סמינר מחלקתי – הנדסת חומרים

הנכם מוזמנים בזאת לסמינר מחלקתי
אשר יתקיים ביום ב', 14 למרץ 2024 , ד' באדר ב' תשפ"ד,
בשעה 11:00, בבניין 59 אולם 235

Multifunctional devices for the study of immune function activity of white blood cells

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The immune activity of lymphocytes is regulated by multiple signals delivered by many activating, costimulatory, and inhibitory receptors. These receptors help lymphocytes discriminate pathogens from healthy cells, which are essential for the specificity of their immune response. However, the mechanism of how different receptors integrate their signals and how their signal integration depends on the receptor spatial organization is still unclear. In recent years, biomimetic devices that control the spatial organization of receptors within the cell membrane have been extensively used to study how the receptor's spatial organization regulates cell function. Such devices have been limited to one receptor type and thus were not used to study signal integration between different receptors. Today, nanoscale tools that manipulate different receptors are required to comprehend the mechanism underlying the immune response.

In this research, we developed an "out-of-the-box" fabrication approach that combined nanoimprint lithography with double-angle evaporation, to produce bimetallic nanoarrays registered with nanoscale accuracy using only one lithographic step and with no need for the alignment between different nanodots. These nanoarrays were used in two applications. The first application, explored in collaboration with Maya Shor and Dr. Avi Niv, was studying the optical second-harmonic generation (SHG) from deep subwavelength gold-silver heterodimers and silver-silver and gold-gold homodimers[1]. The second application, to which this fabrication was initially motivated, was controlling two types of receptors to study the activating-inhibitory balance in Natural Killer (NK) cells. We engineered a device based on pairs of sub-20 nm nanodots of Au and Ti selectively functionalized with activating and inhibitory ligands for NK cells. Using this device, we discovered that activating and inhibitory ligands' spatial arrangement and size matching significantly influence signal integration in NK cells. we found that the 40-nm gap between activating and inhibitory ligands provided optimal inhibitory conditions supported by theoretical simulation[2]. This research suggests that precise spatial control of ligands is crucial for regulating the functional cross-talk in NK cell activation and may have implications for understanding immune cell regulation and potentially informing immunotherapy strategies.

Continuing this work, we explored the role of co-localization and segregation of nanoclusters formed by activating and inhibitory receptors in T cells. For this purpose, we developed a simple and modular fabrication process to create a customizable nanoscale chip that contained nanopatterned domains of activating and inhibitory ligands for T cells. we demonstrated that when the inhibition was blocked, cells became highly responsive to modifications in the nanoscale ligand configuration[3].

Overall, my research presents novel nanofabrication approaches that pave the way for many studies that provide essential insights into the molecular mechanisms of the immune function of cytotoxic lymphocytes. This understanding is crucial for advancing our knowledge of the immune system and designing future immunotherapies with a rational basis.

References:

1. Shor Peled, M. H, **Toledo E***. Second-harmonic generation from subwavelength metal heterodimers. *Opt. Express* **28**, 31468 (2020). (*equal contribution)
2. **Toledo, E**. *et al.* Molecular-scale spatio-chemical control of the activating-inhibitory signal integration in NK cells. *Sci. Adv.* **7**, eabc1640 (2021).
3. **Toledo, E**. *et al.* Multifunctional Nanoscale Platform for the Study of T Cell Receptor Segregation. *ACS Omega* **8**, 28968–28975 (2023).

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