Abstract

Title: HSV-1 mediated COL7A1 (KB103) delivery to keratinocytes and fibroblasts for recessive dystrophic epidermolysis bullosa (RDEB) therapy: preparations for Phase-I clinical trials

Name(s): Marco Prisco[1], Velina Atanasova[1], Ignacia Fuentes[1], Julio Cesar Salas Alanis[2], Pooja Agarwal[3], Suma Krishnan[3], Andrew South[1]

Author affiliation:

1 – Dermatology and Cutaneous Biology, Thomas Jefferson University

2 – Department of Medicine, University of Monterrey

3 – Krystal Biotech Inc.

Text:

Current gene therapy for Recessive dystrophic epidermolysis bullosa (RDEB) requires processing of primary cells ex-vivo resulting in significant costs in manufacturing and lead time in production. We have produced a novel engineered replication defective HSV-1 vector encoding COL7A1 transgene (KB103) for off-the-shelf application in RDEB patients. KB103 can be injected or topically formulated for direct application to open wounds. RDEB primary fibroblasts and keratinocytes are efficiently transduced by KB103 in vitro, leading to detection of recombinant collagen 7 (C7) by immunostaining and Western blotting. COL7A1 corrected RDEB cells showed functional restoration in adhesion assays and KB103 efficiently deposited C7 at the dermal-epidermal junction in organotypic cultures and in mouse skin after intradermal injection. Clinical grade KB103 is currently being manufactured under GMP and will undergo release testing and characterization for optimal formulation, feasibility and safety in animal studies ahead of phase-I clinical trial.