

Funamoto, S., R. Meili, S. Lee, L. Parry and R.A. Firtel (2002). Spatial and temporal regulation of 3-phosphoinositides by PI 3-kinase and PTEN mediates chemotaxis. *Cell* 109:611-623.

We have investigated the mechanisms of leading edge formation in chemotaxing *Dictyostelium* cells. We demonstrate that while phosphatidylinositol 3-kinase (PI3K) transiently translocates to the plasma membrane in response to chemoattractant stimulation and to the leading edge in chemotaxing cells, PTEN, a negative regulator of PI3K pathways, exhibits a reciprocal pattern of localization. By uniformly localizing PI3K along the plasma membrane, we show that chemotaxis pathways are activated along the lateral sides of cells and PI3K can initiate pseudopod formation, providing evidence for a direct instructional role of PI3K in leading edge formation. These findings provide evidence that differential subcellular localization and activation of PI3K and PTEN is required for proper chemotaxis.