Docket #: S21-196

Differential Proliferation of Human HSPCs Using Truncated Erythropoietin Receptors

Researchers at Stanford have developed gene editing methods for modifying hematopoietic stem and progenitor cells (HSPCs) to express truncated forms of the erythropoietin receptor (tEPOR). The expression of tEPOR in the modified cells and their descendants, in particular in the erythropoietic lineage (e.g., red blood cells), leads to enhanced growth and/or proliferation. This enhanced growth and/or proliferation leads to the enrichment of the cells relative to unmodified cells *in vitro* and/or *in vivo*. Accordingly, when coupled with a desired trait or an additional genetic modification (e.g., to effect the expression of a therapeutic transgene), the induction of tEPOR expression in the modified cells can be used to enhance the presence of the desired and/or modified cells *in vitro* or *in vivo*. Currently, edited cell chimerism is one of the greatest bottlenecks to clinical efficacy of gene therapies for hemoglobin diseases. As a result, transplanted genetically modified HSCs often fail to proliferate or be maintained sufficiently to provide therapeutic benefit. This technology can be used to safely and effectively enhance the chimerism of edited red blood cells in patients.

Stage of Development
This method was tested in *in vitro* cell culture on human HSCs. Data were generated from proprietary sgRNA and AAV6 DNA repair templates.

Applications

- Genetically modified HSPCs from patients could be used in treating genetic disorders such as ?-thalassemia, ?-thalassemia, sickle cell disease, hemophilia B, phenylketonuria, mucopolysaccharidosis type 1, Gaucher disease, Krabbe disease, etc.

Advantages

- Could improve efficacy in all current gene therapies for hemoglobinopathies

Patents

- Published Application: WO2023064798
- Published Application: 20240409958

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