Lay Summary

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Single-cell transcriptomics of prion diseases

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Prion diseases are untreatable fatal brain conditions such as Creutzfeldt-Jakob disease in humans and bovine spongiform encephalopathy in cows. These are relatively rare diseases but still affect approximately 150 people per year in the UK. Prion diseases are caused by one of the body's own proteins (prion protein) changing shape into an abnormal or rogue form (a prion) that encourages normal protein to change shape.

Increasingly a view amongst scientists holds that there are shared mechanisms between prion diseases and other dementias. We study prion diseases because of the unmet need for treatment of these devastating diseases.

Although progress has been made towards understanding the mechanisms involved, very little is known about what happens at the cellular level in affected brains.

We have developed a robust protocol to investigate which cells are affected by prion infection, and what makes them different from other cells that remain unaffected. Our goal is to obtain a snapshot of the activity in individual cells of brains affected by prion disease. This protocol requires "single cell sequencing", a cutting-edge technology.

Our experiments in model organisms allow us to understand the development of the disease process in more depth. Our next step is to use this protocol on human tissues. Human samples will enable us to continue our research and hopefully the generated data will benefit dementia research in the wider scientific community.

Abbreviations

PrP: prion protein

sCJD: sporadic Creutzfeldt-Jakob disease

snRNA-seq: single-nucleus RNA sequencing

AD: Alzheimers disease