



**MASTER'S DEGREE IN BIOMEDICAL RESEARCH**

**Research Project Proposal una.**

Academic year 2024-2025

<b>Project Nº 11</b>
<b>Title: Role of antimicrobial peptides in regulating inflammation and intestinal barrier integrity in the context of obesity</b>
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<b>Summary</b> <p><b>Background:</b> Obesity play a key role in the dysregulation of adipose tissue (AT)-gut crosstalk. In this sense, obesity-associated intestinal dysbiosis and permeability are considered key contributors of AT inflammation contributing to systemic chronic inflammation and leading to metabolic diseases. Antimicrobial peptides (AMP) are essential for maintaining intestinal integrity by protecting the gut from microbial infections, regulating the immune response, promoting epithelial cell proliferation and differentiation, enhancing tight junction integrity, and restoring the balance of the gut microbiota.</p> <p><b>Hypothesis:</b> Obesity impairs the production and function of AMP leading to a reduced intestinal integrity and an increased risk of inflammation and metabolic dysfunction. <b>Objective:</b> To understand the underlying mechanisms of AMP signaling in intestinal and AT inflammation as well as in the homeostasis of the intestinal barrier in the context of obesity. <b>Methodology:</b> We will analyze the effects of (i) bacterial components (LPS, LTA), (ii) other metabolites derived (taurine, butyrate, propionate), modified (spermine, histamine) or used (inulin) by bacteria and (iii) <i>Akkermansia muciniphila</i> alive or pasteurized in the expression of AMPs, iron-related molecules and different components of the inflammasome in primary cultures of human visceral adipocytes as well as in HT-29 (HTB-38TM) intestinal cells. We will also evaluate of the effect of the inhibition of AMP (by small interfering RNA) in the processes of intestinal and AT inflammation and intestine barrier dysfunction. The role and functionality of the AMPs will be further addressed in a rat model of bariatric surgery (sleeve gastrectomy and SADI-S).</p> <p>The following <b>techniques</b> will be used:</p> <p><i>Sample processing:</i></p> <ul style="list-style-type: none"><li>- Serum and plasma processing</li><li>- Cellular isolation from adipose tissue</li><li>- RNA isolation from adipose tissue and intestinal biopsies</li><li>- Protein extraction from adipose tissue and intestinal biopsies</li></ul> <p><i>Biology molecular techniques:</i></p> <ul style="list-style-type: none"><li>- Nucleic acid and protein quantification and quality assessment</li><li>- Analysis of gene expression by Real-time PCR</li><li>- Analysis of protein expression by Western-blot</li></ul> <p><i>Analytic techniques:</i></p> <ul style="list-style-type: none"><li>- ELISAs</li><li>- Immunohistochemical analysis of proteins</li></ul>



*In vitro studies:*

- Human intestinal and adipocyte cell cultures
- Treatments with recombinant proteins
- In vitro inhibition of gene expression by siRNA

*Statistical analysis:*

- Learn to carry out the statistical analysis and the representation of the data obtained

yes	
no	X

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?