Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Interaction of voltage-gated potassium channels and large-conductance calcium-sensitive potassium channels in vascular smooth muscle

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Voltage-gated potassium (Kv) channels and large-conductance calcium-sensitive potassium (BK) channels are two major potassium channels identified in vascular smooth muscle cells. It has been demonstrated that Kv7 channels and BK channels, through modulation of membrane potential and Ca^{2+} influx, contribute to the regulation of vascular contractility that determines the resistance of blood vessels to blood flow and regulates blood distribution in the body. Although they have become the spotlight of investigation in recent years there are only a few reports describing their expression and function in skeletal muscle arteries. Moreover, there is no report to clarify the functional interaction of Kv7 and BK channels in intact arteries. Therefore, this study addressed the hypothesis that there is functional interaction between Kv7 and BK channels in skeletal muscle arteries under normal physiological conditions, which contributes to the maintenance of arterial contractility.

The Saphenous artery (A.Saphena, a conduit artery supplying blood to a large part of skeletal muscles on the hind limb) and the Gracilis artery (A. Gracilis, a resistance artery providing blood to the gracilis muscle on the hind limb) from Wistar rats were isolated for this study. The expression of Kv7 and BK channels was detect by use of the qPCR technique; the function of Kv7 and BK channels and their interaction were examined on the A. saphena during methoxamine-induced contractions using wire myography and on the A. gracilis during pressure-induced myogenic responses using pressure myography.

The results show that subfamily members of Kv7 channels (KCNQ) and BK channels are expressed in A. Saphena and A.Gracilis: higher expression was observed for BKα, BKβ1 and KCNQ4. In methoxamine-induced contractions and pressure-induced myogenic responses, inhibition of Kv7 or BK channels by XE991 (a selective Kv7 channel blocker) or IBTX (a selective BK channel blocker) enhanced arterial contractility, whereas activation of Kv7 or BK channels by retigabine (a selective Kv7 channel activator) or NS19504 (a novel BK channel activator) reduced arterial contractility. Furthermore, inhibition of Kv7 channels increased the functional availability of BK channels, while activation of Kv7 channels decreased the functional availability of BK channels. In turn, inhibition of BK channels improved the functional availability of Kv7 channels, while activation of BK channels decreased the functional availability of Kv7 channels.

In conclusion, Kv7 and BK channels are expressed in rat skeletal muscle arteries and function as negative feedback modulators in the regulation of contractility of these arteries. Moreover, there is a dynamic equilibrium between Kv7 and BK channels, in which, membrane potential, concentration of Ca^{2+}, and membrane permeability might be the three major factors to build a bridge between Kv7 and BK channels.