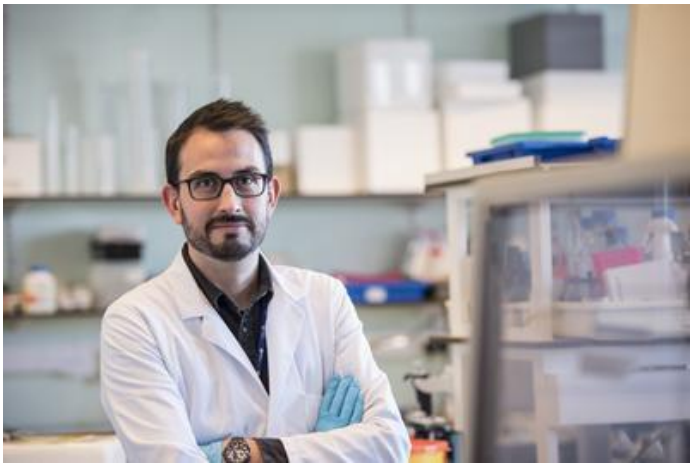


We recently caught up with Dr Diego Gomez-Nicola, a lecturer in neuroscience at the University of Southampton, to find out more about how he has used Brains for Dementia Research tissue in his work.

What aspect of dementia do you work on?

My group focuses on microglia, the resident immune cells in the brain, and studies how these cells change during neurodegeneration. One key hallmark of neurodegeneration is the expansion of the microglial population, with this contributing to the development of pathology. Understanding the processes governing microglial proliferation could highlight potential therapeutic approaches to control neuroinflammation in neurodegeneration.

How has using human brain tissue contributed to your work?

We first decided to use human brain tissue when trying to understand the dynamics and regulation of microglial proliferation and neurogenesis in chronic neurodegeneration. We had been using a mouse model of prion disease to investigate microglia and neurogenesis in chronic neurodegeneration, and so wanted to see whether the changes seen in mice were also seen in humans, in both prion disease (Creutzfeldt-Jakob disease; CJD) and other neurodegenerative conditions. We obtained temporal cortex and hippocampal brain sections from the National CJD Surveillance Unit Brain Bank in Edinburgh, from people with CJD or Alzheimer's disease, and age-matched controls for each condition. By using human tissue, we were able to validate what we had seen in mice, showing that microglial proliferation and neurogenesis occurred in both CJD and Alzheimer's disease, indicating that they are key features of chronic neurodegeneration. Using one set of brain samples, we were able to perform two analyses and gain insight into both microglial proliferation and neurogenesis.

We then turned to the South West Dementia Brain Bank in Bristol to obtain samples for RNA analysis, and were able to obtain matched sections from the same person for some of these samples. Using these samples, we studied microglial proliferation in the brains of people with Alzheimer's, investigating changes in gene expression which could be driving proliferation. Using the human tissue supported and validated the findings we were observing in animal models.

I feel that using human tissue makes our research more robust and relevant to the human diseases we study, but whether that makes our research easier to publish is difficult to say!

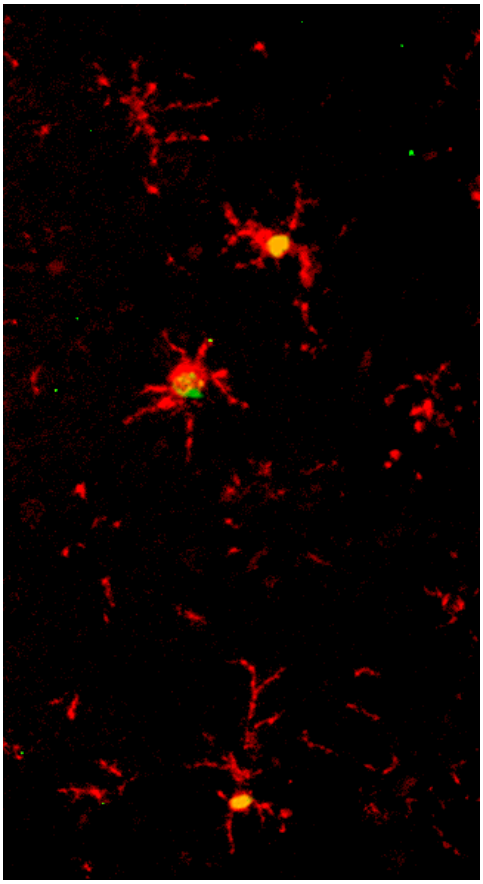
Has using human brain tissue allowed you to explore different avenues of research?

When we first started using human brain tissue, we were comparing brain tissue from CJD and Alzheimer's disease, so also had the age-matched controls for each of these groups. As CJD affects people earlier in life, the age-matched control tissue came from people aged about 23-28, which was much younger than the age-matched control tissue for the Alzheimer's brain

samples. We realised that the control tissue represented two distinct healthy control groups, and that we could perform separate analyses of young versus aged tissue, to understand how ageing affects both microglial number and proliferation. This allowed us to maximise the amount of data we could obtain from this set of tissue, additionally enabling us to understand fundamental aspects of brain ageing.

What are the benefits of BDR?

BDR is a unique resource we have in the UK. While other countries do have brain banks, the variety and number of samples available through BDR has no comparison. Additionally, using BDR streamlines the process of obtaining tissue as we did not have to apply for our own ethics approval as we were covered by the devolved approval from BDR. This is a huge benefit to groups such as mine that do not work exclusively on human tissue.



Proliferating microglia in Alzheimer's disease (Credit – DGN lab)

Another benefit is that BDR has created a network of brain banks. If you go to one brain bank and they don't have the type of tissue you need, they will direct you to another bank that may do. We experienced this recently when trying to get frozen sections of brain tissue from one bank, and they referred us onto another bank with a slightly different process of preserving the tissue, which did have the tissue we needed. The flow of communication between brain banks is fundamental – they know about each other and the speciality of each bank. Using BDR means you don't have to start the process from scratch each time if a bank doesn't have the samples you need.

Initiatives such as BDR have also been successful in highlighting the role that donated brain tissue has in dementia research, raising awareness of brain donation among the wider population. Without people generously deciding to donate their brains, the valuable resource that is BDR would not exist.