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Localization of Divalent Cation-Binding Site in the Pore of a Small Conductance Ca^{2+}-activated K^+ Channel and Its Role in Determining Current-Voltage Relationship

Heun Soh*, Na-Rae Shin and Chul-Seung Park

Department of Life Science, Kwangju Institute of Science and Technology (K-JIST) Gwangju, 500-712 Korea

In our previous study (Soh and Park, 2001), we proposed that the inwardly rectifying current-voltage (I-V) relationship of small-conductance Ca^{2+}-activated K^+ channels (SK_{Ca} channels) is the result of voltage-dependent blockade of K^+ currents by intracellular divalent cations. We expressed a cloned SK_{Ca} channel, rSK2, in *Xenopus* oocytes and further characterized the nature of the divalent cation-binding site by electrophysiological means. Using site-directed substitution of hydrophilic residues in K^+-conducting pathway and subsequent functional analysis of mutations, we identified an amino acid residue, Ser359, in the pore-forming region of rSK2 critical for the strong rectification of the I-V relationship. This residue interacts directly with intracellular divalent cations and determines the ionic selectivity. Therefore, we confirmed our proposition by localizing the divalent cation-binding site within the conduction pathway of the SK_{Ca} channel. Since the Ser residue unique for the subfamily of SK_{Ca} channels is likely to locate closely to the selectivity filter of the channels, it may also contribute to other permeation characteristics of SK_{Ca} channels.