Universidad de Navarra
Facultad de Ciencias

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

Project Nº 11

Title: *A Spatial and Transcriptomic Atlas of Resistant Niches: Identifying Actionable Targets to Restore Radiosensitivity in NSCLC*

Department/ Laboratory
LUNGSearch Laboratory, CIMA

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Summary Non-Small Cell Lung Cancer (NSCLC) remains the leading cause of cancer-related mortality worldwide. While Radiotherapy (RT) is a cornerstone of treatment, its curative potential is severely limited by the development of radio-resistance. Current clinical approaches fail to account for the complex interplay between tumor cells and the Tumor Microenvironment (TME). Our preliminary data indicate that syngeneic murine tumors, which are highly resistant to RT in immunocompetent hosts, become sensitive when grown in immunodeficient mice. This pivotal finding suggests that the TME acts as a protective "shield" against radiation. We hypothesize that resistance is driven not merely by the presence of specific immune cells, but by their precise spatial topology and intercellular crosstalk.

This aims to decipher the spatial architecture of radio-resistance and identify actionable targets to restore radiosensitivity. To achieve this, we will first generate a comprehensive spatial atlas of resistance in humans. We will employ Spatial Transcriptomics on a retrospective cohort of RT-treated NSCLC patients, comparing responders versus non-responders to map cellular neighborhoods and transcriptomic signatures associated with resistant niches. These findings will be validated via multiplexed immunofluorescence in an expanded clinical cohort. To understand the temporal dynamics of this resistance, we will simultaneously characterize our established radioresistant syngeneic mouse models (Lacun3 and CMT167). By performing longitudinal RNA sequencing and multiplexed immunofluorescence before and after irradiation with a clinical-grade SARRP platform, we will track the spatiotemporal evolution of TME remodeling under stress.

Through a systems biology approach, we will integrate these spatial and transcriptomic data to identify key "druggable" ligand-receptor interactions that drive protection against RT.

yes	X
no	

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