

Letter to Editor



Obesity, WISP1, and WISP2: The Effects of Exercise Training and Physical Activity

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DEAR EDITOR

Obesity is a growing health, social, and economic concern worldwide. It is an independent risk factor for type 2 diabetes, cancer, nonalcoholic fatty liver syndrome, and insulin resistance diseases (1). Over the previous decade, the concept of "metabolic inflammation" has been made for the obesity-related dysfunctions, which describes chronic inflammation responses to obesity (2).

The significant increase in adipose tissue can cause obesity-related disorders (3). Studies on mice have revealed that Wingless signaling pathways (WNTs) link with adipogenesis and inflammation. WNT family members are autocrine and paracrine glycoproteins that regulate cell proliferation, differentiation, and growth (1). The WNT signaling system consists of various "central" and "non-central" pathways, influencing cell regeneration. Protein 1 The WNT signaling pathway (WISP1, also known as CCN4) belongs to the CCN family in extracellular matrix proteins. It is a target gene at the central WNT signaling pathway (4). WISP1 is a new adipokine that can stimulate macrophages' cytokine responses (5). It involves the regulation of apoptosis and a wide range of neurological, musculoskeletal, immunological, and cancer diseases (6). Current researches show that other CCN members have a close relationship with adipogenesis, but there is

not sufficient knowledge about the role of WISP1 / CCN4 in obesity and related diseases (7-9).

Visceral fat and subcutaneous tissue produce WISP1 (10), but adipose tissue mainly releases WISP1 in humans (1). WISP1 expression negatively correlates with insulin sensitivity, adiponectin blood levels, and visceral fat content, suggesting that WISP1 may be a valuable indicator of fat accumulation and insulin resistance (1). In one study, weight loss results in WISP1 expression reduction in subcutaneous adipose tissue and blood circulation. Women had higher body fat and WISP1 levels than male subjects (11).

CCN5, also known as WISP-2 (signaling protein from Wnt-1), is a member of CCN [Cyr61 (rich in 61 cysteines), CTGF (connective tissue growth factor), and Nov (a gene that expresses nephrostomy bone), and play a crucial role in cell proliferation (12). WISP2 is an adipokine with 29 kDa weight. WISP2 expression increases in subcutaneous fat tissue in obese individuals (13). WNT signaling pathway can prevent adipogenesis by limiting the adipose tissue storing and directing the lipids to the liver and muscle. So it can cause metabolic complications such as insulin resistance and fatty liver disease (14). The WNT signaling increases insulin resistance through the JNK cascade, JUN kinase, and IRS-1 serine phosphorylation (15).

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Current studies have demonstrated that WNT signaling plays an essential role in inflammatory conditions which connect obesity to metabolic complications (15). On the other hand, physical activity is crucial in preventing obesity prevalence (16). Physical activity and diet are essential in the obesity incidence and its unfavorable consequences (17, 18), such as cardiovascular diseases (19).

However, the underlying mechanism of obesity and its pathological consequences is not

well defined. Various factors can initiate obesity. Physical activity has not had the same influence in all of those conditions. Based on our knowledge in this field, no study has examined the effect of physical training on WISP2 and WISP1. Therefore, analyzing the effects of different exercises (endurance, resistance, and combination) and protocols on WISP2 and WISP1 responses can help recognize the underlying mechanism of obesity-related dysfunctions.

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