Docket #: S22-010

Supplementation with inosine improves CAR-T cell metabolism and anti-tumor effects

Researchers at Stanford have developed a method of culture media supplementation with inosine during the chimeric antigen receptor (CAR)-T cell manufacturing process which can alter and enhance CAR-T cell metabolism and anti-tumor functions. Poor efficacy and persistence have hindered the success of CAR-T cell immunotherapy in many patients and tumor types. To address these challenges, this method adds inosine to culture media, resulting in changes in CAR-T cell phenotype and metabolic features. Supplemented CAR-T cells were shown to use inosine as a carbon source, relieving tumor-imposed metabolic restrictions on T cells and leading to increased anti-tumor potency in vitro. The supplemented CAR-T cells can further improve the efficacy of immune checkpoint blockade and adoptive T cell therapies in vivo, prolonging survival in mouse models of solid tumors unable to metabolize inosine. This method can be used during CAR-T cell manufacturing or in further immunotherapy research and development efforts to improve CAR-T cell function.

Stage of Development:
Prototype

Applications

- This method can be used by stakeholders with an interest in improving CAR-T cell efficacy:
    - Academic researchers
    - Biotech companies
    - Pharmaceutical companies
    - Cell manufacturing centers

Advantages

- Easy method implementation
- Improved anti-tumor potency of CAR-T cells
- Improved persistence of CAR-T cells in vivo
- Improved efficacy of immune checkpoint blockade and adoptive T cell therapies

Publications

- **Dorota D. Klysz**, Carley Fowler, Meena Malipatlolla, Lucille Stuani, Katherine A. Freitas, Yiyun Chen, Stefanie Meier, Bence Daniel, Katalin Sandor, Peng Xu, Jing Huang, Louai Labanieh, Vimal Keerthi, Amaury Leruste, Malek Bashti, Janette Mata-Alcazar, Nikolaos Gkitsas, Justin A. Guerrero, Chris Fisher, Sunny Patel, Kyle Asano, Shabnum Patel, Kara L. Davis, Ansuman T. Satpathy, **Steven A. Feldman**, Elena Sotillo, **Crystal L. Mackall** (2024). Inosine induces stemness features in CAR-T cells and enhances potency. *Cancer Cell*, Volume 42, Issue 2, Pages 266-282.e8, ISSN 1535-6108.

Patents

- Published Application: WO2024010955

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