“Rites of Passage” Seminar

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Assessing APP96-110 as a novel neuroprotective agent against traumatic spinal cord injury.

Tuesday 24 October, 2017 at 1.00pm

Room 1.81, Anatomy, Physiology & Human Biology Building North
The University of Western Australia (off Hackett Entrance No. 2)

The Seminar: Sarah’s PhD thesis entitled “Immunomodulatory and neuroprotective approaches including human mesenchymal precursor cell transplantation for spinal cord injury repair” investigated combined immunomodulatory, drug and cell based therapies for spinal cord injury (SCI) repair in a Nude rat model.

This study investigated the potential neuroprotective effects of the APP96-110 peptide, a heparin binding site at residues 96-110 of the amyloid precursor protein (APP) that has marked neuroprotective effects following traumatic brain injury (TBI). Rats received a moderate contusive thoracic (T10) SCI, and were given a single intravenous injection of APP96-110 (active) or mAPP96-110 (inactive mutant) peptide at 30 minutes post-injury. At 1 week post-injury (wpi), a cohort of animals underwent transplantation of viable or non-viable (nv) human mesenchymal precursor cells (hMPCs) into the spinal cord lesion site. Recovery of hindlimb function was assessed weekly for 8 weeks before animals were euthanised and spinal cord sections were analysed for hMPC survival, cyst formation and spinal cord morphology. There were no significant differences in hindlimb function between treatment groups when assessed during open field locomotion (Basso-Beattie-Bresnahan (BBB) scoring) and no treatment groups recovered to pre-injury scores/performance. APP96-110 or hMPCs alone did not improve tissue morphology, however combined APP96-110 + hMPCs significantly reduced cyst size compared to SCI only. Donor hMPCs also significantly increased βIII tubulin fluorescence intensity, and the amount of $GFAP^+$ and $laminin^+$ tissue, and decreased the amount of $ED1^+$ tissue compared to SCI only.
This study demonstrates that the APP96-110 peptide may have modest neuroprotective effects following SCI, which may be enhanced when combined with hMPC transplantation. Although no functional improvements were reported in these studies, there were significant improvements in tissue morphology with individual and combined therapies, which highlights the potential of combinatorial approaches for SCI. Better understanding of how hMPCs exert neuroprotective and neuroregenerative effects may improve the favourable outcomes reported with hMPC transplantation following SCI. Optimising drug dose/concentration, and the timing and duration of early immunomodulatory and neuroprotective interventions may also significantly improve the efficacy of these therapies. Utilising combinatorial approaches that target specific pathophysiological events at different stages following SCI can significantly improve the efficacy of individual therapies and lead to greater functional and morphological improvements.

The Speaker: Sarah completed her Undergraduate degree with Honours in Neuroscience at UWA in 2010. She worked as a Research Assistant before commencing her PhD in the Spinal Cord Repair Laboratory UWA in 2011, supervised by Associate Professor Stuart Hodgetts, Professor Alan Harvey and Associate Professor Giles Plant. Sarah’s PhD was awarded in June 2017 and she is now working as a Research Officer in the School of Human Sciences, UWA.