OBESIDADE: ADIPÓCITOS E SISTEMA IMUNE

Adipocytes and immune cells cross-talk: the role of catecholamines

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Background

Obesity is reaching epidemic proportions worldwide, being characterised by long-term, low-grade inflammation with detrimental effects on virtually all physiological systems. Adipocyte dysfunction has been recently regarded as the instigator of the main metabolic disturbances observed in obesity and obesity-related comorbidities. Thus, the impact of this dysfunction upon major organic systems involved in obesity clearly needs to be determined.

Given the intimate cross-talk between adipocytes and immune cells, and the recent discovery that immune cells are a source of cathecolamines (CA), we propose that these amines constitute an important link between neuroendocrine and immune networks. Consequently, we need to better understand the role of CA in modulation of the immune response in inflammatory-associated diseases such as obesity.

Immune cell-derived CA alter a wide array of cell functions, including proliferation, differentiation, apoptosis and the pattern of cytokine expression, suggesting a crucial role in the inflammatory outcome. However, the exact mechanisms controlling the release of CA in obesity are not fully understood.

Aim

To investigate the regulation of catecholaminergic system in immune cells by adipose tissue and its relationship with obesity.

Methods

Human visceral and subcutaneous AT cultures, obtained from obese and non-obese patients undergoing surgery, will be established. We will investigate, in peripheral blood mononuclear cells (PBMC) obtained from blood donors and in jurkat cells (a Human T cell lymphoblast-like cell line) the effect of whole adipocyte secretions from those distinct cultures upon the adrenergic system. The influence of physiologically relevant adipokines (leptin, adiponectin and resistin) and fatty acids (oleic, palmitic and arachidonic) upon this system will be also investigated. In some experiments, since 1-methyl-4- phenylpyridinium (MPP^+) and CA possess several structural and functional similarities, we will use ^3H-MPP^+ as a surrogate for CA.

Results

At this time, PBMCs primary cultures and jurkat cells are successfully established, concerning the optimization of cellular viability and growth conditions (in the case of PBMCs, in the presence or absence of phytohemagglutinin (PHA)). Preliminary functional studies performed with ^3H-MPP^+ have shown that, similarly to chromaffin and PC12 cells, PBMCs are able to accumulate this compound.