Gene editing Methods for CD34+ cells to achieve clinically relevant efficacies.

A research group from CIEMAT, FIIS-FJD, CIBER and the company Danaus GT Biotechnology have developed novel methods to achieve clinically relevant efficacies

The Need

Current genome-editing approaches in hematopoietic stem and progenitor cells (HSPCs) can achieve high editing frequencies in vitro, but these efficiencies may not translate into sufficient levels of edited cells after transplantation. There is therefore a need for improved methods that enhance HSPC expansion and maintain their capacity to support clinically relevant gene editing outcomes.

The Solution

The invention proposes a combined approach involving short-term ex vivo pre-stimulation of primary CD34+ HSPCs with hematopoietic cytokines, UM171 and StemRegenin 1, followed by CRISPR/Cas-mediated genome editing and delivery of a homologous donor AAV vector. This integrated procedure is designed to promote cell expansion while enabling targeted gene modification through homologous recombination.

Innovative Aspects

- ✓ **Integrated workflow**: Combines optimized HSPC pre-stimulation, CRISPR/Cas-mediated DNA cleavage and AAV-based donor delivery in a single procedure.
- ✓ **Enhanced HSPC expansion**: The use of UM171 and StemRegenin 1 promotes ex vivo expansion of primary CD34+ HSPCs while maintaining their suitability for subsequent gene editing.
- ✓ **Improved editing potential**: The combination of CRISPR/Cas and a homologous donor AAV vector enables targeted gene modification through homologous recombination.
- ✓ **Clinical relevance**: The overall strategy is designed to increase the frequency of genetically modified HSPCs and potentially achieve clinically relevant levels of gene correction.

Stage of Development:

he technology is at an advanced **preclinical development stage**, with the gene-editing process optimized and validated in primary CD34+ HSPCs through in vitro functional and clonogenic assays. **In vivo validation** in immunodeficient mouse models demonstrates engraftment, multilineage differentiation, gene-editing efficiency and clonal diversity, supporting its potential for clinical translation.

IP status:
PTC filed in 2024
Entry into national phases.

Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

Contact details

Consorcio Centro de Investigación Biomédica en Red *(CIBER)*
otc@ciberisciii.es
https://www.ciberisciii.es/en