

## **Comprehensive Seminar**

## CAR-T Cells: Synthetic biology strategies for overcoming therapeutic barriers

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Chimeric Antigen Receptor (CAR) T-cell therapy has proven to be one of the most promising targeted therapies for treating cancers. CAR-T cells are generated by genetically modifying a patient's own T-cells ex vivo or in vivo to express chimeric receptors against a tumour-specific antigen, enabling them to recognise and eliminate cancer cells. CAR-T cell products are clinically approved for treating B-cell acute lymphoblastic leukemia (ALL) and multiple myeloma.

As effective as CAR-T therapy is, it has several limitations. As living drugs, these cells can become overactivated, potentially leading to severe toxicities such as cytokine release syndrome (CRS), which can cause organ damage. There is a significant unmet need for technologies that can precisely and controllably turn on and off CAR-T cells to mitigate CAR-T-induced side effects. The tumour-killing ability of CAR-T cells also depends on their persistence in tumour tissue and the number of activated cells, which are directly influenced by the nature of the cancer type and microenvironments.

In my talk, I will discuss some of the challenges associated with current CAR-T cell treatment and the synthetic biology-based strategies employed to overcome them. Furthermore, I will describe recent advances in using CAR-T for treating brain cancers such as glioblastoma. I will address our motivation to develop tools for understanding the persistence and phenotypes of these CAR-T cells in the brain and controlling CAR-T-mediated toxicity, where existing strategies are inadequate.

Monday, Jun 30<sup>th</sup> 2025 14:30 Hrs (Tea / Coffee 14:15 Hrs) Trishul Hall, TIFRH