



Research Project Proposal
Academic year 2019-2020

Project Nº 7

Title: Role of GDF15 in the development of obesity-associated insulin resistance and type 2 diabetes.

Department/ Laboratory

Metabolic Research Laboratory, Department of Endocrinology & Nutrition, Clínica Universidad de Navarra (Edificio CIFA).

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Summary:

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 insulin resistance and type 2 diabetes. Preliminary results from our group has shown that circulating concentrations of GDF15 are altered in patients with type 2 diabetes and, therefore, may be involved in the development of insulin resistance.

Hypothesis: This project addresses the hypothesis that GDF15 could play a role in the development of obesity-associated insulin resistance and type 2 diabetes.

Objectives and Methods: Our aim is to analyse the role of GDF15 in the development of insulin resistance and type 2 diabetes in humans and mouse models of diet-induced obesity, studying in which signalling pathways GDF15 is involved in this process. We will study changes related to energy homeostasis, carbohydrate and lipid homeostasis and variables related to inflammation, and oxidative stress, systemically and at the tissue level. In vitro studies in adipocytes, hepatocytes and myotubes will be performed in order to gain insight in the effects of GDF15 in the development of obesity-associated insulin resistance and inflammation.

The following techniques will be used:

Animal handling

- 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.

Cell cultures of adipocytes, hepatocytes and myotubes.

In vitro inhibition of gene expression by siRNAs.

Immunohistochemical analysis of proteins in histological preparations.

Processing of serum and plasma from mice.

ELISAs.

yes	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	