

CARTA AO EDITOR

Mechanisms of subcutaneous adipose tissue formation in experimental lymphedema model

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Our article entitled “Mechanisms of subcutaneous adipose tissue formation in experimental lymphedema model” displays a very interesting and practical way of studying both obesity and lymphedema. Limb lymphedema is a highly prevalent complication of cancer treatment with no available therapy. A 5-year cohort¹ showed 42% lymphedema prevalence in patients who did not undergo axillary lymph node dissection and another 20-year cohort² displayed 50% lymphedema prevalence in patients who underwent axillary lymph node dissection for breast cancer treatment showing how prevalent this condition is. An interesting aspect of lymphedema is that damaged lymphatic vessels or nodes lead to stasis in addition to causing inflammation and adipose tissue accumulation³. Causative mechanisms are still not completely understood.

The objective of the study presented at the XXXV COMU was to establish an experimental model of lymphedema, improving a previously reported one and to describe cellular and molecular processes triggered by lymph stasis. This model consisted of the dissection of a 2-mm circumferential segment of skin, 2 cm distally

from the base of the tail. Patent Blue V stain was injected intradermally, distally to the wound and the deep lymphatic vessels were tied. Twenty male C57BL6 Black mice were submitted to this procedure and were euthanized 3 and 6 weeks later. Tissues from the proximal (Control) and distal (Lymphedema) portions of the tails were collected to histological and molecular analyses. Compared to their controls, Lymphedema group presented early enlargement of the tail on account of edema and inflammatory cells and fibroblasts infiltration. Further, large adipose tissue deposits were formed around vessels and muscles. There was also an early increase in the transcription of genes (measured by quantitative PCR) involved in adipocytes differentiation (CEBP), followed by increased markers of adipocytes maturity (Lipin1 and 2). Markers of lymphatic vessels formation (SLP-76) were increased during the whole follow-up.

Our results validated our adapted mouse-tail model in inducing lymphedema and adipogenesis in both histological and molecular analyses, establishing it as a viable model for studying lymphedema pathophysiology and testing new treatments.

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Recebido: 16.11.2016

Aceito: 12.01.2017