P003 Annexin-dependent rafts act as Ca^{2+}-sensing feedback loops for the regulation of intracellular Ca^{2+}-homeostasis

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Eukaryotic cells harbour numerous, tissue-specific subsets of Ca^{2+}-sensitive, membrane-associated proteins belonging to the annexin family. We have examined the significance of this variety in smooth muscle and demonstrated that different annexins target membrane sites of distinct lipid composition. Moreover, each annexin requires a different $[Ca^{2+}]_i$ for its translocation to the sarcolemma. Our results suggest that the interactions of annexins with distinct plasma membrane regions promote membrane segregation and – in combination with their individual Ca^{2+}-sensitivity – might allow a spatially confined, graded response to a multitude of extra-or intracellular stimuli.

We propose that the members of the annexin family work synergistically to form a broad-range Ca^{2+}-sensor by regulating the spatial architecture of the sarcolemma via a reversible, Ca^{2+}-dependent association of lipid microdomains.

Our results indicate that the stability of lipid microdomains is critical for the regulation of the BK-channel, a major element in defining intracellular Ca^{2+} homeostasis. Thus, annexin-dependent rearrangements of the plasma membrane might provide a feedback mechanism which links Ca^{2+} traffic across the sarcolemma (regulated by the BK-channel) with its actual intracellular concentration (sensed by the annexins).