Docket #: S19-060

Genetically corrected, iPSC-derived epithelial sheets to treat RDEB

Researchers at Stanford have developed a targeted gene therapy approach to treat patients with recessive dystrophic epidermolysis bullosa (RDEB). Epidermolysis bullosa (EB) represents a group of debilitating inherited skin disorders in which blisters develop after minor trauma to the skin. Symptoms and severity depend on type of EB. RDEB is the most severe form of EB. It is caused by the absence of the type VII collagen protein, the main component of the anchoring fibrils which tether the epidermis to the dermal tissue underneath. Patients with RDEB develop large, severely painful blisters and open wounds that eventually lead to infection and development of squamous cell carcinoma. The extensive blistering and open wounds on the skin greatly affect patient quality of life, with patients reporting severe daily pain, especially during wound care. Currently, there is no cure for RDEB as existing treatments are only supportive in nature. To help meet this need, the inventors have developed a scalable and cGMP compatible gene therapy approach. This approach uses CRISPR to correct mutations in the COL7A1 gene, where type VII collagen is encoded, in patient-derived induced pluripotent stem cells (iPSCs). These gene-corrected iPSCs are then used to generate keratinocyte sheets for grafting to treat RDEB. This technology provides a much-needed treatment for RDEB.

Stage of Research
Proof-of-concept studies show this approach can be used to correct mutations at different sites within the COL7A1 locus to make COL7A1-corrected iPSCs. Further, the iPSCs can generate graftable keratinocytes.

Applications

- Therapy for RDEB
- Wound healing

Advantages

- Helps meet serious unmet need to provide treatment for RDEB
- Streamlined and shortened manufacturing process
- iPSCs provide scalable source of material for cell therapy
- Potential to relieve patients' significant suffering and improve quality of life

Publications

- Gernot Neumayer, Jessica L. Torkelson, Shengdi Li, Kelly McCarthy, Hanson H. Zhen, Madhuri Vangipuram, Joanna Jackow, Avina Rami, Corey Hansen, Zongyou Guo, Sadhana Gaddam, Alberto Pappalardo, Lingjie Li, Amber Cramer, Kevin R. Roy, Thuylinh Michelle Nguyen, Koji Tanabe, Patrick S. McGrath, Anna Bruckner, Ganna Bilousova, Dennis Roop, Irene Bailey, Jean Y. Tang, Angela Christiano, Lars M. Steinmetz, Marius Wernig, Anthony E. Oro (2023). A scalable, GMP-compatible, autologous organotypic cell therapy for Dystrophic Epidermolysis Bullosa. *bioRxiv* 2023.02.28.529447.

Patents

- Published Application: WO2021133724
- Published Application: 20230045590

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