



Universidad
de Navarra

Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA

Research Project Proposal

Academic year 2025-2026

Project Nº 19

Title: *The Intricate role of G9a in hepatocarcinogenesis and its potential as effective Therapeutic Target.*

Department/ Laboratory *Hepatology: Molecular Mechanisms and Targets in Liver Carcinogenesis group. Solid Tumors Program. CIMA – University of Navarra.*

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Summary

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. Unfortunately, it is frequently diagnosed at advanced stages, when curative treatments such as surgery or locoregional therapies are no longer viable, leading to a very poor prognosis. This is largely due to the tumors' limited responsiveness to conventional chemotherapy and the modest success of existing targeted therapies. In contrast, immune checkpoint inhibitors (ICIs) have shown promise in a subset of HCC patients, yet their overall efficacy remains suboptimal. Therefore, it is crucial to uncover the molecular drivers that contribute to HCC aggressiveness and to explore more effective treatment approaches. Epigenetic mechanisms play a key role in maintaining cellular identity and function, and their disruption can promote oncogenesis through aberrant activation of proto-oncogenes and silencing of tumor suppressor genes. We recently identified the histone methyltransferase G9a as a significant contributor to hepatocarcinogenesis and demonstrated the therapeutic potential of targeting it pharmacologically. However, further investigation into G9a's role is warranted. The general aim of this project is to elucidate G9a's mechanistic involvement in HCC development and assess the therapeutic benefits of its inhibition. First, we will study G9a's role in liver injury and regeneration—two fundamental processes in HCC development—using acute and chronic injury models (via CCl₄) and regeneration after partial hepatectomy in G9a^{ΔhepKO} and wild-type mice. We will analyze liver damage, inflammation, repair, and cell proliferation. Second, we will assess G9a's role in tumorigenesis using human-relevant genetic HCC models via hydrodynamic tail vein injection, evaluating tumor dynamics, histopathology, immune contexture, and signaling pathways.

yes	X
no	

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