Universidad de Navarra
Facultad de Ciencias

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

Project Nº 30

Title: Generating self-amplifying RNA vectors able to propagate through the generation of extracellular vesicles for cancer therapy

Department/ Laboratory *Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.*
Laboratory of Cancer Gene Therapy , Program of RNA Biology and Therapy, Division of DNA and RNA Medicine, CIMA

Director 1 *Name and surname of the director (If there will be two co-directors indicate both)*
Contact: *Cristian Smerdou Picazo*
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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used*

In our laboratory we have extensively worked with a self-amplifying RNA viral vector based on Semliki Forest virus (SFV). This vector has shown remarkable antitumor properties when used to express immunostimulatory molecules, such as cytokines or antibodies against immune checkpoints. Although the SFV vector can provide high expression levels of therapeutic proteins in tumors, this expression is very transient due to the fact that the vector is unable to propagate.

In this project we propose to modify the vector genome to allow it to generate extracellular vesicles that could transfer the self-amplifiying RNA from the initial infected cells to neighbouring cells, increasing in this way the mass of the tumor reached by the vector and potentially enhancing its antitumor effects.

For that purpose, the following partial objectives are proposed:

- Construction of SFV plasmids with modifications in the replicase gene of SFV that have been described to promote the production of extracellular vesicles

- Generating viral vectors containing the modified SFV RNA coding for reporter proteins, like GFP or luciferase and for therapeutic proteins, like antibodies against PD-1 and PD-L1 immune checkpoints

- Testing these new RNA vectors in cell culture, analyzing their propagation and the production of infectious extracellular vesicles

- Testing the antitumor activity of these vectors in an animal model of cancer comparing them with conventional non-propagative vectors expressing the same transgenes

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The project will involve the use of many different techniques, including molecular biology, cell culture, virus production, analysis of protein expression, imaging techniques, immunological techniques, animal models of cancer etc.

Note: There is the possibility of performing a PhD thesis after the TFM provided a fellowship is obtained (minimun score required in universty studies: 2 in the scale 1-4)

yes	X
no	

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