NANYANG TECHNOLOGICAL UNIVERSITY
SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Synthetic Macromolecules That Overcome Resistance in Infection and Cancer

Date: 14 October 2019
Time: 1.30 p.m.
Venue: Classroom 4, SBS
Hosted By: A/P Koh Cheng Gee

Speaker:

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With the increased prevalence of drug resistance in cancer and infection, and the lack of new therapeutics, there is an urgent need for development of innovative antimicrobial and anticancer therapeutics. Macromolecular antimicrobial agents including cationic polymers and peptides have recently received increasing attention as they can selectively target and disintegrate bacterial membranes *via* electrostatic interaction and insertion into the membrane lipid domains, avoiding potential bacterial resistance. Many antimicrobial peptides have seen limited clinical applications in treatment of systemic infections due to toxicity and rapid degradation. As a result, a plethora of bio-inspired synthetic polymers have been developed and are achieving considerable success in overcoming many drawbacks found in using peptides.

In this talk, biodegradable antimicrobial polymers will be discussed. The antimicrobial polymers are based on biodegradable guanidinium-functionalized polycarbonates, which are synthesized *via* organocatalytic living ring-opening polymerization. This synthetic platform yields polymers with well-defined molecular weight and structure, which is crucial in the future clinical applications as individual molecular weight fractions of a polydisperse system are expected to exhibit distinct pharmacological activities *in vivo*. Polycarbonates with various molecular compositions have been designed and synthesized. These polymers killed bacteria based on a unique mechanism - membrane translocation followed by precipitation of cytosolic materials. The polycarbonates with optimal hydrophilicity/hydrophobicity balance have strong activity against multidrug-resistant (MDR) Gram-positive and Gram-negative bacteria without inducing significant toxicity both *in vitro* and *in vivo*. The optimized polymers have been tested in several MDR bacterial infection mouse models, and the results are promising. Unlike antibiotics, multiple treatments using these polymers do not cause resistance. In addition, novel macromolecules have also been designed and synthesized to overcome drug resistance in cancer. These macromolecules have been demonstrated to be effective against various cancer cell lines *in vitro* and in a PDX HCC mouse model. Repeated use of the macromolecules does not induce resistance in cancer cells. In addition, the macromolecules prevented cancer metastasis in a 4T1 mouse breast cancer model. These synthetic macromolecules hold potential for use in the treatment of MDR infection and cancer.