

UK Dementia Research Institute Sefydliad Ymchwil Dementia y DU



UK Dementia Research Institute at Cardiff University

New scientific discoveries, new hope to stop dementia



Principal funder:



Medical Research Council Dementia is one of our greatest global health challenges, and it is growing rapidly. The number of people in the UK living with dementia is projected to increase to 1.6m by 2040, with global cases set to triple to 153m by the year of 2050. The economic and personal cost of these figures is staggering. Although a handful of drugs that modestly slow disease progression have emerged in the last few years, we still do not have a single treatment that can prevent the disease or stop dementia progressing. In part, this is because dementia research has been chronically underfunded globally, which has negatively impacted progress.

The **UK Dementia Research Institute (UK DRI)** was established to change this. Working across the UK, we are conducting world-leading discovery science to fill the knowledge gap in dementia. Our unique structure draws together the expertise of six great universities across the UK and the diverse skills in their research teams, as well as attracting the best scientific talent from overseas. The resulting community is a highly multidisciplinary ecosystem of researchers, working together to answer fundamental questions about the brain. The UK DRI was founded in 2017 by principal funder the Medical Research Council (MRC), alongside Alzheimer's Research UK and Alzheimer's Society, and was recently re-funded for a further five years.



Researchers at the **UK DRI at Cardiff University** are harnessing cuttingedge techniques to interrogate the genetic variations linked with neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and Huntington's disease. Our new genetic discoveries direct and inform our research into disease processes and mechanisms; these in turn will help accelerate progress towards better disease detection and new treatments.

Meet the Group Leaders at UK DRI Cardiff

The UK DRI has established itself as a world leader in discovery science in neurodegeneration, quickly becoming one of the most cited institutes in the field. The Group Leaders and Emerging Leaders at UK DRI Cardiff are fundamental to this effort, leading multidisciplinary teams to interrogate the biological processes that underpin neurodegenerative diseases. Find out more about the work of our Cardiff centre at <u>ukdri.ac.uk/centres/cardiff</u>.



Prof Paul Morgan (Interim UK DRI Centre Director) is investigating how inflammatory pathways, identified by genetics, contribute to disease development in Alzheimer's disease and other neurodegenerative disorders. His work has clarified the processes by which inflammation contributes to neurodegeneration and highlighted novel targets for drug therapies. Currently, his group is exploring in preclinical models of dementias whether drugs that are known to modify these targets in other diseases can be delivered to the brain to prevent neurodegeneration. Their aim is to deliver these re-purposed therapies for use in the clinic in the next few years.



Prof Julie Williams conducts pioneering research into how our genes influence our risk of Alzheimer's disease and co-led international Genome Wide Association Studies discovering over 100 risk genes. These findings also provide clues about how the disease develops, including the roles of inflammation and the immune system. Prof Williams is also leading on a major new stem cell platform to model the combination of risk genes contributing to common forms of Alzheimer's disease. This resource will be available to researchers around the world. In addition, Prof Williams leads the IPSC Platform to Model Alzheimer's Disease Risk (IPMAR), which aims to become one of the largest cellular model resources. Prof Williams has been awarded a CBE for Alzheimer's research and a British Neuroscience Association Prize for Outstanding Contribution to Neuroscience.



Prof Philip Taylor is exploring the biological consequences of gene variants known to influence a person's risk of developing Alzheimer's disease, to dissect how immune cells called "microglia" contribute to disease development. Microglia have important roles in keeping the brain healthy. Our evidence suggests that risk genes change the way these cells behave, contributing directly to the development of Alzheimer's disease.



Prof Vincent Dion is aiming to develop effective new treatments for "trinucleotide repeat disorders" – a group of inherited neurodegenerative conditions, including Huntington's disease. He is adapting the use of sophisticated gene-editing technologies to correct the mutation that causes the disease.



Prof Caleb Webber (also UK DRI Director of Informatics) is developing state-of-the-art stem cell models and human cellular atlases of neurodegeneration using bioinformatics and Omics approaches that advance our understanding of both Parkinson's and Alzheimer's diseases. By identifying new risk pathways and genes, he is opening up new therapeutic avenues for treatment.



Dr Dayne Beccano-Kelly studies the complex communication between brain cells using research models of Parkinson's disease. His team is aiming to decipher the type of miscommunication that arises and what is driving it. He is doing this at the earliest stages of Parkinson's disease and assessing how this changes over time – ultimately trying to find new ways of correcting it before there is a significant loss of cells in the brain and symptoms appear.



Prof Valentina Escott-Price uses and develops statistical methods to identify individuals at high risk of neurodegenerative disease, utilising polygenic risk scores, biomarkers and environmental risk factors. She is focused on leveraging artificial intelligence and machine learning methods to enhance disease risk prediction and patient stratification in large population-level data. She also employs cutting-edge federated and swarm learning approaches for remote and secure data analyses.



Dr Tom Massey is a Clinical Scientist focused on developing effective drugs for Huntington's disease. His team uses human genetics and stem cell models to identify novel targets that are then taken forward into drug screens.

Meet the Emerging Leaders at UK DRI Cardiff



Dr Natalie Connor-Robson investigates the molecular mechanisms underlying the most common form of Alzheimer's Disease using stem cell models. Her work concentrates on genetic changes in the endocytic pathway. This is a pathway that is used by all of our cells to sort and recycle cellular components. It is particularly important to neurons and microglia, the cells of the brain impacted by the disease. Her work aims to identify how these genetic changes alter cell behaviour and function and ultimately uncover new targets for future therapies.



Dr Wioleta Zelek is an immunologist researching roles of the part of the immune system called complement system in the brain. She has developed a toolbox of novel complement inhibitors, including patent protected drug candidates, immune assays, cell-based assays other tool reagents enabling the study of complement in vitro and in animal models. She holds a prestigious Race Against Dementia fellowship.

Affiliates at UK DRI Cardiff

UK DRI Associate Member is a highly respected scientist that brings mutual benefit through their association with the UK DRI. Prof Valerie O'Donnell is the UK DRI Cardiff Associate Member.

UK DRI Co-Investigators are close collaborators. There are six Co-Investigators at UK DRI Cardiff; Prof Peter Holmans, Dr Georgina Menzies, Dr Gaynor Smith, Dr Rebecca Sims, Dr Mariah Lelos & Dr Owen Peters.





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