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The ghrelin receptor regulates obesity by modulating heat production

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Abstract

Aging is associated with increased adiposity in white fat and impaired thermogenesis in brown fat, both of which contribute to increased incidences of obesity and type 2 diabetes. Ghrelin is the only known circulating orexigenic hormone that promotes adiposity. We previously showed that the stimulatory effect of ghrelin on appetite is mediated though the ghrelin receptor (growth hormone secretagogue receptor, GHS-R). Here, we show that ablation of GHS-R reduces adiposity and improves insulin sensitivity during aging. Compared to wild-type mice, old *Ghsr*-/- preserve a healthier lipid profile and exhibit elevated energy expenditure, yet the Ghsr-/- mice have similar food intake and locomotor activity. GHS-R expression in white and brown fat increases with age. GHS-R ablation reduces glucose/lipid uptake and lipogenesis in white fat, but increases lipid reserves and enhances thermogenic capacity in brown fat of old mice. Moreover, old *Ghsr*-/- mice have higher core body temperate and show increased expression of mater thermogenic regulator UCP1. Furthermore, in brown adipocyte cultures, ghrelin suppresses the expression of lipogenic and thermogenic genes, while GHS-R antagonist enhances the expression of these genes and abolishes ghrelin's effect. These findings collectively suggest GHS-R is important novel regulator of thermogenesis in brown fat. GHS-R ablation prevents decline of thermogenesis during aging, thus attenuating age-associated obesity and insulin resistance. GHS-R antagonists may represent a novel approach to combat obesity during aging without the need for dieting or exercise.

Biography

Yuxiang Sun received her MD from Beijing Medical University, P. R. China and PhD at the University of Manitoba, Canada. She subsequently received postdoctoral training at Baylor College of Medline. She is currently a principle investigator at Baylor College of Medicine. Her research interests are obesity, diabetes and metabolic regulation. He has published more than 40 peer reviewer papers many of which are in high ranking journals such as Cell Metabolism, JCI, PNAS, amd Aging Cell. Currently, she serves as reviewer for a number of endocrine journals, and she is the Editorial Board Member of *World Journal of Diabetes* (*WJD*).