Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2026-2027

Project Nº 02

Title: Developing novel EPIgenetic drugs for advanced cardiac FIbrosis Therapy

Department/ Laboratory Bioquímica y Genética / Ischemic Heart Disease & Regenerative Medicine Group (https://sites.google.com/unav.es/i-heartgroup/portada)

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Summary

Cardiac disease, primarily driven by adverse remodeling and fibrotic scar formation, remains the leading cause of mortality and morbidity worldwide. Despite significant progress in research, an effective anti-fibrotic treatment has yet to become clinically available. However, promising advances are emerging through the exploration of novel epigenetic therapies.

Our group has employed both bulk and single-cell CRISPR perturbation in primary cardiac fibroblasts (CFs), alongside *ex vivo* functional assays, to identify **key chromatin factors involved in fibrotic processes**. Subsequent ATAC-seq analyses have uncovered the roles of various transcription factors regulated by these chromatin factors, highlighting their crucial involvement in fibrosis (Aguado-Alvaro *et al.* **Nat Commun**. 2025; doi: 10.1038/s41467-025-66597-9).

Building upon these findings, we aim **to develop a first-in-class epigenetic-based drug** that will effectively treat the disease by reversing fibrotic scarring in the heart. The three top-score inhibitors available against this chromatin factor will be tested *in vitro* in a primary murine CF platform (previously developed by our group). Dose and specificity of action of the molecules will be determined, and the best molecule will be chosen for further analysis. **Functional *in vitro* assays, as well as NGS techniques,** will be also performed to elucidate the molecular mechanisms underlying the inhibitor´s regulatory effect.

Our major innovative outcome will be to **deliver a novel epigenetic molecule** with a great impact on reducing cardiac fibrosis, and potentially other kind of fibrosis. For future clinical translation, the therapeutic potential of this novel drug could be tested, in a second stage project, in **human organoids and** a **murine model of myocardial infarction** that greatly resemble the damaged heart in humans**.**

The development of a new drug for fibrosis not only tackles key global research objectives but also holds promise for lowering healthcare expenses, reducing hospital stays, and enhancing the well-being of patients.

yes	X
no	

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