



## Hopewell M.I.N.D. Prize 2022 Finalists

### [Dr Peter Stys](#)

**Title of Project:** *“Non-immune role of B cells in the pathogenesis of multiple sclerosis”*

**Dr. Stys** completed his medical studies at the University of Ottawa. He went on to complete his specialty training in Neurology at the University of Toronto, then engaged in post-doctoral studies at Yale University, supported by a Centennial Fellowship from the Medical Research Council (CIHR). There he worked on the fundamental mechanisms of injury to nerve fibres in the brain and spinal cord. In 1992 he returned to Canada to set up his own research laboratory and an academic clinical neurological practise, at the Civic Campus of the Ottawa Hospital. In 2007, he was recruited to the Hotchkiss Brain Institute (HBI) at the University of Calgary.

Dr. Stys is a neurologist/neuroscientist and a world leader in the detailed study of pathophysiological mechanisms of white matter injury in stroke and trauma. He has extensive expertise in electrophysiological recording methods in myelinated axons, and his team has recently developed confocal, multi photon and coherent anti-Stokes Raman scattering (CARS) imaging techniques for both fixed immunostained and live myelinated axons and glial cells.

Dr. Stys' team discovered several novel injury mechanisms responsible for axo-glial damage in ischemia/trauma and glutamate excitotoxicity, due to reversal of Na-dependent glutamate transport in damaged spinal axons. Dr. Stys' insights provide a rational basis for devising drug therapy for the acute phases of stroke, spinal cord injury, brain trauma, and neuroinflammatory conditions (such as EAE/MS), in which axons, oligodendrocytes, and myelin are prominent targets of damage.

Dr. Stys is the recipient of the Dr. Frank LeBlanc Chair in Spinal Cord Research, Canada Research Chair (Tier 1) in Axo-glial biology, and Alberta Heritage Foundation for Research (AHFMR) scientist award. He is an Adjunct Research Professor at the Department of Systems and Computer Engineering at Carleton University, an Adjunct Professor at the Cumming School of Medicine at the University of Ottawa and a Visiting Assistant Professor at the Department of Neurology at Yale School of Medicine. In addition, Dr. Stys has published 88 peer reviewed articles, 17 book chapters, and two books. His work is supported by a number of important funding partners (in addition to the ones mentioned above), including the Canadian Foundation for Innovation (CFI), Canadian Institutes for Health Research (CIHR), Multiple Sclerosis Society of Canada, Neuroscience Canada, HBI, Canadian Stroke Network (CSN), NSERC, Alberta Paraplegic Foundation, Adelson Foundation for Medical Research, and the National Institutes of health (NIH).

(University Profile - <https://cumming.ucalgary.ca/departments/dcns/about/faculty/stys>)



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### **Summary of Proposed Innovation:**

MS is one of the commonest causes of neurological disability in young adults, with Canada having one of the highest rates in the world. The cause is unknown, but it is clear that both autoimmune inflammation and an underlying CNS degeneration operate in concert from the start, eventually culminating in a progressive course and irreversible disability. Strong evidence for T- and B-cell-driven autoimmunity has spurred development of over a dozen therapeutic agents currently in routine use, that are highly effective at reducing inflammatory relapses. Unfortunately, these are largely ineffective in the progressive disabling stage of MS, raising important questions about MS pathogenesis: might this disease be a degenerative disorder at its core? We have generated recent data suggesting that like many other neurodegenerative diseases, MS might also be a protein misfolding disorder, with autoimmune inflammation an important secondary reaction. What could be the trigger? Evidence suggests that an unknown toxic factor circulates in the CSF to induce myelin damage, and that such damage is often found in proximity to aggregates of B cells in the brain. Moreover, B cells from MS patients secrete an unidentified toxin that is not an immunoglobulin or other immune effector. The hypothesis underpinning this project proposes that MS B cells are transformed to secrete an agent that induces cytodegeneration and spread of protein misfolding pathology in a prion-like manner (like Alzheimer's, Parkinson's and most other neurodegenerations). Aims will include study of human B cells from MS patients in culture in an attempt to characterize this putative factor; transmission of MS-like pathology from human B cells or their products to humanized transgenic mice (for which we already have evidence using human white matter homogenates); and given the universal requirement of prior infection with Epstein-Barr virus in MS, the role of this virus in the putative transformation of B cells into long-lived toxin-producing factories that take up residence in the CNS and chronically fuel the degenerative process. Success of this project would upend our understanding of MS and usher in next-generation therapies that could be particularly effective in progressive MS.