

Research Project Proposal
Academic year 2016-2017

Project Nº 24
Title: Role of osteopontin in colon cancer development in the context of obesity.
Department/ Laboratory Metabolic Research Laboratory, Department of Endocrinology & Nutrition, CUN (Edificio CIFA)
Director: Dr. Javier Gómez Ambrosi Contact: jagomez@unav.es Codirector: Dra. Gema Frühbeck Contact: gfruhbeck@unav.es
<p>Summary</p> <p>Background: Obesity has become in a real pandemic threatening many of the health gains achieved in the last decades. In this sense, obesity is associated with the development of colon cancer, with colorectal cancer being the most prevalent cancer among the Spanish population. Moreover, during the expansion of adipose tissue that takes place in obesity the expression of osteopontin (OPN) is dramatically increased. Furthermore, the expression of OPN significantly increases in many cancers, including colon cancer, which appears to indicate a worse prognosis.</p> <p>Hypothesis: This project addresses the hypothesis that OPN could play a major role in the development of obesity-associated colon cancer.</p> <p>Objectives and Methods: Our aim is to analyse the role of OPN in the development of colon cancer in a mouse model of diet-induced obesity. Colon tumours will be induced by subcutaneous inoculation of the adenocarcinoma cell line MC38 in wild type and OPN knockout animals fed either control or high-fat diets. We will study changes related to energy homeostasis, carbohydrate and lipid homeostasis and variables related to inflammation, oxidative stress, and angiogenesis, systemically and at the tissue level. Macroscopic changes in tumours will be determined, including size, markers of inflammation, apoptotic and Ki67-positive cells. Molecular studies will be performed in order to analyse the changes in gene expression profile in the tumours as well as in epididymal and mesenteric adipose tissues.</p> <p>The following techniques will be used:</p>



Animal handling (including wild type and OPN knockout mice)

- Control of food intake, energy expenditure and weight changes.

Gene expression analysis.

- RNA extraction from tissue.
- Nucleic acid quantitation and quality assessment.
- Real Time RT-PCR.

Protein expression analysis.

- Protein extraction from tissue.
- Protein amount quantitation (*Bradford*).
- Western blot.

Immunohistochemical analysis of proteins in histological preparations.

Processing of serum and plasma from mice.

ELISA.

References

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Catalán V, Gómez-Ambrosi J, Rodríguez A, Ramírez B, Silva C, Rotellar F, Hernández-Lizoain JL, Baixauli J, Valentí V, Pardo F, Salvador J, Frühbeck G. Up-regulation of the novel proinflammatory adipokines lipocalin-2, chitinase-3 like-1 and osteopontin as well as angiogenic-related factors in visceral adipose tissue of patients with colon cancer. *J Nutr Biochem* 2011;22:634-41.

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POSSIBILITY OF PhD

YES *

*(PhD grant required)