Dr Giovanna Lalli, UK DRI Director of Scientific Affairs at the UK DRI Early Career Researchers' Workshop on Neuroinflammation, April 2019.

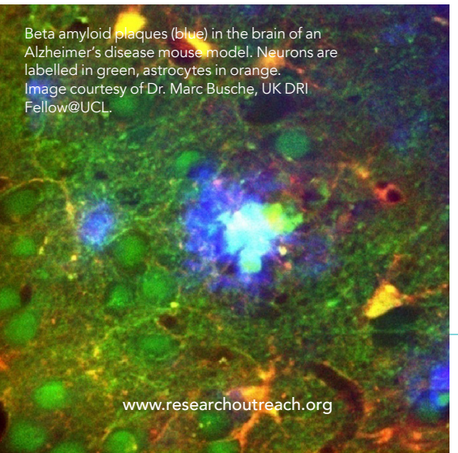
It's not only about neurons:

How the UK Dementia Research Institute is facilitating an interdisciplinary approach in the global fight against neurodegenerative conditions

Dementia is the world's biggest challenge in terms of social and health costs. In the UK, we're projected to have 1 million dementia patients in 2020 at a cost of £26bn; by 2040, costs are projected to reach £55bn. Globally, 50 million people are affected by dementia and this will increase to 152 million by 2050. But, looking beyond the statistics, almost everyone knows somebody who suffers from dementia. The UK Dementia Research Institute aims to unite researchers, clinicians and scientists in the battle against this little understood range of conditions; its Director of Scientific Affairs, Giovanna Lalli, tells us more.

The UK Dementia Research Institute (UK DRI), set up to work on the future of dementia care and research, is committed to driving meaningful development in an understanding of the hugely complex area of neurodegenerative disorders.

Director of Scientific Affairs at UK DRI Giovanna Lalli explains more about what motivates her and her colleagues in the ongoing struggle to understand why dementia happens – and to develop therapeutic and preventative measures.



Beta amyloid plaques (blue) in the brain of an Alzheimer's disease mouse model. Neurons are labelled in green, astrocytes in orange. Image courtesy of Dr. Marc Busche, UK DRI Fellow@UCL.

Hi Giovanna. Can you tell us more about your journey to where you are at UK DRI today?

I'm a neuronal cell biologist, by training. I trained in Italy, the States and then London, where I got my PhD and continued as a post-doc. I got a lectureship at King's College London, where I was investigating neuronal stem cells in the mammalian brain. I then moved to the Wellcome Trust where I was overseeing the molecular and cellular neuroscience portfolio. I was there for three years including as acting head of neuroscience and mental health for ten months – and it was an incredible learning experience. From working in the lab studying my favourite signalling pathways, suddenly this entire portfolio of neuroscience research projects was in front of me. I had to adopt a broader perspective and 'stretch' much beyond my immediate area of expertise.

Can you explain the vision of UK DRI and how you're working to realise that vision?

Our mission is to lead multidisciplinary research, not only into Alzheimer's but the spectrum of neurodegenerative conditions causing dementia. We want to drive a step change in how we understand these diseases; to accelerate the discovery and delivery of interventions to diagnose but also treat and ultimately prevent dementia.

We've also recently opened a new care research and technology centre so that we can hopefully have an even quicker impact on dementia patients. We're gaining momentum and the fact we're able to attract young talent from across the world is exciting – we need fresh thinking, fresh perspectives to tackle this problem.

Our founding funders are the Medical Research Council and the two biggest UK Alzheimer's charities, Alzheimer's Research UK and the Alzheimer's Society, who between them have made a total investment of £290m for the first five years. We are assembling a critical mass of excellent researchers who can then catalyse and engage with the rest of the UK dementia and non-dementia research landscape and bring back partnerships with the biopharmaceutical sector.

Would you say collaboration is instrumental in moving forward?

Collaboration is essential and we see this quite clearly within the UK DRI, as we have seven centres in six institutions, three in London, and others in Cardiff, Cambridge and Edinburgh. We strongly promote collaboration within and between centres, but we are aware that the UK DRI cannot be a silo community; we have to build upon the strength of research and science already present in the UK and build bridges across borders as well.

If we want to develop new interventions and treatments, we can't do it on our own; we must also engage in partnerships with industry, biotechs and others.

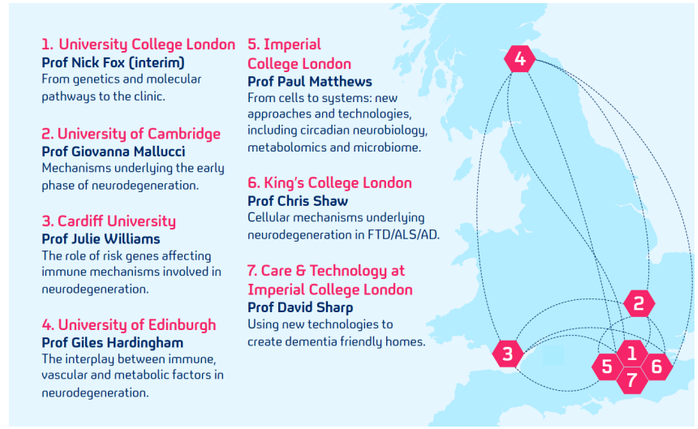
Can you tell us more about UK DRI's new partnership with Eisai?

We've recently completed a partnership with Eisai, with whom we're launching a co-funded post-doctoral programme to identify new biomarkers or biological mechanisms that can lead to targets for therapeutic development. This partnership delivers a very important message in this field, especially at a time when many companies are pulling out of research into neurodegeneration after the failure of big clinical trials. We need to re-engage with industry, and this is only the first of our partnerships.

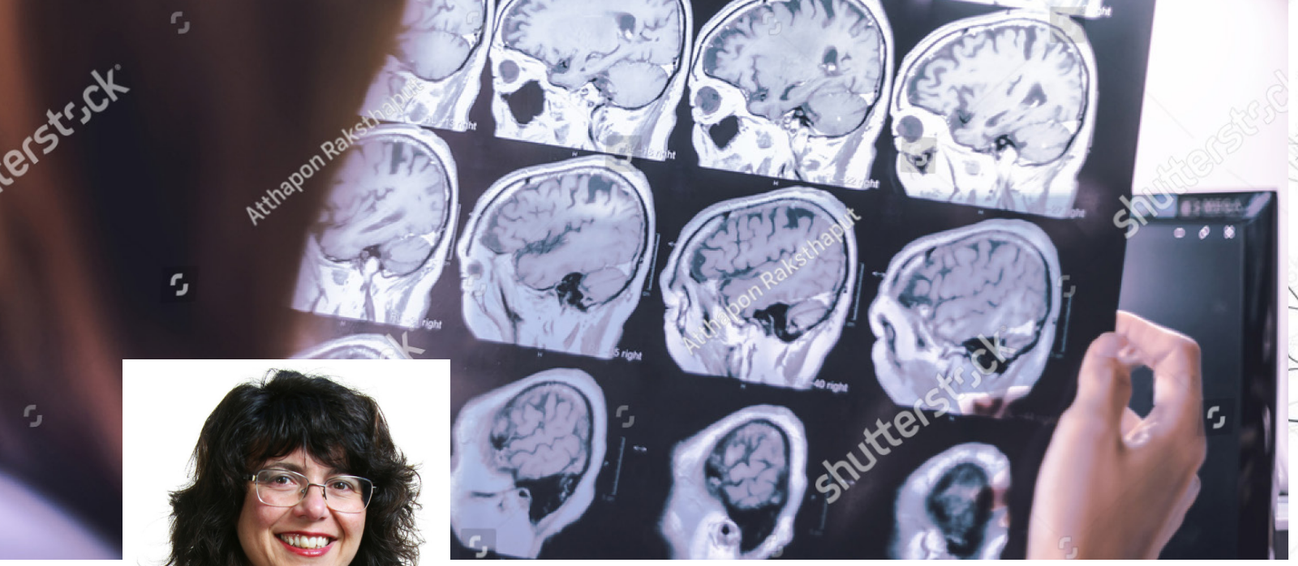
To what extent do basic, or lab-based, research and clinical research, which works with patients and data, translate into medical outcomes?

It's important to have the freedom to do 'blue sky research' to advance knowledge, but, it's crucial to have a real impact on human health. We focus on basic mechanisms underlying

Across all populations and countries – we need to work together to defeat dementia.



The UK DRI: a national virtual institute formed by a hub (located at UCL) and six centres.



Dr Giovanna Lalli, UK DRI Director of Scientific Affairs.

neurodegeneration but we also have clinical research going on – and we want to promote interactions between basic and clinical streams. A successful outcome for us is not only going to be highly-cited publications but also work that can lead to novel approaches in therapies, because this is what we want to achieve: ways to diagnose early and maybe prevent but also treat dementia.

Where do you see research into dementia going, and do you feel the aims are changing?

We have new methods and technologies to study how different types of cells in the brain interact – for example, high-resolution microscopy, single-cell sequencing, cutting-edge neuro-imaging, and special probes able to record the activity of hundreds of neurons simultaneously – harnessing the power of all these techniques together with insights from genetic studies in patients can help us better understand not only how the brain works but also how dementia develops.

Genetic studies point to an important role of microglia, the immune cells in the brain involved in the response to the amyloid plaques that are a typical feature of Alzheimer's disease. Microglia can be protective, but some studies clearly point to these cells as a key cell type involved in Alzheimer's disease. The brain includes neurons and other types of cells like astrocytes, microglia, endothelial cells, and new directions in neurodegeneration research are investigating the cross-talk between these different cell types. Genetics, immunobiology, vascular biology – bringing all these together gives us a better understanding about what happens in neurodegeneration; it's not only about neurons!

Prof David Sharp, Director of the UK DRI Care Research & Technology Centre at Imperial College London.

Does dementia research have any take-outs for other degenerative conditions such as multiple sclerosis?

It's very important not to think in silos; we're investigating different types of dementia, which are characterised by inflammatory states, by misfolding or aggregation of toxic proteins. These principles and phenomena are also found in other degenerative conditions. We can learn a lot; by understanding how these processes are malfunctioning, we can also better understand other types of conditions.

Is the DRI helping initiate those conversations between different researchers?

Our basic scientists are keen to learn more about the clinical manifestations of different types of dementia. We have clinician scientists distributed throughout the network, with many of them embedded in basic research labs, so we're asking, 'How do we promote these interactions, and how do we make the most of the expertise that is available?'

There should be more dialogue between the clinicians: the people who are actually seeing the patients and analysing their symptoms, and the basic researchers, who are sometimes just confined in their own labs studying their own proteins. Having a broader view of how the patients and their symptoms differ can provide important clues into the basic mechanisms of these diseases. We're still fairly early in our development as we only started in 2017, but we have plans to engage more with the health network systems, so we are trying now to reach out to NIHR [the Clinical Research Network] to look for ways to better collaborate and make use of clinician/patient data. Additionally, we have established a patient involvement panel so our researchers can gather first-hand feedback.

We need to try to re-engage with industry; and this is only the first of our partnerships – we hope to announce many more in the future.

Can you tell us more about the newest UK DRI centre at Imperial College and technologies to create dementia-friendly 'healthy homes'.

The UK DRI Care Research & Technology Centre opened in June at Imperial College London (ICL). It's creating monitoring technologies for key dementia-related measures such as sleep disturbance, infection, diagnosis in the home; research streams that require substantial patient input.

The centre is led by Professor David Sharp at ICL in collaboration with colleagues at the University of Surrey. They will optimise a series of technologies in a model home environment to look at ways to monitor dementia progress at home. The point is to really keep the patient at home instead of having to be referred to hospital. They are going to also develop a safe AI [artificial intelligence] system that will improve health autonomy by predicting clinical events and develop robotic devices that can monitor and manage the environment for improved patient safety and quality of life, so the clinical team can deliver a highly personalised health care plan.

Do you collaborate with researchers from overseas?

The majority of our researchers already have collaborations with investigators around the world. Brexit could have an important effect on how the UK is able to attract researchers from across the EU and whether our own researchers will be able to access EU funding, such as from the European Research Council – there is still no clarity on that.

I hope that measures can be taken to continue to enable effective collaboration and funding across borders with the EU, enabling movement of researchers and access to funding, otherwise, this could have huge effects on our research – and on UK research in general.

I've had interactions with the Alzheimer's Association and National Institutes of Health in the States, who are trying to really push dementia research. When we speak to patients who, because of genetic mutations, were going to develop dementia early in their life, they say, 'I don'twant this to happen to my children'.

Direct contact with patients always opens a different perspective and reminds us why we are here and why we need to tackle this devastating disease. Across all populations and countries – we need to work together to defeat dementia.

If you would like to find out more about dementia or are interested in UK DRI's research, you can visit their website at: https://ukdri.ac.uk

UK Dementia Research Institute

UK Dementia Research Institute HQ
6th Floor, UCL Maple House
Tottenham Court Road
London W1T 7NF

E: g.lalli@ucl.ac.uk
W: www.ukdri.ac.uk

www.researchoutreach.org