Docket #: S20-297

Target-Recognition of Antigen-MHC Complex Reporter (TRACeR) Platform

Researchers at Stanford have created a de novo protein design platform that designs binding proteins specifically interacting with the MHC-peptide complex.

MHC (major histocompatibility complex) are protein molecules that bind peptide fragments derived from pathogens and display them on the surface of cells for recognition by the immune system. T cell receptors (TCRs) have evolved to recognize the peptide identities on the MHC-peptide complexes via interaction with both the antigenic peptide and the MHC. There have been significant efforts to engineer TCRs to allow improved recognition and destruction of virus-infected cells or cancer. However, TCR engineering remains a challenge due to its structural complexity.

Stanford inventors have created a non-TCR protein platform to design functional mimetics of TCRs that recognize the MHC-peptide complexes. Proteins that specifically bind to an MHC-peptide complex of interest are designed using computer-based protein engineering and high throughput screening assays. The designed binding protein, or TRACeR, is simpler in structure than TCRs, and comprises an antigenic peptide recognition element and an MHC recognition element. Selected binders are screened for binding strength against thymic epithelial cells to minimize cross-reactivity with self-MHC-peptides. The antigenic peptide binding region of TRACeR can be developed into a therapeutic agent that activates cytolytic pathways to kill viruses or cancerous cells. For autoimmune indications, the antigenic peptide binding region can be engineered to block interactions without activating immune cytotoxic pathways.

If interested in this technology, please respond by Tuesday, September 15, 2020.

Applications

- Platform can be used to design therapeutic agents targeting:
  - viral epitopes from infections
  - tumor specific / associated antigens, including neoantigens
  - autoimmune targets
- Research or clinical use such as imaging, labeling and drug delivery

Advantages

- Compared to engineered TCRs:
  - easier to engineer and produce
  - better binding affinity and specificity with MHC-peptides
  - better stability and shelf life
- Computational protein design combined with high throughput screening allows faster turnaround

Patents

- Published Application: WO2022026926
- Published Application: 20230265195

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