

Towards a Wound Healing Treatment for Recessive Dystrophic Epidermolysis Bullosa

A Case Study on RDEB Wound Healing

A 12-year old child with EB suffered from non-healing leg ulcers for 4 years. Since there is no way to prevent the damage from occurring, the child's condition kept progressing worse, continuously damaging the body tissue. A clinician decided to apply a solution of ReGeneraTing Agent (RGTA) to the lower extremity ulcers of the patient as the last resort.

The RGTA topical treatment was applied to the wounded site twice weekly for 4 weeks with maintained dressing change. Within the span of 5 minutes on the first administration, the patient experienced significant pain relief. The pain slowly faded with the help of the RGTA treatment.

The external and internal layers of the skin slowly became less inflamed, with granulation and healing subsequently becoming evident. At the end of the trial, the wounded area closed completely and no recurrence happened over the period of 2 years. This is the only report showcasing the positive effect of RGTA treatment on the chronic wounds of RDEB, which can potentially be the treatment of RDEB chronic wounds.



Figure 1. RDEB Patient with chronic leg ulcers treated with RGTA solution showed skin color change and wound size reduction (Barritault & Malaq 2012)

Tissue Regeneration with RGTA

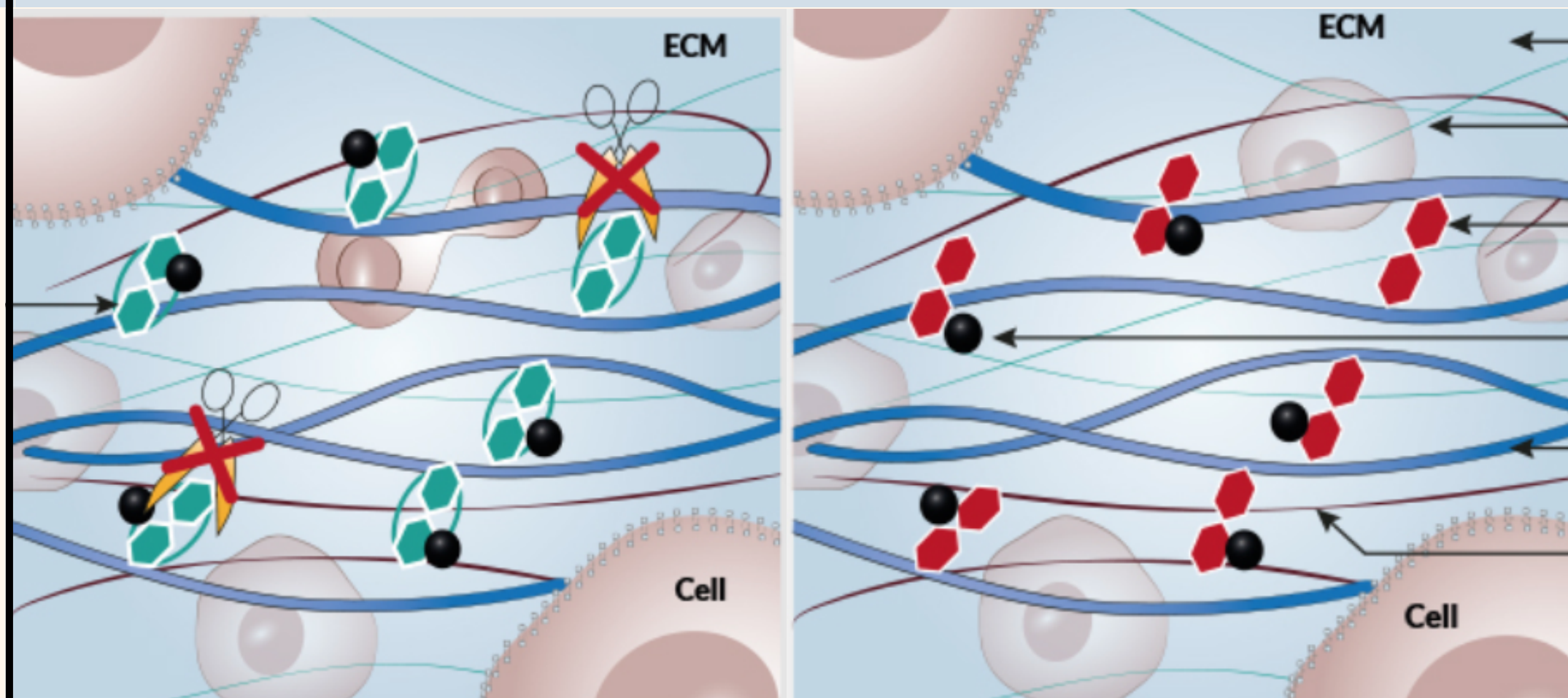


Figure 2. Endogenous Heparan Sulfates in the damaged Extracellular Matrix being replaced by RGTA, promoting tissue regeneration by binding with peptides and protecting ECM proteins (OTR3)

RGTA molecules has the same functionality of Heparan Sulfates and are designed to be more resistant to enzymatic degradation. It reconstructs the spatial organization of the ECM by attaching to communication peptides, collagen and hyaluronic acid. The less inflamed areas with neighboring cells resume tissue regeneration process, making natural HS and will recover their role in healing the tissue. RGTA molecules are designed to support natural tissue regeneration process to occur, restoring initial tissue homeostasis.

Determining the Effects of RGTA and Hyaluronic Acid on RDEB and non-RDEB Keratinocytes

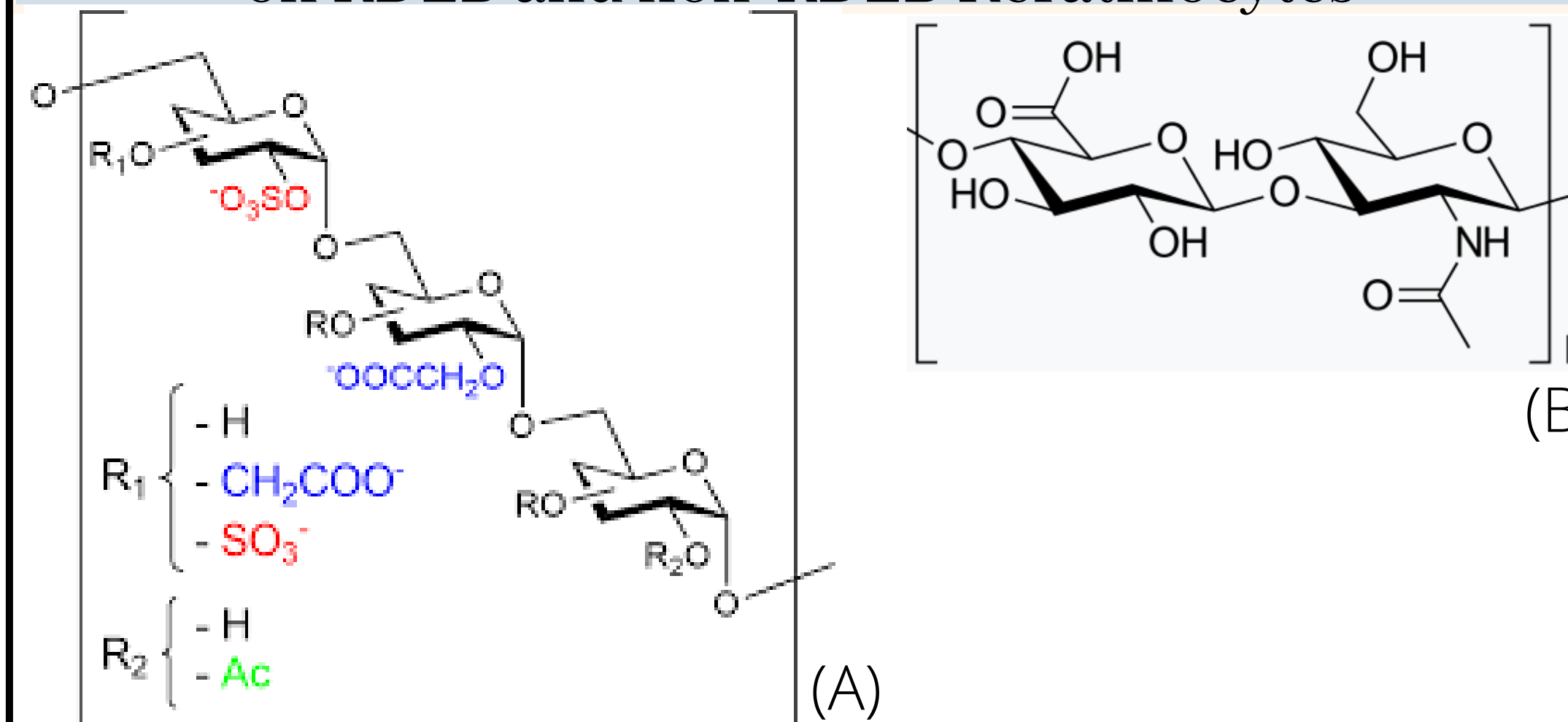


Figure 3. (A) Molecular Structure of Regenerating Agents (RGTA) and (B) Molecular Structure of Hyaluronic Acid

The objective of this ongoing study is to determine the effects of RGTA OTR4120 combined with Hyaluronic Acid on the proliferation, migration, and growth of RDEB and non-RDEB Keratinocytes. The growth of these cells contribute to the overall wound healing response in the injured skin, thus it is important to examine the interaction between the treatment and cells.

Results of RGTA and HA on RDEB Keratinocytes

A wound healing assay was performed to examine the cell migration and cell interactions with RGTA and HA treatment. The area coverage by the growth of RDEB and non-RDEB keratinocytes was recorded by the IncuCyte platform. RGTA OTR4120 combined with HA has a positive effect on migration and proliferation of RDEB Keratinocytes, whereas it has a negative effect on non-RDEB keratinocytes. This study does not fully reflect the effect of RGTA in keratinocytes and the overall wound healing process. However, it can be hypothesized that RGTA and HA may act as an activator in RDEB keratinocytes growth and may possess an inhibitory effect on non-RDEB keratinocytes.

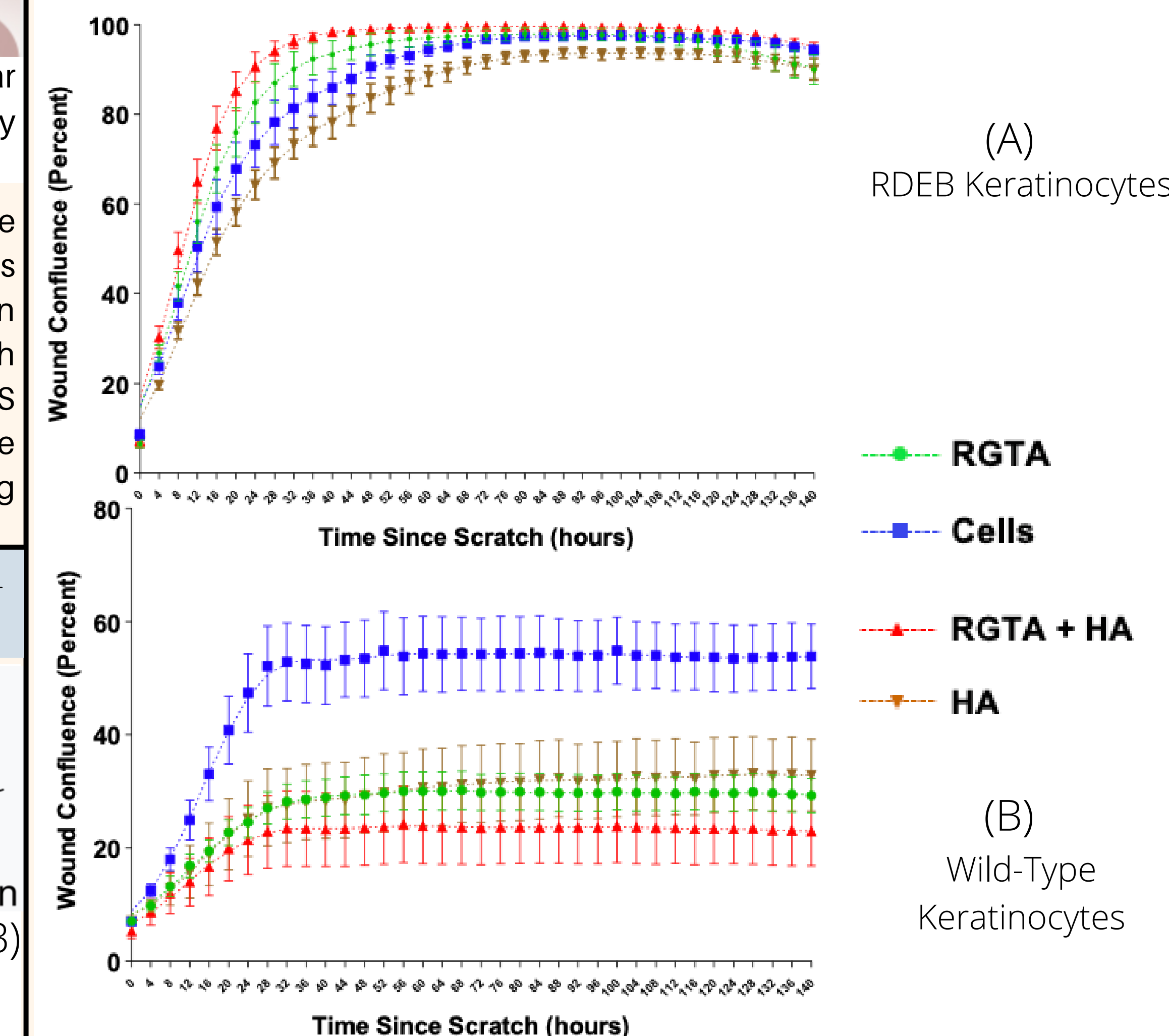


Figure 4. The effects of RGTA and 0.2% HA on keratinocyte growth. The figure represents the percentage area covered by the growth of keratinocytes in a 140-hour time of incubation. Both keratinocytes are treated with 25 µg/ml RGTA and 0.2% HA, and compared with keratinocytes only keratinocyte SFM.

References

[1] Barritault, D & Malaq A 2012, 'A rapid response to matrix therapy with RGTA in severe epidermolysis bullosa', *Eplasty*, viewed 26 April 2022, National Library of Medicine database, PMID 23479950
[2] Barritault, D, Gilbert-Sirix, M, Rice, K, Si eriz, F, Papy-Garcia, D, Baudouin, C et al. 2016, 'RGTA or ReGeneraTing Agents mimic heparan sulfate in regenerative medicine: from concept to curing patients', *Glycoconj*, viewed 26 April 2022, National Library of Medicine database, DOI 10.1007/s10719-016-9744-5