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TITLE: Expression profiles and coexpression network analyses of long noncoding RNAs in brown adipose tissue of obesity-prone and obesity-resistant mice fed a high-fat diet

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ABSTRACT

An obesity-prone (OP) or an obesity-resistant (OR) phenotype exists under the same diet type, including a high-fat diet (HFD). Brown adipose tissue (BAT) functions to dissipate energy in response to cold exposure or overfeeding. Long noncoding RNAs (LncRNAs) are an important class of pervasive genes involved in a variety of biological functions. However, the potential biological functions of lncRNAs related to OP or OR phenotype in BAT have not been fully understood.

Here, we constructed a high-fat diet-induced OP and OR mouse model. Transcriptome analyses were performed to obtain the expression profiles of mRNAs and lncRNAs in the BAT of the OP and OR mice. We detected 228 differentially expressed lncRNAs and 1159 differentially expressed mRNAs between the OP and OR groups. We further analysed differentially expressed Genes (DEGs) , using Gene set enrichment, Gene Ontology, and Kyoto Encyclopedia of Genes and Genomes pathway analysis. Co-expression analysis and target gene prediction were further performed to determine the transcriptional regulatory relationship of the differentially expressed lncRNAs and mRNAs between the OP and OR groups. The expression levels of the candidate lncRNAs and mRNAs were validated in brown adipocytes activated with norepinephrine bitartrate monohydrate (NE) and Forskolin in vitro and in the BAT from cold-induced thermogenesis mice in vivo by qPCR. Our data suggest that two candidate lncRNAs (A530050N04Rik and 4930528G23Rik) and four candidate mRNAs (Lep, Oxtr,Cars2, and Gmpr) were involved in weight and metabolism regulation by cAMP and thermogenesis pathways.

Significant differences were detected between the transcriptomes of the BAT from OP and OR mice. The differentially expressed lncRNAs and mRNAs were enriched in two potential pathways involved in weight and metabolism regulation. These results provide clues to the molecular mechanisms of metabolic disorders as well as candidate biomarkers of risk for obesity.

BIOGRAPHY

Dr.Zhu is a Qiushi Professor at Zhejiang University, CMB Distinguished Professor, a Professor at Children's Hospital of Zhejiang University School of Medicine, and a Professor at the University of Toronto (Status Only), the Founding Director of Chronic Disease Research Institute, and the Chair of Department of Nutrition and Food Hygiene at Zhejiang University School of Public Health, the Founding Director of Obesity and Body Composition Research Center at Zhejiang University School of Medicine. Dr.
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Dr.Zhu graduated from Nagoya University School of Medicine, Japan, and obtained PhD in 1997, was an Assistant Professor at Nagoya University from 1997 to 2000. From 2000 to 2003, he received Post-doctoral training at Obesity Research Center, Human Nutrition Institute at Columbia University College of Physicians and Surgeons. He joined the faculty as an Assistant Professor (tenure-track) from 2003 to 2007 at Medical College of Wisconsin and Adjunct Associate Professor from 2008 to 2010. Dr. Zhu received US CMB Distinguished Professorship Award in 2009, University Silver Medal from Heidelberg University in 2012, and the Most Cited Chinese Researchers in Medicine (Elsevier) in 2014 to 2020.

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