EUH : ENGINEERING γ9δ2 T CELLS TO UNDERSTAND AND HARNESS THEIR ANTI-TUMOR POTENTIAL (C. HARLY)

Promising immunotherapeutic strategies against cancer are based on adoptive transfer(s) of circulating anti-tumor T cells that can specifically recognize and eradicate tumor cells. Human γ9δ2 T cells are particularly promising for the development of broadly applicable cheap strategies. However, advances in understanding and improving γ9δ2 T cells anti-tumor functions have been impeded by issues that could only be addressed by precise engineering of these cells, which was not possible until now. In this project, we propose to take advantage of cutting-edge genetic editing approaches to better understand how γ9δ2 T cells recognize tumor cells, and improve their performance against solid tumors. Our team has long been committed to understand and to harness the mechanisms of γ9δ2 T cells anti-tumor functions to design and improve immunotherapeutical strategies. We have recently re-enforced our commitment by applying newly developed virus like particles to deliver CRISPR/Cas9 genetic deletions tools to γ9δ2 T cells with high efficiency. We now propose to implement complementary approaches for genetic insertion, and use both approaches to address two new research hypotheses. The infrastructure put in place in this project, as well as the results obtained, should provide the groundwork needed to put us in a highly competitive position to subsequently obtain funds though national and international agencies, for both basic and applied research programs.