Armoured CAR T-cells: utilizing cytokines and pro-inflammatory ligands to enhance CAR-T-cell anti-tumour efficacy

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Recently published reports support the novel approach of treating cancer with patient derived T-cells genetically modified to express artificial T-cell receptors, termed chimeric antigen receptors (CARs), targeted to tumour associated antigens. Initial clinical trial outcomes of patients with relapsed B cell acute lymphoblastic leukemia (B-ALL) treated with T-cells genetically modified to express a CAR specific to the CD19 antigen demonstrate that this approach is a very promising therapeutic intervention which potentially may dramatically alter the standard of care in this disease. In contrast far more modest clinical responses were seen in patients with relapsed low grade B cell malignancies including chronic lymphocytic leukemia (CLL) and B cell non-Hodgkins lymphomas (NHL), not only at our center but at other centers including UPenn and the NCI. The discordant clinical outcomes between B-ALL and CLL patients treated with CD19 targeted CAR T-cells remains a subject of conjecture although the tumour microenvironment is a strong focus for further investigation. To this end, we will present data on a next generation of CAR T-cells, termed “armored CARs” further genetically designed to overcome an immune suppressive tumour microenvironment through further genetic modification of CAR T-cells secrete the pro-inflammatory IL-12 cytokine or constitutively express the CD40L T-cell co-stimulatory ligand. Promising preclinical studies utilizing these “armored CAR” T-cell approaches and their role in future clinical trials will be discussed.