

Abstract of Presentation

Presentation Title:

Guanine nucleotide exchange factors for Rho GTPases in endothelial cells: critical transducers of angiogenic signals

Abstract:

G protein coupled receptors activate signaling pathways related to endothelial cell migration and angiogenesis. We studied the role of $G\beta\gamma$ and P-Rex1, a Rac guanine exchange factor, as mediators of angiogenic signals. We characterized a differential inhibitor of $G\beta\gamma$, derived from Phosducin-like protein (PhLP-M1-G149), able to interfere with the interaction between $G\beta\gamma$ and $PI3K\gamma$, which inhibits AKT signaling, endothelial cell migration and tubulogenesis. In addition, we tested the hypothesis that P-Rex1 is required for the angiogenic response stimulated by SDF1 and characterized the role of P-Rex1-interacting proteins in cell migration. We found that P-Rex1 is an effector of the mammalian target of Rapamycin, linking this kinase to Rac activation and cell migration, and demonstrated a critical participation of P-Rex1 in the migration and in vitro angiogenic response of endothelial cells stimulated with SDF-1/CXCL12. Together, our data indicate an important role of the $G\beta\gamma/PI3K\gamma/P\text{-Rex1}$ signaling pathway in angiogenic responses.