

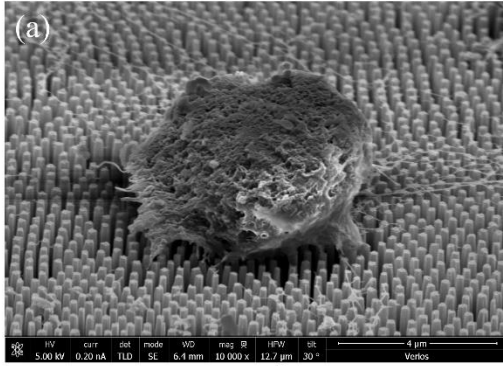
Fabrication of nano and micro devices with varying rigidity to understand various T cell interaction mechanisms

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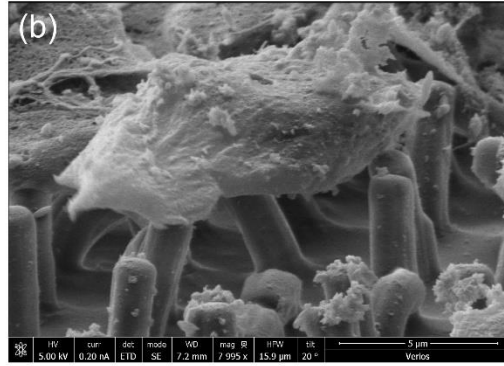
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A new emerging paradigm is that immunotherapies are revolutionizing cancer treatments by showing promising anti-tumor effects derived from body's internal immune defense mechanism. Cells such as NK cells and T cells, belonging to the innate and adaptive immune systems can be activated by transient interactions between supramolecular assemblies of receptors and ligands. The mechanism of immune cell's activation has been traditionally studied based on biochemical interaction of the immune cell receptors with the ligands presenting on target cells. Ligands immobilized on flat surfaces rendering minimum topography have been mostly used to understand the interaction mechanisms of immune cells at molecular scale. The mechanical properties of the target substrate can influence several immune cell mechanisms such as activation, proliferation and spreading. Here, we explored the influence of different nanodevices with distinct topography and rigidity to understand immune cell interaction mechanisms. We present two different nanofabrication approach for fabrication of nanodevices, (a) rigid Silicon Nanowires with Metal Assisted Chemical Etching (MACE) and (b) softer micropillars manufactured from polydimethylsiloxane (PDMS) a bio-compatible elastomer. Both the substrates demonstrated a simple system consisting of TCR/CD3 complex and CD28 receptors with variable rigidity. The topography, elasticity, and the immobilized antigens, deliver physical and chemical cues, respectively, enabling systematic study of combined effect of these cues on T cells immune response. We found that T cells can sense and respond to the topographic changes and which in turn modulates their signaling and proliferation with the variation in these physical features. Our study provides an important insight into the physical mechanism of T cell activation and proliferation and paves the way to novel nanomaterials for better understanding of T cell interaction mechanisms at molecular scale.



T cell on Si NWs



T cell on PDMS pillars

Figure 1: (a) T cells immobilized on Silicon Nanowires (Si NWs) which were functionalized with a mix of CD3 and CD28 activating receptors (b) T cells immobilized on short PDMS micro pillars pre-functionalized with CD3 and CD28 activating receptor; to understand the interaction mechanism of T cells with different types of nano and micro platforms