



Master project

Start date: September 1st, 2026

Latest start date: March 31st, 2027

Project duration: 1 year

Supervisor/Co-supervisor: Diogo Silva and João F. Lacerda

Lab: João Lacerda Lab

GIMM site: Lisbon

Project title: Molecular Engineering of Chimeric Antigen Receptors for Precision Cancer Therapy

Project synopsis:

Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the treatment of hematological malignancies, particularly B cell leukemias/lymphomas and multiple myeloma by targeting CD19 and BCMA proteins. Yet significant challenges remain in expanding its efficacy to a broader range of cancers and patient populations particularly given the lack of cancer-specific antigens in other forms of cancer. Therefore, in this line of research, our group focuses on advance molecular designs of novel CAR constructs to address current limitations in target selectivity, therapeutic scope, and clinical applicability.

By exploring innovative CAR architectures and novel target antigens — including disease-specific cell surface markers and non-conventional molecular targets — this work seeks to develop next-generation immunotherapeutic tools with improved precision and versatility. Research lines encompass the engineering of CARs directed against specific tumors in hematological malignancies with particular interest in acute myeloid leukemia and the



targeting of leukemic stem cells while avoiding permanent toxicities over CD34+ cells, but also solid tumors, by targeting unconventional cancer markers expressed due to aberrant post-translational modifications. Hence, we seek to develop novel CAR molecules generating novel CAR T cell therapies and validate their clinical potential in in vitro preclinical models, by testing not only the ability of our constructs to improve anti-tumor responses by T cells but also the immunological characteristics of our CAR T cells regarding phenotype, persistence potential and cytokine production.

Students joining this project will gain hands-on experience in molecular biology (DNA cloning), CAR construct design and validation, and functional immunological assays (cell culture and flow cytometry), working at the interface of fundamental research and clinical translation.

Application: Applications should include a current CV and a letter of motivation, and must be submitted by email directly to the Supervisor and Co-supervisor by email:

diogo.silva@gimm.pt ; jlacerda@medicina.ulisboa.pt