Abstract

The exocyst is a hetero-octameric protein complex which mediates tethering secretory vesicles to specific sites of plasma membrane for polarized exocytosis. The exocyst was long known to contribute to processes such as yeast budding, cytokinesis, epithelia polarization and neurite outgrowth. Recently, the role of the exocyst in regulation of actin cytoskeleton and cell migration was discovered.

It was shown, that the exocyst is important for formation of cell migration structures such as lamellipodia and filopodia in motile cells and invadopodia in invasive cancer cells. These structures are all actin-based membrane protrusions and the exocyst can through its Exo70 subunit interact with the Arp2/3 complex, the activator of actin nucleation. By binding and activating the Arp2/3 complex, the exocyst mediates actin polymerization resulting in formation of these membrane protrusions. Furthermore, the exocyst probably targets the Arp2/3 complex to specific sites of plasma membrane that are intended to become membrane protrusions. In addition, the exocyst mediates secretion of matrix metalloproteinases (MMPs) in invadopodia. MMPs are important for degradation of the extracellular matrix, an essential process in cancer cell invasion.

The exocyst seems to be part of the cascade downstream of cytokines TNF-α and IL-1 leading to filopodia formation. TNF-α and IL-1 activate Cdc42 GTPase, which in turn activates RalA GTPase. Activated RalA GTPase consequently interacts with exocyst subunit Sec5 and induces filopodia formation. For invadopodia formation and function the interaction between exocyst subunits Sec3/8 and IQGAP1 under the control of Cdc42 and RhoA GTPases is needed.