Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by Prof. Wang Yue:

Date: 10 September 2014, Wednesday
Time: 10:00AM – 11:00AM
Venue: Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Speaker: A/Prof. Scott Summers, Duke-NUS Graduate Medical School, Singapore and the Stedman Center for Metabolic Research, USA
Title: Sphingolipids and Metabolic Disease

During obesity, sphingolipids such a ceramides accumulate in the liver and other tissues, where they have deleterious effects on tissue metabolism and function. Notably, genetic or pharmacological inhibition of enzymes that drive ceramide synthesis (e.g. serine palmitoyltransferase, dihydroceramides desaturase, etc.) in mice ameliorates virtually all complications of obesity including insulin resistance, steatosis, diabetes, hypertension, cardiomyopathy, and atherosclerosis.

Ceramides are actually a diverse family of molecules that differ in the composition of their acyl-chain. This molecular entity is added by a family of six ceramide synthases (CerS) that differ by substrate preference and tissue distribution. One family member, ceramide synthase 2 (CerS2), exclusively makes long-chain ceramides (C22-24) and is expressed at particularly high levels in the liver. To understand what these long-chain ceramides do to liver metabolism, we challenged heterozygous $CerS2^{+/-}$ mice, which appear phenotypically health on a chow diet, with a high fat feeding regimen. $CerS2^{+/-}$ mice were highly susceptible to insulin resistance, hepatic steatosis, and steatohepatitis. Expectedly, liver sphingolipids were slightly devoid of very long acyl chains. However, they demonstrated remarkable increases in C16-ceramides and sphinganine following high fat feeding, owing in part to increased expression of ceramide synthase-5 and -6. The increased steatosis was attributable to large deficits in mitochondrial respiration leading to impaired lipid oxidation and increased expression of PPARgamma and its downstream targets CD36 and Fsp27. Together these observations suggest that minor adjustments to the sphingolipids milieu has profound effects on liver metabolism and nutrient homeostasis. Moreover, they provide the first evidence in vivo regarding which ceramides (C16-ceramides) are involved in the onset of metabolic disease.

Biography:
Dr. Summers' interest in diabetes originated when he was a teenager, and his father was diagnosed with the disease. Currently Dr. Scott Summers holds joint appointments with the Stedman Center in Durham and the new Duke-NUS Medical School in Singapore. His integrated laboratories at these two locations study the relationship between the accumulation of ectopic fats during obesity with the development of diabetes and cardiovascular disease. In particular, Dr. Summers' group made the observation in 2007 that a particular derivative of fat, termed ceramide, is one of the more toxic metabolites which accumulates in the obese. His current efforts are directed at assessing the

therapeutic potential of modulating levels of ceramides in the treatment of metabolic diseases and elucidating the molecular networks controlling ceramide production and action. At Duke-NUS he directs the metabolomics and mouse metabolic phenotyping facilities.

Prior to joining Duke, Dr. Summers held faculty appointments at Colorado State University and the University of Utah, and he conducted postdoctoral training at the University of Pennsylvania. He has received grant support from the USA National Institutes of Health, American Diabetes Association, American Heart Association, March of Dimes, the National Medical Research Council of Singapore, the Ministry of Education of Singapore, and the Agency for Science, Technology and Research (A*STAR) of Singapore.

ALL ARE WELCOME *(No registration required)*