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RESPONSE TO 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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We appreciate the comments by Moro and Bourlier (1) regarding our recent study (2), which shows the capacity of visceral fat–derived adipocytes from obese patients to promote inflammation and atrophy of muscle cells. Briefly, we identified interleukin (IL)-6 and IL-1β as drivers of the inflammatory burst of cocultured cells and a substantial amelioration of the atrophic phenotype by IGF-II/insulin growth factor binding protein-5. Given that our data do not support the direct role of IL-6 or IL-1β in promoting atrophy in muscle cells, we agree that further research is needed to determine the molecular effectors responsible.

Histological analysis of skeletal muscle from obese mice revealed the presence of intermuscular adipocytes, named as intermuscular adipose tissue (IMAT). We agree with Moro and Bourlier that phenotyping IMAT-derived adipocytes and exploring their contribution in the promotion of muscle wasting are important goals for future studies. IMAT differs from intramyocellular lipids in terms of where fat is accumulated. However, both phenomena are considered negative consequences of obesity. In this line, it is important to bear in mind that IMAT has been extensively reported as a relevant player in muscle insulin resistance (3), exacerbating inflammation and muscle wasting through local productions of adipokines.

We are aware that our in vitro experiments may more closely mimic interorgan visceral adipose tissue/skeletal muscle cross talk rather than intercellular as presumed for IMAT-myocytes interaction. Nevertheless, we believe that replicating that specific interplay in vitro may not be technically possible at the present moment for the following reasons: *1*) for ethical reasons in humans it is difficult to obtain sufficient amounts of muscle to isolate intramuscular adipocytes and *2*) the amount of fat accumulation in nutritional or genetic models of obesity is relatively low (2) when compared with other models of experimentally induced IMAT accumulation (e.g., intramuscular injection of glycerol) (4). Currently, the improvement of new technologies, such as laser microdissection of muscle samples in combination with multiplex gene expression profiling (5), may facilitate the direct study of IMAT-muscle cross talk in the near future.

Interestingly, the information obtained from our ex vivo experiments suggests a strong correlation between adipocyte accumulation in muscle (increased leptin expression) and subsequently muscle atrophy (decreased muscle marker expression). Although these data do not show a causative effect per se, we believe the data may help to establish a common ground to study other pathologies, such as myopathies of genetic and autoimmune

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origins where fat accumulation is associated with muscle loss (6), and to identify novel therapeutic targets in the context of myopathies associated with metabolic disorders.

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

References

1. Moro C, Bourlier V. Comment on Pellegrinelli et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. Diabetes 2015;64: 3121–3134 (Letter). Diabetes 2015;64:e22. DOI: 10.2337/db15-0296

2. Pellegrinelli V, Rouault C, Rodriguez-Cuenca S, et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. Diabetes 2015;64: 3121–3134

3. Boettcher M, Machann J, Stefan N, et al. Intermuscular adipose tissue (IMAT): association with other adipose tissue compartments and insulin sensitivity. J Magn Reson Imaging 2009;29:1340–1345

4. Pisani DF, Bottema CDK, Butori C, Dani C, Dechesne CA. Mouse model of skeletal muscle adiposity: a glycerol treatment approach. Biochem Biophys Res Commun 2010;396:767–773

5. Flagella M, Bui S, Zheng Z, et al. A multiplex branched DNA assay for parallel quantitative gene expression profiling. Anal Biochem 2006;352:50–60

6. Chan WP, Liu G-C. MR imaging of primary skeletal muscle diseases in children. AJR Am J Roentgenol 2002;179:989–997