4D Quantification on Complex Wave-Formation of Phosphatidylinositol Lipids Signaling in Dictyostelium

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The ability of cells to sense an external chemical gradient is essential to cellular functions such as chemotaxis and other diverse processes. To sense a chemical gradient, eukaryotic cells have to detect differentials in the concentration of chemicals along the periphery of cells without rapid motile translocation. A concentration differential of a few percent across a cell body of a few tens of micrometers can be sufficient to induce directional migration. The phosphatidylinositol (PtdIns) lipids reaction is a key signaling event responsible for gradient sensing for eukaryotic cell chemotaxis. The self-organization activity of the PtdIns lipids reaction induces an inherent polarity even in the absence of an external chemoattractant gradient by producing a localized domain of PI(3,4,5)P3 on the membrane. It is shown experimentally in 2D observations that in Dictyostelium cell such a domain can exhibit two kinds of behavior: 1) persistent domain formation that travels on the membrane over time, and 2) stochastic formation of transient domains. [1, 2]

On the basis of 3D time-resolved observations on actin-polymerisation-inhibited Dictystelium cells using ultra-fast spin confocal microscopy, we systematically analyze and map the dynamics and pattern formation of Dictystelium-membrane-bounded PI(3,4,5)P3 molecules. We show that a whole zoo of pattern formation is possible, such as periodic target waves, bouncing waves, 'standing' waves, and rotating waves along and perpendicular to the cell-equator. We discuss geometrical constrains by the shape of cell membrane, and propose a possible mechanism that may explain the origin of the polarity of PI(3,4,5)P3 domain formation in the absence of an external chemoattractant gradient. Additionally, we discuss our finding with previously observed 2D observations.

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2. Shibata, T., Nishikawa, N., Matsuoka, S. and Ueda, M. 2012. "Modeling the self-organized phosphatidylinositol lipids signaling system in chemotactic cells based on quantitative image analysis", *Journal of Cell Science*, **125**, 5138-5150 (2012).