

Mendoza, M.C., E.O. Booth, G. Shaulsky and R.A. Firtel (2007). MEK1 and protein phosphatase 4 coordinate Dictyostelium development and chemotaxis. *Mol. Cell. Biol.* 27:3817-3827.

The MEK and extracellular signal-regulated kinase/mitogen-activated protein kinase proteins are established regulators of multicellular development and cell movement. By combining traditional genetic and biochemical assays with a statistical analysis of global gene expression profiles, we discerned a genetic interaction between *Dictyostelium discoideum* *mek1*, *smkA* (named for its role in the suppression of the *mek1* mutation), and *pppC* (the protein phosphatase 4 catalytic subunit gene). We found that during development and chemotaxis, both *mek1* and *smkA* regulate *pppC* function. In other organisms, the protein phosphatase 4 catalytic subunit, PP4C, functions in a complex with the regulatory subunits PP4R2 and PP4R3 to control recovery from DNA damage. Here, we show that catalytically active PP4C is also required for development, chemotaxis, and the expression of numerous genes. The product of *smkA* (SMEK) functions as the *Dictyostelium* PP4R3 homolog and positively regulates a subset of PP4C's functions: PP4C-mediated developmental progression, chemotaxis, and the expression of genes specifically involved in cell stress responses and cell movement. We also demonstrate that SMEK does not control the absolute level of PP4C activity and suggest that SMEK regulates PP4C by controlling its localization to the nucleus. These data define a novel genetic pathway in which *mek1* functions upstream of *pppC-smkA* to control multicellular development and chemotaxis.