Department of Biomedical Sciences
&
State Key Laboratory in Marine Pollution

Present a seminar

"Marine Invertebrates and their Associated-Microorganisms, Untapped Resources for Novel Drug Leads to Treat Metabolic Diseases and Osteoporosis"

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Date : 29 August 2018
Time: 3:00pm to 5:00pm
Venue: Chu Wong Yim Fong Classroom (P4704), 4/F, Yeung Kin Man Academic Building

Abstract

Obesity- and bone-related diseases such as diabetes, atherosclerosis, and osteoporosis are becoming more and more of a threat to public health. Mimicking physical workout, precise blocking of the physiological processes or in combination will eventually lead to innovative drugs for treatment of the diseases.

Marine invertebrates, such as sponges, have been known to be the richest source of bioactive natural products. Nearly 30% of marine natural products discovered so far have been isolated from sponges alone. Marine sponges contain diverse microorganisms such as archaea, bacteria, cyanobacteria, algae, phytoplankton and fungi in the inner tissues up to 50% of dry weight. Recently microbial symbionts of sponges were demonstrated to be the real producers of bioactive natural products isolated from marine sponges and can be regarded as an untapped resource for innovative drug discovery. We established diverse libraries of marine invertebrates and their symbiotic microorganisms for facilitating discovery of novel bioactive compounds.

The CMDD has a powerful drug lead discovery platform including a robotic system equipped with a variety of biochemical instruments along with LC-tandem MS, NMR, synthetic and animal facilities. We utilized both molecular and empirical approaches to discover novel drug leads from marine natural products to treat metabolic and bone diseases. The molecular approaches were target-based high throughput screenings with nuclear receptors, kinases/phosphatases and ion-channels, which regulate many aspects of metabolism, inflammation, and muscle fiber transformation. In the other hand, we adopted phenotypic screening methods to identify bioactive compounds with novel underlying mechanisms to treat the diseases.

Our approaches led to identification of novel compounds as ligands of the nuclear receptors, blockers of ion channels, modulators of bone remodeling pathways. Pharmacological treatment of mice with bioactive compounds totally reversed drug-induced and high fat diet-induced hepatic steatosis *in vivo*. They ameliorated diabetes and protected mice from obesity in diet-induced and genetically disposed models. The compounds also gave potent anti-atherogenic effect in mice models. In addition, we developed potent ligands for nuclear receptors in combination with molecular modeling and medicinal chemistry. The ligands improved physical endurance performance 2-3 folds, which eventually led to anti-obesitic and anti-diabetic effect with challenge of high fat-diet. The compounds gave the physiological effect through inducing muscle fiber transformation, insulin sensitivity, and increasing β-oxidation *in vivo*. Finally one of the bone remodeling modulators with dual activity in both osteoclast and osteoblast differentiation *in vitro* showed good efficacy in an animal disease model of bone formation. These results clearly demonstrate that bioactive compounds from marine sources and their synthetic derivatives have potential for drug candidates to treat human diseases such as obesity, diabetes, fatty liver, atherosclerosis, and osteoporosis.

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All are welcome!