CASE STUDY

Microglia and motor neuron disease/amyotrophic lateral sclerosis

Who: Julie Simpson, PhD Department of Neuroscience Sheffield Institute for Translational Neuroscience, University of Sheffield

Julie Simpson PhD is currently a Lecturer in Translational Neuropathology at the University of Sheffield. Her research focusses on identifying and understanding neuroinflammatory contributions to neurodegenerative diseases, using the complementary approaches of detailed immunohistological characterisation and gene expression profiling of specific cell populations in post-mortem brain. Investigating glial activation and function is crucial to understanding the inflammatory response in neurodegenerative diseases, including motor neuron disease.

nCounter® Assay selection:

nCounter Human Neuroinflammation Panel

Project Summary:

MND (also known as Amyotrophic Lateral Sclerosis or Lou Gehrig's disease) is a fatal, neurodegenerative disease that lacks an effective treatment. Microglia are the resident immune cells of the brain with many different functions. Autopsy studies of MND have demonstrated elevated levels of microglia-related chemokines and mRNA species. Marked microglial reactions have been demonstrated in both sporadic MND (sMND) and MND caused by C9orf72 mutations (the most common genetic cause of MND). The severity of the microglial reaction correlates with the rate of disease progression, clinical symptoms and level of pathology. We have shown that motor neurons express inflammation-related genes in proportion to the levels of other pathology markers and that knockdown or mutation of C9orf72 is associated with widespread immune abnormalities.

Most studies that examine which immune functions are affected have used animal models. These have confirmed the involvement of microglia, but yielded inconsistent results with respect to which functions are important. We propose to use NanoString's Neuroinflammation Panel to perform a human autopsy study to discern how the immune profile differs between MND and healthy spinal cords. The findings generated by the NanoString Neuroinflammation Panel will be a vital, starting dataset in this research project. The data will be interpreted in the light of other gene expression technologies as well as immunohistochemistry and state of the art image analysis. The outcome of these investigations will be mapped to multiple other brain regions in order to find correlates of disease survival as targets for downstream experiments. The Grant also offers an exciting opportunity for our PhD student, Bridget Ashford, who will commence her research by using this NanoString panel.

"Trying to identify what specific aspects of neuroinflammation are relevant has been attempted in animal models and it's led to some inconsistent results. We want to use human tissue to try and pin down in greater detail specifically what that microglial response may be. We're looking at multiple different CNS areas principally the spinal cord and the lower motor neurons plus the corticospinal tract that project to them. We have a lot of immunohistochemistry markers against microglial and other inflammatory cell markers. But we were keen to explore some more open-ended gene expression and that's where we thought the NanoString technology would fit in."

Julie Simpson, PhD

To learn more about Neuroinflammation Panels, visit nanostring.com/neuroscience

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