

Research Project Proposal
Academic year 2016-2017

Project Nº 43
Title: Adipose tissue, macrophages and immunomodulation. Role of interleukin-1 β in infiltration and polarization of macrophages in adipose tissue.
Department/ Laboratory Functional Metabolomic Laboratory, Department of Endocrinology & Nutrition. Clínica Universidad de Navarra. CIMA
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Summary Background: The obesity-associated low-grade chronic inflammation results from the interaction between adipocytes and cells from the immune system, mainly macrophages. Obesity induces a phenotypic switch from an anti-inflammatory M2-polarized state to a pro-inflammatory M1 state mediated through different cytokines. Hypothesis: This project addresses the hypothesis that the adipose tissue excess and the glycemic state underlay the changes in the gene expression of interleukin-1 β . In this way, interleukin-1 β may play a role in the macrophage polarization, aggravating the inflammatory state of obese patients. In addition, the blockade using siRNA of interleukin-1 β may contribute to improve the inflammation of adipose tissue associated to obesity. Objectives and Methods: The involvement of interleukin-1 β in M1 polarization will be determined in human adipocytes and macrophages cell cultures as well as the potential use of blockade of interleukin-1 β in the improvement of the obesity-associated inflammatory state. In addition, the effect of conditioned medium secreted by adipocytes, with normal expression of interleukin-1 β or silenced, on gene expression profile of macrophages will be studied. Moreover, the relationship with other inflammatory markers as well as extracellular matrix components will be also studied. The following techniques will be used: Sample processing: - Serum, plasma and buffy coat extraction - Cellular isolation from adipose tissue



- RNA isolation from adipose tissue and peripheral blood mononuclear cells
- Protein extraction from adipose tissue

Biology molecular techniques:

- Nucleic acid and protein quantification and quality assessment
- Analysis of gene expression by Real-time PCR
- Analysis of protein expression by Western-blot

Analytic techniques:

- ELISAs
- Large-scale cytokine analyses Multiplex (Luminex™ 200)
- Immunohistochemical analysis of proteins

Human macrophage and adipocyte cell cultures

References

Catalán V, Gómez-Ambrosi J, Rodríguez A, Pérez-Hernández AI, Gurbindo J, Ramírez B, Méndez-Giménez L, Rotellar F, Valentí V, Moncada R, Martí P, Sola I, Silva C, Salvador J, Frühbeck G. Activation of non-canonical Wnt signaling through WNT5A in visceral adipose tissue of obese subjects is related to inflammation. *J Clin Endocrinol Metab* 2014; 99:E1407-17

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POSSIBILITY OF PhD

YES*

* (PhD grant required)