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COMMENT ON PELLEGRINELLI ET AL.

Human Adipocytes Induce Inflammation and Atrophy in Muscle Cells During Obesity. Diabetes 2015;64:3121–3134

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Loss of muscle mass and strength contributes to functional limitations and disability (1). This age-related muscle wasting has been termed sarcopenia and has been originally seen as a basic decline in muscle mass with aging (2). Interestingly, obesity is also an independent predictor of sarcopenia, defining the so-called concept of sarcopenic obesity (3). Therefore, there is a pressing need to understand the molecular mechanisms of sarcopenia to identify potential preventive measures. The study by Pellegrinelli et al. (4) provides compelling evidence that excess adipose tissue, particularly in the visceral fat depot, may contribute to skeletal muscle wasting. Using a combination of three-dimensional coculture and conditioned media experiments, they showed that the secretome of inflamed human visceral adipocytes induces atrophy in human skeletal muscle cells. Interestingly, this effect is more potent with visceral than with subcutaneous adipocytes. The atrophic response in skeletal muscle appears independent of proinflammatory signaling as immunoneutralization of the cytokines interleukin-1β and interleukin-6 cannot rescue the phenotype. Thus, adipocytes may produce peptide and/or lipid factors that are secreted into the systemic bloodstream and negatively influence skeletal muscle mass. This underlying mechanism may involve a reduced activation of protein synthesis signaling in response to anabolic signals, such as insulin, amino acids, and insulin-like growth factors, rather than to increased atrophy signaling. These data add novel mechanistic knowledge to the current literature, suggesting that anabolic resistance may be a key factor in the development and progression of sarcopenia (5). However, it is still unclear if adipocytes from other depots, such as intramuscular adipocytes, also emerging in the context of obesity and aging (6) can influence skeletal muscle metabolism, function, and mass. It will be interesting to investigate the specific role of intramuscular adipose tissue in the near future and its causal association with muscle dysfunction in vivo. Future studies should also focus on identifying the molecular triggers of this adipocyte-skeletal muscle cross talk. This may help researchers to identify novel strategies to reduce lipotoxicity and prevent muscle wasting associated with obesity and aging.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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