Docket #: S19-057

Generating Type 1 Regulatory T Cells Through Transcription Factor Targeting

Researchers in the Roncarolo have discovered transcription factors that enable the tracking and differentiation of type 1 T regulatory (Tr1) cells for the treatment of autoimmune conditions.

Type 1 regulatory (Tr1) cells are a subset of T regulatory cells that have been shown in clinical trials to successfully treat graft versus host disease, with the potential to treat other autoimmune diseases as well. Unlike other T regulatory cells, they are not governed by FOXP3 master control and their transcriptional machinery is ill-defined, making it challenging to engineer or induce cells that exhibit their antigen-specific tolerogenic behavior.

Researchers in the Roncarolo lab have discovered key transcription factors that govern the Tr1 cell phenotype via RNA-seq transcriptome analysis. They have proposed a method to utilize these factors to more readily induce Tr1 cell differentiation *in vivo* or *in vitro* from CD4+ T cells or iPSCs (induced pluripotent stem cells). While other methods have been described to produce these cells, they are difficult to execute, requiring the coordinated collection of donor CD4+ T cells and recipient monocytes and/or tedious clonal expansion from single cells. This invention simplifies this process, requiring just a single collection of blood and making Tr1 production more robust and scalable for therapeutic use.

Stage of Development

Research *in vitro*

Applications

- Production of Tr1 cells from CD4+ T cells or iPSCs for cell therapy to treat autoimmune conditions
- Use of transcription factors to identify, quantify, and track Tr1 cells *in vivo*
- Development of small molecule agents to induce Tr1 differentiation *in vitro* or *in vivo*

Advantages

- Simpler protocol for Tr1 cell production than existing methods
- Enables both differentiation and tracking of Tr1 cells
- Differentiation can potentially be induced either *ex vivo* or *in vivo* with the use of a small molecule agent
- Tr1 cells can be potentially generated from CD4+ T cells or iPSC lines

Publications

- Uyeda, M. J., Freeborn, R. A., Cieniewicz, B., Romano, R., Chen, P. P., Liu, J. M. H., ... & Roncarolo, M. G. (2021). BHLHE40 Regulates IL-10 and IFN-? Production in T Cells but Does Not Interfere With Human Type 1 Regulatory T Cell Differentiation. Frontiers in immunology, 12, 2705.

Patents

- Published Application: WO2020167648
- Published Application: 20220162553
- Issued: 12,319,935 (USA)

Innovators

- Maria-Grazia Roncarolo
- Molly Kathryn Uyeda

Licensing Contact

Eileen Lee

Email