Abstract "Characterization of the *in vivo* function of PACSIN 2" by Jan Kormann

The F-BAR protein PACSIN 2 is expressed in many vertebrate cell types and, like other members of the PACSIN-protein family, after dimerization binds to negatively-charged phospholipids via its F-BAR domain. Its C-terminal SH3-domain mediates the interactions with numerous binding partners, including dynamin, N-WASP, different cargo molecules and EHD proteins. Overexpression or knockdown studies unraveled an *in vitro* role for PACSIN 2 in clathrin-dependent and –independent endocytic pathways. To characterize its *in vivo* role PACSIN 2-deficient mice were studied.

PACSIN 2-deficient mice appear healthy and fertile, however they show defects in thrombopoiesis. The platelet number is decreased and the platelet volume increased and in the spleen the number of megakaryocytes is increased. Furthermore, PACSIN 2-deficient mice show defects in locomotor activity, but histological analysis of the muscle architecture and of brain revealed no abnormalities. Parasympathic stimulation in PACSIN 2-deficient mice leads to massive Mobitz type II AV-blocks, indicating a role in the excitation conductance from the atrium to the ventricle. Isolated atrial cardiomyocytes show a reduced beating frequency as well as an increase in action potential duration in PACSIN 2-deficient mice.

In fibroblasts PACSIN 2-deficiency leads to an enhanced attachment on fibronectin and a defect in cell migration. In PACSIN 2-deficient fibroblasts activated β1 integrin accumulates at the plasma membrane. This acculumation might be caused by a defective β1 integrin internalisation via tubular structures. PACSIN 2 colocalizes with EHD1 at tubular structures. Both, PACSIN 2 and EHD1 are essential for the maintenance of tubular structures as a lack of either proteins leads to a loss of these structures, which blocks endocytosis of GPI-anchored proteins. Colocalization studies with GRAF1 identified these tubular structures as CLICs.

Overall PACSIN 2 plays an important role in tubular associated transport, which is not essential for survival but appears to be relevant under stress conditions.