Adipose-Specific MIMS1 Overexpression Preserves Brown Adipose Tissue Function and Improves Metabolic Adaption to Chronic High-Fat Diet

Yung-Yu Cheng[1], Yubo Wang[1], Yumei Zhou[1], Miguel A. Gutierrez-Monreal[2], Zhiyong Cheng[3,4,5,6], Karyn A. Esser[2,5], Feng Yue[1,2,4,5,6*]

[1]Department of Animal Sciences, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611, USA
[2]Department of Physiology and Aging, College of Medicine, University of Florida, Gainesville, FL 32610, USA
[3]Department of Food Science and Human Nutrition, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611, USA
[4]Nutritional Science Doctoral Program, Center for Nutritional Science, University of Florida, Gainesville, FL 32611, USA
[5]Center for Integrative Cardiovascular and Metabolic Diseases, University of Florida, Gainesville, FL 32610, USA
[6]UF Diabetes Institute, University of Florida, Gainesville, FL 32611, USA

Brown adipose tissue (BAT) is a mitochondria-rich thermogenic tissue that contributes to systemic energy and metabolic homeostasis. MIMS1 (formerly FAM210A) is a mitochondrial inner membrane protein required for cristae remodeling and BAT thermogenic function. Clinically, adipose MIMS1 expression is inversely associated with waist-to-hip ratio and body mass index, whereas adipocyte-specific loss of MIMS1 exacerbates HFD-induced metabolic dysfunction in mouse. However, the effects of increasing adipose MIMS1 expression remain unclear.

We generated adipose-specific inducible MIMS1-overexpressing (Adipoq-rtTA;MIMS1) mice and fed adult mice with chow or HFD containing doxycycline (200 mg/kg diet) for six months. Metabolic phenotypes were assessed by body weight and composition, glucose and insulin tolerance tests, indirect calorimetry, and thermal imaging. BAT was evaluated by histology and Western blotting for mitochondrial proteins. In a developmental cohort, dams received doxycycline during pregnancy and lactation, and offspring were maintained on doxycycline chow after weaning until one month of age.

MIMS1 overexpression was confirmed in BAT under chow and chronic HFD conditions. Under chow-fed conditions, BAT morphological and histology, and glucose and insulin tolerance were comparable between groups. Under chronic HFD conditions, MIMS1-overexpressing mice showed preserved BAT morphology, prevention of HFD-induced whitening, increased BAT thermogenic activity, and enhanced insulin responsiveness despite comparable body weight and composition. Oxygen consumption and carbon dioxide production were consistently higher but did not reach statistical significance. OPA1, OXPHOS proteins, and UCP1 were not detectable altered. In the developmental cohort, MIMS1 overexpression increased BAT thermogenic activity without apparent changes in OPA1 and OXPHOS proteins.

These findings indicate that adipose MIMS1 overexpression preserves BAT function and improves systemic metabolic adaptation to chronic HFD.