A platform to study the role of forces in T lymphocyte activation

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T cell activation requires the recognition by T-cell receptors (TCR) of peptide-major histocompatibility complex molecules (pMHC) presented by antigen-presenting cells (APC). This process also involves engagement of costimulatory receptors, cytoskeletal components and adhesion molecules recognizing ligands on APC, finally forming a special cell-cell structure-immunological synapse (IS) [1].

Although the biochemical and molecular aspects of this cell-cell interaction have been well studied, the possible role of mechanical forces in receptor assembly at the IS and T cell activation has only recently been investigated. Experimental evidence shows that the T cell surface is subjected to tensile and traction forces which could be transmitted to TCR-pMHC or other receptor pairs [2]. T cells could also use forces to sense the physical properties of the APC to translate them into biochemical signals. In current models of APC-T cell interactions, the mechanical engagement of costimulatory receptors and adhesion molecules have rarely been considered. So in our project, we will use hydrogel to fabricate artificial APCs recapitulate both mechanical and biochemical information which could be recognized by T cells, to study how mechanical engagement of individual receptors correlates with activation levels in T cells.

[1] Monks CRF, et al., Nature, 395, 82-86 (1998)

[2] Keenan T.Bashour, etal, PNAS,111, 2241-2246 (2014)