Abstract Information

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Title :	When the secondary role plays its full part: the story of the Kv3.1 channel in neuropathologies

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Abstract :

Introduction and objectives: Kv3.1 channels are of critical importance to the functioning of the nervous system. These channels, which are abundantly expressed in fast-firing neurons, as inhibitory GABAergic interneurons and cerebellar neurons, are essential for the rapid repolarization of action potentials.

Neurological disorders are marked by neuronal loss leading to cognitive and motor dysfunctions. Recent research highlights the involvement of oligodendrocytes in the pathogenesis of these disorders due to their rising susceptibility to damage. This vulnerability might be exacerbated by the dysregulation of voltage-gated potassium channels like Kv3.1, impacting cell proliferation, migration, and axon myelination.

Our research has focused on examining the various pathophysiological implications of this channel, including K+ hemostasis, neurodegeneration in Alzheimer's disease cell models, and its relationship with serotonergic mechanisms. We finally used an active scorpion venom fraction to identify a molecule that modulates Kv3.1 currents (Cheikh et al., 2013).

Results: Our research findings suggest that the lipid environment affects Kv3.1b channel expression and/or functionality and that subsequent rupture of K? homeostasis is associated with oligodendrocytes and microglial cell damage. Actually, a positive correlation seems to exist between Kv3.1b or the intracellular K? concentration, loss of transmembrane mitochondrial potential, and increased plasma membrane permeability in these cells (Bezine et al., 2018)

We have also confirmed that Kv3.1b channel is significantly expressed in 1C11 cell line, as an in vitro model for serotonergic release, and that fluoxetine affects Kv3.1b expression but increases cell proliferation. Finally, we highlighted its role during cell differentiation (Tabka et

al., 2020).

Moreover, we used a combined optimization through advanced biochemical purification and patch-clamp screening steps to characterize, for the first time, the peptide in Aah venom active on Kv3.1 channels (Maatoug et al., 2021).

Discussion: Kv3.1's frequently secondary or indirect contribution to pathophysiological mechanisms does not in any way diminish its crucial role. Targeting Kv3.1 inhibition selectively could yield treatments for diseases involving altered neuronal excitability, such as epilepsy, ataxia, or auditory processing disorders. While these findings provide promising perspectives, advances in pharmacology and personalized medicine will likely to make Kv3.1 modulation a viable therapeutic strategy in the near future.