KCNK2 Regulates the Nanoscale Formation of Immune Docking Structures on Brain Endothelial Cells Under Autoinflammatory Conditions

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Abstract

KCNK2 was previously shown to regulate immune-cell trafficking into the central nervous system (CNS). Kcnk2−/− mice demonstrated a more severe disease course in experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis, due to an increased immune-cell migration into the CNS. An upregulation of the cellular adhesion molecules ICAM1 and VCAM1 on brain endothelial cells in Kcnk2−/− was proposed as underlying mechanism. The exact molecular pathways involved are currently unknown. By using super resolution microscopy methods, we were able to identify an altered surface morphology of brain endothelial cells upon inflammation indicated by 200-300 nm high membrane protrusions. Analysis of atomic force microscopy (AFM) images of Kcnk2−/− mouse brain endothelial cells showed a significant increase in number and volume of membrane protrusions. Confocal imaging identified these membrane protrusions as ICAM1- and VCAM1-containing immune-cell docking structures. Kcnk2−/− cells showed alterations of the actin cytoskeleton and an increase of stress fibers already under basal conditions, indicating a regulation of cytokine rearrangement by KCNK2 channels. KCNK2 regulates the nanoscale formation of adhesion molecule-containing immune docking structures on brain endothelial cells under autoinflammatory conditions, thereby regulating leukocyte adhesion and migration into the CNS.

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