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Molecular Mechanism for Targeting of Na^+/Ca^{2+} Exchanger to Basolateral Membrane in Renal Epithelial Cells and Its Pathophysiological Significance

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Summary

Na^+/Ca^{2+} exchanger type 1 (NCX1) is ubiquitously expressed in the plasma membrane of various cell types including heart, smooth muscle, nerve and renal tubule. This transporter bidirectionally exchanges 3 Na^+ with 1 Ca^{2+}, depending on the electrochemical gradients across the plasma membrane. In renal tubule, NCX1 is localized to the basolateral membranes of distal convoluted tubule cells, and is considered to be involved in Ca^{2+} reabsorption. However, the molecular mechanisms for its membrane sorting remain to be elucidated. In the present study, we found that the intracellular domain of NCX1 interacts with the adaptor protein using yeast two-hybrid screening in murine kidney cDNA library. Using GST pull-down assays, we further identified the binding motif in NCX1 molecule. We also found that the mutations in the binding motif of NCX1 affect its membrane sorting in epithelial MDCK cells, suggesting the interaction between NCX1 and the adaptor protein plays a key role in NCX1 basolateral sorting.