TAK1

TAK1 (Transforming growth factor beta-activated kinase 1) is a protein kinase that is involved in various cellular processes such as inflammation, immune response, and cell survival. It is activated by various stimuli, including cytokines, growth factors, and cellular stress, and it then phosphorylates downstream signaling molecules to initiate specific signaling pathways.

TAK1 is part of the MAPK (mitogen-activated protein kinase) signaling pathway and plays a crucial role in the regulation of the NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) pathway, which is involved in the regulation of genes related to inflammation, immunity, and cell survival. Dysregulation of TAK1 has been implicated in various diseases, including cancer, inflammatory disorders, and cardiovascular disease.

Several drugs that target TAK1 are currently under development, and they have shown promising results in preclinical studies for the treatment of various diseases. However, more research is needed to fully understand the role of TAK1 in these diseases and to develop effective therapies targeting TAK1.

Khan et al. investigated the cellular role of TAK1 in experimental epilepsy. C57Bl6 and transgenic mice with inducible and microglia-specific deletion of Tak1 (Cx3cr1CreER: Tak1fl/fl) were subjected to the unilateral intracortical kainate mouse model of temporal lobe epilepsy (TLE). Immunohistochemical staining was performed to quantify different cell populations. The epileptic activity was monitored by continuous telemetric electroencephalogram (EEG) recordings over a period of 4 weeks. The results show that TAK1 was activated predominantly in microglia at an early stage of kainate-induced epileptogenesis. Tak1 deletion in microglia resulted in reduced hippocampal reactive microgliosis and a significant decrease in chronic epileptic activity. Overall, the data suggest that TAK1-dependent microglial activation contributes to the chronic epilepsy pathogenesis [1].

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Khan D, Bedner P, Müller J, Lülsberg F, Henning L, Prinz M, Steinhäuser C, Muhammad S. TGF-β Activated Kinase 1 (TAK1) Is Activated in Microglia After Experimental Epilepsy and Contributes to Epileptogenesis. Mol Neurobiol. 2023 Mar 2. doi: 10.1007/s12035-023-03290-2. Epub ahead of print. PMID: 36862288.