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Forcing it on: Cytoskeletal dynamics during lymphocyte activation

ARPITA UPADHYAYA, Department of Physics, University of Maryland, College Park

Formation of the immune synapse during lymphocyte activation involves cell spreading driven by large scale physical rearrangements of the actin cytoskeleton and the cell membrane. Several recent observations suggest that mechanical forces are important for efficient T cell activation. How forces arise from the dynamics of the cytoskeleton and the membrane during contact formation, and their effect on signaling activation is not well understood. We have imaged membrane topography, actin dynamics and the spatiotemporal localization of signaling clusters during the very early stages of spreading. Formation of signaling clusters was closely correlated with the movement and topography of the membrane in contact with the activating surface. Further, we observed membrane waves driven by actin polymerization originating at these signaling clusters. Actin-driven membrane protrusions likely play an important role in force generation at the immune synapse. In order to study cytoskeletal forces during T-cell activation, we studied cell spreading on elastic gels. We found that gel stiffness influences cell morphology, actin dynamics and receptor activation. Efforts to determine the quantitative relationships between cellular forces and signaling are underway. Our results suggest a role for cytoskeleton driven forces during signaling activation in lymphocytes.