The mechanical response of T cells during activation

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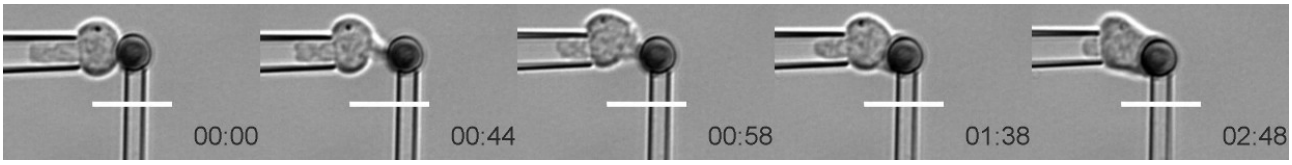
T cells activate upon antigen recognition on the surface of antigen-presenting cells (APCs). The interface between a T cell and an APC – the information that is read there, its integration, and the launch of the functional response of T cells – remains an active field of study. In particular, there is a growing interest in the mechanics of the process, as forces generated by T cells at the contact area with the APC were linked with the T cells biological function [1].

We measure forces that T cells exert perpendicular to the contact area (perpendicular to the immunological synapse plane), using the Micropipette Force Probe [2]. When a T cell pushes or pulls on its target, the holding micropipette bends, and its tip moves along the horizontal axis (figure below). Force developed by the cell is then directly proportional to the displacement of the micropipette measured in the microscope image. With this setup, we track also the morphology of the cell, as seen from the profile, after the contact with an activating bead.

Within first minutes of the activation process T cells follow a conserved sequence of events: they first push, then pull on their target. Both pushing and pulling forces change with the bending stiffness of the micropipette that holds the bead. This means that T cells adapt their mechanical response to the mechanical cues from the environment. Pushing forces start as soon as 30 s after the contact, marking them as one of the earliest events in the process. We will further study the role of cytoskeleton in the major changes in T cell morphology (figure below), to elucidate the mechanism of T cell activation.



Human primary CD4+ T cell, held in a micropipette, activated with an anti-CD3/anti-CD28 bead. Left to right: contact, pushing, collapse, spreading, pulling. Time in minutes:seconds, scale bar is 10 μm.

[1] Basu, Husson, Whitlock et al. Cytotoxic T Cells Use Mechanical Force to Potentiate Target Cell Killing. Cell 165, 100–110, 2016, doi: 10.1016/j.cell.2016.01.021
[2] Sawicka et al. Micropipette Force Probe to quantify single-cell force generation: application to T cell activation. Molecular Biology of the Cell, published online before print, September 20, 2017, doi: 10.1091/mbc.E17-06-0385