Chapter 3

POTASSIUM CHANNELS

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Introduction

Potassium (K^+) channels are membrane proteins displayed in excitable and non-excitable cells. These channels provide the conduction of signaling in the central nervous system and the rate of heart, release of synthesized hormones into the blood, muscle contraction, insulin secretion, epithelial electrolyte transport, cell volume regulation, cell profiling, and the central nervous system (Shieh, 2000).

Neuronal K^+ channels have a key role in the control of neuronal activity and the spread of signal transduction throughout the nervous system (Brandsgaard, Barrett & Rosenzweig-Lipson, 2000; Kobayashi, Washiyama & Ikeda, 2004a; MacKinnon, 2003; Wu & Dworetzky, 2005). Blockade of neuronal K^+ channels inhibits K^+ efflux from the cell leading to prolonged depolarization of the neuron and consequently an increase in neurotransmitter release (Glover, 1981).

K^+ channels are responsible for the repolarization phase of the action potential in the heart (Karczewski et al., 2009). In vascular smooth muscle, these channels are responsible for maintaining resting potential and repolarization of the depolarized cell, regulation of cell metabolism and excitability (vasoconstriction and vasodilatation) (Ko et al., 2008).

The ion channels in the vascular endothelium play an important role in resting membrane potential, signal transduction and stimulus-secretion match. Both smooth muscle cells and channel activity of endothelial cells function in determining blood flow. The K^+channel currents in the endothelium are affected by the secretion of vasoactive factors, blood flow, pressure and metabolic status (Emre, Özcal & Şan, 2004).

There are various types of K^+ channels in the respiratory tract tissues and activation of these channels lead to the modulation of various respiratory tract functions such as bronchoconstriction, neurotransmitter release from autonomic nerves, and electrolyte secretion from epithelial cells as a result of hyperpolarization or repolarization of the cell (İncesu-Gürel & Yılmaz-Sipahi, 1998; Tamaoki et al., 1997).

Four subunits of the Kir3 channel family are defined in the mammals. The Kir3.1 and Kir3.2 of these channels are common in the brain and especially important in pain pathway (not Kir3.3). Kir3.2 is homomultimer structure that is particularly intense in the substantia nigra and ventral tegmental area and cause spontaneous epileptic attack when blocked. Kir3.1 and Kir3.4 are heteromultimeric structures that are dense in the atrium and cause tachycardia when blocked. These channels have an important role in the regulation of neuronal excitability and heart rate (Kobayashi, Washiyama & Ikeda, 2004a, 2004b; Kobayashi, Washiyama & Ikeda, 2006).

Kir channels are dense in small-diameter arteries and contribute to the preservation of vascular tone and membrane resting potential (Ko et al., 2008).

Various vasoconstrictors such as angiotensin, endothelin, vasopressin, norepinephrine, histamine, serotonin and neuropeptide Y inhibits the function of a Kir6 channel after "protein kinase C" (PKC) activation in vascular smooth muscle. Direct-acting vasodilator agents such as calcitonin gene-related peptide (CGRP), adenosine and isoprenaline act through "protein kinase A" (PKA) to activate Kir6 channels (Ko et al., 2008).

Two pore domain K^+ channels

In mammals, 15 members of the 2-pored K^+ channel (K_{2P}) family have been described (Lenguel, Czirjak & Enyedi, 2018). The K2P channel, which contains two α-structures, consists of two pore with a transmembranal structure that spanning the cell membrane four times (Ocaña et al., 2004).

The pharmacological characteristics of these channels are not well known.They are especially concentrated in the superficial layer of the spinal cord dorsal horn (laminae I and II) and the trigeminal ganglion (Lenguel, Czirjak & Enyedi, 2018; Gabriel et al., 2002),is thought to play a key role in the pain pathway (Ocaña et al., 2004). They are activated by increasing in the cytoplasmic Ca^{+2} concentration (Lenguel, Czirjak & Enyedi, 2018).

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