Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2024-2025

Project Nº 19

Title: Inhibition of caspase-2 activity to fight metabolic dysfunction-associated steatohepatitis and hepatocellular carcinoma development

Department/ Laboratory Hepatology: Metabolism, Epigenetics and Carcinogenesis Laboratory, Solid Tumors Program, CIMA.

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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used*

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most prevalent chronic liver disease in Western countries. It ranges from steatosis to metabolic dysfunction-associated steatohepatitis (MASH) and can lead to advanced liver damage, including fibrosis, cirrhosis, and hepatocellular carcinoma (HCC), the most common form of primary liver cancer. However, the specific mechanisms of MASH progression towards HCC are not fully understood. Currently, prescribed medications for patients with MASH are nonspecific, and there is no effective therapy for HCC. Caspases, a protein family involved in apoptosis and inflammation, are crucial in the pathogenesis of obesity and MASH-associated HCC. This project focuses on studying caspase-2 inhibitors, which play a role in metabolic homeostasis and contribute to MASH progression. Our preliminary data suggest that caspase-2 is upregulated in MASLD patients' livers as the disease advances. In animal models, caspase-2 inhibition protects against MASH, obesity, and type 2 diabetes. We will use hepatocyte cell cultures stimulated to mimic MASH, and a mouse model of diet-induced MASH to study the effect of caspase-2 inhibition. In these models, we will examine the therapeutic properties of innovative and highly selective caspase-2 inhibitors targeting lipogenesis, apoptosis, and inflammation pathways to prevent MASLD/MASH progression. This project aims to characterize the therapeutic inhibition of caspase-2 in MASLD/MASH to halt its progression to HCC. The ultimate goal is to provide new avenues to treat MASH and prevent its progression to HCC, addressing a previously unmet medical need.

yes	x
no	

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