Mouse models of sporadic CJD.
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Prion diseases are transmissible, invariably fatal neurodegenerative diseases of mammals. They are an example of an unconventional infectious disease as they are transmitted through a unique pathogen; a misfolded form of a host-encoded protein referred to as a prion. Very little is known about the process by which this aberrant misfolding occurs but it is pervasive as prion diseases have been described in many mammalian species and even exhibit different strains within the one species. The array of clinical signs associated with prion diseases is quite broad; including general dementia and motor signs through to more specific clinical signs such as persistent insomnia or pruritus. As prion diseases are considered to be a class of neurodegenerative diseases the different clinical signs seen between strains are generally thought to be due to damage to different areas of the brain but how prions can target different brain regions is unknown.

In order to investigate how prions target particular brain regions and inflict damage appropriate models of disease are required. To date most prion research has focused on agricultural animal derived strains with little attention directed at medically relevant human prion strains. Recently the Lawson lab has generated three, mouse-adapted strains of prion disease that represent different strains of the most common form of human prion disease; sporadic CJD (Creutzfeldt–Jakob disease). These strains exhibit remarkably different incubation times and clinical presentations. We wish to further characterise the prions that cause these different manifestations of disease to understand

- What part of the brain they affect and how this relates to their clinical presentation?
- What determines the regions of the brain that they affect?
- How this affects our ability to detect (or diagnose disease)?
- Whether these different strains respond differently to treatment?

Answers to these questions are directly relevant to patients and their families as they can help to explain why prion diseases are so difficult to diagnose and hopefully identify common features or early symptoms that can be better utilised by clinicians. It will also establish whether a treatment that shows promise in one patients will be equally effective in a patient with another ‘strain’ of prion disease. We are also hopeful that by understanding why different strains of prion target different regions of the brain we can determine a factor that facilitates disease that could be targeted for drug development.

Laura Ellett has been a research assistant in the Lawson lab since 2008. She has contributed to several significant publications and has been extensively involved in the development of these prion strains that we only now are in a position to use to answer questions that will benefit patients and families with CJD.

Due to Laura Ellett's fantastic academic record she has been awarded an APA scholarship, to fully fund her stipend and is appreciative of the 'CJDSGN top up scholarship for 2017 in memory of Frank Burton. I anticipate that she will be competitive for the Willesee scholarship or equivalent memorial scholarship top up in the future.

The commitment from the CJDSGN to support Laura's project (if required) for the duration of her candidature (3-4 years) has secured Laura's candidature. The $40,000 'CJDSGN grant in memory of Frank Burton' for 2017 will contribute to a very cost intensive first two years of the project and has enabled us to commit to significant experiments aimed at understanding the basis for different clinical presentations of prion diseases and determining how this affects diagnosis and treatment.

We anticipate that the final 12-24 months of her candidature will be less cost intensive. I have applied for funding for her project (NHMRC) and if that were successful I would of course advise the CJDSGN that this commitment could be used for other research in Australia.

I cannot emphasise enough how important Laura is to my overall research program or the role she plays in prion research in Australia. She has provided the 'hands' for collaborations I have with Steve, Andy, Simon and Cath. Without her these collaborations would not be possible and so some of this work would not have occurred.

If I had not had the funds to support Laura's PhD project this work would have ceased at the end of June 2017 and the knowledge and skills she has developed over the last 9 years would have been lost. I am grateful to the CJDSGN for their support which will enable Laura and I to continue prion disease research and train future prion disease research scientists.