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Alteration of Ion Selectivity by Mutations within the Pore-forming Region of Small Conductance Ca^{2+}-activated K^+ Channels

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Small conductance Ca^{2+}-activated K^+ channels (or SK_{Ca} channels) are a group of K^+-selective ion channels activated by sub-micromolar concentrations of intracellular Ca^{2+} independent of membrane voltage. We expressed a cloned SK_{Ca} channel, rSK2, in *Xenopus* oocytes and investigated the monovalent cation selectivity of the channels. We have used site-directed mutagenesis and macro-channel recordings to identify amino acid residues influencing the ion selectivity. Currents were recorded in bi-ionic conditions with K^+ as the external cation and the test ion as the sole internal monovalent cation. Calculated permeability ratios (P_X/P_K) for the wild-type rSK2 channels yielded the sequence K^+ (1) > Rb^+ (0.80) > $NH4^+$ (0.19) ≥ Cs^+ (0.18) > Li^+(0.13) ≥ Na^+ (0.12). Although this sequence is similar to those of other K^+ channels, the permeability of Na^+ ion is relatively high. Ala substitution of Ser359 residue, which is located near to K^+ selectivity filter, GYG, in the pore-forming region, enhanced the passage of other test ions against K^+. However, Ser359Thr mutation did not show the significant difference compared with wild-type. These results suggest that the hydroxyl group of Ser359 is critical for selecting ions prior to the K^+ selectivity filter in rSK2 channels.