



Editorial: Gene, Cell and Protein Replacement Therapy for Genetic Muscle, Bone and Skin Disorders

Holm Schneider^{1*} and Michele De Luca²

¹Department of Pediatrics, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany,

²Centre for Regenerative Medicine "Stefano Ferrari", University of Modena and Reggio Emilia, Modena, Italy

Keywords: gene therapy, myogenic cell transplantation, protein replacement, ectodermal dysplasia, duchenne muscular dystrophy (DMD), epidermolysis bullosa

Editorial on the Research Topic

Gene, Cell and Protein Replacement Therapy of Genetic Muscle, Bone and Skin disorders

Over the past decade, various cell and gene therapy approaches have led to advanced therapy medicinal products that offer tremendous hope for patients suffering from rare genetic diseases. This especially applies to conditions affecting the musculoskeletal system or the skin, which represent the largest organs in the human body. The impairment of muscles, bone or skin due to a genetic abnormality usually has a large impact on the whole organism, and some severe hereditary conditions, such as Duchenne muscular dystrophy, are not particularly rare.

In this research topic on novel therapies, we aimed to highlight promising recent developments, challenges, and interdisciplinary scientific questions. We encouraged our colleagues to submit relevant articles of all types and included very different contributions, ranging from original research findings in a mouse model of human disease and with patient-derived induced pluripotent stem cells (iPSC) to a phase II/III clinical trial protocol.

The introductory perspective article by Koch and Koster outlines the rationale of studying rare diseases and the recent approaches they and others are applying to tackle the complexity of two developmental disorders that belong to the group of ectodermal dysplasias. They discuss the challenges for researchers in this field and focus on correcting phenotypes in the most severely affected tissues, such as wounded skin, by cell therapy strategies using genetically corrected iPSC.

Boyer et al. review myogenic cell transplantation for various genetic and acquired muscle disorders including Duchenne muscular dystrophy, oculo-pharyngeal muscular dystrophy, mitochondrial myopathies, inclusion body myositis, and sphincter incontinence. This paper provides deep insights into common or disease-specific problems that have so far limited the clinical success of myogenic cell therapy. It highlights the need for scientific, pharmaceutical and regulatory communities "to join forces and work together to produce mutual guidelines for preclinical core requirements" as well as for openness to innovative study designs in order to facilitate the translation of promising experimental results into clinical trials. This is also true for an unprecedented strategy to treat the most frequent ectodermal dysplasia (Schneider et al., 2018; Körber et al., 2020) which is based on the prenatal replacement of a missing protein, the signaling molecule ectodysplasin A1 (EDA1). For ectodermal dysplasias and some other developmental disorders, temporary protein replacement actually represents a more promising approach than cell or gene therapy attempts. An original research article by Kossel et al. illustrates this point with data showing that disturbed vertebral bone development in EDA1-deficient mice can be corrected by timely EDA1 replacement. It emphasizes tissue-specific requirements for the timing of interventions and an opportune way to overcome drug-targeting hurdles.

OPEN ACCESS

Edited and reviewed by:

Jordi Pérez-Tur,
Instituto de Biomedicina de Valencia,
Spain

*Correspondence:

Holm Schneider
holm.schneider@uk-erlangen.de

Specialty section:

This article was submitted to
Genetics of Common and Rare
Diseases,
a section of the journal
Frontiers in Genetics

Received: 06 September 2021

Accepted: 28 September 2021

Published: 18 October 2021

Citation:

Schneider H and De Luca M (2021)
Editorial: Gene, Cell and Protein
Replacement Therapy for Genetic
Muscle, Bone and Skin Disorders.
Front. Genet. 12:771611.
doi: 10.3389/fgene.2021.771611

The two final chapters of this research topic address new gene and cell therapy approaches to treat epidermolysis bullosa, a severe genodermatosis characterized by blistering of the skin upon minor mechanical trauma. Koller and Bauer discuss emerging treatment concepts based on gene replacement or genome editing, while De Rosa et al. present the protocol of a planned clinical trial of combined cell and gene therapy, which was prompted by the successful treatment of two adults and one

severely affected child with junctional epidermolysis bullosa (Hirsch et al., 2017).

AUTHOR CONTRIBUTIONS

Both authors contributed to the writing of this article and approved its publication.

REFERENCES

- Hirsch, T., Rothoef, T., Teig, N., Bauer, J. W., Pellegrini, G., De Rosa, L., et al. (2017). Regeneration of the Entire Human Epidermis Using Transgenic Stem Cells. *Nature* 551, 327–332. doi:10.1038/nature24487
- Körber, I., Klein, O. D., Morhart, P., Faschingbauer, F., Grange, D. K., Clarke, A., et al. (2020). Safety and Immunogenicity of Fc-EDA, a Recombinant Ectodysplasin A1 Replacement Protein, in Human Subjects. *Br. J. Clin. Pharmacol.* 86, 2063–2069. doi:10.1111/bcp.14301
- Schneider, H., Faschingbauer, F., Schuepbach-Mallepell, S., Körber, I., Wohlfart, S., Dick, A., et al. (2018). Prenatal Correction of X-Linked Hypohidrotic Ectodermal Dysplasia. *N. Engl. J. Med.* 378, 1604–1610. doi:10.1056/NEJMoa1714322

Conflict of Interest: MD is co-founder and member of the Board of Directors of Holostem Therapie Avanzate, S.r.l., Italy, and consultant for Japan Tissue Engineering Co., Ltd.; HS is an inventor on patents related to the treatment of

ectodermal dysplasias and consultant for the Pierre Fabre Group. He received research grants from Edimer Pharmaceuticals, Ltd., and the EspeRare Foundation, Switzerland, for investigating a potential prenatal therapy for X-linked hypohidrotic ectodermal dysplasia.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Schneider and De Luca. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.