Phosphorylation-dependent structural changes in the N-terminal extension of SUR2A NBD1

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Abstract

ATP-sensitive potassium (K\textsubscript{ATP}) channels are involved in many biological processes and play an important role in sustaining healthy functioning organs. K\textsubscript{ATP} channels are composed of four copies of a pore-forming Kir6.x protein that is surrounded by four copies of regulatory sulfonylurea receptor (SUR) proteins. SUR proteins are members of the ATP-binding cassette (ABC) superfamily. Nucleotide binding and hydrolysis at the SUR proteins results in channel opening, which is potentiated by SUR protein phosphorylation. The studies conducted during this thesis aimed to understand how phosphorylation of the N-terminal extension (N-tail) of the first nucleotide binding domain (NBD1) of SUR2A alters its structure and influences the N-tail’s interaction with the core NBD1. This biophysical study utilizes nuclear magnetic resonance (NMR) and other biophysical techniques to understand these structural and dynamic changes in N-tail with phosphorylation. Through the investigation of the phosphorylation-dependent structural changes of N-tail, we will complete our understanding on how phosphorylation regulates ATP-binding at SUR2A NBD1 and thus contributes to the control of K\textsubscript{ATP} channel conductance.