



Research Project Proposal
Academic year 2023-2024

Project Nº 14	
Title: <i>Vaccination to improve the efficacy of CAR-T cells in Glioblastoma</i>	
Department/ Laboratory Laboratorios de “Terapia celular adoptiva” y “Terapia Génica para Cáncer” del Programa de “Inmunología e Inmunoterapia” y “Terapia Génica”, respectivamente. Centro de investigación Médica Aplicada (CIMA).	
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Summary <p>Chimeric antigen receptor (CAR) T cells (CAR-T) represent a revolutionary treatment for hematological tumors but their efficacy in solid tumors has not been yet supported. In the case of solid tumors, the recognition of the CAR antigen (CAR-Ag) and activation of CAR-T cells occur exclusively in the tumor microenvironment (TME). However, the immunosuppressive TME prevents the efficient activation of CAR-T cells. We hypothesized that the use of vaccines expressing the CAR-Ag could exert a boosting effect and substantially improve the efficacy of CAR-T therapy in solid tumors. Using a vaccine based on a RNA virus expressing the CAR-Ag, we have demonstrated that the combination of CAR-T cells with the vaccine fosters the antitumor efficacy of CAR-T therapy in preclinical models of breast cancer. We want to delve into the mechanism of action of this combination, while applying it to the treatment of glioblastoma (GBM), a frequent type of brain tumor with very poor prognosis. For that purpose, the following objectives are proposed: (1) To study the effect of the vaccine on (i) the expansion and persistence of CAR-T cells <i>in vivo</i> and (ii) other cells present in the tumor, such as endogenous T cells, myeloid suppressor cells, macrophages, Tregs...); (2) To test the antitumoral activity of the CAR-T-cell/vaccine combination in mouse models of GBM. The project will involve the use of many different techniques, including genetic modification of T-cells, virus production, analysis by flow cytometry and immunohistochemistry, animal models of cancer (breast and GBM), <i>in vivo</i> experiment of CAR-T therapy...</p>	
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	
yes	√
no	