

Protein 4.1N is required for inositol 1,4,5-trisphosphate receptor type 1 translocation to the basolateral membrane domain in polarized Madin-Darby canine kidney cells

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We identified Protein 4.1N as a binding molecule for the C-terminal cytoplasmic tail of inositol 1,4,5-trisphosphate receptor type 1 (IP₃R1) using a yeast two-hybrid system. 4.1N and IP₃R1 associate in both subconfluent and confluent Madin-Darby canine kidney (MDCK) cells, a well-studied tight polarized epithelial cell line. In subconfluent MDCK cells, 4.1N is distributed in the cytoplasm and the nucleus; IP₃R1 is localized in the cytoplasm. In confluent MDCK cells, both 4.1N and IP₃R1 are predominantly translocated to the basolateral membrane domain; whereas 4.1R, the prototypical homologue of 4.1N, is localized at the tight junctions and other endoplasmic reticulum (ER) marker proteins are still present in the cytoplasm. Moreover, the 4.1N-binding region of IP₃R1 is necessary and sufficient for the localization of IP₃R1 at the basolateral membrane domain. A fragment of the IP₃R1-binding region of 4.1N blocks the localization of co-expressed IP₃R1 at the basolateral membrane domain. These data indicate that 4.1N is required for IP₃R1 translocation to the basolateral membrane domain in polarized MDCK cells.

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