Modulating Cdc42 activation
by mitogen activated kinase signaling permits gradient sensing

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Abstract

Directional cell growth requires that cells generate and read shallow chemical gradients. We use live single cell analysis in microfluidic gradient chips combined with mathematical modeling to elucidate the directional response of yeast cells exposed to pheromone gradients. We find that cells establish a polarity site independent of the gradient direction. Restricted Cdc42 activation leads to lateral site movement to align with the gradient before directional growth is initiated. Chemical genetic and mutational analysis identifies a MAPK driven incoherent feed forward loop regulating Cdc42 activation by sequestration of its activator, Cdc24. Computational analysis defines restricted Cdc42 activation and resultant limited directed receptor trafficking as central in a spatial double positive feedback system sufficient for chemical gradient amplification. Cells deficient in Cdc24 sequestration or regulated directed receptor trafficking are unable to align their polarity axis with the external gradient. Our results define the core network for how cells can sense and interpret chemical gradients. Given the high conservation of many network components we suspect that similar mechanisms operate in many eukaryotic gradient-sensing systems.