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Session 138 - G protein coupled inwardly rectifying K+ channels: from structure to function.
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Title Molecular and cellular diversity of GIRK channels in the brain.

Text G protein-gated inwardly rectifying potassium (GIRK) channels regulate cellular excitability and neurotransmission. GIRK channels are activated by the direct action of G β - γ subunits released from G α 1/o proteins in response to a number of G protein-coupled receptors. Four GIRK subunits (GIRK1-4) have been identified in the brain, which assemble as either homo- or hetero-tetrameric complexes. Three GIRK channel subunits (GIRK1-GIRK3) exhibit broad and overlapping distributions in the brain, whereas the fourth subunit (GIRK4) is found primarily in cardiac tissue. Several studies indicate that neuronal GIRK channels may consist primarily of GIRK1 and/or GIRK2. In agreement with that data, using a combination of biochemical and morphological techniques, including light and electron microscopic immunohistochemistry, we have found that hippocampal pyramidal cells mainly express GIRK1 and GIRK2, while dopaminergic neurons in the substantia nigra mainly express GIRK2. However, our laboratory has obtained compelling data demonstrating that other subunit combinations are also possible in other brain regions like the cerebellum. Indeed, we found a high degree of molecular diversity in the cerebellar GIRK channel repertoire as suggested by immunolabelling seen in various cerebellar neuron populations, including granule cells (GIRK1/GIRK2/GIRK3), Purkinje neurons (GIRK1/GIRK2/GIRK3), basket cells (GIRK1/GIRK3), Golgi cells (GIRK2 and GIRK2/GIRK4), stellate cells (GIRK3), and unipolar brush cells (GIRK2/GIRK3). High-resolution immunoelectron microscopy have shown that while GIRK1 and GIRK2 shares virtually the same subcellular localization in the extrasynaptic plasma membrane of pyramidal cell spines, GIRK2 but not GIRK1 are present in the postsynaptic density of asymmetrical synapses between Schaffer's collateral axon terminals and dendritic spines. All together, our findings demonstrate that GIRK subunits are distributed in a cell type-dependent manner, as well as in a subcellular compartment-dependent manner, supporting the existence of significant molecular and cellular diversity in the brain GIRK channel population.
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