Progress Report

Author: A/Prof Susanna Park
Qualification: PhD
Institution: University of Sydney
Date: 26 October 2023

Title of Project: Measuring Nerve Damage after Chemotherapy Treatment

Summary:

Chemotherapy-induced nerve damage or peripheral neuropathy (CIPN) is a major side effect of cancer treatment, leading to early cessation of treatment and long-lasting disability. Despite successful treatment, up to 40% of cancer survivors may be left with long-term disability and reduced quality of life due to CIPN following treatment with neurotoxic chemotherapies. This project will measure the trajectory of nerve degeneration in patients with CIPN through innovative methods of assessing nerve dysfunction, including specialised nerve testing methods and analysis of protein markers of axon degeneration in blood.

The key aims of the project are to:

1. Determine association between neurophysiological and serum markers of axonal degeneration in chemotherapy-induced neurotoxicity.
2. Define the trajectory of axonal degeneration and neurotoxicity in this cohort over time.

The main serum marker of nerve damage that we will test is called neurofilament light chain (NfL). This protein forms the structure of nerves, and is released during injury. NfL has been identified as a marker of axonal damage in animal models of CIPN, and in clinical studies with certain chemotherapies. However, it has never been examined with sensitive neurophysiological measures of CIPN such as nerve excitability studies. Our project will use clinical phenotyping, longitudinal assessment, functional outcomes coupled with these specialised neurophysiological and protein biomarker approaches, to determine key mechanisms underlying the development of nerve damage following chemotherapy treatment.

In 2023, our research team received an equipment grant from University of Sydney and National Health and Medical Research Council which enabled us to purchase a Quanterix SR-X digital immunoassay testing suite. This has led to the establishment of in-house capability for ultrasensitive immunoassay techniques – meaning that we can test for NfL and other relevant proteins in our own facility, rather than sending

samples to another testing site as proposed in our original project. This provides enormous scope to test further patient groups and samples. Our progress on this project to date has also included the collection of longitudinal serum samples and matched clinical and neurological data from 89 patients treated with neurotoxic chemotherapies. This data is also matched with neurophysiological data, including nerve excitability studies which can provide more detailed information regarding axonal function and membrane properties than conventional nerve testing. The comparison between serum markers of nerve damage such as NfL and nerve excitability findings has not yet been completed but will enable development of monitoring strategies to identify early nerve damage following chemotherapy.