Docket #: S20-068

Genetically modified immune cells increase potency of adoptive immunotherapy

The potency of cancer immunotherapies for solid tumors are often diminished by inadequate metabolic reprogramming and resulting immune evasion in cancer. To acquire a fully activated state upon antigen encounter, T cells must undergo metabolic reprogramming to support cell growth, proliferation, and cytotoxic function. This reprogramming is sensitive to regulation of nutrient transporters and nutrient availability. Unfortunately, the tumor microenvironment in cancer is associated with limited nutrients due to competition between the tumor cells and infiltrating immune cells.

The Mackall lab invented a method to metabolically enhance immune cells during immunotherapy. Through the regulation of a group of genes, the invention leads to enhanced metabolic reprogramming and subsequently increases immune cell activation, cytokine secretion and tumor killing. The invention also functionally restores exhausted T cells and can be applied to immune cells expressing natural receptors, or those engineered to express antigen specific receptors such as chimeric antigen receptors (CARs) and recombinant TCRs.

Stage of Development
Proof of concept – in vivo

Patent Status
PCT application filed

Applications

- CAR-T Cell Therapy
- TCR Therapy

- Other adoptive cell therapies

Advantages

- Enhancement of immune cell cytotoxic function, proliferation and persistence
- Improvement of effector function of exhausted and non-exhausted cells
- Can be regulated by drug on/off systems

Publications

- Guerrero, J.A., Klysz, D.D., Chen, Y. et al. GLUT1 overexpression in CAR-T cells induces metabolic reprogramming and enhances potency. Nat Commun 15, 8658 (2024).

Patents

- Published Application: WO2022011130
- Published Application: 20230248824

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