



**Research Project Proposal**  
Academic year 2018-2019

**Project Nº 39**

**Title:** *Cancer Gene Therapy based on local expression of immunostimulatory genes*

**Department/ Laboratory** *Gene Therapy and Regulation of Gene Expression Program. CIMA. Laboratories 4.06 and 4.04.*

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**Summary**

Previous work from the host laboratories has demonstrated a significant antitumor effect of gene therapy vectors (Adenovirus and Semliki Forest Virus) encoding a monoclonal antibody against the immune checkpoint protein PD-L1. In the present project we aim to optimize the efficacy of this approach by testing different antibody conformations, as well as combination with other immune modulation molecules. In particular, we will explore the synergy between PD-1/PD-L1 blockade and the interference with galectin pathways, using chemical and genetic approaches.

For safety and efficacy evaluation we will use syngeneic tumor models based on subcutaneous and orthotopic inoculation of cancer cells (colon cancer, pancreatic cancer) in mice.

Vectors will be characterized in vitro (titration and transgene expression by qRT-PCR, Western blot and ELISA), and then administered intratumorally in mice. In vivo transgene expression will be determined by ELISA from serum and tumor samples. Survival, biochemical markers of toxicity and tumor progression will be monitored for at least one month after vector inoculation. Immune responses against tumors will be analysed in mice treated with the optimized protocol.

yes	X
no	

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