CHEMICAL ENGINEERING

DISTINGUISHED YOUNG SCHOLARS SERIES

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Exploiting the Interactions between Nanomaterials and Circulatory Barriers to Combat Vascular Diseases

ABSTRACT: One-dimensional (1D) nanoparticles and two-dimensional (2D) nanosheets have demonstrated tremendous potential for a variety of nanomedicine and theranostic applications, particularly for drug delivery, biomedical imaging, and disease diagnostics.[1,2] However, due to the inability of these nanomaterials to overcome the different biological phenomena taking place in the circulatory system (i.e., circulatory barriers), such as biomolecule adsorption, blood flow shear stress, phagocytic clearance, and limited diffusion across vascular endothelium, the nanomaterial delivery and theranostic efficacies remain poor.[3,4] Startlingly, the average delivery efficiency of nanomaterials towards target tissues over the past decade has been reported to be less than 1%.[4] Numerous attempts have been made to mitigate circulatory barriers by controlling the behaviors of nanomaterials in physiological environments, which so far, has been achieved primarily through manipulating nanomaterial properties. Many of these efforts, nevertheless, fail to adequately address the issue of circulatory barriers due to a lack of fundamental understanding of the nanomaterial-barrier interactions. Moreover, most studies have varied only one or two nanomaterial properties when investigating the impact of nanomaterial design on barrier interactions. Crucially, the interrelationship of several properties of nanomaterials in influencing their interactions with circulatory barriers remains unclear.

In this seminar, I will present my research on the interactions of nanomaterials with circulatory barriers and how these findings can be translated into universal principles for guiding more effective design of theranostic nanoagents to overcome multiple circulatory barriers and combat vascular diseases (Fig. 1A). First, employing graphene oxide (GO) nanosheets as model 2D nanomaterials, I will describe my PhD work in formulating biocompatible GO nanosheets resistant to non-specific biomolecule adsorption for preventing

and minimizing thrombosis (Fig. 1B).[5-8] Second, using polymeric nanoparticles as model 1D nanomaterials, I will discuss my recent postdoctoral work in formulating nanocarriers for vascular imaging capable of evading immune surveillance and localizing preferentially at the vascular endothelium (Fig. 1C).[9] These theranostic nanoagents were designed through systematic interrogations of the interactions between nanomaterials and biological entities responsible for circulatory barriers, including plasma proteins, blood cells, macrophages, and endothelial cells. Importantly, the interdependent effects of numerous nanomaterial properties, specifically size, size distribution, surface functionality, surface charge, and lipophilicity, on the triggered biological responses from molecular to organism levels were comprehensively evaluated.

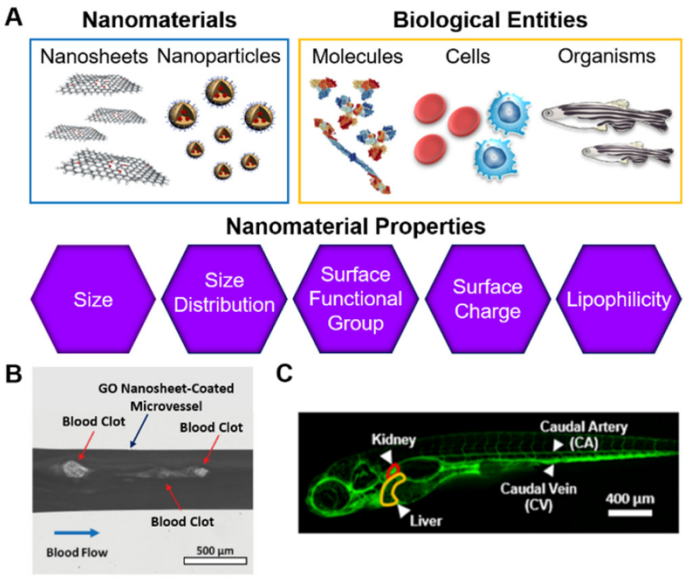

Figure 1. (A) Schematic of the study on the interactions between nanomaterials and biological entities responsible for circulating barriers from molecular to organism levels, considering the interdependency of multiple nanomaterial parameters. **(B)** GO nanosheets for thrombosis prevention and therapy. **(C)** Polymeric nanocarriers (in green) for vascular imaging.

Overall, this talk will shape our understanding on how the exploitation of nanomaterial-barrier interactions improves the rational engineering of theranostic nanoagents to conquer multiple biological barriers and fight vascular diseases. Furthermore, the design framework originated from this study can be readily translated into the formulation of nanoagents for diagnosing and treating other diseases. The work presented here has been recognized with several awards, notably JSPS HOPE Fellowship from the Japan Society for the Promotion of Science, Young Scientist Award from the European Materials Research Society and NUSS Outstanding Achievement Award from the National University of Singapore.

BIOGRAPHY: Kenry is a Research Fellow at the Department of Imaging, Dana-Farber Cancer Institute and Harvard Medical School. His research focuses on understanding and modulating the interactions between nanomaterials and biological barriers to improve the formulation of theranostic nanoagents with enhanced delivery and theranostic efficacies. Prior to his current appointment, Kenry did his postdoctoral research at the Department of Chemical and Biomolecular Engineering, National University of Singapore. He received his Ph.D. in Biomedical Engineering from the same institution and B.Eng. in Electrical and Electronic Engineering (First Class Honors) from Nanyang Technological University, Singapore. Kenry has received numerous awards and honors for his academic and research achievements, notably JSPS HOPE Fellowship (Japan Society for the Promotion of Science), Young Scientist Award (European Materials Research Society), ASEAN Outstanding Engineering Achievement Award (ASEAN Federation of Engineering Organizations), and NUSS Outstanding Achievement Award (National University of Singapore). Apart from research, he is passionate about mentorship and entrepreneurship.

LECTURE 1:00 - 2:00 Zoom
Networking Hour on Zoom Following

[1] Chen et al., Chemical Reviews 2016, 116, 2826-2885.
[2] van der Meel et al., Nature Nanotechnology 2019, 14, 1007-1017.
[3] Meng et al., Biomaterials 2018, 174, 41-53.
[4] Wilhelm et al., Nature Reviews Materials 2016, 1, 16014.
[5] Kenry et al., Small 2015, 11, 5105-5117.
[6] Kenry et al., Nanoscale 2016, 8, 9425-9441.
[7] Kenry et al., NPG Asia Materials 2017, 9, e422
[8] Kenry et al., Nanoscale 2017, 9, 14065-14073.
[9] Kenry et al., ACS Nano 2020, 14, 4509-4522.