

## Physiological role of a novel hormone FNDC5/irisin revealed in humans

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A research team led by Dr. Christos Mantzoros, MD, PhD, at Beth Israel Deaconess Medical Center, Harvard Medical School, has published new findings elucidating the molecular and clinical role of FNDC5/irisin in humans.

Irisin is a recently identified hormone secreted from <u>muscle cells</u> that has been found to serve as a <u>chemical messenger</u> providing key exerciseinduced health benefits in mice. In these earlier studies, irisin showed direct effects on 'browning' of white fat which would lead to burning of excess calories. Discovery of irisin therefore raised expectations of potential for developing new therapies for <u>metabolic diseases</u>.

In their study, Dr. Mantzoros and his team of researchers went one step further by uncovering the role of irisin in humans. They reported that whereas the cleaved soluble part of the FNDC5 molecule (irisin) is readily detectable in <u>human</u> plasma, the uncleaved and unprocessed molecule FNDC5 is only rarely detectable.

They studied possible predictors of circulating irisin concentrations by performing cross-sectional and interventional studies in humans. They found that irisin levels reflect muscle mass primarily and are higher in younger male athletes than in older women. Also, muscle mRNA expression of FNDC5 was strongly and positively correlated with PGC1- $\alpha$  mRNA levels which confirms irisin as a myokine, a hormone secreted by muscle.



The Mantzoros group addressed the controversy of whether irisin levels change in humans during exercise by comparing levels in young healthy males who performed acute sprint runs and chronic sprint training for eight weeks. The results showed that irisin levels increase in response to acute exercise and irisin levels are closely and negatively associated with muscle ATP levels, pointing to a need for a prompt secretion of irisin after acute exercise to meet the needs for ATP and <u>metabolite</u> synthesis in muscle. Also reported were associations of irisin with growth factors, which increase muscle mass and metabolic outcomes in normal humans; a finding which will require confirmation by future studies.

Although this clinical study has revealed a significant amount of novel information regarding the physiological role of irisin in humans, much remains unknown regarding its function as a hormone and the regulation of FNDC5 synthesis and irisin secretion.

**More information:** This article is "FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise" by Huh JY, Panagiotou G, Mougiosb V, et al. (DOI <u>10.1016/j.metabol.2012.09.002</u>). The article will appear in *Metabolism*, Volume 61, Issue 12 (December, 2012), published by Elsevier.

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