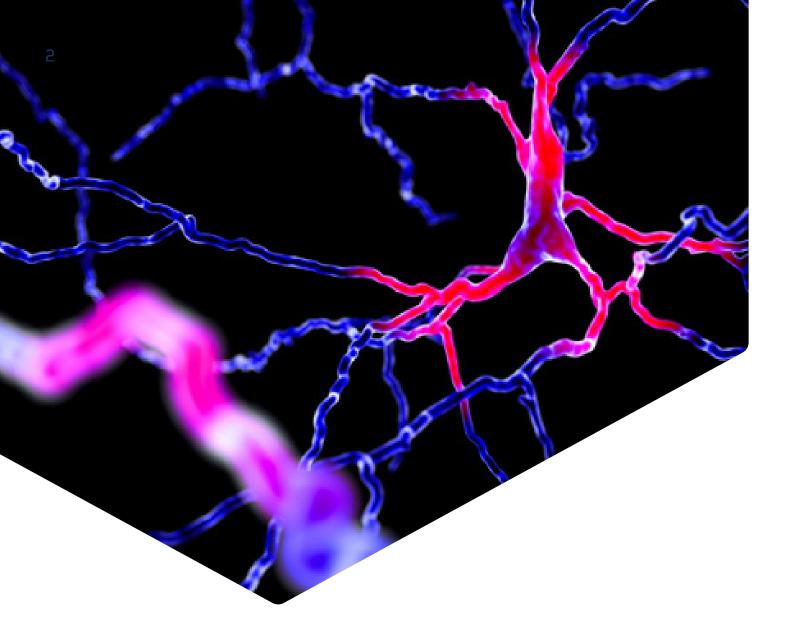


UK Dementia Research Institute at five years





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Foreword by William Rucker

Chairman, UK Dementia Research Institute (UK DRI)

Five years ago, when the UK DRI was established and I became its Chair, there was a sense that bold action was needed. Dementia was affecting over 850,000 people in the UK, and numbers were growing (it's now closer to a million) – and yet we had not found a single drug that could stop or slow the condition. Meanwhile, we knew that 1 in 3 people being born would develop dementia in their lifetime. It was clear that investment into research could not wait.

The commitment to establish the UK DRI was unprecedented. The Medical Research Council joined forces with charities Alzheimer's Research UK and Alzheimer's Society to create and fund a collective of dementia researchers

on a scale never seen in the UK – and five years later, I am immensely proud of the thriving community that has emerged.

Today, more than 800 researchers across the UK, from a spectrum of scientific disciplines, are united at the UK DRI behind a common mission: to fill the knowledge gap in dementia, and transform that knowledge into new tools, technologies and treatments. The UK DRI has assembled a critical mass of the brightest minds from around the globe and created an intensely collaborative environment for them to tackle dementia from every possible angle.

We have already seen significant progress. The UK DRI has quickly established itself as a world

leading institute, making important contributions to dementia research and becoming one of the most cited research institutes in the field. These contributions and the UK DRI's ambition have recently been rewarded by a panel of international experts and peers, who scored the institute as excellent in its first major review in 2022. I am thrilled that this will enable the UK DRI to continue driving its ambitious agenda of research, building on its early successes to make a real difference in the fight against dementia.

The day I interviewed to become the UK DRI's Chair also happened to be the day that my own mother was diagnosed with dementia. This was not a shock – the signs and symptoms many of us are sadly familiar with were becoming clear before that date - but it was nonetheless devastating. Five years on, that sadness remains, but alongside it I also have hope. The scientists I speak to are confident that the discoveries made by the UK DRI, and the thriving wider community of partners and collaborators, will yield breakthroughs. If we continue to take strides forwards as we have in the last few years, I am confident that for our children's generation, things will be different.





Discovering hope for dementia

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. In the UK, the estimated cost of dementia to our economy is £35bn per year, equivalent to nearly a quarter of the NHS budget. Currently, 1 in 4 NHS hospital beds is occupied by a person living with dementia.

Historically, the level of investment into dementia research has not reflected the devastating scale of the problem. Dementia research is **chronically underfunded** globally, and this has negatively impacted progress, with our understanding of neurodegenerative diseases **lagging far behind that of other disease areas**.

Glimmers of hope are emerging. At the end of 2022, a new drug, lecanemab, demonstrated for the first time that Alzheimer's disease can be slowed, offering hope to millions of people. This is a momentous scientific breakthrough, and it shows beyond doubt that our researchers are on the right track. But the effects of the drug are relatively modest, and it will be difficult to deliver as things stand. Lecanemab is an exciting step forwards, but there is plenty more to do.

The UK DRI is filling the dementia knowledge gap by conducting world-leading discovery science. The institute's unique structure draws together the expertise of six great universities across the UK, and the diverse skills in their individual teams, as well as attracting the best talent from overseas to the UK: 1 in 3 of the UK DRI's group

leaders relocated from overseas to take up their posts. The resulting community is a highly multidisciplinary ecosystem of researchers, working together to answer fundamental questions about the brain. Crucially, the institute is also leveraging private investment from charities and industry to take its discoveries out of the lab and translate them into treatments.

The UK DRI's contributions and achievements have now been recognised by an international panel of experts and peers, who recently undertook a rigorous review process of its first five years.

The UK DRI was scored "excellent" in its first five-year review (2022) and awarded £150m over five years to continue its ground-breaking research. This sustained funding is essential for progressing the field, and will enable us to deliver

an ambitious, multidisciplinary programme across the whole spectrum of neurodegeneration.

Now is the time to capitalise on early signs of progress and double down on our efforts. To create space for more breakthroughs,

sustained strategic funding across the whole dementia research ecosystem is needed. With that support, the UK can lead the world in the fight against neurodegenerative diseases.

We have:

- Assembled a critical mass of the brightest minds studying the whole spectrum of neurodegenerative diseases
- Attracted global scientific talent to the UK and built much needed research capacity in neurodegeneration
- Established major programmes in Alzheimer's disease, motor neuron disease (MND), Parkinson's disease and several other neurodegenerative conditions, with a clear translational pathway to accelerate patient benefit
- Brought together a multi-disciplinary community and created a unique operating structure for intensive collaboration

We will:

- Continue to drive forward an ambitious research agenda, contributing to the scientific breakthroughs
- Build on our scientific excellence to provide a central role in convening the UK dementia research ecosystem
- Contribute to the national policy debate to ensure that UK science continues to thrive

We are:

- Conducting world-leading discovery science in neurodegeneration
- Tackling neurodegeneration from multiple angles, to leave no stone unturned
- Partnering to take our discoveries out of the lab and into the lives of people who need them
- Leveraging the UK's strengths across life sciences and biomedical research to accelerate progress

We need:

- Sustained public funding for dementia research to fill the knowledge gap
- A renewed national focus on discovery science, recognising that it attracts investment and is the foundation for driving real impact for those living with dementia



Discovery science:

The crucial first step towards treatment and cures

Discovery science is the engine that drives all subsequent stages of research. We cannot develop new drugs to help patients until we understand the biological processes that underpin neurodegenerative diseases, what causes them and the mechanisms that drive them. The success of lecanemab would not have been possible without decades of previous research into the mechanisms of Alzheimer's disease. UK DRI Group Leader Professor Sir John Hardy first

identified the link between amyloid plaques in the brain and cognitive impairment thirty years ago, opening a new avenue of research that led to this breakthrough.

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. Through our Research Themes, we are uniting experts across the institute, the UK and the global research

community, to foster collaboration in key areas of scientific inquiry and drive progress. UK DRI scientists have already been at the forefront of major advances in dementia discovery science, including studies on the genes that underlie Alzheimer's disease, Parkinson's disease and Huntington's disease; the identification of changes in the diseased brain that contribute to nerve cell loss; and a new form of testing for motor neuron disease (MND). Every new discovery brings us closer to finding new cures.

Unravelling the causes of dementia

Brain Prize winners **Professor** Sir John Hardy (UK DRI Group Leader, UCL) and **Professor Bart De Strooper** (UK DRI Director) are working to understand the role of amyloid proteins in cognitive decline. In 1991, Hardy's team uncovered the first mutation directly implicated in Alzheimer's disease, leading to the formulation of the highly influential 'amyloid-cascade' hypothesis. De Strooper's team is probing the response of brain cells to abnormal clusters of proteins. Both have made important contributions to the field, paving the way for the development of new anti-amyloid drugs, including lecanemab.

Harnessing the UK's rich research talent

The UK DRI Emerging Leaders programme supports talented early career researchers on their journey to building an independent laboratory, helping to bring their exciting research ideas to fruition. One of our Emerging Leaders, Dr Sarah Marzi (UK DRI at Imperial), is uncovering how our environments interact with our genes to affect cells in the brain. Her team combines experimental genomic and epigenomic techniques with innovative statistical and computational analyses to understand our gene regulatory mechanisms, and how these contribute to the earliest stages of neurodegenerative disease.

Creating the right environment

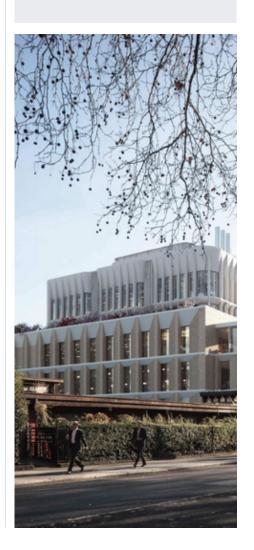
Building has begun on a new 17,500m² state-of-theart neuroscience facility at University College London. The new building will provide a headquarters for the UK DRI and house the largest of the Institute's seven research facilities, to provide the optimum environment for our researchers. Importantly, the UK DRI's discovery scientists will work side by side with translational and clinical researchers under one roof, facilitating knowledge exchange across the research pathway.

Understanding genetic risk

Professor Julie Williams (UK DRI Centre Director, Cardiff) is conducting pioneering research into how our genes influence our risk of Alzheimer's disease, including working on a recent study that identified 42 new risk genes. These findings also provide clues about how the disease develops, including the roles of inflammation and the immune system. Williams is also leading on a major new cell platform, IPMAR, to explore risk factors that contribute to the development of Alzheimer's disease. This resource will be available to researchers around the world.

Linking heart and brain health

Internationally renowned researcher **Professor** Joanna Wardlaw (UK DRI Group Leader, Edinburgh) is working to pinpoint changes in blood vessels linked to neurodegeneration. This will not only lead to new treatment opportunities, but could also help predict who is most at risk of certain types of dementia. Her team aims to translate this knowledge into effective treatments for the NHS. improving lives for people at risk of dementia.



From bench to bedside

The UK DRI is committed to ensuring that the knowledge we generate is translated into tools and therapies that make a real, tangible difference. From the institute's inception, it was set up to ensure that our discoveries can be taken out of the laboratory and into the lives of people that need them – "from bench to bedside".

Since 2017, the UK DRI has signed five major strategic industry partnerships, launched a major new spinout, filed 27 patents, and negotiated at least 350 industry collaborations, non-disclosure agreements, MoUs and translational projects. The UK DRI's collaborative, open, operating model and uniquely competitive IP structure have been critical to these deals.

In 2022, the UK DRI announced a £30m translational partnership with medical research char

with medical research charity LifeArc. This investment will accelerate our activities in this space, funding a wide-ranging programme of translational science across the institute's whole portfolio. Projects will be announced later in 2023.

Bridging the gap between discovery and translational research

The UK DRI's Translation Award programme is an initiative to kick-start promising ideas and projects that have the potential to transform lives. Dr Gabriel Balmus (UK DRI Group Leader, Cambridge) was chosen for his work in targeting DNA repair for the treatment of Huntington's disease. There is evidence that a subset of genes involved in DNA repair is important in the onset and progression of Huntington's disease, and that inhibiting just one gene can delay disease onset. If successful, it could lead to an entirely new approach to treatment, complementing emerging therapies that target the main Huntington's gene.

Translation leading to new companies

The UK DRI's first major spinout company, AviadoBio, recently secured an investment of \$80m in its Series A funding round.

Professor Chris Shaw (UK DRI Group Leader, King's College London) is translating his UK DRI discoveries to develop innovative gene therapies for people living with frontotemporal dementia and MND. This latest investment will allow the company to take their research through to in-human clinical trials.

Collaborating with industry to accelerate new therapies

The UK DRI's £2m partnership with Eisai supports post-doctoral research into dementia. One of the projects selected, led by Professor Valentina Escott-Price (UK DRI Group Leader), is leveraging human genetics to identify target populations for dementia therapeutics. To slow Alzheimer's disease, we need to administer treatment early, so the team is looking to identify those at highest risk and tailoring therapeutics to them.

Pioneering new tools and treatments

The UK DRI is committed to innovation. From brand new techniques for treatments, to cutting edge platforms and tools to support research, the institute has already invested significantly in innovative, promising new avenues with the potential to galvanize progress and accelerate new discoveries.

The UK DRI will continue to invest in ambitious initiatives to drive progress across the field. A brand new, soon-to-launch Transcriptomics platform will expand our capabilities to study gene expression, and a new programme of data science will capitalise on the institute's strengths by harnessing the data generated from a range of cutting-edge techniques.

UK DRI Biomarker Factory

New ultrasensitive tests. many from blood samples, can detect subtle biological changes, facilitating early diagnosis and, eventually, treatment at the earliest possible stage of disease. In clinical trials, biomarkers help recruit the right patients and measure their progress. Prof Henrik Zetterberg (UK DRI Group Leader, UCL) is a world expert on biomarkers, having published over 1,100 papers on the subject and won numerous awards. With Zetterberg at the helm, we launched the **UK DRI Biomarker Factory**

in 2021, a world leading platform that identifies, validates and measures biomarkers. Supported by a team of expert technical staff, the platform is already expanding to accommodate high demand for its services and is providing new insights to researchers around the world.

Non-invasive deep brain stimulation therapy

Multi-award-winning researcher Dr Nir Grossman (UK DRI Group Leader, Imperial) is pioneering a non-invasive deep brain stimulation therapy, with the potential to be an innovative treatment for Alzheimer's disease. There is growing evidence that electrical currents can be used to target specific regions of the brain, to change their activity or alleviate neurological symptoms like the tremors associated with Parkinson's disease. But the most common techniques carry risks due to their invasive nature, with electrodes being implanted deep into the brain. Grossman's new, non-invasive technique has already shown promise in humans. The next stage is a study using it to boost memory in early-stage Alzheimer's Disease.

Helping people living with dementia today

We are committed to finding treatments to help people in the future, but we must also work to improve the lives of people with dementia today. Our Care Research and Technology Centre, led by Professor David Sharp, has launched a new platform, "Minder", to deliver personalised care to people with dementia in their own home. Currently in its pilot stage, the UK DRI is developing plans to expand the programme, to help as many people with dementia, their families and their carers, as possible.

The "Minder" platform to personalise at-home care

The UK DRI Care Research & Technology Centre, based at Imperial College London and the University of Surrey, develops and translates technologies to enable people with dementia to live well. A diverse team of doctors, engineers and scientists is harnessing advances in artificial intelligence, engineering, robotics and sleep science, building a new platform that delivers the highest quality care

to people with dementia in their own homes. The team is guided by people with dementia and their caregivers, and investigates ways to keep people independent, improve their general health and sleep, and reduce confusion and agitation. The Minder platform synthesises data from sensors and devices around the home, such as sleep sensors or Alexa devices, to detect signs of problems early and minimise the risk of hospitalisations.



Founding funders and key partners

The UK DRI would not have been possible without the bold ambition and steadfast commitment of its three founding funders: the Medical Research Council, Alzheimer's Research UK and Alzheimer's Society. We are immensely grateful for their vision and support in establishing the UK DRI, and our ongoing partnerships as we continue to work together to unite the UK's whole dementia research community.





Prof John Iredale, Executive Chair of the Medical Research Council, said:

"We are immensely proud of the entire UK DRI community and their collaboration across the seven centres to advancing our detailed understanding of dementia and neurodegeneration and its translation.

"With renewed investment of £150m that will build on the excellent progress over its first 5 years, UK DRI is in a wonderful position to marshal the internationally renowned research of the UK and its partners to help transform the research field and the lives of those living with dementia and other neurodegenerative conditions and those who care for them.

"The MRC looks forward to celebrating future successes for UK DRI and supporting it as a key national asset to further the UK's reputation as a leader in research and innovation."

Fiona Carragher, Director of Research and Influencing at Alzheimer's Society, said:

"As a founding partner and funder of the UK DRI we are very proud of what the institute has achieved since its launch in 2017. We congratulate everyone involved in placing it on the map as a global leader in dementia research and for the great impact it has had so far. This has included critical research into developing new diagnostic tools to ensure people living with dementia receive an early and accurate diagnosis, potentially giving them access to one of the disease-modifying treatments we hope to see emerging from the clinical trials pipeline in the coming years.

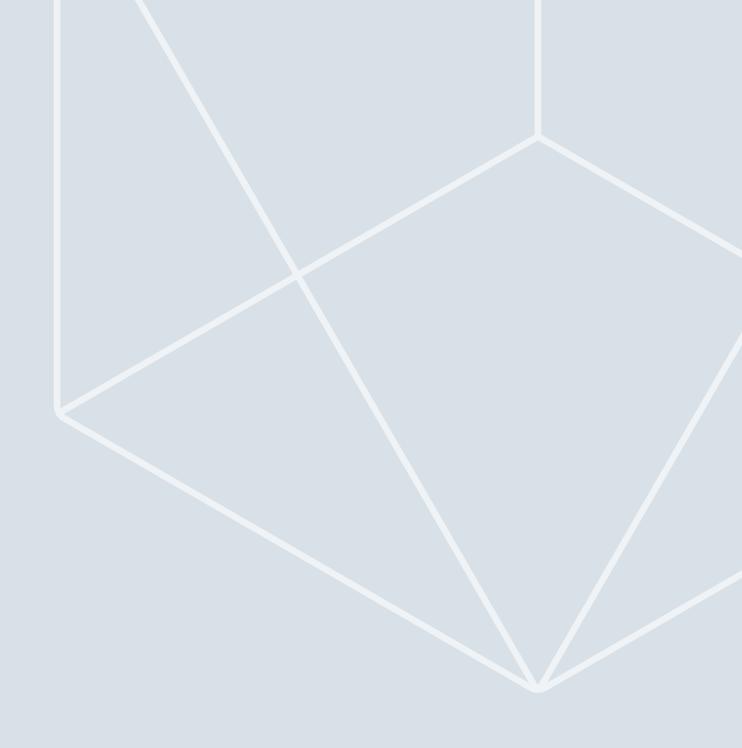
"We are also passionate about the work of the Care Research and Technology centre which is revolutionising the way people living with dementia are cared for, to help them live better for longer today. So much has been accomplished by the UK DRI so far and we look forward to working with this vibrant community of researchers in the future."



Dr Susan Kohlhaas, Executive Director of Research and Partnerships at Alzheimer's Research UK, said:

"When you consider the UK Dementia Research Institute's impressive achievements, it is easy to forget that it was established just five years ago. It is fantastic to see a critical mass of talented, passionate and hard-working scientists coming together to answer the most pressing questions in dementia research. It's hard to overstate how important the UK DRI is, not just to the wider UK research community, but in providing the answers that people living with the heartbreak of dementia need and deserve."

"The next five years will doubtless see the team at the UK DRI build on their incredible track record, making vet more fundamental discoveries that will get us closer to new treatments, diagnostic tools and preventative strategies for people living with neurodegenerative conditions like dementia. As a world-class research institute, the UK DRI is well placed to forge new collaborations and partnerships, both in the UK and internationally that will further accelerate global progress. At Alzheimer's Research UK we're proud to be a strategic partner and founding funder of the UK DRI and look forward to our continued partnership to deliver real progress for the field."





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