Docket #: S21-023

CRISPR-based FOXP3 gene Engineered T cells and Hematopoietic Stem Cell Precursors to treat IPEX syndrome patients

IPEX syndrome is a severe autoimmune disease with limited treatment options caused by mutations in the forkhead box protein 3 (FOXP3) gene, which plays a critical role in immune regulation. As a monogenic immune disease, IPEX is an ideal candidate for a gene therapy approach whereby patient hematopoietic stem and progenitor (HSPC) cells or T cells are gene corrected ex vivo and reinfused in the patient. The Bacchetta, Roncarolo, and Porteus Labs at Stanford developed a CRISPR-based FOXP3 gene correction approach that uses homology directed repair to insert a FOXP3 cDNA into the endogenous gene locus and permit regulated expression of wild-type FOXP3 protein irrespective of downstream mutations. This site-specific approach is designed to benefit a broad range of IPEX patients, given that the causative mutations are located downstream of the insertion site. The technique permits gene delivery to patient-derived HSPCs for an autologous transplant or to T cells for autologous cell therapy. The method uniquely restores physiological expression of FOXP3 and repairs the function of multiple cell lineages disrupted by the FOXP3 mutations that is responsible for disease manifestations. This novel approach is thus suitable for developing therapies for IPEX patients with diverse FOXP3 mutations.

Applications

- IPEX syndrome therapies
- Autoimmune disease
- Cell therapies
- CRISPR-based therapies

Advantages

- Compatible with all patients and is site-specific
- Restores multiple lineages and targets multiple mutations

Publications

- Goodwin, M., Lee, E., Lakshmanan, U., Shipp, S., Froessl, L., Barzaghi, F., ... & Bacchetta, R. (2020). "CRISPR-based gene editing enables FOXP3 gene repair in IPEX patient cells". Science advances, 6(19), eaaz0571.

Patents

- Published Application: WO2021163642
- Published Application: 20230081343
- Issued: 12,540,311 (USA)

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