The Chinese University of Hong Kong

Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

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Date	:	28 May 2019 (Tuesday)
Time	:	3:30 p.m.
Venue	:	Room 513, William M W Mong Engineering Building (ERB)

Title: Harnessing Cell Receptor–Ligand Interactions via Tunable Nanostructures to Regulate Cellular Behaviors

Cells can sense and react to the surrounding microenvironment through transmembrane protein – integrin binding to cell adhesive ligand, such as Arg-Gly-Asp (RGD) peptide. Cells respond to nanoscale surface feature, with changes in cell proliferation, migration, polarization and differentiation by alterations in cell surface receptor and ligand binding. Previously studies have shown different strategies to control cell adhesion and spreading through different nanotopographies and external stimulations. However, few studies have demonstrated strategies to represent anisotropic nanoscale of RGD and magnetically control the tether mobility to regulate cell fates on substrate. In this dissertation, we present platforms of ligand bearing novel nanomaterials to physically regulate the nanoscale receptor-ligand interactions, which govern the outside-in and inside-out cellular signalling.

The mechanism of cell sense to nanoscale anisotropic pattern (micro/nanotopography) of bioactive ligands in the extracellular matrix regulate cell adhesion behaviors remain unexplored. We developed a platform of RGD-bearing gold nanorods (AuNRs) composed of different aspect ratios (ARs, from 1 to 7) and fixed surface area, particles density and RGD density on cell culture substrate, to decouple the effect of nanoscale anisotropic presentation RGD to cell adhesion from macroscopic cells alignment. Our finding demonstrated that the cultured stem cells had better attachment and induced osteogenic differentiation to large ARs AuNRs through recruitment of -β_3 and -β_1 class integrins to promote focal adhesion toward fibrillar adhesion whereas these were inhibited in small ARs. Moreover, our results also showed an enhanced macrophages adhesion to large ARs through recruitment of -β_1 to promote Rho-associated protein kinase (ROCK) signaling and M2 polarization, but a weaker adhesion that favored M1 polarization of macrophages in smaller ARs. This nanoscale anisotropic nanogeometry of cell adhesive ligands suggests a novel and critical parameter to unravel the fundamental mechanisms of cell adhesion and associated signaling at the molecular level and to guide rational design of biomaterials with tailored bioactive functions.

Apart from nanogeometry of RGD presentation, we also report a novel strategy to dynamically adjust the ligand tether mobility by a monolayer of RGD-bearing magnetic nanoparticles (Fe3O4, MNPs) conjugated to a glass substrate by a flexible and coiled poly(ethylene) glycol linker of large molecular weight. Such platform provides a magnetic-controllable integrin-ligand binding tether mobility and oscillating motion. Our results suggested that a low tether mobility under magnetic attraction and slow ligand oscillation frequency (0.1 Hz) promoted adhesion, spreading and osteogenic differentiation of stem cell; while a high tether mobility without magnetic attraction and high ligand oscillation frequency (2 Hz) dampened such stem cell mechanosensing signalling. Therefore, our platform demonstrated a simple, physical, noncontact and non-invasive external stimuli strategy to control cellular adhesion that elucidates the fundamental understanding of the dynamic of integrin-ligand binding and sheds some light into the design consideration of biomaterials.

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

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