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Trish Translational Research Project Grants

Commencing January 2023, **Professor Paul Stupple, The Monash Institute of Pharmaceutical Sciences (MIPS) and Dr Steven Petratos, Monash University,** have been awarded a 2-year Trish Translational Research Project Grant of $250,000. Professor Stupple's and Dr Petratos' Project is titled, **"Development of Small Molecules to Promote Remyelination in Multiple Sclerosis".**

Consistent with the funding principles of the Trish MS Research Foundation, **Professor Stupple and Dr Petratos** aim to develop a small molecule-based treatment to reverse progressive MS through promoting remyelination of neurons. Of the 19 FDA approved disease-modifying therapies for MS, there remains a lack of tangible options for progressive MS, for which Professor Stupple and Dr Petratos aim to develop new therapeutic agents to solve this unmet need. They aim to carry out translational research to translate results from their academic research into results that directly benefit progressive MS patients.

MS is the most common demyelinating disease, where the protective covers (myelin) of nerve cells in the central nervous system (CNS) are damaged. Absence of myelin can lead to degradation, resulting in permanent neurological complications such as complete loss of function for motor control or cognition. Remyelination is the formation of myelin-producing cells to generate new myelin sheaths on demyelinated nerve cells. While myelin can be regenerated through remyelination, degenerated nerve cells cannot be regenerated, therefore making research to promote remyelination more important in treating progressive MS.

Diiodothyropropionic acid (DITPA) is a small molecule that exerts neurobiological effects in the CNS. We hypothesise that DITPA can promote remyelination and protect the CNS through increased production of myelin-producing cells as well as maintenance of mature myelinating oligodendrocytes. We have shown that DITPA encourages precursor cells to become myelin producing cells, hence enhancing the myelination of nerve cells. Now we are working to synthesise and screen DITPA derivatives to study the structure–activity relationship, which data are lacking in the literature. Preliminary assays have identified certain DITPA analogues with promising activity, where we now plan for the next generation of optimised compounds. Ultimately, we aim to obtain an optimised drug candidate to expand the options for neurologists for treating their patients living with progressive MS if these can be licenced and taken through to clinical trials.

Also commencing January 2023, **Professor Trevor Kilpatrick and Dr Vivien Li, University of Melbourne,** have been awarded a 3-year Trish Translational Research Project Grant of $250,000. Professor Kilpatrick and Dr Li's Project is titled, **"Advancing tolerogenic dendritic cell therapy for multiple sclerosis toward clinical translation".**

Professor Kilpatrick, Dr Li and their team aim to develop a new way to treat MS based on using patients' own blood immune cells. These immune cells are treated with anti-inflammatory signals in the laboratory and then re-administered to the patient, where they selectively target and dampen down the disease-causing immune cells that promote inflammation and lead to nerve cell damage in MS. This approach has benefits over existing therapies as it targets key initiating events in MS and could treat all disease stages. The targeted cells can cross into the central nervous system to dampen down disease-causing immune cells that are otherwise hidden from current treatments.

This project will advance the team's existing work towards clinical translation. They have developed techniques to grow these immune cells from patient blood samples and defined culture conditions that can modify their behaviour to assume protective/anti-inflammatory rather than disease-inducing/pro-inflammatory characteristics. They have identified relevant proteins involved in MS which can enable selective targeting of the disease-causing immune cells rather than broadly suppressing the immune system.

The next steps focusing on clinical translation will involve identifying target patient populations who may be suitable candidates for this therapy and partnering with a commercial organisation to manufacture this cellular therapy for clinical trials.