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Proteomic analysis of human obesity reveals differential expression of the epigenetic factor HDAC4 and role of physical exercise in correcting its expression

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Abstract

The modern increase in sedentary lifestyles and excessive food intake are considered as key contributing factors to a group of obesity-associated disorders such as insulin resistance, diabetes, and cardiovascular complications. Proteomic profiling strategy was used to identify proteins that are differentially expressed and might play a role in obesity and the potential modulation of their expression by physical exercise.

PBMCs and subcutaneous adipose tissue biopsies from 48 male non-diabetic subjects were collected before and after exercise. Proteins were extracted from PBMCs, and digested SCX beads and analyzed by LC-Orbitrap Velos. Label-free method was then used to quantify identified proteins. Data were validated by Q-PCR and immunohistochemistry. Circulating cytokine and metabolic markers were investigated by multiplexing technology.

A total of 47 proteins were found to be differentially expressed (more than 1.5-fold changes) between normal-weight and obese volunteers. Proteins that were upregulated in obese volunteers included thrombospondin 1 (TSP1), nuclear receptor co-regulator (NCoR) whereas; the histone deacetylase 4 (HDAC4) protein was reduced in obese subjects. After exercise, expression of these proteins was restored to the level observed in control group. Our initial analysis on HDAC4 indicated that it negatively correlated with leptin (P=0.008; r^2=-0.59) and PAI1 (P=0.04; r^2=-0.46) as well as IP-10 (P=0.02; r^2=-0.5) and MIP-1a (P=0.03; r^2=-0.53).

The downergulation of HDAC4 in obese subjects, its restoration with physical exercise and its correlation with inflammatory and metabolic markers may suggest a protective role of HDAC4 against obesity and could therefore represent a potential therapeutic target for management of obesity and insulin resistance.