Max-Planck-Institut für biophysikalische Chemie
Am Fassberg 11, 37077 Göttingen

DOKTORANDENSEMINAR

Mittwoch, den 5.3.2008
11 Uhr c.t.
im Großen Seminarraum

Isabella Gekel
Membrane Biophysics

Epac: a novel cAMP-target modulating neurotransmitter release

In the brain, cyclic AMP (cAMP) activity regulates the communication between nerve cells. cAMP alters the signal across a synapse, the point of contact between two neurons, by modulating the activity of proteins crucial for neuronal information exchange. A rise in the intracellular cAMP level enhances glutamate release from presynaptic terminals at excitatory mammalian cerebral synapses. This can be attributed to an increase in the release probability of glutamate containing vesicles or to a change in the number of releasable vesicles.

Although cAMP-dependent protein kinase A (PKA), the first cAMP target known, had become a model of protein kinase structure and regulation, it turned out that not all of the cAMP-related effects are mediated by the general activation of PKA: The novel cAMP-target Epac contributes to cAMP-signaling.

Electrophysiological recordings from dissociated cultured autaptic neurons of the *Dentate Gyrus* show that activation of Epac by specific cAMP-analogues increased both the action potential-evoked excitatory postsynaptic currents (EPSCs) during low frequency (0.2 Hz) stimulation and the number of spontaneous fusion events (miniature EPSCs, mEPSC). The number of releasable vesicles remained unchanged upon Epac activation. In conclusion, Epac-mediated cAMP-signaling increases the mean release probability of a vesicle. In addition, Epac activity augmented a subsequent enhancement of evoked EPSC amplitudes by phorbol ester (PDBu). PDBu has been reported to modulate both the number of readily releasable vesicles as well as the vesicular release probability.The amount of enhancement of the PDBu-response depended on the time interval between Epac activation and PDBu application, and developped slowly over several minutes. Since downregulation of PKC activity abolished the presynaptic PDBu-response, Epac activation leads to presynaptic changes involving Epac-to-PKC signaling.

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