



**Project title:** “Development of Novel Cellular Platforms for Immunotherapies”  
**Group Leader:** Georges Lacaud  
**Research Group:** Stem Cell Biology

Blood transfusions, bone marrow stem cell transplants, and immunotherapies are fundamental procedures in the treatment of malignant and non-malignant disorders. Among these, cell-based cancer immunotherapy has revolutionised the treatment of haematological malignancies. Specifically, autologous chimeric antigen receptor-engineered T (CAR-T) cell therapies have received approvals for treating leukaemia, lymphoma, and multiple myeloma following unprecedented clinical response rates.

A critical barrier to the widespread usage of current CAR-T cell products is their autologous nature. These cellular products are patient-selective, and therefore very costly and challenging to manufacture. In contrast, allogeneic cell products can be scalable and readily administrable. However, these procedures face critical concerns of graft-versus-host disease, a life-threatening adverse event in which therapeutic cells attack host tissues, and rejection, by host immune cells, limiting their antitumor efficacy.

Stem cell-derived immune cells could represent potential alternatives to overcome these limitations and offer off-the-shelf therapies. These stem cell-engineered allogeneic cell therapies could include conventional  $\alpha\beta$  T cells as well as unconventional T cells, natural killer cells and myeloid cells. Most of these cells could be generated independently from haematopoietic stem cells through an endothelial to haematopoietic transition.

In this project, we aim to establish human cell production platforms to generate immune cells for therapeutic production. We will thoroughly define optimal protocols to efficiently and robustly generate these specific therapeutic cells, and then evaluate the therapeutic potential of these cells. This project will provide outstanding training in the field of cellular and molecular haematopoiesis, oncology, immune cellular assays, *in vivo* mouse models, flow cytometry and single-cell omics approaches.