

Identifying 8-11B as a Novel Anti-Inflammatory Compound on Attenuating Neuroinflammation and Disease Severity in MS

Noah Bergsma¹, Jimmy Yen PhD²

¹Doctor of Medicine Program and ²Department of Microbiology and Immunology, Indiana University School of Medicine, Fort Wayne

Background and Hypothesis: Multiple sclerosis (MS) arises due to impairments in immune cell regulation, leading to neuroinflammation via alterations in microglial activation and pathogenic T cell differentiation. One novel compound developed from IUSM Fort Wayne and Manchester University, 8-11B, was recently associated with an in vitro reduction of inflammatory cytokine IL-6. 8-11B was thus analyzed in modulating pro-inflammatory cytokine and chemokine expression in microglia, attenuating pathogenic T cell differentiation, and ameliorating disease in MS animal models.

Experimental Design and Methods: The first phase of the experiment incorporated a quantitative polymerase chain reaction (qPCR) to determine if 8-11B would reduce IL-27p28, CCL2, and CCL3 expression in primary microglia in vitro. The second phase of the experiment was performed by flow cytometry to analyze 8-11B in suppressing Th1 and Th17 differentiation via reducing IFN- γ , GM-CSF, and IL-17 production in CD4⁺ splenocytes in vitro. Finally, MS animal models were employed to assess the therapeutic effect of 8-11B in vivo.

Results: We found 8-11B enabled a dose-dependent reduction in IL-27p28, CCL2, and CCL3 RNA expression in microglia in vitro. Furthermore, 8-11B inhibited pathogenic T cell activation and differentiation by suppressing the production of IFN- γ and GM-CSF from Th1 cells and IL-17 from Th17 cells in a dose-dependent manner in vitro. Finally, our in vivo results showed 8-11B administration delayed disease onset and reduced disease severity in MS animal models.

Conclusion and Potential Impact: Our study demonstrated that 8-11B attenuates neuroinflammation through modulating microglial activation and pathogenic T cell differentiation. Most importantly, the in vivo analysis showed the ability of 8-11B to ameliorate disease severity in MS animal models. Thus, it suggests that 8-11B can be developed as a novel therapeutic agent for MS treatment.