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1029 Differences in inflammasome activation between metabolically healthy and unhealthy obese individuals

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The pro-inflammatory cytokine interleukin-1 beta (IL-1 β) is involved in the pathogenesis of obesity-related insulin resistance through the activation of the NLRP3 inflammasome. Obesity is a heterogeneous disease; some patients are obese but metabolically healthy (MHO) whereas others develop metabolic disorders (MUO). The aim of this study is to determine if differences in inflammasome activation and cell composition play a role in such paradoxical phenotype.

The MHO phenotype was defined as the absence of metabolic syndrome. Paired subcutaneous (SAT) and visceral (VAT) adipose tissue samples were obtained from a total of 23 MUO subjects, 21 age- and BMI-matched MHO subjects and 9 age-matched lean subjects.

We found relevant and significant differences among the three phenotypes but only in the VAT, including a higher expression of IL-1 β and NLRP3 mRNA, a more important IL-1 β secretion, a higher level of adipose tissue macrophages (ATMs) and a lower percentage of T regulatory cells in the VAT of MUO compared to MHO and lean subjects. Moreover, the caspase-1 activity and IL-1 β release were higher in the ATMs from VAT of MUO compared with MHO. We also showed similar significant differences between the SAT and VAT of MUO subjects.

Metabolic abnormalities are associated with an activation of the inflammasome in the ATMs infiltrating the VAT. MHO subjects have a more favorable adipose tissue inflammatory profile. These findings may be the key to protecting obese individuals from the adverse metabolic effects associated with increased fat mass.

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