



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

Project Nº 15
Title: Understanding resistance to immunotherapy in pancreatic cancer
Department/ Laboratory: Tumor evasion and new targets lab (2.04), Solid Tumors Program (CIMA)
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Summary: Immunotherapy and, in particular, immune checkpoint blockade (ICB) have revolutionized cancer treatment in the last years and has shown long-term responses in several different cancer types. However, only a residual fraction of pancreatic cancer (PanC) patients treated with immunotherapy exhibit clinical benefits. Genetic and epigenetic programs modulate the tumor immune microenvironment (TME) and can regulate the antitumor immune responses which ultimately result in immunotherapy failure. We use a multiomic approach to identify the tumor intrinsic mechanisms that hinder anti-tumor responses for overcoming resistance to immunotherapy in PanC. Additionally, we perform a comprehensive analysis of the infiltrate and the tumor alterations induced by deletion of selected genes to understand the mechanisms of immune suppression in PanC. Our ultimate goal is to discover novel treatments that synergize with ICB for the treatment of PanC. The proposed research will provide: i) mechanistic evidence of the genetic programs that cause resistance to immunotherapy and ii) strong basis for new combinatorial strategies to improve antitumoral responses with ICB in PanC.
GOALS:
- To generate KO tumor cell lines for candidate genes using CRISPR/Cas9 gene editing technology.
- To functionally validate the effects of genetic deletion of candidate genes in the context of irradiation in vitro and in vivo
METHODOLOGY:
The candidate will learn standard techniques for in vitro and in vivo work such as: cell culture, manipulation of recombinant DNA for CRISPR/Cas9 gene editing, western blot, multiparametric flow cytometry, in vivo tumor models, etc.
yes X
no
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?