementia research is significantly underdeveloped when compared to the scale of the challenge. As the nation's largest single dementia research institute, the UK DRI has an important role in building capacity now and for the years to come. We must develop the next generation of high-calibre biomedical researchers and equip them with necessary skills to succeed at the UK DRI and beyond. Our training and career development strategy has five streams: