Ron Receptor Tyrosine Kinase Regulates CNS Inflammatory Response in a Murine Model of Multiple Sclerosis

Experimental autoimmune encephalomyelitis(EAE) is a well characterized murine model of Multiple Sclerosis(MS) applied for detection and validation of new targets for MS treatments. The overarching impact of our proposal is to study a particular gene, Receptor d'origine Nantais(Ron) and its potential as a novel target for MS treatments. Our lab has reported the role of Ron in promoting the expression of genes associated with anti-inflammatory M2 macrophage activation and conversely inhibiting classical M1 macrophage activation. Current therapies for MS do not attenuate the progression of symptoms, instead patients are afflicted with systemic inflammatory responses. Thus, it is becoming more critical to develop therapies targeted to cellular populations of the CNS. Preliminary data for this proposal demonstrates that Ron deletion/knock-out(KO) mice are susceptible to increased severity of symptoms following EAE induction compared to Wild-Type mice. The proposed study is based on the hypothesis that Ron KO animals' exhibit greater severity in clinical symptoms due to heightened CNS innate immune response, mediated by increased activation of M1 macrophages. The maintenance and/or expansion of Ron expressing M2 macrophages could then be a potential therapeutic approach to treating MS symptoms.