

P025 Effects of phosphoinositide identity and lateral organization on PTEN binding and structure

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Recent reports have shown that PTEN is activated by PI(4,5)P₂ and that this activation requires a polybasic region located at the N-terminus of the protein. It was hypothesized that PI(4,5)P₂ aids membrane recruiting and induces a conformational change in PTEN. This study characterizes PTENs binding preferences, investigates its contact points with the lipid bilayer and highlights structural changes upon membrane interaction. Fluorescence quenching experiments involving PC/phosphoinositide vesicles yielded results consistent with an enhanced PTEN binding to PI(4,5)P₂ or PI(5)P containing vesicles, while the interaction with all other phosphoinositide derivatives was only minor. Addition of PS to these vesicles increased the overall binding but did not alter the binding preferences. Experiments with a truncated PTEN₁₆₋₄₀₃ showed a strongly reduced phosphoinositide affinity and a loss of specificity, while experiments using a peptide representing PTENs N-terminus (PTEN₁₋₂₁) showed preferential PI(4,5)P₂ binding. Infrared spectroscopic measurements furnished results consistent with an increased α -helical secondary structure content in the presence of PI(4,5)P₂/PC vesicles, while other phosphoinositides like PI(3,5)P₂ or PI(3,4,5)P₃ did not cause a structural change. Although PS induced a structural change towards more β -sheet, it did not alter the structural effect of PI(4,5)P₂. PTENs structural changes were also associated with a marked change of Trp fluorescence.