Nanoscale ligand spacing influences receptor triggering in immunological synapses

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Immunological synapses, domains of close adhesive intercellular contact, play a crucial role in key decision-making processes in the immune system. By creating a stable connection, they enable immune cells to integrate signals from a complex range of ligand molecules on the surfaces of target or information-bearing cells. Such processes enable the immune system to distinguish harmless molecules and cells from those that pose a threat, and are of vital clinical interest in infection, cancer and autoimmune disease [1].

Here, we create biomimetic ligand nanoarrays that actively control the spatial distribution of cell surface molecules in a model immunological synapse. By using these to stimulate immune cells we show that this spatial distribution acts directly to determine the outcome of the decision-making process. The nanoarrays were formed from gold nanospheres with controlled interparticle spacing in the range 25–104 nm [2]. These were biofunctionalized with ligand molecules that stimulate activating receptors on T cells and natural killer (NK) cells. In both cases, the strength of response decreased strongly with increasing spacing, falling to background levels by 69 nm in the T cell system and 104 nm for the NK cell system [3]. These results demonstrate that immune receptor triggering is influenced by the nanoscale spatial organization of receptor/ligand interactions.

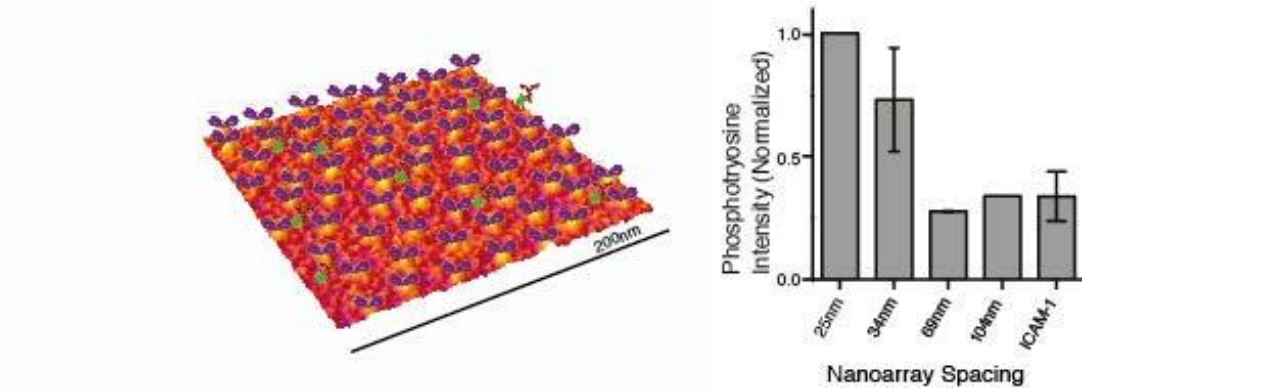

Fig. 1. (Left) T cell activating nanoarray formed by functionalizing a gold nanoparticle array with T cell-binding proteins and antibody fragments. The figure shows structures of immobilized proteins superimposed on a 3D plot of a scanning electron micrograph of a representative gold nanosphere array, with T cell stimulating $F(ab')_2$ fragments shown in purple, cell adhesion ligands in red and streptavidin used for functionalization in green. (Right) Dependence of T cell early stage activation signaling, indicated by phosphotyrosine intensity, on the spacing of stimulating nanoarrays.

[1] Xie *et al*., *Immuol. Rev.*, 251, 65 – 79 (2013)
[2] Calvacanti-Adam *et al., Biophys. J.*, 92, 2964 – 2974 (2007)
[3] Delcassian *et al., Nano Letters*, 13, 5608 – 5614 (2013)