Differential modulation of Kv1.3/Kv1.5 complexes by Kcne4

SY04-07

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The voltage-dependent potassium channel Kv1.3 is widely expressed in the immune system. Kv1.3 is present in T and B-lymphocytes as well as macrophages and dendritic cells, controlling their activation and proliferation. This channel is one of the responsible actors of the chronic activation during autoimmune diseases, such as multiple sclerosis. In fact, a pharmacological control of the channel alleviates symptoms of disease.

Kv1.3 may interact with a large collection of proteins. Thus, other Kv1 subunits, regulatory β-subunits (i.e. Kcne4) and other proteins like caveolin may form a heteroligomeric complex named the Kv1.3 channelosome. These interactions modify either Kv1.3 traffic or tune the functional activity resulting in potential alterations in cell physiology. Here we analysed the effect of both Kv1.5 and Kcne4 in the functional activity of a Kv1.3 functional complex.

As Kv1.3 and Kv1.5 can form functional heterotetramers with a variable stoichiometry, we generated a Kv1.3-Kv1.5 protein tandem chimera of a 1:1 fixed ratio. We describe the behaviour of the heterotetramer in this ratio regarding traffic and function. As Kcne4 is able to interact and modulate Kv1.3, but not Kv1.5, homotetrameric channel, we performed experiments in the presence or absence of KCNE4. We describe a differential effect of Kcne4 over the Kv1.3 channelosome depending on the presence of Kv1.5. Also, we demonstrate that our model recapitulates what it is found in dendritic cells.

Supported by MINECO (Spain) and FEDER (BFU2014-54928-R and BFU2015-70067-REDC)