Irisin, a Novel Myokine Responsible for Exercise Induced Browning of White Adipose Tissue

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Dear Sir,

Exercise is known to induce weight loss which is more than expected due to energy expenditure during exercise. Till now the molecular mechanism of this disproportionate loss in weight was not known. A novel myokine, Irisin named after Greek goddess iris, discovered by Bruce M. Spiegelman et al. in 2012 [1] has been found to be the hormone responsible for exercise induced improvement in glucose homeostasis. It is a 112 AA polypeptide secreted from muscle into the bloodstream in response to exercise. There is 100 % homology in structure of Irisin between human and mice suggesting it to be a highly conserved hormone during evolution. It is found to be responsible for browning of subcutaneous adipose tissue and thus it is responsible for antiobesity and antidiabetic effect [1].

Regarding the biochemical nature, Irisin is a cleaved and secreted fragment of FNDC5 (FRCP2 and PeP). FNDC5 is synthesised as a type I membrane protein which undergoes proteolytic cleavage and this results in release of *N* terminal part of protein into extracellular space. FNDC5 consists of three parts, a signal peptide, two fibronectin domains, hydrophobic domain and a *C*-terminal peptide. FNDC 5 is a glycoprotein. It is released from muscle in response to exercise [2, 3].

As per the molecular mechanism, exercise is the stimulus for release of PGC1 α (PPAR-co-activator-1 α) which is

a coactivator of PPAR γ (involved in energy metabolism). This in turn stimulates expression of FNDC5 which in turn is proteolytically cleaved to release the active hormone, irisin. Irisin has cell surface receptors. It increases the expression of UCP1 and Cidea mRNA, which causes browning of primarily subcutaneous and also of visceral adipose tissue and thereby inducing thermogenesis [4]. White adipose tissue, which is a storehouse of energy, is converted to brown adipose tissue which dissipates energy as heat. This in turn causes increase in total body energy expenditure.

As far as the potential biochemical implication is concerned, Irisin causes browning of adipose tissue and thereby inducing thermogenesis, white adipose tissue is primarily composed of triglycerides and fatty acids (mainly responsible for insulin resistance). Irisin causes white adipose tissue to get converted to brown adipose tissue and thereby reduction of insulin resistance and improvement of glucose homeostasis. It may be useful as anti obesity treatment by weight loss and antidiabetic treatment by virtue of improved glucose homeostasis.

To conclude, it may be useful in treatment of obesity, diabetes, and metabolic syndrome. It will be specially useful to people who cannot exercise because of physical limitations. However, it can not act as a substitute for exercise. All its effects are presently seen in mice, because of its 100 % sequence homology, it is being assumed to have same effect in humans for which clinical trials are being conducted (Fig. 1).

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Fig. 1 Mechanism of exercise induced weight loss by Irisin

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