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Adiponectin and the cardiometabolic syndrome: An epidemiological perspective

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Adiponectin is an adipocyte-derived plasma protein with cardiovasculo-protective and anti-diabetic properties. Plasma adiponectin levels are low in patients with the cardiometabolic syndrome (a cluster of multiple risk factors based on visceral fat accumulation). Routine measurement of plasma adiponectin may be useful to encourage life-style changes.

Introduction

The metabolic syndrome (or cardiometabolic syndrome), a tetrad of hypertriglycidemia, low serum high-density lipoprotein cholesterolemia (HDL-C), hyperglycaemia, and hypertension, has become the common basis of atherosclerotic cardiovascular diseases (CVD). Accumulation of intra-abdominal visceral fat stands upstream of various risk factors. Dysfunction of adipocyte is the cellular basis of this cascade.

Adiponectin is an adipocyte-specific protein abundantly present in the plasma. Since its discovery, numerous experimental and clinical studies have demonstrated that adiponectin has anti-atherogenic, anti-diabetic and anti-inflammatory properties. However, plasma adiponectin levels are low in subjects with visceral fat accumulation. Hypoadiponectinemia seems to play an important role in the pathogenesis of visceral fat syndrome. In this chapter, we discuss the concept and molecular mechanisms of visceral fat syndrome, discovery of adiponectin and epidemiological perspective of this molecule in the visceral fat syndrome.

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Visceral fat syndrome

The World Health Organization has declared CVD as a global health problem in both developing and developed countries accounting for almost 30% of deaths worldwide. Various pathogenetic conditions contribute to the development of CVD. Firstly, high levels of low-density lipoprotein cholesterol (LDL-C) have been identified as the most important culprit. The molecular mechanism responsible for the high levels of LDL, oxidized LDL and their receptors have been clarified and strategies against high LDL-C levels have been established using effective cholesterol-lowering drugs such as statins.

Impaired glucose tolerance, hypertension and lipid disorders, including hypertriglyceridemia and low levels of high-density lipoprotein cholesterol (HDL-C), were recognized as weaker risk factors for CVD compared with high level of LDL-C. However, the coexistence of multiple risk factors apart from LDL-C is considered as important as hypercholesterolemia. Independent control of each risk factor was discussed first. Such disorders are commonly found in obesity, but not in all obese subjects. There is considerable variation in fat distribution in obesity as assessed by computed tomography (CT) [1]. Visceral fat accumulation contributes to the development and/or worsening of various disorders, such as glucose intolerance, hyperlipidemia [2], hypertension [3], cardiac dysfunction [4] and sleep apnoea syndrome [5]. Even in mildly obese individuals, visceral adiposity is related to a cluster of risk factors and coronary artery disease (CAD) [6,7]. This pathogenetic condition, in which visceral fat accumulation locates upstream of various disorders related to CVD is conceptualized as visceral fat syndrome. Visceral fat syndrome is currently considered a common cause of CVD in many countries, in association with nutritional oversupply and physical inactivity.

Adipocytokines

We analyzed the gene expression profile of human adipose tissue in collaboration with the'human body map' project team to determine the reasons for atherogenicity in visceral fat syndrome. Up until recently, the adipose tissue was regarded as a passive tissue for storage of excess energy in the form of triglyceride. However, it became clear that the adipose tissue, especially visceral fat, expresses a variety of genes for secretory proteins (Fig. 1) [8,9]. Approximately 30% of the genes expressed in visceral fat are those encoded for secretory proteins, suggesting that adipose tissue is a large endocrine organ that

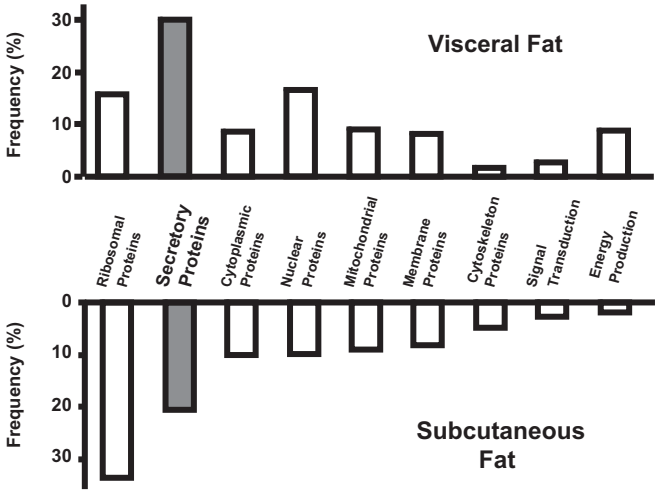

Fig. 1. The frequency of categorized expressed genes in human visceral (top) and subcutaneous (bottom) adipose tissues. Data show the frequency of the genes in each category such as functions and subcellular localization in both visceral and subcutaneous fat. Adipose tissue expresses a variety of genes of secretory proteins. Notably, approximately 30% of the genes expressed in visceral fat encoded secretory proteins. Reproduced from Fig. 2 in Ref. [9] with permission of Japanese Society of Internal Medicine.