

INVITED LECTURE T11

Imaging of cell signaling pathways

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The directed cell migration towards a chemotactic source, chemotaxis, involves three complex and interrelated processes: directional sensing, cell polarization and motility.

Directional sensing allows migrating eukaryotic cells to chemotax in extremely shallow gradients (< 2% across the cell body) of the chemoattractant. Although directional sensing has been observed as spatially restricted responses along the plasma membrane, our understanding of the cell's compass that controls the gradient-induced translocation of proteins during chemotactic movements is still largely lacking. Until now, the dynamical behaviour and mobility of the chemoattractant-receptor molecule has been neglected in models describing the directional sensing mechanisms. Here we show by single-molecule microscopy an agonist-induced increase in the mobile fraction of cAMP-receptor at the leading edge of chemotacting *Dictyostelium discoideum* cells. The on-set of receptor mobility was correlated to the uncoupling and activation of the G α 2-protein. A finite-element simulation showed that the increase in mobile fraction of the activated receptor enabled the amplified generation of activated G $\beta\gamma$ -dimers at the leading edge of the cell, faithfully representing a primary linear amplification step in directional sensing. We propose here that modulation of the receptor mobility is directly involved in directional sensing and provides a new mechanistic basis for the primary amplification step in current theoretical models describing directional sensing.