Universidad de Navarra

Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 13
Title: *Modulating the Innate Immune Response mediated by Complement to Enhance Lung Cancer Immunotherapy*
Department/ Laboratory *Translational Oncology. Program in Solid Tumors. Division of Cancer. Cima Universidad de Navarra*
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Summary

Immunotherapy targeting the PD-1/PD-L1 axis has emerged as a powerful approach for the treatment of lung cancer, restoring antitumor immune responses by reversing T-cell inhibition. However, not all patients benefit from this strategy, as PD-1/PD-L1 blockade alone is insufficient to overcome all resistance mechanisms.

Over the past years, our research has focused on understanding the role of complement activation in lung cancer, particularly the contribution of the C5a/C5aR1 axis. We have demonstrated that complement component C5a, through its receptor C5aR1, promotes the development of an immunosuppressive tumor microenvironment that supports cancer progression. Importantly, our preclinical studies have shown that pharmacological inhibition of C5a synergizes with PD-1 blockade, leading to enhanced control of lung tumor growth and suppression of metastatic dissemination. Building on these findings, a Phase I/II clinical trial (STELLAR-001) was launched to assess the safety and efficacy of combined C5a/C5aR1 and PD-1/PD-L1 inhibition in patients with advanced solid tumors.

In this context, we propose a research project aimed at further dissecting the mechanisms by which C5a/C5aR1 signaling influences lung tumor development. Additionally, the immunological impact of dual C5a and PD-1 blockade will be investigated in syngeneic *in vivo* models, with the goal of optimizing this combinatorial approach and overcoming resistance to immunotherapy.

This project will contribute to a deeper understanding of the interplay between cancer and innate immunity, identify novel therapeutic targets, and potentially support the development of more effective treatments for lung cancer.

yes	x
no	

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