

The project aims to investigate the relationship and complexity of the processes involved in the interaction between cancer cells and programmed T-cells in the tumour microenvironment, focusing on CAR-T cell activation, and minimizing the effects of off-target targeting and CAR-T exhaustion. The success of CAR-T cell technology has been remarkable for blood cancers, and the FDA and EMA have already approved some CAR-T cell therapies. However, CAR-T therapy faces challenges in the treatment of solid tumours due to the complex microenvironment, limited infiltration, and CAR-T cell exhaustion.

The project will compare a lung cancer model with a breast cancer model. These are groups of aggressive, genetically complex and difficult-to-treat cancers. Striving to understand the mechanisms of cancer cell destruction by controlling the activation of T-lymphocytes will increase the effectiveness of therapy in treating cancer. Directing CAR-T cell activation is one way to understand their exhaustion due to their interaction with cancer cells. For a deeper understanding of this phenomenon, we will use the optogenetic system to locally control the activation of CAR-T cells and study the process of their activation and exhaustion.

Implementing the project's objectives will contribute directly to the scientific understanding of CAR-T cell exhaustion and off-target effects. It will also allow for broadening of knowledge about increasing the effectiveness of CAR-T cell therapy, and thus improving the treatment of solid tumours.