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Tubular Invagination of the Plasma Membrane by SNX9 is Regulated by Dynamin and the Actin Cytoskeleton

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Sorting nexin 9 (SNX9, also called SH3PX1), which contains SH3, LC, and PX domain, is a member of the sorting nexin family of proteins. The C-terminal part of SNX9 contains a putative BAR (Bin-Amphiphysin-Rvs) domain, which displays a coiled-coil nature with a characteristic set of conserved hydrophobic, aromatic and hydrophilic residues. BAR domain proteins such as amphiphysin and endophilin, is known to be involved in membrane deformation and vesicle budding during clathrin-mediated endocytosis. Since SNX9 shows a similar domain organization with amphiphysin and endophilin although in an opposite direction, we tested the role of SNX9 BAR domain during clathrin pit formation. Although SNX9 only shows a distant homology at the sequence level, a helical wheel alignment of its BAR domain revealed a similar amphipathic pattern with that of amphiphysin. The structural modeling using Arfaptin as a template showed a similarity with amphiphysin BAR domain as well. When transfected in COS-7 cells, SNX9 formed tubular invaginations originating from the plasma membrane. The C-terminal BAR domain as well as LC and PX domains is required for tubular membrane invagination. Furthermore, BAR domains of two SNX9 dimerizes with each other to form V shaped dimer to sense and/or induce membrane bending. Notably, the ability of SNX9 BAR domain to induce tubular invagination is enhanced by disruption of the actin cytoskeleton and is antagonized by dynamin, thus suggesting that plasma membrane curvature formation and actin dynamics are tightly interconnected during clathrin pit formation.