ATP-sensitive potassium channels (K\textsubscript{ATP} channels) are ion channels that selectively allow potassium ions to permeate the cell. Their channel activities are tightly regulated by endogenous nucleotide metabolites. Specifically, in particular, they are inhibited by ATP and activated by Mg-ADP\textsubscript{2}. By sensing the intracellular ADP/ATP ratio, K\textsubscript{ATP}-these channels tune the potassium ion efflux across the plasma membrane and adjust the membrane potential. Therefore, K\textsubscript{ATP} channels convert the cellular metabolic status into electrical signals, which provide a unique output that has with broad physiological effects.

K\textsubscript{ATP} channels are widely distributed in many several tissues, including those of the pancreas, brain, heart, and smooth muscle, and they play important roles in many physiological processes, such as hormone secretion and vasodilatation. Genetic mutation of genes that encode K\textsubscript{ATP} channel subunits can lead to several metabolic diseases and neuronal diseases. Therefore, K\textsubscript{ATP}-these channels are important drug targets. Clinically relevant sulfonylureas inhibit pancreatic K\textsubscript{ATP} channels and serve as insulin secretagogues for the treatment of type II diabetes, whereas K\textsubscript{ATP} activators, such as potassium channel openers (KCOs) activate K\textsubscript{ATP} channels, are used for treating hypoglycemia, and show promise for myoprotection. Previous studies have established that the functional K\textsubscript{ATP} channel is a hetero-octamer composed of four inward-rectifying potassium channel 6 (Kir6) subunits and four sulfonylurea receptor (SUR) regulatory subunits. The Kir6 subunits are encoded by either KCNJ8 (Kir6.1) or KCNJ11 (Kir6.2). Kir6 subunits and harbor sites for inhibitory ATP binding. The activities of Kir6 can be enhanced by PIP\textsubscript{2}, which is a signaling lipid present in the inner leaflets of the plasma membrane. The SUR subunits are composed of the N-terminal transmembrane domain 0-loop 0 (TMD0-L0) and ATP-binding cassette (ABC) transporter-like modules.