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Effect of substrate mechanical properties on T cell activation

KING LAM HUI, ARPITA UPADHYAYA, Department of Physics, University of Maryland, College Park, MD — T cell activation is a key process in cell-mediated immunity, and engagement of T cell receptors by peptides on antigen presenting cells leads to activation of signaling cascades as well as cytoskeletal reorganization and large scale membrane deformations. While significant advances have been made in understanding the biochemical signaling pathways, the effects imposed by the physical environment and the role of mechanical forces on cell activation are not well understood. In this study, we have used anti-CD3 coated elastic polyacrylamide gels as stimulatory substrates to enable the spreading of Jurkat T cells and the measurement of cellular traction forces. We have investigated the effect of substrate stiffness on the dynamics of T cell spreading and cellular force generation. We found that T cells display more active and sustained edge dynamics on softer gels and that they exert increased traction stresses with increasing gel stiffness. A dynamic actin cytoskeleton was required to maintain the forces generated during activation, as inferred from small molecule inhibition experiments. Our results indicate an important role for physical properties of the antigen presenting cell as well as cytoskeleton-driven forces in signaling activation.

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