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Invited critical review

The protective functions of omentin in cardiovascular diseases

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ABSTRACT

Adipose tissue is considered as a large gland that can produce paracrine and endocrine hormones. Growing evidence suggests that adipocytes may link obesity to cardiovascular diseases (CVD). Adipose tissue produces a large number of mediators, which affect metabolism, inflammation and coagulation. Omentin, a novel adipocytokine, has come into the center of interest due to its favorable effects on inflammation, glucose homeostasis and CVD. The present review provides a concise and general overview on the roles of omentin in CVD. The knowledge of these concepts may provide a new strategy to reduce disease risks on CVD in the future.

Contents

Abbreviations: CVD, cardiovascular disease; CAD, coronary heart disease; PAH, pulmonary arterial hypertension; MIRI, myocardial ischemia–reperfusion injury; TGF-β, transforming growth factor-β; ICAM-1, intercellular adhesion molecule-1; VCAM-1, vascular cell adhesion molecule-1; MCP-1, monocyte chemoattractant protein-1; PI3K, phosphatidylinositol 3-kinase; AKT, protein kinase B; AMPK, AMP-activated protein kinase; TNF-α, tumor necrosis factor-α; JNK, c-Jun N-terminal kinase; VSMC, vascular smooth muscle cell; COX-2, cyclooxygenase-2; PDGF-BB, platelet-derived growth factor-BB; NO, nitric oxide; BNP, brain natriuretic peptide; MetS, metabolic syndrome; SCF, slow coronary flow phenomenon; LV, left ventricular; AMI, acute myocardial infarction; THRT, thyroid hormone replacement therapy; c-IMT, carotid intima-media thickness; DM, diabetes mellitus; IBD, inflammatory bowel disease; CD, Crohn's disease.

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1. Introduction

Adipose tissue is not only an energy storage, but also the largest endocrine organ in the body. The fat factors (adipokines), secreted by the adipose tissue, include dozens of members, such as leptin, adiponectin, resistin glycolipids, tumor necrosis factor, interleukin-6, visfatin, omentin and retinol binding protein. These factors participate in various physiological and pathophysiological processes in the body involved in energy metabolism, lipid metabolism and inflammatory responses in cardiovascular system [1]. However, few of these adipokines play a role in the positive metabolism promoting good health. Omentin is a recently identified novel adipocytokine, and belongs to the category of good adipokines. Plasma omentin levels are significantly decreased in patients with obesity, insulin resistance, and diabetes that contribute to the major components of the metabolic syndrome and other disease conditions like atherosclerosis, coronary artery disease (CAD) and heart failure, etc. [2]. This review expands upon several papers [3–5] that provided commentaries on specific aspects of omentin biology and functions in cardiovascular disease (CVD).

2. Omentin structure and distribution

Omentin was identified in an omental fat cDNA library in 2005 [6,7] and was initially described in intestinal Paneth cells [8,9] with the name intelectin-1 and intestinal lactoferrin receptor [9,10]. It was also detected in endothelial cells and referred to as endothelial lectin [10]. Omentin is composed of 313 amino acids, and mainly expressed in visceral adipose tissue. More specifically, it is expressed in visceral adipose stromal vascular cells, rather than in subcutaneous adipose tissue [7]. Omentin is encoded by 2 genes, omentin-1 and omentin-2, and the former is the major circulating form. Omentin-1, with uniprot code Q8WWAO and gene bank expression number AY549722, has been more intensively studied than omentin-2 [11]. In this article, we refer to omentin-1 as omentin.

Omentin, a hydrophilic protein with a molecular weight of 35 kDa, is scarce in subcutaneous fat depots and mature adipocytes, and specifically secreted from the stromal vascular cells within the fat depots. It is also expressed in other tissues, such as endothelial cells, epicardial fat, thymus, small intestine, colon, eticulocytes, ovary, lungs and placenta [6,7].

Omentin-1 is a new type of Ca^{2+}-dependent lectin with affinity for galactofuranosyl residues [6]. It may therefore be implicated in the recognition of specific pathogens and bacterial components [12]. Omentin-2 is a homolog of omentin-1 with 83% of amino acid identity. The genes of these two homologs are adjacent to each other in the 1q22–q23 chromosomal region linked to type-2 diabetes mellitus (T2DM) in several populations [13] (Table 1).

Table 1
The characteristics of omentin.

Different names	Isoforms	Half ife in RC	Plasma concentration	Gene location	SNP ID*
IntL/ECtin/ILFR	Omentin-1/2	30 h	100 ng–1 μg/m l	1q22–q23	rs2274907

IntL: intelectin-1; ECtin: endothelial lectin; ILFR: intestinal lactoferrin receptor; half life in RC: half life in reticulo cytes; 1q22–q23: 1q22–q23 chromosomal region; SNP ID*: polymorphism identity, the first identified single nucleotide polymorphisms in the genes of omentin.

3. Omentin and inflammation

Accumulating evidence indicates that the obese state is characterized by chronic low-grade inflammation, which leads to the initiation and progression of obesity-related disorders, such as T2DM, hypertension, CVD, and atherosclerosis. Omentin, as a newly discovered adipokine, plays an anti-inflammatory role, as reported by several groups [11,14,15]. In addition, the role of omentin has been implicated in the gut defensive mechanism to pathogenic bacteria such as *Escherichia coli* [6]. Rheumatoid arthritis, another studied inflammatory condition, has low omentin levels in synovial fluid when compared with healthy condition, suggesting that omentin can be a possible biomarker for degenerative process in osteoarthritis [16]. The gene expression of omentin is enhanced in the airway epithelial cells of patients with asthma [17,18]. Lower levels of omentin in smokers seem to be related to a susceptibility of infections. Omentin levels are decreased in psoriasis, but increased levels of omentin in psoriatic arthritis [19]. Turkcu et al. [20] demonstrated that the plasma omentin level was decreased, whereas the TNF-α levels and TNF-α/omentin ratio were increased in Behcet disease patients. The ratio may be used in the presentation of deviation in the inflammatory and anti-inflammatory balance in Behcet disease. The elevation of omentin levels in rats was observed in the early stage of pancreatitis. The elevated omentin levels improved insulin resistance and caused a significant reduction in glucose levels [21].

It remains challenging to determine the inflammatory activity in Crohn's disease (CD) due to the lack of specific laboratory markers. Recent studies suggest that serum omentin is associated with inflammatory response. The serum and colonic omentin expression is decreased in active CD patients. The correlation of serum omentin with disease activity of CD is superior to that of C-reactive protein. Serum omentin is a potential marker for CD disease activity [6,22]. Background inflammation is involved in the mechanism of inflammatory bowel disease (IBD). Decreased serum omentin levels could be considered as an independent predicting marker of the presence and disease activity of IBD [23,24]. In a recent study of acute mesenteric ischemia (AMI), Sit and colleagues [25] demonstrated that serum omentin level in sham group was significantly elevated compared to rats in ischemia–reperfusion group. Acute mesenteric ischemia is an intestinal vascular disease with high mortality. Clinical diagnosis of acute mesenteric ischemia is difficult. Serum omentin level may predict early diagnosis of acute mesenteric ischemia before development of transmural ischemia. Omentin levels may be a biochemical indicator to detect acute mesenteric ischemia. However, further human studies are needed.

Omentin is also increased in non-alcoholic fatty liver disease (NAFLD), and is an independent predictor of hepatocyte ballooning [26]. This finding appears controversial, because non-alcoholic fatty liver disease is mostly found in obesity, which has been linked with low levels of omentin (see below). Furthermore, patients with end stage renal disease who are in haemodialysis have higher levels of omentin versus control subjects [27]. The patients with diabetes mellitus (DM) have lower levels of omentin than patients with end stage renal disease on haemodialysis without DM. Pregnant women

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