Actin Dynamics Spatially Organize Plasma Membrane Biophysical Properties

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Biological membranes are assemblies of lipids forming fluid bilayers. The physicochemical properties of membranes play crucial roles in cellular functions. However, the mechanisms regulating membrane properties and particularly their interplay with live cell processes remain poorly understood. In this study, we investigated the effect of forces on the plasma membrane in vitro and in cells. For this, we employed the synthetic probe Flipper-TR (1-2), which measures molecular forces at the plasma membrane and can be imaged by fluorescence lifetime microscopy (FLIM).

First, we examined the spatial distribution Flipper-TR lifetime in various primary and cultured cell types and found consistent gradients in migrating cells, with high Flipper-TR lifetime observed at the leading edge. Next, we reconstituted tension gradients in lipid bilayers in vitro with different lipid compositions. The results demonstrated that the Flipper-TR lifetime gradients correspond to tension gradients. Further experiments on micropatterned cells allowed us to standardize cell shape and adhesion, confirming an increase in Flipper-TR lifetime at cell edges, consistent with results from migrating cells. Surprisingly, we found a decrease in Flipper-TR lifetime specifically at the edges of adhesive patterns, regardless of shape.

Our findings using a variety of drugs indicate that a dynamic actin cytoskeleton is critical for spatially organizing the membrane biophysical properties, since: 1) Flipper-TR lifetime locally correlates with the magnitude of actin flows, and 2) arresting actin dynamics abolished Flipper-TR lifetime patterns. Analysis of lipid diffusion by pair correlation function (pCF) analysis confirmed the existence of lipid diffusion barriers and lipid flows at the bottom membrane. We conclude that, even in non-motile cells, actin dynamics can sustain gradients of membrane tension at the plasma membrane due to the combination of adhesion and actin flows, spatially organizing membrane biophysical properties in live cells.

References:

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