The 147th iCeMS SEMINAR

Fri 15 Nov 2013
16:30-18:00

Venue:
2nd Floor Seminar Room (#A207)
iCeMS Main Building (#70), Kyoto University

<Part 1: 16:30-17:15>

Prof Dennis E Vance

School of Molecular and Systems Medicine
University of Alberta, Canada

"Phospholipid Methylation Has an Unexpected Role in Obesity and Insulin Resistance"

<Part 2: 17:15-18:00>

Prof Jean E Vance

Department of Medicine
University of Alberta, Canada

"Cholesterol Transport in the Brain and Niemann-Pick C Disease"

Contact: iCeMS Ueda Group at ueda-g@icems.kyoto-u.ac.jp
Hosted by: iCeMS (Institute for Integrated Cell-Material Sciences), Kyoto University

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Abstracts for November 15 iCeMS Seminar

Prof Dennis E Vance <*Part 1: 16:30-17:15*>

Phosphatidylcholine is made in the liver via the choline pathway and via the conversion of phosphatidylethanolamine to phosphatidylcholine by 3 transmethylation reactions from AdoMet catalyzed by phosphatidylethanolamine N-methyltransferase (PEMT). PEMT is a 22.3 kDa integral transmembrane protein of the endoplasmic reticulum and mitochondria-associated membranes. The only tissue with quantitatively significant PEMT activity is liver. PEMT activity is regulated by thee concentration of substrates (phosphatidylethanolamine and AdoMet) as well as the ratio of AdoMet to AdoHcy. Studies with mice that lack PEMT have provided novel insights into the function of this enzyme. PEMT activity is required to maintain hepatic membrane integrity and for the formation of choline when dietary choline supply is limited. PEMT is required for normal secretion of very low-density lipoproteins. The lack of PEMT protects against diet-induced atherosclerosis in two mouse models. Most unexpectedly, mice that lack PEMT are also protected from diet-induced obesity and insulin resistance. However, mice lacking PEMT have increased susceptibility to diet-induced fatty liver and steatohepatitis.

Prof Jean E Vance <*Part 2: 17:15-18:00*>

Niemann-Pick type C (NPC) disease is an inherited neurodegenerative disease in which the egress of cholesterol from late-endosomes/lysosomes is impaired. We have studied cholesterol metabolism and trafficking in primary neurons and glial cells isolated from a mouse model of NPC disease. Recent experiments indicate that a low (0.1 mM), but not a high (>1mM), dose of the cholesterol-sequestering agent, cyclodextrin, normalizes cholesterol metabolism and trafficking in these neurons and glial cells, and markedly increases lifespan of the mice. In NPC neurons and glia, the cyclodextrin mobilizes stored cholesterol from the lysosomes, thereby increasing the cholesterol content of the endoplasmic reticulum, the site at which cholesterol homeostasis is regulated. These studies support the use of low doses of cyclodextrin for treatment of NPC patients.

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