The Chinese University of Hong Kong
Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

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Date	***:***	30 May 2022 (Monday)
Time	***:***	2:00 pm
Zoom Link	***:***	https://cuhk.zoom.us/j/9326341067?pwd=UUNiUkJwbnlubzg0OGdBTGlEbXA1Zz09
Meeting ID	***:***	932 634 1067
Password	***:***	566889

Title: Anisotropic Nanoscale Presentation of T cell Stimulatory Ligands Promotes T cell activation

Adoptive cancer therapy (ACT) tailors the treatment by incorporating patients' immune systems and has durable side effects. Using inherent patient-specific biology can design a treatment direction specifically for the individual patient instead of relying on tumor biology. The ACT consists of several steps from collection to administration. Treatment requires collecting patients' immune cells, sorting and selectively growing the specific T cell population to large numbers in the lab, then administering the extracted and grown T cells back to the patients through the bloodstream. The key to success in the ACT is depending on the effective and successful stimulation of T cells. To help the *ex vivo* expansion process, scientists have put effort to designed biomaterials that mimic antigen-presenting cells to promote T cell activation *in vitro* within a short period and with a high yield of cancer-specific T cells. Especially, gold nanoparticles have been extensively used in biomedical applications due to their excellent biocompatibility, easy modification of the shape and size, as well as simple functionalization of the particles' surface. Modulating the shape of nanoparticles is known to contribute to therapeutic performance. However, the mechanism of extracellular ligand nano-geometry in *ex vivo* T cell activation for immunotherapy remains elusive. Herein, we demonstrate large aspect ratio (AR) of gold nanorods (AuNRs) conjugated on cell culture substrate enhances both murine and human T cell activation through the nanoscale anisotropic presentation of stimulatory ligands (αCD3 and αCD28). AuNRs with large AR bearing αCD3 and αCD28 antibodies significantly promotes T cell expansion and key cytokine secretion including IL-2, IFN-γ, TNF-α. High membrane tension observed in large AR AuNRs regulates actin filament and focal adhesion assembly and develops maturation-related morphological features in T cells such as membrane ruffle formation, cell spreading, large TCR cluster formation. Anisotropic stimulatory ligand presentation promotes differentiation of naïve $CD8^+$ T cells towards the effector phenotype inducing CD137 expression upon co-culture with human cervical carcinoma. Those findings suggest the importance of manipulating extracellular ligand nano-geometry in optimizing T cell behavior to enhance therapeutic outcomes.

***** ALL ARE WELCOME *****

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