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Reply: Phenotypic Analysis of Stromal Vascular Fraction after Mechanical Shear Reveals Stress-Induced Progenitor Populations

Derek A. Banyard, M.D., M.B.A. and Alan D. Widgerow, M.B.B.Ch., M.Med

Center for Tissue Engineering, Department of Plastic Surgery, University of California, Irvine, Orange, Calif

Sir

We thank Dr. Chaput et al. for their kind and insightful letter regarding our recent article identifying the phenotypic up-regulation of stromal vascular fraction progenitor cell fractions after the application of mechanical shear stress.¹ Indeed, our investigation focused on the analysis of intersyringe-processed unfiltered fat that was subjected to collagenase digestion before single-cell analysis. We have conducted internal experiments on the cellular constituency of the filtrate and filtrand of intersyringe-processed fat and observed a significant number of retained cells in the filtrand, indicating a large portion of regenerative cells that are closely intimated to the adipose extracellular matrix. Although our results are not directly comparable to the filtrate analysis performed by Tonnard et al.,² we do not believe our results represent a completely different cell population, but rather a more complete picture of the effects of intersyringe processing on the phenotypic properties of standard lipoaspirate. In fact, we have recently presented phenotypic data of mechanically processed lipoaspirate that is more analogous to nanofat processing and observed the same populations with similar effect.³

In addition, we would like to congratulate your group on your well-written and comprehensive article comparing the phenotypic, clonal, and immunomodulatory properties of enzymatically processed fat versus that which is mechanically processed.⁴ We too have observed a significant decrease in the total number of cells recovered after mechanical processing and filtration,³ but of the cells that remain, there was a significant increase in the proportion of adipose-derived stem cells (CD45⁻/CD31⁻/CD13⁺/CD73⁺) and endothelial progenitor cells (CD45⁻/CD31⁺/CD34⁺/CD146⁺). We do concede that broadly defining mesenchymal stem cells as CD45⁻/CD34⁺ captures a progenitor population that includes endothelial cells; however, the relationship of mesenchymal stem cell enrichment mirrored that of both adipose-derived stem cells and mesenchymal stem cells in the mechanically processed groups in our study.¹ We are encouraged by your findings that demonstrated a

Correspondence to Dr. Widgerow, Center for Tissue Engineering, Department of Plastic Surgery, 200 South Manchester Avenue, Suite 650, Orange, Calif. 92868, awidgero@uci.edu.

DISCLOSURE

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significant enrichment of adipose-derived stem cells (CD45⁻/CD31⁻/CD34⁺) that corroborates our findings, and we suspect that the key difference in subpopulations observed is related to your use of a 100-µm filter without collagenase.

Our methodology involved the analysis of the cells still bound to the extracellular matrix after intersyringe processing, and includes subpopulations that were likely excluded during the filtration step in your study. There is currently a shift toward stromal vascular fraction as a therapeutic for regenerative applications, and we believe that a number of these subpopulations, in addition to the extracellular matrix, act synergistically for regenerative applications.^{5,6} We are currently working in earnest to further characterize the differentiation capacity, transcriptional profile, secretome, and clonal properties of mechanically processed adipose-derived stem cells and other constituents of the stromal vascular fraction. We thank you for your letter and look forward to the growing body of knowledge regarding the mechanical processing of adipose tissue and its potential regenerative applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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