The Chinese University of Hong Kong

Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

Student	:	Miss YIN Bohan
Supervisor	:	Prof. CHOI Chung Hang Jonathan
Date	:	9 January 2020 (Thursday)
Time	:	2:30 p.m.
Venue	:	Room 215 William MW Mong Engineering Building (ERB)

Title: Journey of Nanoparticles Inside the Cell and Inside the Lung: Effect of Functional Groups

In the past decades, bionanomaterials were designed from the bottom up by assembling different types of biomolecules (*e.g.,* nucleic acids, proteins, and lipids) as into ordered nanostructures for targeted delivery. A contemporary and reductionist approach to elucidating "bio-nano" interactions is to zoom in from the biomolecule level to the functional group level and to interrogate how different functional groups contribute to the interactions between bionanomaterials and the living system at the organ, tissue, and cellular levels.

In this thesis, we firstly explore how the surface chemistry of nanoparticles (NPs) and the extracellular microenvironment jointly affect "bio-nano" interactions of cells. Our model particle for incubation with cells entails a 20 nm gold nanoparticle (AuNP) core and an outer shell of polyethylene glycol (PEG) strands that bear hydrocarbyl functional groups with different carbon numbers and structures. To elucidate the effect of nanoscale localization of hydrocarbyl functional groups in the extracellular microenvironment on "cell-nano" interactions, we further immobilize the same set of hydrocarbyl-terminated NPs onto a glass substrate before seeding cells atop and incubating the seeded cells with the model NPs. Our results demonstrate that the functional groups on the surface of NP and those localized on the substrate play a synergistic role in mediating the endocytosis and exocytosis of NPs. They reveal the importance of the extracellular microenvironment in mediating the uptake and clearance of NPs by cells.

Secondly, we investigate how aerosolized NPs that contain different functional groups interact with the lungs following their inhalation by mice. Our model particle entails a 20 nm AuNP core and an outer shell of PEG strands that bear defined functional groups found in atmospheric particulates. Regardless of functional group, these ~50 nm NPs remain colloidally stable following aerosolization and incubation in bronchoalveolar lavage fluid (BALF), without pronouncedly crossing the air-blood-barrier. The type of BALF proteins adhered to the NPs is similar, but the composition of protein corona depends on functional group. By exposing mice to aerosolized NPs for 6 h, we demonstrate that the intrapulmonary distribution of NPs among the various types of cells (both found in BALF and lavaged lung) and the inflammatory responses are sensitive to the functional group of NPs and post-inhalation period (0 h, 24 h, or 48 h). By evaluating the pairwise correlations between the three variables of "lung-nano" interactions (protein corona, intrapulmonary cellular-level distribution, and inflammatory response), we reveal strong statistical correlations between the (1) fractions of albumin or carbonyl reductase bound to NPs, (2) associations of inhaled NPs to neutrophils in BALF or macrophages in the lavaged lung, and (3) level of total protein in BALF. Our results provide insights into the effect of functional group on lung-nano interactions and health risks associated with inhalation of PM0.1.

In conclusion, these results offer in-depth mechanistic information into "bio-nano" interactions of nanoparticles with cells as a function of functional group at in vitro and in vivo contexts. They offer new insights into the design of nanoparticles for targeting or evading certain cell types on the basis of functional group.

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