Docket #: S21-181

A Method to Enhance CAR T Efficacy through Adenosine Deaminase Overexpression

Stanford Scientists have developed an innovative approach that enhances the antitumor efficacy of CAR T cells by overexpressing Adenosine Deaminase 1 (ADA), an enzyme responsible for metabolizing adenosine into inosine, to attenuate the immunosuppressive tumor microenvironment.

Although promising, CAR T cell therapy efficacy in solid tumors is limited by hostile tumor microenvironments, limited CAR T persistence, and lack of tumor killing. Extracellular adenosine contributes to the hostile tumor microenvironment by binding the adenosine A2a receptor on immune cells. Blocking A2aR or enhancing ADA-mediated adenosine metabolism to inosine protects T cells from adenosine-mediated immunosuppression. Stanford scientists showed that human CAR T cells are also susceptible to adenosine-mediated immunosuppression. They developed an approach where they overexpressed ADA in exhausted and non-exhausted CAR T cells leading to a higher frequency of stem cell-like memory T cell effectors, and a simultaneous decrease of exhausted subpopulations. Both antigen-driven proliferation and effector function of CAR T cells also significantly improved after ADA overexpression. Therefore, overexpression of adenosine deaminase in CAR T cells is a novel and efficient way to evade immunosuppression.

Stage of Development

Research – in vitro

Applications

- CAR T immunotherapy, especially for solid tumors

Advantages

- Brand new approach
- Can increase resistance to immunosuppression and improve potency of existing cancer immunotherapies against solid tumors

Publications

- Dorota D. Klysz, Crystal L. Mackall, et al.. "Inosine Induces Stemness Features in CAR T cells and Enhances Potency." bioRxiv 2023.04.21.537859.

Patents

- Published Application: WO2023034742

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