The Chinese University of Hong Kong
Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

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Supervisor : Prof. CHOI Chung Hang Jonathan
Date : 22 July 2022 (Friday)
Time : 10:30 am
Venue : Room 1118, William MW Mong Engineering Building
Zoom Link : https://cuhk.zoom.us/j/96551753698?pwd=K08zSXZkbjhQUzZaaUFHbFRNbTZ2Zz09
Meeting ID : 965 5175 3698
Password : 145755

Title: Systemic Delivery of microRNA-146a for Reducing Atherosclerosis via RNA-coated Iron Oxide Nanoparticles

Atherosclerosis is a pathological process that underpins the progression of cardiovascular diseases such as stroke and coronary heart disease, both causing high mortality rates globally in the past 15 years according to the World Health Organization. As current forms of surgical intervention are invasive, the development of innovative, effective, and non-invasive technologies for inhibiting atherosclerosis are in great demand. Atherosclerosis treatments by gene regulation are garnering attention, yet delivery of gene cargoes to atherosclerotic plaques remains inefficient.

To improve the systemic delivery efficiency to the atherosclerotic plaque, we assemble the therapeutic microRNA-146a oligonucleotides, which regulate the NF-κB pathway, into a three-dimensional spherical nucleic acid for the treatment of atherosclerosis. Upon intravenous injection into apolipoprotein E knockout ($ApoE^{-/-}$) mice fed with a high-cholesterol diet, this nanoparticle naturally targets the SR-A scavenger receptor on plaque macrophages and endothelial cells, contributing to elevated delivery to the plaques (~1% of the injected dose). Repeated injections of the nanoparticle down-regulate genes related to immune response and vascular inflammation (e.g., TNF-α, IL-1β, and VCAM-1). Additionally, this treatment not only reduces the plaque size but also leads plaques to a more stabilized phenotype by enhancing the collagen content and reducing the necrotic core area. Finally, we find this non-cationic nanoparticle is significantly cleared 4 weeks post-treatment and does not change body weight, histological structure of major organs, liver function, or blood cell composition of mice. Hence, we conclude it is safe to deliver microRNA-146a-coated nanoparticles for alleviating atherosclerosis without inducing toxicity.

In summary, this thesis offers mechanistic insights into the in vivo interactions of microRNA-based nanostructures in atherosclerotic plaques. Our findings show a safe and effective treatment of atherosclerosis and reveal the promise of nucleic acid nanotechnology for cardiovascular disease.

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

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