



Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 17		
Title: Development of improved CAR T cells for immunotherapy against Multiple Myeloma		
Department/ Laboratory: <i>Immunology and Immunotherapy program.</i> <i>Lab 3.02. CIMA.</i>		
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<p>Summary: Multiple Myeloma (MM) remains an incurable disease despite therapeutic advances. Chimeric Antigen Receptor T cells (CAR T) are one of the most promising immunotherapies for the treatment of cancer. CAR T showed great efficacy against hematological malignancies. However, CAR T against MM were not successful in clinical trials due to the poor persistence of CAR T after transfer, and the loss of antigen expression in MM cells. In order to develop more efficient and persistent CAR T, we have identified a way to improve their long-term survival by including the pro-survival cytokine IL-15 and its receptor in the anti-MM CAR. We have also identified a way to overcome antigen loss by generating a CAR that expresses APRIL, a molecule that has several binding partners in MM cells. Using novel MM murine models we want to test the efficacy of these improved CARs.</p> <p>Goal: The overarching goal of this project will be to generate CAR T cells against MM that are more effective and persistent.</p> <p>Methodology: This project will include the use of common laboratory techniques including Molecular Biology (vector construction, cloning, qPCR), cell culture, and virus production, and immunology techniques like flow cytometry, ELISPOT or ELISA. Animal tumor models will be used to test the efficacy and characterize CAR T immunotherapies against MM. The roles of the student are:</p> <ul style="list-style-type: none"> - Construction and production of retroviral vectors able to successfully express CARs. - Production of retrovirus to engineer T cells to express the CARs. - <i>In vitro</i> characterization: analyse expression and functionality of CAR T cells using different techniques. - <i>In vivo</i> characterization of the CAR T cells anti-tumor immune response using MM murine models. 		
yes	x	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no		