Docket #: S22-364

CD39 to enhance or reduce cytotoxicity of chimeric antigen receptor modified or otherwise genetically engineered T regulatory cells

Stanford researchers have defined subgroups of regulatory T cell (Tregs), CD39+ and CD39-, that can be genetically engineered to produce enhanced or reduced cytotoxicity without affecting their ability to suppress the immune system.

Tregs suppress immune response to maintain homeostasis. Chimeric antigen receptor (CAR) engineered T cells (CAR-Treg) are antigen specific, as the CAR is a receptor that selectively binds to antigens present on a target cell population. Stanford researchers have identified T regulatory cell subsets CD39+ and CD39-. Populations of CAR-Treg cells are bimodal with respect to expression of the surface marker CD39, where the cytotoxic potential of these cell population depends on the expression of CD39. Selection for a CD39+ CAR-Treg population provides for a population with significantly reduced cytotoxic risk toward the cell population targeted by the CAR. Conversely, selecting the CD39- CAR-Treg subgroup can enhance cytotoxicity toward CAR-targeted cells.

The CD39+ cell subgroup has potential to improved immunoregulatory function, which are useful in the treatment of autoimmune disease, to provide tolerance in transplantation, to promote wound healing or tissue regeneration etc. The CD39- cell populations on the other hand can be used for depletion of targeted populations, e.g. in cancer, depletion of undesirable antigen-presenting cells such as those present in transplantation rejection, autoimmune or inflammatory diseases.

Stage of Development
In vitro

Applications

- Type I Diabetes
- Cancer
- Immune disorders
- Transplantation
- Autoimmune diseases

Advantages

- Manipulate cytotoxic function
- Targeted cell population

Publications

- Wu X, Chen PI, Whitener RL, MacDougall MS, Coykendall VMN, Yan H, Kim YB, Harper W, Pathak S, Iliopoulou BP, Hestor A, Saunders DC, Spears E, Sévigny J, Maahs DM, Basina M, Sharp SA, Gloyn AL, Powers AC, Kim SK, Jensen KP, Meyer EH. CD39 delineates chimeric antigen receptor regulatory T cell subsets with distinct cytotoxic & regulatory functions against human islets . Front Immunol. 2024 Jun 28;15:1415102. doi: 10.3389/fimmu.2024.1415102. PMID: 39007132; PMCID: PMC11239501.

Patents

- Published Application: WO2024107410

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