

ATP-sensitive potassium channels (~~K<sub>ATP</sub> 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<sub>i</sub>. By sensing the intracellular ADP/ATP ratio, ~~K<sub>ATP</sub> these~~ channels ~~then~~regulate the potassium ion efflux across the plasma membrane and adjust the membrane potential. Therefore, ~~K<sub>ATP</sub> channels they~~ convert the cellular metabolic status into electrical signals, which provide a unique output ~~that has with~~ broad physiological effects.

**Comment [A1]:** Making sure an abbreviation and its spelled out form match is essential to avoid any confusion to readers. Here, the abbreviation of "ATP-sensitive potassium channels" has been revised to "K<sub>ATP</sub> channels" for accuracy.

K<sub>ATP</sub> 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~~Mutation of genes that encode K<sub>ATP</sub> channel subunits can lead to cause several metabolic ~~diseases~~ and neuronal diseases. Therefore, ~~K<sub>ATP</sub> these~~ channels are important drug targets. Clinically relevant sulfonylureas ~~drugs~~ inhibit pancreatic K<sub>ATP</sub> channels and serve as insulin secretagogues for ~~the treatment of~~treating type II diabetes, ~~while whereas~~ ~~K<sub>ATP</sub> activators, such as~~ potassium channel openers (KCOs) activate K<sub>ATP</sub> channels, are used for treating hypoglycemia, and show promise for myoprotection. Previous studies have established that the functional K<sub>ATP</sub> 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 K<sub>CNJ8</sub> K<sub>CNJ8</sub>~~ (Kir6.1) ~~or or~~ ~~K<sub>CNJ11</sub>~~ (Kir6.2). ~~Kir6 subunits and~~ harbor sites for inhibitory ATP binding. ~~The activities of~~ Kir6 can be enhanced by PIP<sub>2</sub>, ~~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 ~~cassettes~~cassette (ABC) transporter-like modules.

**Comment [A2]:** Excessive repetition of nouns or noun phrases can hamper readability. Therefore, pronouns should be used instead of repeating nouns at multiple instance.