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Nanoscale Mechanosensing of Natural Killer Cells is Revealed by Antigen-Functionalized Nanowires

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Cells sense their environment by transducing mechanical stimuli into biochemical signals. Commonly used tools to study cell mechanosensing provide limited spatial and force resolution. Here, we report a novel nanowire-based platform for the detection and monitoring of cell forces, which integrates both mechanical and chemical cues. We used this platform to explore mechano-sensitivity of Natural Killer (NK) cells, whose mechano-regulation has been mostly unexplored up to date. To enable antigen-specific interaction between the nanowires and NK cells, we functionalized the nanowires with Major Histocompatibility Complex I (MICA) – ligands that are recognized by NKG2D activating receptors of NK cells (Fig. 1a). We stimulated NK cells on MICA-functionalized nanowires, and found that nanowires permit enhanced cell contraction, whereas such contraction is impossible on flat surfaces functionalized with MICA. We used high resolution fluorescence microscopy and SEM to discover that NK cells anchor and bend nearby nanowires during their stimulation (Fig. 1b). The nanometric radius and ultra-high aspect-ratio of nanowires allowed us to monitor cell forces with ultra-fine mechanical and spatial resolutions Based on the magnitude of the nanowire bending, we assessed that the mechanical load applied by NK cells on a single nanowire is of the order of 10pN, which is the smallest mechanical force recoded for a spreading cell. Finally, we studied the effect of nanowire topography and MICA functionalization on the immune function NK cells. We found that, whilst each of these two factors alone was insufficient to stimulate significant cell immune response, their combination substantially boosted NK cell degranulation (Fig. 1c). This finding indicates that NK cells use mechanical forces to sense their environment, and that this sensing is based on an independent mechanotransduction pathway which is costimulatory to the chemical signaling. In this sense, NK cells can be analogous to a Boolean AND gate, whose independent mechanical and chemical signaling provides two logic inputs. Our findings provide an important insight into the underlying mechanism of NK cell immune function, as well as demonstrate a novel toolbox for detecting cellular forces with an unprecedented spatial and mechanical resolution.

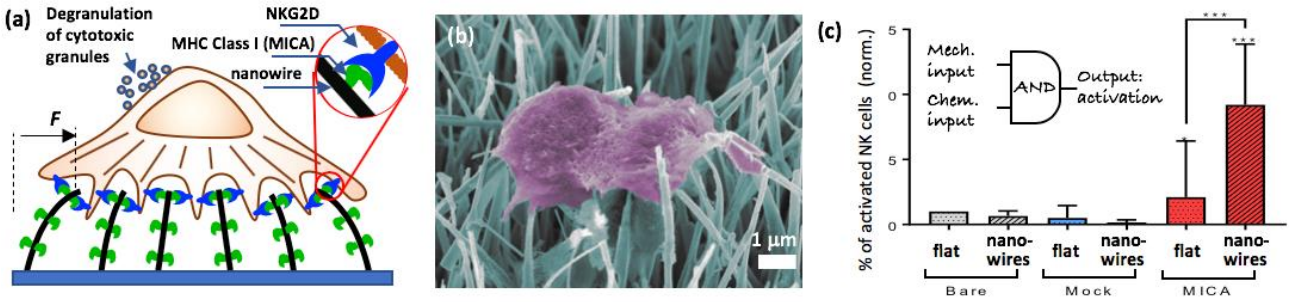

Fig.1. (a) Scheme of nanowire functionalization. (b) Scanning electron microscope of NK cells bending the nanowires. (c) Enhanced immune stimulation of NK cells by antigen-functionalized nanowires

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