



MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 28
Title: RNA-targeted therapeutics to sensitize tumor cells to immunotherapy.
Department/ Laboratory: Molecular Therapeutics, RNA Aptamer Therapeutics, CIMA
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Summary
There is an unmet need to develop a feasible clinical therapeutic platform to increase the rate of response to cancer immunotherapy. We have experience with a novel biotechnological RNA aptamer platform aimed to modulate the immune response and facilitate the antitumor immune attack. Aptamers are high-affinity targetable oligonucleotide ligands that allow the precise delivery of different types of therapeutic cargos including RNA drugs. We will use this platform to tackle one of the most resilient tumor cells that account for circulating tumor cells (CTCs), which are responsible for tumor relapse and therapy resistance. To select anti-CTC aptamers, we will perform an in-vivo SELEX to screen RNA aptamers using different tumor murine models (Maite Sola et al Molecular Therapy Nucleic Acids 2020). The selected aptamers will be screened using high-throughput sequencing (HTS) techniques combining different bioinformatic pipelines. The selected aptamer will be tested using different devices and techniques to determine the affinity and specificity of the top enriched aptamers. The best aptamer candidates will be conjugated with immunomodulatory RNA cargos to improve the antigen presentation in the context of cancer immunotherapy with immune-checkpoint blockade agents.
The master's thesis student will be exposed to many technologies during the timeframe of the master's program: molecular biology techniques (cloning, RNAi, mRNA synthesis and aptamer in vivo SELEX), cell and tissue culture, in vivo animal experiments, different immunoassay techniques, flow cytometry, image confocal microscopy, and different bioinformatic pipelines for HTS analysis.
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator? yes