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1. *Title:*

BCMA and SLAMF3 (CD229) chimeric antigen receptor T-cell immunotherapy in multiple myeloma.

2. Scientific abstract:

Multiple myeloma (MM) is the second most common hematologic malignancy. In the last years, the outcome of MM patients has shown remarkable improvements primarily due to the incorporation of novel therapeutic agents, like proteasome inhibitors (bortezomib, carfilzomib), immunomodulatory agents (lenalidomide, pomalidomide), and monoclonal antibodies (elotuzumab and daratumumab). However, MM remains incurable for most patients. In recent years, immunotherapy treatment infusing autologous Chimeric Antigen Receptor (CAR)-modified T cells have shown outstanding responses in B cell malignancies. Regarding MM, BCMA and SLAMF3 has appeared as the most suitable targets to produce CART cells against MM, due to specific expression in MM cells, mostly absent in the rest of tissues. In the clinical setting, BCMA-CAR T cells have shown excellent results in patients with relapsed/refractory MM, with 70-100% objective responses. Regarding SLAMF3-CAR T cells in the preclinical setting, there is data that illustrate therapeutic potential against this antigen. However, two of the main problems associated with CART immunotherapy are the disappearance of CART cells and the tumor antigen escape from CART cells. At Hospital Clínic, we have developed a GMP facility to produce our own CART cells. We have designed and successfully tested a BCMA-CAR T cell against malignant plasma cells. In the proposed project, we will create an academic CD229-CAR T cell, humanize it to increase its persistence, demonstrate its efficacy in vitro and in vivo. To solve the problem of tumor antigen scape, we will evaluate the efficacy of the dual target approach against BCMA and SLAMF3 using a bicistronic or a tandem CAR T cell.

3. Keywords: *multiple myeloma; immunotherapy; T-cell; chimeric antigen receptor, BCMA, CD229*