

Probing the role of microglia in Relapsing-Remitting EAE

Microglia are the specialized phagocytes of the brain parenchyma. In multiple sclerosis (MS), an autoimmune disease targeted at the CNS, microglia phagocytose cell debris and upregulate immune-related transcripts. However, it is not clear whether microglia play a beneficial or detrimental role, whether they interact with the infiltrating immune cells and whether or not these cells mediate recovery. Here, we used the Relapsing-Remitting Experimental Autoimmune Encephalomyelitis (RR-EAE) mouse model for MS on SJL*B6 F1 hybrids to study the role of microglia in different stages of the disease, focusing on their contributions to recovery and relapse. Using the RiboTag approach in Cx3cr1CreER:Rpl22HA mice (1), we revealed that microglia actively translate inhibitory molecules such as Lag3, PDL1 and IL18bp. Depletion of microglia in Cx3cr1CreER:Rosa26iDTR mice resulted in delayed recovery accompanied by T cell accumulation in the brain. Wiskott Aldrich Syndrome protein (WASP) is a regulator of actin filament reorganization, crucial for the execution of the immune response in hematopoietic cells. Cx3cr1creER:Wasf1/y mice, that lack WASP in microglia, fail to recover during RR-EAE. Together these results suggest that the presence and immune competence of microglia might be important for the recovery phase in RR-EAE. Inhibitory molecules expressed by microglia could mediate recovery, however the precise molecular mechanism by which this takes place remains under investigation.

Keywords :

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