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TDAG51 is a novel mediator of age-onset obesity, hepatic steatosis and insulin resistance

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Abstract

Regulation of energy metabolism plays a critical role in the prevention of obesity, diabetes and hepatic steatosis. T-cell death associated gene 51 (TDAG51), a pleckstrinhomology-like domain family member, has been associated with enhanced apoptosis when overexpressed. However, we report here that TDAG51 deficiency contributes to the development of age-onset obesity, hepatic steatosis and insulin resistance.To assess the effects of TDAG51 on energy metabolism, cell culture studies and TDAG51-deficient (*TDAG51*$^{-/-}$) mice were utilized in these studies. TDAG51 expression was examined during adipocyte differentiation and its role in adipogenic potential was determined in TDAG51-deficient preadipocytes. Weight gain, insulin sensitivity, metabolic rate, and liver lipid content were assessed in*TDAG51*$^{-/-}$mice and compared with wild type (WT) C57BL/6 mice. In addition to its high expression in liver, TDAG51 was detected in several other murine tissues including white adipose tissue (WAT) and lung. TDAG51 is down-regulated during adipogenesis and *TDAG51*$^{-/-}$ preadipocytes exhibit greater lipid accumulation and adipogenic potential. *TDAG51*$^{-/-}$ mice fed a standard chow diet exhibit greater body and WAT mass, have reduced energy expenditure, display mature-onset insulin resistance, and are predisposed to hepatic steatosis. *TDAG51*$^{-/-}$ mice have increased hepatic triglyceride content and SREBP-1 target gene expression. Further, TDAG51 expression is dramatically reduced in multiple mouse models of hepatic steatosis that develop insulin resistance. Taken together, our findings suggest that TDAG51 is a novel mediatorof energy homeostasis and adipogenesis, and thus, may be a therapeutic target for the treatment of obesity and insulin resistance.

Biography

Richard Austin obtained his PhD in Medical Sciences at McMaster University and trained as a postdoctoral fellow in the Department of Human Genetics, Hospital for Sick Children, Toronto. He is currently a Professor in the Department of Medicine, McMaster University and is the Amgen Canada Research Chair in Nephrology, St. Joseph's Healthcare Hamilton. He is also the Research Director at the Hamilton Centre for Kidney Research and is a Career Investigator of the Heart and Stroke Foundation of Canada. Dr. Austin holds multiple peer-reviewed research grants and has published over 100 peer-reviewed papers, book chapters and review articles.