



Research Progress of Omentin-1 in Disease Diagnosis: A Review

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Abstract: Omentin-1, an adipokine secreted by visceral adipose tissue, plays a key role in various diseases by regulating insulin sensitivity, inflammation, and vascular health. Its diagnostic value is increasing, although challenges remain due to limited standardization and an incomplete understanding of its mechanisms. These challenges highlight the need for further research to improve its clinical application for the early detection and prognosis of metabolic and inflammatory conditions.

Keywords: Omentin-1, disease diagnosis, biomarker, metabolic diseases, cardiovascular diseases, inflammation

1. Biological characteristics and mechanism of action of Omentin-1

1.1 Molecular Structure and Expression Characteristics of Omentin-1

Omentin-1 (ITLN1) is an adipokine primarily found in visceral adipose tissue, especially omental fat, and also expressed in various other tissues like airway goblet cells and vascular cells, highlighting its broader physiological significance[1-2]. Omentin-1 is a secreted lectin that binds to the sugar moiety galactofuranose. This binding affects the interaction between omentin-1 and microbes, thereby influencing innate immunity. Additionally, omentin-1 modulates cell signaling pathways involved in metabolic homeostasis and inflammation. Its plasma levels can serve as indicators of specific metabolic and inflammatory conditions[1]. Importantly, omentin-1 expression is inversely correlated with obesity and related metabolic dysfunctions[3-4]. Omentin-1 expression varies between visceral and subcutaneous adipose tissue. This variability highlights the importance of considering tissue-specific profiles in research and clinical evaluations[4]. The molecular structure and expression patterns of omentin-1 specific to various tissues support its functions in cellular signaling, metabolic balance, and immune responses.

1.2 Mechanisms of Omentin-1 in Metabolic Regulation

Omentin-1 significantly regulates metabolism by activating the AMP-activated protein kinase (AMPK) pathway. This activation enhances glucose uptake and fatty acid oxidation, thus improving insulin sensitivity in adipocytes and skeletal muscle cells. Omentin-1 enhances glucose uptake and glycolytic activity in human myotubes but does not enhance insulin-stimulated glucose uptake in these cells, suggesting that its effects are tissue-specific and may differ from those in other tissues such as adipocytes[1, 5]. Omentin-1 suppresses inflammatory cytokines like TNF- α and IL-1 β , reducing chronic inflammation linked to insulin resistance and metabolic syndrome[3, 6]. The anti-inflammatory effect is partly due to inhibiting NF- κ B and MAPK pathways, which regulate inflammatory gene expression[3]. Omentin-1 modulates lipid metabolism by enhancing cholesterol efflux in macrophages through upregulation of ATP-binding cassette transporter A1 (ABCA1), which decreases foam cell formation and slows atherosclerosis progression[7]. Omentin-1 administration in diabetes and metabolic disease models enhances glucose tolerance, lowers serum free fatty acids, and normalizes insulin signaling components like PI3K, AKT, and GLUT4, indicating its therapeutic potential[8]. These mechanisms highlight omentin-1's crucial role in metabolic homeostasis by improving glucose and lipid metabolism and reducing inflammation.

1.3 Relationship Between Omentin-1 and Immune Regulation

Omentin-1 is crucial for immune modulation beyond metabolic regulation, influencing macrophage polarization toward an anti-inflammatory (M2) phenotype, which aids in tissue repair and reduces excessive inflammation[2, 9]. This immunomodulatory property is seen in conditions like psoriasis and rheumatic diseases, where omentin-1 levels relate to disease activity and inflammation[9, 10]. Omentin-1 regulates pro- and anti-inflammatory cytokines, fine-tuning the immune balance[2]. Omentin-1's anti-fibrotic effects in cardiac fibroblasts and neuroprotective actions in cerebral ischemia are mediated by immune-response-related signaling pathways like Src/PI3K/Akt and GAS6/Axl[11-12]. Omentin-1 regulates macrophage function and cytokine networks to maintain immune homeostasis, protect tissues from inflammation, and support repair, making it a potential therapeutic target for metabolic and inflammatory diseases.

2. Omentin-1 in the Diagnosis of Metabolic Diseases

2.1 Type 2 Diabetes Mellitus and Insulin Resistance

Clinical studies show that plasma omentin-1 levels are lower in type 2 diabetes mellitus (T2DM) patients, correlating with insulin resistance, and omentin-1, an adipokine from visceral fat, is vital for glucose homeostasis; meta-analyses confirm lower serum levels in T2DM compared to healthy controls, with no significant changes in type 1 diabetes[13-14]. Reduced omentin-1 is associated with impaired insulin signaling in T2DM, and lower levels correlate with high fasting glucose, insulin resistance, and adverse lipid profiles, indicating its role as a potential biomarker for early diagnosis and monitoring[15-16]. Omentin-1 levels are inversely related to diabetic complications like peripheral artery disease and nephropathy, with lower levels linked to increased severity and progression of these diseases[17, 18]. Omentin-1 protects by enhancing endothelial function, reducing inflammation, and improving mitochondrial function, often compromised in diabetes[19-20]. Therapeutic interventions like insulin therapy and exercise training increase circulating omentin-1 levels, improving metabolic parameters and supporting its role as a dynamic biomarker and potential therapeutic target[21-22]. These findings highlight omentin-1's potential as a biomarker for early T2DM detection, monitoring insulin resistance, and its role in diabetic complications.

2.2 Metabolic Syndrome and Obesity-Related Diseases

Omentin-1 levels are linked to metabolic syndrome (MetS) and obesity; they are lower in MetS individuals than healthy controls and correlate inversely with body mass index (BMI), waist circumference, insulin resistance, and triglycerides, while positively with high-density lipoprotein cholesterol (HDL-C)[23-24]. Studies show an inverse relationship between omentin-1 and insulin resistance, indicated by negative correlations with HOMA-IR and the triglyceride-glucose index, both markers of metabolic dysfunction[25-26]. Omentin-1 levels are reduced in hypertensive patients and those with nascent metabolic syndrome, indicating its potential as an early metabolic derangement marker[24, 27]. Omentin-1 concentrations are lower in obese adults and children, with reductions linked to increased adiposity and metabolic risks, indicating its potential as a biomarker for adipose tissue dysfunction[23, 28]. Studies suggest that omentin-1 levels reflect metabolic syndrome severity and cardiovascular risks, with lower levels linked to greater carotid intima-media thickness and aortic valve sclerosis, indicators of subclinical atherosclerosis[26, 29]. Interventional studies show that lifestyle changes, such as exercise, can increase omentin-1 levels and improve inflammatory markers and metabolic parameters, highlighting their effectiveness in therapy[23, 30]. Omentin-1 is a biomarker for metabolic syndrome and obesity-related diseases, potentially mediating metabolic health by reflecting adipose tissue inflammation and insulin sensitivity balance.

2.3 Non-Alcoholic Fatty Liver Disease (NAFLD)

Omentin-1 shows abnormal expression in non-alcoholic fatty liver disease (NAFLD), linking it to hepatic lipid metabolism and inflammation. Studies indicate dysregulation of omentin-1 levels in NAFLD, suggesting its role in autophagy and lipid accumulation via the AMPK α /mTOR pathway[5]. Altered omentin-1 levels in obese and overweight children correlate with hepatic steatosis severity and metabolic parameters, indicating its potential as a non-invasive biomarker for disease prognosis[31]. Omentin-1's anti-inflammatory and insulin-sensitizing effects may help in NAFLD, which involves chronic inflammation and insulin resistance[32]. Omentin-1 shows potential as a novel biomarker for early diagnosis, classification, and monitoring of NAFLD, warranting further research into its clinical use and therapeutic strategies.

3. Omentin-1 in Cardiovascular Diseases and Inflammatory Diseases Diagnosis: Research Progress

3.1 Coronary Heart Disease and Atherosclerosis

Omentin-1, an adipokine from visceral adipose tissue, is linked to cardiovascular diseases like coronary heart disease (CHD) and atherosclerosis, with evidence showing that lower circulating omentin-1 levels correlate with more severe coronary artery disease (CAD) and vascular dysfunction[33]. Mechanistically, omentin-1 exerts protective effects on vascular endothelium by enhancing endothelial nitric oxide synthase (eNOS) activity and promoting nitric oxide (NO) bioavailability, which improves endothelial function and vasodilation[34-35]. Moreover, omentin-1 inhibits vascular smooth muscle cell (VSMC) proliferation and migration, key processes in atherogenesis, through modulation of signaling pathways such as AMPK/ERK and PI3K-Akt[7, 34]. Omentin-1 is a promising biomarker for early diagnosis and risk stratification in CHD, with Receiver operating characteristic (ROC) analyses showing moderate to good diagnostic accuracy when combined with markers like MALAT1 in type 2 diabetes patients[33]. These findings show a negative correlation between omentin-1 levels and coronary artery disease and atherosclerosis,

indicating its potential as a non-invasive biomarker for early cardiovascular diagnosis.

3.2 Pulmonary Arterial Hypertension and Heart Failure

Emerging research shows that omentin-1 significantly affects pulmonary arterial hypertension (PAH) and heart failure (HF), as it improves endothelial function, enhances AMP-activated protein kinase (AMPK) phosphorylation, reduces endoplasmic reticulum (ER) stress, and boosts NO production in pulmonary arteries[36]. AMPK signaling is crucial for omentin-1's vascular benefits, which include anti-inflammatory and anti-oxidative effects that mitigate PAH-related vascular remodeling[37]. In heart failure, especially heart failure with preserved ejection fraction (HFpEF), omentin-1 levels decrease and are inversely related to inflammation markers (e. g. , TNF- α , IL-6) and cardiac dysfunction indicators like E/e' ratio and NT-proBNP. Omentin-1 is a protective factor for HFpEF, showing diagnostic performance similar to NT-proBNP, especially in the elderly[38]. Omentin-1 activates cardioprotective pathways like AMPK and PI3K/Akt, reducing myocardial apoptosis and enhancing mitochondrial function[19, 39]. Higher serum omentin-1 levels in hemodialysis patients are linked to fewer major adverse cardiac and cerebrovascular events (MACCE), indicating its role in inflammation and lipid metabolism[40]. Omentin-1 administration enhances vascular insulin resistance and hypertension in obesity-related cardiovascular disease animal models[41]. These data highlight omentin-1 as a key regulator of vascular tone and myocardial protection, serving as a biomarker and potential therapeutic target in PAH and heart failure.

3.3 Diagnostic Value in Inflammatory Diseases

Omentin-1 shows promise in diagnosing and treating chronic inflammatory diseases like rheumatoid arthritis (RA) and inflammatory bowel disease (IBD), with elevated serum and synovial levels in RA correlating with disease activity indices such as CRP, ESR, and DAS28, indicating its role in synovitis and joint damage[42]. Omentin-1 modulates macrophage polarization to an anti-inflammatory M2 phenotype through IL-4 and STAT6 signaling, reducing pro-inflammatory cytokines and joint damage[43]. In systemic sclerosis and chronic inflammatory states, omentin-1 expression changes indicate disease activity and microvascular involvement. Omentin-1 reduces lipopolysaccharide-induced macrophage activation in cellular models by inhibiting TLR4/MyD88/NF- κ B pathways and promoting Nrf2 nuclear translocation[44]. Omentin-1 is identified as a biomarker for inflammatory disease activity and an immune response modulator, offering potential for diagnosis, monitoring, and therapy in inflammatory disorders.

4. Conclusion

Omentin-1 is a complex adipokine crucial for metabolic control, immune response, and heart health, showing promise as a biomarker for metabolic and cardiovascular disorders. However, the translation of Omentin-1 research into clinical application faces challenges, like inconsistent detection methods and unclear disease-specific pathways. Integrating Omentin-1 into multi-marker diagnostic strategies may enhance accuracy. Future research should focus on large-scale trials and standardized testing methods to fully harness its clinical potential.

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