

Mendoza, M.C., F. Du, N. Iranfar, N. Tang, H. Ma, W.F. Loomis and R.A. Firtel (2005). Loss of SMEK, a novel, conserved protein, suppresses mek1 null cell polarity, chemotaxis, and gene expression defects. *Mol. Cell. Biol.* 25, in press.

MEK/ERK MAP kinase signaling is imperative for proper chemotaxis. *Dictyostelium* mek1⁻ (MEK1 null) and erk1⁻ cells exhibit severe defects in cell polarization and directional movement, but the molecules responsible for the mek1⁻ and erk1⁻ chemotaxis defects are unknown. Here, we describe a novel, evolutionarily conserved gene, smkA (suppressor of mek1⁻), whose loss partially suppresses the mek1⁻ chemotaxis phenotypes. SMEK also has MEK1-independent functions: SMEK, but not MEK1, is required for proper cytokinesis during vegetative growth, timely exit from the mound stage during development, and myosin II assembly. SMEK localizes to the cell cortex through an EVH1 domain at its N-terminus during vegetative growth. At the onset of development, SMEK translocates to the nucleus via an NLS (nuclear localization signal) at its C-terminus. The importance of SMEK's nuclear localization is demonstrated by our findings that a mutant lacking the EVH1 domain complements SMEK deficiency, whereas a mutant lacking the NLS does not. Microarray analysis reveals that some genes are precociously expressed in mek1⁻ and erk1⁻ cells. The mis-expression of some of these genes is suppressed in the smkA deletion. These data suggest that loss of MEK1/ERK1 signaling compromises gene expression and chemotaxis in a SMEK-dependent manner.