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

Project Nº 20
Title: New Epigenetic Mechanisms and Innovative Therapeutic Interventions in Hepatocellular Carcinoma**.**
Department/ Laboratory Hepatology: Metabolism, Epigenetics and Carcinogenesis Laboratory, Solid Tumors Program, CIMA.
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Summary
Hepatocellular carcinoma (HCC) is the predominant form of primary liver cancer and one of the deadliest malignancies globally. A considerable portion of HCC cases receive diagnosis only at an advanced stage, rendering curative surgery impractical. Consequently, systemic therapies, predominantly multi-tyrosine kinase inhibitors (TKIs) like sorafenib, have shouldered the treatment burden for decades. Recent strides in immune checkpoint inhibitors (ICIs) have heralded hope for treating unresectable HCCs. Nevertheless, the modest response rates witnessed in HCC patients underscore the imperative for further research to enhance ICI efficacy. Epigenetic mechanisms, nestled at the nexus of microenvironment and genome, have emerged as pivotal orchestrators of metabolic pathways and cellular destinies. Perturbations in epigenetics not only fuel HCC progression but also sculpt the tumor microenvironment, shielding it from immune evasion. These epigenetic signatures could serve as vital indicators for immunotherapy response and potential targets to thwart ICI resistance, boasting reversibility, flexibility, and intricate interplays amenable to pharmacological intervention.

Recent investigations have spotlighted protein arginine-methyltransferase 4 (PRMT4), or CARM1, as a prominently expressed, tumor-promoting gene in HCC. Our interdisciplinary endeavor aims to: i) scrutinize CARM1's role in HCC pathogenesis; ii) evaluate the anti-tumoral potential of CARM1 inhibition and its synergy with ICI therapy in HCC—utilizing diverse HCC cell lines and preclinical models of liver disease and carcinogenesis. This initiative aspires to unravel the pathological nuances of CARM1 across HCC's trajectory and guide future clinical trials for a tumor type with a dismal prognosis.

yes	x
no	

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