

Park, K.C., F. Rivero, R. Meili, S. Lee, F. Apone and R.A. Firtel (2004). Rac regulation of chemotaxis and morphogenesis in Dictyostelium. EMBO J. 23:4177–4189.

Chemotaxis requires localized F-actin polymerization at the site of the plasma membrane closest to the chemoattractant source, a process controlled by Rac/Cdc42 GTPases. We identify Dictyostelium RacB as an essential mediator of this process. RacB is activated upon chemoattractant stimulation, exhibiting biphasic kinetics paralleling F-actin polymerization. *racB* null cells have strong chemotaxis and morphogenesis defects and a severely reduced chemoattractant-mediated F-actin polymerization and PAKc activation. RacB activation is partly controlled by the PI3K pathway. *pi3k1/2* null cells and wild-type cells treated with LY294002 exhibit a significantly reduced second peak of RacB activation, which is linked to pseudopod extension, whereas a PTEN hypomorph exhibits elevated RacB activation. We identify a RacGEF, RacGEF1, which has specificity for RacB in vitro. *racgef1* null cells exhibit reduced RacB activation and cells expressing mutant RacGEF1 proteins display chemotaxis and morphogenesis defects. RacGEF1 localizes to sites of F-actin polymerization. Inhibition of this localization reduces RacB activation, suggesting a feedback loop from RacB via F-actin polymerization to RacGEF1. Our findings provide a critical linkage between chemoattractant stimulation, F-actin polymerization, and chemotaxis in Dictyostelium.