Il-6 Receptor Alpha-Binding Protein And Its Use In Controlling Cytokine Release Syndrome In Immunotherapy

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SUMMARY

UCLA researchers in the Department of Chemical and Biomolecular Engineering have developed a novel protein that binds to and inhibits human IL-6 receptor alpha (IL-6Rα), which can be used to modulate and/or prevent cytokine release syndrome in immunotherapy.

BACKGROUND

Severe cytokine release syndrome (CRS), or a sudden and dramatic increase in cytokine production caused by an intensely overstimulated immune system, has been implicated in the death of multiple patients treated with adoptive T-cell therapy. In particular, IL-6 has been shown to be highly upregulated in patients experiencing severe CRS, and tocilizumab—an anti-IL-6Rα antibody—is an effective treatment for CRS in many patients. However, real-time detection of cytokine levels remains unfeasible at this time. As a result, clinical decisions on when to treat a patient with tocilizumab or other pharmaceutical interventions such as corticosteroids must be made based on indirect symptoms such as fever and rising blood pressure. Consequently, the treatment timing of CRS is imprecise and susceptible to missing the optimum treatment window.

INNOVATION

The inventors developed a single-chain variant of tocilizumab that efficiently binds to and inhibits human IL-6 receptor alpha (IL-6Rα). This synthetic protein can be used to modulate and/or prevent cytokine release syndrome in immunotherapy, particularly adoptive T-cell therapy. When stably expressed in tumor-targeting T cells, this invention can potentially increase the precision and effectiveness of CRS intervention by enabling T cells to perform real-time modulation of cytokine signaling, within the cellular milieu where CRS originates. The invention could regulate cytokine signaling in both engineered T cells and the surrounding endogenous immune cells, which are also important contributors to CRS.

APPLICATIONS

- Prevent and/or ameliorate cytokine release syndrome
- Suppress undesirable inflammatory responses

ADVANTAGES

- Self-regulating
- Real-time detection
- Effective and precise

STATE OF DEVELOPMENT

Primary human T cells that constitutively express an anti-CD19 chimeric antigen receptor (CAR) and the anti–IL-6Rα protein have been shown to significantly reduce cytokine production upon antigen stimulation, without compromising target-cell lysis or T-cell proliferation *in vitro*. It has also been shown that constitutive anti–IL-6Rα protein production does not alter CD19 CAR-T cells' subtype differentiation pattern, nor does it trigger premature exhaustion of the CAR-T cells. Finally, it has been confirmed that CD19 CAR-T cells that stably express the anti–IL-6Rα protein retain equally robust anti-tumor functions *in vivo* compared to conventional CD19 CAR-T cells.

PATENT STATUS

Country	Type	Number	Dated	Case

CONTACT

UCLA Technology Development Group
ncd@tdg.ucla.edu
tel: 310.794.0558.

INVENTORS

- Chen, Yvonne Y.

OTHER INFORMATION

KEYWORDS

Immunotherapy, T cell therapy, sequence, modulate, cytokine release syndrome, single-chain variable fragments, IL-6 receptor alpha

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2017-453-0

Australia	Issued Patent	2017319702	02/27/2025	2017-453
Germany	Issued Patent	60 2017 087 584.8	01/29/2025	2017-453
European Patent Office	Issued Patent	3506943	01/29/2025	2017-453
France	Issued Patent	3506943	01/29/2025	2017-453
United Kingdom	Issued Patent	3506943	01/29/2025	2017-453
China	Issued Patent	ZL 201780067444.9	03/15/2024	2017-453
United States Of America	Issued Patent	11,701,384	07/18/2023	2017-453
United States Of America	Published Application	20230372400	11/23/2023	2017-453
Canada	Published Application	WO 2018/042385	08/03/2018	2017-453

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Single-Chain Bispecific Chimeric Antigen Receptor Targeting BCMA And CS1 For The Treatment Of Multiple Myeloma

UCLA Technology Development Group
10889 Wilshire Blvd., Suite 920,Los Angeles,CA 90095
https://tdg.ucla.edu
Tel: 310.794.0558 | Fax: 310.794.0638 | ncd@tdg.ucla.edu