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Oral Presentation

Kynurenine Impairs MbMEC Function in Vitro Through Arylhydrocarbon Receptor Activation

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Abstract

In the development of neuroinflammatory diseases, alterations of the blood brain barrier (BBB) represent key events. The integrity of the BBB is partially maintained by endothelia cells (ECs), since they actively limit the transmigration of immune cells. However, the factors that cause endothelial cells to develop an immune cell-permissive phenotype are poorly understood. In general, it has been shown that vascular dysfunction can be caused by kynurenine pathway (KP) metabolites. In the initial step of the KP, the bioactive intermediate synthesized is kynurenine (Kyn). It is known to activate the arylhydrocarbon receptor (AhR), a ligand binding transcription factor that mediates immune responses. To examine if this pathway has an effect on the BBB, we investigated the effects of Kyn-mediated AhR activation in primary isolated murine brain microvascular endothelial cells (MbMECs) in vitro. First, we confirmed AhR expression in MbMECs at RNA and protein levels. Transendothelial electrical resistance (TEER) of MBMEC monolayers was unaffected by Kyn treatment. However, treatment with Kyn did cause an increased migration of T-cells. Addition of MNF, an AhR specific inhibitor, reversed this effect. These findings were further confirmed by an increase in the intracellular adhesion protein 1 (ICAM-1) expression in KYN-treated MBMECs. These results suggest a role of KYN in MBMEC dysfunction via AHR activation.

Keywords: Brain, Immune Cells, Adhesion Protein

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