Identification of Inflammasome Expression and Activity in Experimental Autoimmune Encephalomyelitis

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Background Experimental Autoimmune Encephalomyelitis (EAE) is an immune-mediated animal model of Multiple Sclerosis (MS). In this model, mice have multiple demyelinated lesions distributed throughout the central nervous system (CNS). Inflammasomes are intracellular, innate immune complexes known to have a pathogenic role in EAE development. In EAE inflammasomes are activated by danger-associated molecular patterns to mature and release pro-inflammatory cytokines, IL-1beta and IL-18. Objectives To identify inflammasome activity in different CNS cells of the spinal cord; we aimed to establish immunofluorescent staining of inflammasome components. To assess the effect of IL-1beta on oligodendrocytes. Methods To establish immunohistochemistry protocols, spinal cord sections from EAE mice were stained for inflammasome components AIM2, ASC and IL-1beta. To test the effect of IL-1beta on oligodendrocytes, oligodendrocyte lineage cells were derived from frontal cortices of postnatal mice and treated with IL-1beta. Cultures were stained for oligodendrocyte lineage and myelin markers. Results We established immunofluorescent staining for AIM2, ASC and IL-1beta, and thus identified inflammasome activity in demyelinated spinal cord lesions. In vitro, exogenous IL-1beta significantly enhanced myelin protein production from oligodendrocytes. IL-1beta did not increase the number of mature oligodendrocytes. Conclusions AIM2, ASC and IL-1beta immunohistochemistry demonstrated inflammasome activity in demyelinated spinal cord lesions. Future studies will develop co-staining for CNS markers to determine which cells express inflammasomes in EAE-induced lesions. Our studies show that IL-1beta drives oligodendrocyte maturation and myelin protein production in glial cultures. Future work will assess the effect of the inflammasome product IL-18 on oligodendrocyte cells.