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Physical Foundations of PTEN/Phosphoinositide Interaction
ARNE GERICKE, ZHIPING JIANG, ROBERTA E. REDFERN, EDGAR E. KOOIJMAN, Kent State University, ALONZO H. ROSS, University of Massachusetts Medical School — Phosphoinositides act as signaling molecules by recruiting critical effectors to specific subcellular membranes to regulate cell proliferation, apoptosis and cytoskeletal reorganization, which requires a tight regulation of phosphoinositide generation and turnover as well as a high degree of compartmentalization. PTEN is a phosphatase specific for the 3 position of the phosophoinositide ring that is deleted or mutated in many different disease states. PTEN association with membranes requires the interaction of its C2 domain with phosphatidylserine and the interaction of its N-terminal end with phosphatidylinositol-4,5-bisphophate ($PI(4,5)P_2$). We have investigated PTEN/$PI(4,5)P_2$ interaction and found that Lys13 is crucial for the observed binding. We also found that the presence of cholesterol enhances PTEN binding to mixed $PI(4,5)P_2$/POPC vesicles. Fluorescence microscopy experiments utilizing GUVs yielded results consistent with enhanced phosphoinositide domain formation in the presence of cholesterol. These experiments were accompanied by zeta potential measurements and solid state MAS ^{31}P-NMR experiments aimed at investigating the ionization behavior of phosphoinositides.

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