

Lee, S., F. Rivero, K.C. Park, E. Huang, S. Funamoto and R.A. Firtel (2004). Dictyostelium PAKc is required for proper chemotaxis. *Mol. Biol. Cell* 15:5456–5469.

We have identified a new Dictyostelium p21-activated protein kinase, PAKc, that we demonstrate to be required for proper chemotaxis. PAKc contains a Rac-GTPase binding (CRIB) and autoinhibitory domain, a PAK-related kinase domain, an N-terminal phosphatidylinositol binding domain, and a C-terminal extension related to the Gbg binding domain of *Saccharomyces cerevisiae* Ste20, the latter two domains being required for PAKc transient localization to the plasma membrane. In response to chemoattractant stimulation, PAKc kinase activity is rapidly and transiently activated, with activity levels peaking at 10 s. *pakc* null cells exhibit a loss of polarity and produce multiple lateral pseudopodia when placed in a chemoattractant gradient. PAKc preferentially binds the Dictyostelium Rac protein RacB, and point mutations in the conserved CRIB that abrogate this binding result in misregulated kinase activation and chemotaxis defects. We also demonstrate that a null mutation lacking the PAK family member myosin I heavy chain kinase (MIHCK) shows mild chemotaxis defects, including the formation of lateral pseudopodia. A null strain lacking both PAKc and the PAK family member MIHCK exhibits severe loss of cell movement, suggesting that PAKc and MIHCK may cooperate to regulate a common chemotaxis pathway.