Intramyocellular Lipid Accumulation After High-Fat Diet Is Associated with the Gene Expression Involved in Lipid Metabolism in Skeletal Muscle of Non-Obese Men

SAORI KAKEHI*1) 2), YOSHIYUKI TAMURA*1) 2), KAGEUMI TAKENO*1), YUKO SAKURAI*1), MINAKO KAWAGUCHI*1), TAKAHIRO WATANABE*1), TAKASHI FUNAYAMA*1), FUMIHiko SATO*1), SHIN-ICHI IKEDA*1) 2), AKIO KANAZAWA*1), YOSHIO FUJITANI*1), RYUZO KAWAMORI*1) 2), HIROTAKA WATADA*1) 2) 3) 4)

*1) Department of Metabolism and Endocrinology, Juntendo University Graduate School of Medicine, Tokyo, Japan, *2) Sportology Center, Juntendo University Graduate School of Medicine, Tokyo, Japan, *3) Center for Therapeutic Innovations in Diabetes, Juntendo University Graduate School of Medicine, Tokyo, Japan, *4) Center for Molecular Diabetology, Juntendo University Graduate School of Medicine, Tokyo, Japan

Insulin resistance in skeletal muscle is one of the main features of metabolic syndrome, and it has been associated with lifestyle factors including diet 1) 2). Whereas the mechanisms underlying the development of insulin resistance have not been fully elucidated, the accumulation of intramyocellular lipid (IMCL) is recognized as an important determinant of insulin resistance, and is increased by a high-fat diet (HFD) 3) 4). The fat content of food is a determinant of the accumulation of IMCL. The effects of HFD on IMCL and insulin sensitivity are highly variable, although, it had shown that a short term (3-day) high-fat diet (HFD) in human increases the IMCL level and impairs insulin sensitivity in skeletal muscle 3) 5).

The aim of this study was to identify the genes in muscle that are related to this inter-individual variation. Fifty non-obese healthy men were recruited for this study. Before and after HFD for 3 days, IMCL levels in the tibialis anterior were measured by 1H-magnetic resonance spectroscopy, and peripheral insulin sensitivity was evaluated by glucose infusion rate (GIR) during the euglycemic–hyperinsulinemic clamp. We observed a significant increase in TA-IMCL by HFD. GIR was significantly decreased by HFD. We also observed a negative correlation between changes in TA-IMCL and GIR by HFD (r = -0.37, p < 0.01). Subjects who showed a large increase in IMCL and a large decrease in GIR by HFD were classified as the high-responder (HR), and the subjects who showed a small increase in IMCL and a small decrease in GIR were classified as the low-responder (LR). In 5 subjects in each group, the gene expression profile of the vastus lateralis muscle was analyzed by DNA microarray analyses. Before HFD, gene expression profiles related to lipid metabolism were comparable between the 2 groups. Gene Set Enrichment Analysis demonstrated that 5 gene sets related to lipid metabolism were up-regulated by HFD in the HR group, but not in the LR group. Changes in gene expression patterns were confirmed by qRT-PCR using more samples (LR: n = 9; HR: n = 11). These results suggest that IMCL accumulation/impaired insulin sensitivity after HFD is closely associated with changes in the expression of genes related to lipid metabolism in muscle.

Key words: high fat diet, intramyocellular lipid, insulin sensitivity, skeletal muscle

Corresponding author: Saori Kakehi
Sportology Center, Juntendo University Graduate School of Medicine
2-1-1 Honcho, Bunkyo-ku, Tokyo 113-8421, Japan
TEL: +81-3-3813-3111 FAX: +81-3-3813-5996 E-mail: skakehi@juntendo.ac.jp
The 2nd Congress, International Academy of Sportology (Held on Sep. 12, 2015)
[Received Dec. 18, 2015]
References


