P2C-Type ATPases and Their Regulation

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Abstract

P2C-type ATPases are a subfamily of P-type ATPases comprising Na+/K+-ATPase and H+/K+-ATPase. Na+/K+-ATPase is ubiquitously expressed and has been implicated in several neurological diseases, whereas H+/K+-ATPase is found principally in the colon, stomach, and kidney. Both ATPases have two subunits, α and β, but Na+/K+-ATPase also has a regulatory subunit called FXYD, which has an important role in cancer. The most important functions of these ATPases are homeostasis, potassium regulation, and maintaining a gradient in different cell types, like epithelial cells. Na+/K+-ATPase has become a center of attention ever since it was proposed that it might play a crucial role in neurological disorders such as bipolar disorder, mania, depression, familial hemiplegic migraine, rapid-onset dystonia parkinsonism, chronic stress, epileptogenesis, and Alzheimer's disease. On the other hand, it has been reported that lithium could have a neuroprotective effect against ouabain, which is the best known Na+/K+-ATPase inhibitor, but and high concentrations of lithium could affect negatively H+/K+-ATPase activity, that has a key role in regulating acidosis and potassium deficiencies. Finally, potassium homeostasis regulation is composed of two main mechanisms, extrarenal and renal. Extrarenal mechanism controls plasma levels, shifting potassium from the extracellular to the intracellular, whereas renal mechanism concerns with body balance and is influenced by potassium intake and its urinary excretion. In this article, we discuss the functions, isoforms, and localization of P2C-type ATPases, describe some of their modulators, and discuss their implications in some diseases..

Keywords

Potassium, Na+/K+-ATPase, H+/K+-ATPase, Alzheimer's disease, Hypertension.