Signaling through BK_{Ca} channels - a view by functional proteomics

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Cellular and fast intercellular signaling mainly occurs through proteins integral to the plasma membrane such as ion channels and G protein-coupled receptors. The respective signalling processes are highly specific and often tightly restricted in time and space - functional characteristics that result from integration of channels and receptors into 'macromolecular complexes' (termed signaling supercomplexes or microdomains). So far, however, membrane protein-associated signalling supercomplexes have largely escaped molecular analysis predominantly for technical reasons arising from their poor solubility and low stability.
Our group has developped a novel approach for isolation of such signaling supercomplexes from plasma membranes and identification and analyses of their individual protein constituents.

In this presentation I will show application of our *functional proteomics* to Ca^{2+} and voltage-activated potassium channels of the BK-type (BK_{Ca}). These channels are fundamental modulators of signaling in the brain by contributing to action potential repolarization, mediating the fast phase of afterhyperpolarization, controlling dendritic Ca^{2+} spikes and establishing a feedback loop between membrane potential and cytosolic Ca^{2+} that regulates the release of hormones and transmitters. I will discuss organisation and working of BK_{Ca} channel complexes and show how they reconstitute 'Ca^{2+} *nano-domains*' where Ca^{2+} influx through the co-assembled voltage-gated Ca^{2+} channels (Cav) activates BK_{Ca}. Moreover, I will discuss how other constituents fine-tune the operation of BK_{Ca} supercomplexes and thus promote the specificity of their signaling required in different types of cells and distinct subcellular compartments.

Literature

Berkefeld H, Sailer CA, Bildl W, Rohde V, Thumfart JO, Eble S, Klugbauer N, Reisinger E, Bischofberger J, Oliver D, Knaus HG, Schulte U, Fakler B (2006) BK_{Ca}-Cav channel complexes mediate rapid and localized Ca^{2+}-activated K^+ signaling.
Science 314: 615-620.

Schulte U, Thumfart JO, Klöcker N, Sailer CA, Bildl W, Biniossek M, Dehn D, Deller T, Eble S, Abbass K, Wangler T, Knaus HG, Fakler B (2006) The epilepsy-linked Lgi1 protein assembles into presynaptic kv1 channels and inhibits inactivation by Kvβ1.
Neuron 49: 697-706.