S18-2 Pathophysiological roles of TRP channels in glial cells

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Glial cells are abundant in the CNS and play diverse roles in the regulation of neuronal activity, vascular function, and gliotransmitter release, whereas pathologically activated glial cells have been reported to disturb brain function in conjunction with Ca^{2+} signaling, however there is no enough explanation for a unique Ca^{2+} entry. Transient receptor potential (TRP) superfamily comprises a group of non-selective cation channels that open in response to divergent stimuli in their environment. Although TRP channels are widely distributed in the mammalian brain, their roles remain to be elucidated. Here we provide an overview of the roles of TRP channels in pathophysiological processes, especially focusing on TRPC3 and TRPV4 channels in glial cells. Using rat cortical astrocytes, we found that TRPC3 was upregulated by thrombin, a major blood-derived serine protease, via ERK, JNK, NF-κB and Ca^{2+} signaling through TRPC3 itself. Thrombin also upregulated S100B, a marker of reactive astrocytes, and increased cell proliferation, both of which were inhibited by Ca^{2+} signaling blockers. Specific knockdown of TRPC3 using siRNA also suppressed the thrombin-induced S100B up-regulation, suggesting that TRPC3 contributes to the pathological activation of astrocytes in part through a feed-forward upregulation of its own expression. Moreover, we found that TRPV4 stimulation by its agonist 4α-PDD suppressed LPS-induced microglial activation while TRPV4 mRNA was downregulated in LPS-treated cultured microglia. We will mention their possibility of being targets for drugs in such stressful conditions.