Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 8
Title: Adipose tissue, macrophages and immunomodulation: Role of interleukin-32 in infiltration and polarization of macrophages in adipose tissue.
Department/ Laboratory Functional Metabolomic Laboratory, Department of Endocrinology & Nutrition. Clínica Universidad de Navarra.
Director 1: Victoria Catalán **Contact:** vcatalan@unav.es **82 5133**
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 citokines. **Hypothesis:** This project addresses the hypothesis that the adipose tissue excess and the glycemic state underlay the changes in the gene expression of different interleukins (IL), especifically IL-32. In this way, IL-32 may play a role in the macrophage polarization, aggravating the inflammatory state of obese patients. In addition, the blockade using siRNA of Il-32 may contribute to improve the inflammation of adipose tissue associated to obesity. **Objectives and Methods:** The involvement of IL-32 in M1 polarization will be determined in human adipocytes and macrophages cells culture as well as the potential use of blockade of IL-32 in the improvement of the obesity-associated inflammatory state. In addition, the effect of conditioned medium secreted by adipocytes, with normal expression of IL-32 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. *Biology molecular techniques:* - Nucleic acid and protein quantitation 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^{TM} 200).
- Immunohystochemical analysis of proteins.

Human macrophage and adipocyte cells culture.

References

Catalán V, Gómez-Ambrosi J, Rodríguez A, Ramírez B, Rotellar F, Valentí V Silva C, Gil MJ, Salvador J, Frühbeck G. Increased tenascin C and Toll-like receptor 4 levels in visceral adipose tissue as a link between inflammation and extracellular matrix remodeling in obesity. J Clin Endocrinol Metab. 2012;97:E1880-9.

Catalán V, Gómez-Ambrosi J, Ramirez B, Rotellar F, Pastor C, Silva C, Rodríguez A, Gil MJ, Cienfuegos JA, Frühbeck G. Proinflammatory cytokines in obesity: impact of type 2 diabetes mellitus and gastric bypass. Obes Surg. 2007;17:1464-74.

POSSIBILITY OF PhD

YES*

* (PhD grant required)