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Endogenous pathways to limit inflammation in the CNS

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Many members of NLR family of proteins play an important role in human diseases including diabetes, Crohn's disease, cancer, etc. We concentrated on the role of NLRs in neurodegenerative diseases. We postulate that NLRs serve as sensors that detect intracellular stress. They can bind multiple proteins thus redirecting molecular signalling. In our work, we study mechanisms of neuroinflammatory responses and neuronal death. Using a mouse model of multiple sclerosis, experimental autoimmune encephalomyelitis, we demonstrate that Nlrp1 and Nlrp12 inhibit inflammation and improve biochemical and behavioural outcomes of the disease. Furthermore, Nlrp1 acts at the level of mitochondria promoting DRP1 dependent mitochondrial fission. In inflammatory cells such as microglia and astrocytes, this results in inhibition of assembly of proinflammatory pathways including Type I interferon and NFkB. Accordingly we observed reduction in the secretion of cytokines including IL-1beta and TNF-alpha. Using N2A cell line, we demonstrated that Nlrp1 protects cells from rotenone toxicity. We demonstrated that Nlrp1 overexpressing cells were more viable and ration of apoptosis to necrosis was shifted to necrosis in cells that lacked Nlrp1. In conclusion, both Nlrp1 and Nlrp12 decrease inflammatory responses in the CNS and, therefore, present as a target for treatments in neurodegenerative diseases.

Biography

Denis Gris is a Head of neuroimmunology laboratory at the University of Sherbrooke QC Canada. He graduated from University of Western Ontario from Dr. Weaver's laboratory where he studied inflammation after spinal cord injury. He then moved to pursue his Postdoctoral studies with Dr. Ting at University of North Carolina at Chapel Hills NC, USA where he began to investigate role of NLRs in neurodegeneration. His main interest is to discover novel anti-inflammatory pathways within the central nervous system and use this knowledge to design therapies for neurological diseases including multiple sclerosis amyotrophic lateral sclerosis autism and epilepsy.

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