Nanodevices for the Study of NK Cell Function

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Immune cells recognize cancer and viral cells by binding their activating receptors to ligands presenting on the membrane of target cells. Although this recognition and following immune activation are extensively studied today, their exact mechanism is barely understood. Here, we engineered a biochip that act as an "artificial antigen presenting cell", and used it to study the role of the ligand arrangement in the activation Natural Killer cells – lymphocytes that belong to the innate immune system (Fig.1). The chip contained nanopatterned matrices with sub-10 nm metallic nanodots and functionalized with activating ligands. By studying the cell response to the matrix geometry, we discovered the minimal ligand distribution needed to stimulate cell adhesion and immunity.

Remarkably, in-vivo function of NK cells is regulated by the signaling balance of activating and inhibitory receptors. To study the spatila aspects of this signaling crosstalk, we engineered a novel multifunctional biochip that simultaneously regulates both receptors. The chip contains mixed nanodots of different metals, selectively functionalized with activating and inhibitory ligands. We fabricated the chip using novel nanoimprint lithography and sequential angle evaporation, combined with our recently developed orthogonal biofunctionalization[2].

Finally, we explored the nanoscale mechanical sensitivity of Natural Killer cells, by interfacing them with vertical ligand-functionalized nanowires. We indicated mechanical forces applied by the cells via enhanced cell contraction and the nanowire bending (Fig.2). Furthermore, we found that while ether nanowire topography or ligand presence was insufficient to stimulate cell immune response, their combination substantially boosted NK cell degranulation. In this sense, NK are analogous to a "Boolean AND gate" with two independent mechanical and chemical 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 the study of the cell immune activation with an unprecedented spatial and mechanical resolution.

References

[1] Keidar et al , Nanoscale, in press
[2] Le Saux et al, ACS Appl. Mater. Interfaces 10(4) 11486 (2018)

Figures

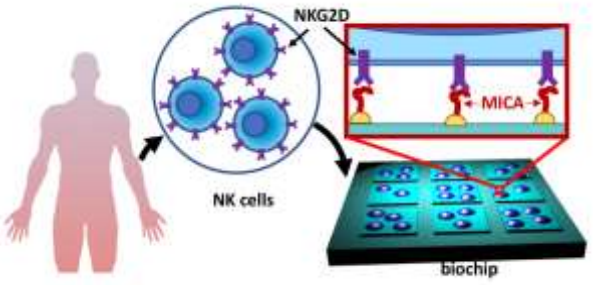

Figure 1. Scheme of the nanochip for NK cell study

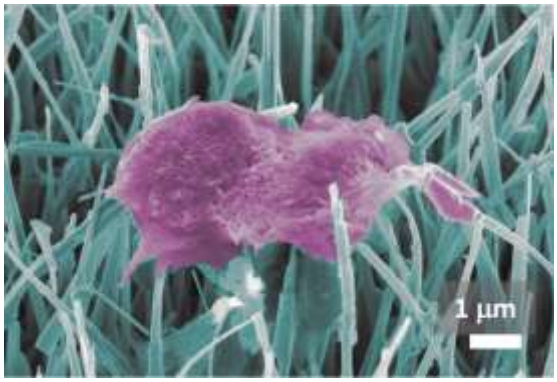

Figure 2. NK cells stimulated on nanowires - SEM