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The expression of rat resistin isoforms is differentially regulated in visceral adipose tissues: effects of aging and food restriction

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Abstract

Two variants of the adipose hormone resistin are generated by alternative splicing in Wistar rats. Here we analyzed the expression of these resistin variants in 2 main visceral adipose depots, epididymal and retroperitoneal, as well as the resistin serum concentration during aging and food restriction. Total protein levels of resistin were also analyzed in extracts from both visceral adipose depots. Resistin variants show similar patterns of relative expression in visceral adipose tissues in 3-month–old rats, representing the short variant, s-resistin, which is 15% of the full-length transcript. However, only epididymal, but not retroperitoneal, fat pad shows a decrease in both messenger RNA and protein levels of resistin isoforms with aging. Food restriction decreases adiposity index in 8- and 24-month–old animals to values even lower than those of 3-month–old animals. Food restriction decreases resistin expression in both adipose tissues in 8-month–old but not in 24-month–old rats. Interestingly, concomitant with the improvement of insulin sensitivity asserted by homeostasis model assessment, resistin serum levels decrease only in food-restricted 8-month–old animals. In contrast, food restriction up-regulates s-resistin messenger RNA in epididymal adipose tissue, whereas no significant changes are appreciated in retroperitoneal adipose tissue. These data indicate that both forms of resistin are differentially regulated by fat depot location, aging, and even nutritional status, suggesting that alternative splicing plays a key role in this differential regulation.

1. Introduction

Resistin is a cysteine-rich hormone secreted by adipose tissue that belongs to the resistin-like molecules family [1]. Early studies showed that in vivo administration of recombinant resistin impairs glucose tolerance and insulin actions in normal mice, whereas administration of anti–resistin antibody enhances the insulin sensitivity of insulin-resistant and obese mice [2]. This initial observation led to the hypothesis that resistin could act in promoting insulin resistance in different tissues, linking obesity and type 2 diabetes mellitus [2]. It has been reported that mice lacking resistin display low blood glucose levels after fasting and decreased expression of gluconeogenic enzymes, suggesting a role for resistin in mediating hyperglycemia associated with obesity [3]. In agreement with these proposals, several reports seem to confirm that chronic hyperresistinemia impairs glucose metabolism, leading to hyperinsulinemia; hypertriglyceridemia; insulin resistance in skeletal muscle, liver, and adipose tissue; and glucose intolerance [4,5].

Visceral fat has been identified as a risk factor for the development of insulin resistance and type 2 diabetes mellitus. Increased levels of visceral adipose tissue (VAT) are correlated with decreased sensitivity to insulin [6,7]. Visceral adipose tissue is a major source of resistin [8], and increased adiposity correlates well with increased resistin plasma levels [9]. In agreement to this, Gabriely and coworkers [6] demonstrated the improvement of peripheral and hepatic insulin sensitivity in aged rats by removing the retroperitoneal and epididymal fat pads. These results

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