The Chinese University of Hong Kong

Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

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Date	:	26 September 2018 (Wednesday)
Time	:	2:30 p.m.
Venue	:	Room 222 Ho Sin Hang Engineering Building

Title: The Journey of Alkyl-Terminated Gold Nanoparticles into, En Route, and Out of the Cell

Alkyl groups (CnH2n+1) are prevalent in engineered bionanomaterials used for intracellular biomedical applications, like phospholipid-coated quantum dots for molecular imaging, lipid nanoparticles for gene delivery, and cholesterol-coated or vitamin E-coated nanoparticles for drug delivery. When elucidating the fundamental "bio-nano" interactions between alkyl-containing nanoparticles and the cell, previous researchers mostly treated alkyl-containing nanoparticles as a single hydrophobic entity and studied how hydrophobicity dictates the interactions between nanoparticles and mammalian cells. Yet the effect of alkyl as a functional group on the “bio-nano” interactions remains incomprehensively investigated.

We propose a platform for specifically addressing the role of alkyl groups in the interactions between nanoparticles and the cell. Termed “alkyl-PEG-AuNP", this largely hydrophilic platform contains a gold nanoparticle (AuNP) core, a shell of polyethylene glycol (PEG) strands, and minute amounts of alkyl groups at the periphery. Its key advantage lies in modularity, allowing for flexible adjustment of the density and type of alkyl groups to be attached. Specifically, we prepare PEGylated AuNPs that bear alkyl chains of varying carbon chain lengths (n) and loading densities, followed by investigating their journey into, en route, and out of Kera-308 keratinocytes.

Strikingly, provided a modest alkyl mass percentage of 0.2% (2 orders of magnitude lower than that of conventional lipid-based NPs) in their PEG shells, dodecyl-PEG-AuNPs (n=12) and octadecyl-PEG-AuNPs (n=18) enter Kera-308 cells up to 30-fold more than methoxy-PEG-AuNPs (no alkyl groups) and hexyl-PEG-AuNPs (n=6). Such strong dependence on n is valid for all serum concentrations considered, although enhanced serum levels can trigger the agglomeration of alkyl-PEG-AuNPs (without permanent aggregation of the AuNP cores) and attenuate their cellular uptake. Additionally, alkyl-PEG-AuNPs enter Kera-308 cells via the filipodia-mediated pathway and adopt the “endo-lysosomal” route of trafficking, but ~15% of them accumulate in the cytosol. Regardless of intracellular location, alkyl-PEG-AuNPs appear as individual entities after 24 h of incubation.

For Kera-308 cells treated with dodecyl-PEG-AuNPs or octadecyl-PEG-AuNPs, up to 87% of NPs leave the cell 24 h post-treatment, and their exocytosed amount is up to 2 orders of magnitude higher than that of methoxy-PEG-AuNPs. Dodecyl-PEG-AuNPs and octadecyl-PEG-AuNPs loaded with 0.5% alkyl chains leave Kera-308 cells three times more than those loaded with 6% alkyl chains. Moreover, the pathway for the exocytosis of alkyl-PEG-AuNPs is independent of uptake duration: upon either 1 h or 10 h of uptake and subsequent incubation in NP-free medium, we observe the excretion of dodecyl-PEG-AuNPs inside or near membrane-bounded vesicles. We demonstrate that the exocytosis of dodecyl-PEG-AuNPs involves unconventional organelle-based secretion but not cholesterol trafficking or recycling.

Results from our “bio-nano” studies accentuate the promise of incorporating alkyl groups as a strategy for boosting intracellular delivery of NPs. While many bionanomaterials rarely depart from the cell in abundant amounts after cellular entry due to their entrapment or degradation inside organelles, large fraction of alkyl-PEG-AuNPs can be excreted. With their high levels of endocytosis and exocytosis, our work offers insights into the design of alkyl-containing bionanomaterials with high cellular uptake, cytosolic accumulation with intracellular stability, and limited cellular retention.

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

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