# pH AND NUCLEOTIDE MODULATION OF MITOCHONDRIAL ATP-REGULATED POTASSIUM CHANNEL

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**Ion channels selective for potassium ions are present in the inner mitochondrial membranes. The mitochondrial ATP regulated potassium channel (mitoK$_{ATP}$ channel) was identified by patch-clamp recordings in the inner membrane of liver mitochondria. Later, a similar channel was described in heart, brain and skeletal muscle mitochondria. Similarly to the plasma membrane K$_{ATP}$ channel, the mitochondrial channel is inhibited by antidiabetic sulfonylureas and activated by potassium channel openers such as diazoxide or nicorandil. However, molecular properties and regulation by endogenous effectors of the mitoK$_{ATP}$ channel remain unclear.**

**In our study, inner mitochondrial membranes from bovine heart were reconstituted using planar lipid bilayer technique. After incorporation, a potassium selective current was observed. The mean conductance was about 103 pS in symmetrical 150/150 mM KCl (*cis/trans*) solution. The effects of different K$_{ATP}$ channel modulators on single channel activity were examined. The channel activity was inhibited by ATP/Mg$^{2+}$ complex and 5-hydroxydecanoic acid. After ATP/Mg$^{2+}$ inhibition activity of the channel was reversed upon BMS191095 application. Apart from this, inhibitors of a mitochondrial Ca$^{2+}$ activated, large conductance potassium channel (mitoBK$_{Ca}$ channel) – iberiotoxin and charybdotoxin had no effect on channel activity.**

**In further experiments the effects of pH on mitoK$_{ATP}$ channel activity were studied. During *trans* side alkalization an increase in the current amplitude and opening probability was observed. The effect was reversed after perfusion. The *cis* side was not sensitive for alkalization. On the other hand, we observed that acidification of the *cis* side decreased opening probability of the channel. This effect was reversed by perfusion with neutral pH medium.**

**Next, the effects of different nucleotides on single channel activity were examined. The channel activity was inhibited by ATP/Mg$^{2+}$ complex and activated by GDP or GTP. Detailed analysis of regulation of the mitoK$_{ATP}$ channel by ATP-PNP/Mg$^{2+}$ complex was performed. We did not observe inhibition of the mitoK$_{ATP}$ channel activity by non-hydrolysable ATP analogues. Additionally we observed "run down" of the mitoK$_{ATP}$ channel activity. Re-activation of the mitoK$_{ATP}$ channel was observed upon transient/perfusion with ATP/Mg$^{2+}$ complex. We conclude that ATP/Mg$^{2+}$ complex regulate activity of the cardiac mitoK$_{ATP}$ channel probably by phosphorylation reaction.**

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