第135回スポーツサイエンス研究会

日時　2014年5月20日（火）　16:30より

場所　早稲田大学　所沢キャンパス　100号館 205室

演題　Muscle phosphatidylethanolamine synthesis maintains sarcoplasmic reticulum integrity to regulate contractile function and insulin sensitivity

Dr. Katsuhiko Funai
（East Carolina University, USA）

Skeletal muscle insulin resistance is an early and essential defect in the development of type 2 diabetes. Molecular mechanisms responsible for reduction in skeletal muscle insulin-stimulated glucose disposal remain elusive. Previously we implicated that alteration in phospholipid composition at the sarcoplasmic reticulum (SR) may contribute to this process. Here we show that choline/ethanolamine phosphotransferase-1 (CEPT1), a terminal enzyme in Kennedy pathway's phosphatidylethanolamine (PE) synthesis, regulates muscle insulin sensitivity. In C2C12 cells, lentivirus-mediated knockdown of CEPT1 resulted in altered SR phospholipid compositions and calcium flux. In mice and in humans, muscle CEPT1 abundance was associated with obesity and inversely correlated with insulin sensitivity. Mice with skeletal muscle-specific knockout of CEPT1 exhibited improved insulin sensitivity measured by glucose and insulin tolerance tests, hyperinsulinemic euglycemic clamp and 2-deoxyglucose uptake in isolated muscles. In CEPT1 deleted muscles, altered SR phospholipid milieu reduced sarco/endoplasmic reticulum Ca2+ ATPase (SERCA)-dependent calcium uptake. This led to the activation of calcium signaling pathways, a known insulin sensitizer. However, dysregulated muscle SR calcium handling made these mice weak and exercise intolerant. Herein we propose that aberrant lipid flux in muscles can place metabolic stress on SR, an "SR stress", that could compromise muscle contractile property through its action on membrane phospholipid composition. Diet-induced increase in skeletal muscle CEPT1 protects muscles from developing diet-induced SR stress. Paradoxically, this appears to come at the expense of promoting skeletal muscle insulin resistance.

早稲田大学 スポーツ科学学術院
Faculty of Sport Sciences, Waseda University

世話人：正木宏明・紙上敬太
早稲田大学　スポーツ科学学術院
E-mail: k-kamijo@aoni.waseda.jp