Sun, B. and R.A. Firtel (2003). A regulator of G protein signaling-containing kinase is important for chemotaxis and multicellular development in Dictyostelium. Mol. Biol. Cell 14:1727-1743.

We have identified a gene encoding RGS domain-containing protein kinase (RCK1), a novel regulator of G protein signaling domain-containing protein kinase. RCK1 mutant strains exhibit strong aggregation and chemotaxis defects. rck1 null cells chemotax ~50% faster than wild-type cells, suggesting RCK1 plays a negative regulatory role in chemotaxis. Consistent with this finding, overexpression of wild-type RCK1 reduces chemotaxis speed by ~40%. On cAMP stimulation, RCK1 transiently translocates to the membrane/cortex region with membrane localization peaking at ~10 s, similar to the kinetics of membrane localization of the pleckstrin homology domain-containing proteins CRAC, Akt/PKB, and PhdA. RCK1 kinase activity also increases dramatically. The RCK1 kinase activity does not rapidly adapt, but decreases after the cAMP stimulus is removed. This is particularly novel considering that most other chemoattractant-activated kinases (e.g., Akt/PKB, ERK1, ERK2, and PAKa) rapidly adapt after activation. Using site-directed mutagenesis, we further show that both the RGS and kinase domains are required for RCK1 function and that RCK1 kinase activity is required for the delocalization of RCK1 from the plasma membrane. Genetic evidence suggests RCK1 function lies downstream from G2, the heterotrimeric G protein that couples to the cAMP chemoattractant receptors. We suggest that RCK1 might be part of an adaptation pathway that regulates aspects of chemotaxis in Dictyostelium.