

Takeda, K., A.T. Sasaki, H. Ha, H. Seung and R.A. Firtel (2007). Role of phosphatidylinositol 3-kinases in chemotaxis in *Dictyostelium*. *J. Biol. Chem.* 282:11874-11884.

Experiments in several cell types revealed that local accumulation of phosphatidylinositol 3,4,5-triphosphate mediates the ability of cells to migrate during gradient sensing. We took a systematic approach to characterize the functions of the six putative Class I phosphatidylinositol 3-kinases (PI3K1–6) in *Dictyostelium* by creating a series of gene knockouts. These studies revealed that PI3K1–PI3K3 are the major PI3Ks for chemoattractant-mediated phosphatidylinositol 3,4,5-triphosphate production. We studied chemotaxis of the *pi3k1/2/3* triple knock-out strain (*pi3k1/2/3* null cells) to cAMP under two distinct experimental conditions, an exponential gradient emitted from a micropipette and a shallow, linear gradient in a Dunn chamber, using four cAMP concentrations ranging over a factor of 10,000. Under all conditions tested *pi3k1/2/3* null cells moved slower and had less polarity than wild-type cells. *pi3k1/2/3* null cells moved toward a chemoattractant emitted by a micropipette, although persistence was lower than that of wildtype or *pi3k1/2* null cells. In shallow linear gradients, *pi3k1/2* null cells had greater directionality defects, especially at lower chemoattractant concentrations. Our studies suggest that although PI3K is not essential for directional movement under some chemoattractant conditions, it is a key component of the directional sensing pathway and plays a critical role in linear chemoattractant gradients, especially at low chemoattractant concentrations. The relative importance of PI3K in chemotaxis is also dependent on the developmental stage of the cells. Our data suggest that the output of other signaling pathways suffices to mediate directional sensing when cells perceive a strong signal, but PI3K signaling is crucial for detecting weaker signals.