



## 2023 Hopewell M.I.N.D. Prize Finalists



**Finalist:** [Dr V. Wee Yong](#)

**Bio:** Dr. Wee Yong is a Professor at the University of Calgary. He leads the Multiple Sclerosis (MS) Brain and Mental Health Team of the Hotchkiss Brain Institute at the university and he directs the provincial Alberta MS Network. Dr. Yong is a past chair of the Medical Advisory Committee of the MS Society of Canada. He has been the President of the International Society of Neuroimmunology, and he continues to co-direct its Americas and Global Schools of Neuroimmunology. Dr. Yong's research interests lie in the area of neuroimmunology, neuroprotection and CNS regeneration, and his projects are guided by MS and brain tumors. He has published 340 peer-reviewed manuscripts and his research has been translated into Phase II

and III clinical trials in MS; his team has initiated a Phase I/IIa trial in glioblastoma. His work has been cited over 33,000 times (h-index of 102) according to Google Scholar. Dr. Yong is an elected fellow of both the Canadian Academy of Health Sciences and the Royal Society of Canada. He received the 2017 Allyn Taylor International Prize in Medicine for 'transformational discoveries in MS'. Dr. Yong was singly profiled in the August 2021 issue of the world's #1 clinical neurology journal, Lancet Neurology.

**Proposal Title:** Overcoming CNS fibrosis for neuroregeneration

### Summary:

Wound healing after an injury to peripheral tissue is normally a well-orchestrated response leading to recovery. In the central nervous system (CNS), however, an injury often results in a fibrotic scar comprised of the aggregation of many cell types. These cell types involved in the scar creation include fibroblasts, pericytes, astrocytes, microglia and infiltrated leukocytes. There is also the substantial deposition of extracellular matrix (ECM) molecules. The CNS fibrotic scar of cells and ECM is well documented to be inhibitory for the regeneration and recovery of axons. We described that the accumulation of chondroitin sulfate proteoglycans (CSPGs), a key component of ECM, inhibits oligodendrocyte differentiation and re-myelination. This promotes T helper 17 inflammation. Attempts to counter CNS fibrotic scars include the use of proteases to degrade deposited ECM, preventing the migration of fibroblasts into the evolving scar, or by use of inhibitors that block the interaction between cells and ECM.

Despite the intense interest in overcoming CNS fibrotic scars, many gaps of knowledge remain including the following: Identifying key regulators of the fibrotic scar as a lesion evolves from early to active and inactive states; Whether there are unidentified inhibitory ECM for repair; The influence of age on the potential for immune cells to interact with scar-forming cells and ECM components, to become injurious or beneficial for recovery. Other gaps include whether the different cells types populating a fibrotic scar have distinct and heterogeneous roles, such as the potential capacity of subpopulations of microglia to enhance injury or to help remove the scar. To address these gaps of



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knowledge, we bring together world class expertise of fibrotic and immune cells, ECM, phagocytosis and design of novel therapeutics to overcome CNS fibrotic scars to enhance recovery from insults.

We will test the overarching hypothesis that reducing the content of inhibitory ECM and pro-fibrotic cells with lesion-targeting novel therapeutics, and elevating phagocytic and pro-regenerative immune cells, will result in lesions with enhanced repair capacity and reduced cytotoxic neuroinflammation.