RNA-sequencing based mechanistic insights support the use of HTL biopolymers as regenerative platforms

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Company Overview

- **HTL Biotechnology** is a global leader in the development and responsible bioproduction of pharmaceutical-grade biopolymers (Hyaluronic Acid, Recombinant Collagen, Polynucleotides).
- **These biopolymers** are used by healthcare companies for the development of treatments in various cutting-edge therapeutic areas such as ophthalmology, dermatology, medical aesthetics and rheumatology.

HTL's HA in the unique form of fiber

- **Our mission** is to unlock the potential of biopolymers to enhance patient's health and well-being worldwide.
- **By 2030**, our biopolymers aim to benefit over 500 million patients affected by age-related diseases and conditions, supporting the advancement of regenerative medicine.

Current applications

Ophthalmology
Use of HA in ophthalmic viscosurgical devices (OVDs)

Ageing of the skin
Use of biopolymers in dermal fillers

Dry eye syndrome
Use of HA in eye hydration

Rheumatology
Use of HA as viscosupplementation

New applications

Regenerative medicine

Drug delivery
(micro-needles, ocular, vaccines, oncology)

Innovative biopolymers at HTL addressing today's and tomorrow's **unmet medical needs**

Introduction

- **Skin** is the human body's largest and heaviest organ, covering an average of 22 square feet and accounting for roughly 15% of total body weight. It protects against external threats, regulates body temperature, and provides sensory input. Epidermis and dermis are main skin layers represented by two major cell types – keratinocyte and fibroblast.
- **Skin ages** due to intrinsic and extrinsic factors (e.g., chronological aging, pollution, UV exposure) result in thinning of epidermis, hyperpigmentation, dehydration, flattening of dermal-epidermal junction (DEJ), and degradation of ECM components (e.g. collagen and elastin) at molecular level.
- Many **natural biopolymers** have been investigated/used for skin regeneration such as **hyaluronic acid, collagen and DNA**.

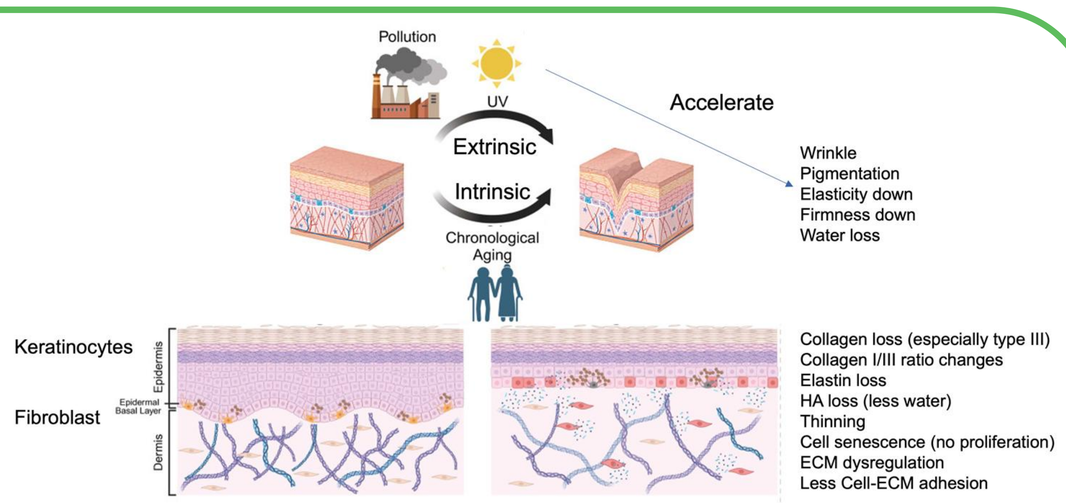

Figure 1. Skin aging and related processes. Adapted from Toby Chin, Xin Er Lee, Pei Yi Ng, Yaelim Lee, Oliver Dreesen, The role of cellular senescence in skin aging and age-related skin pathologies. *Front Physiol*, 2023.

Methods

Cell culture and RNA-sequencing

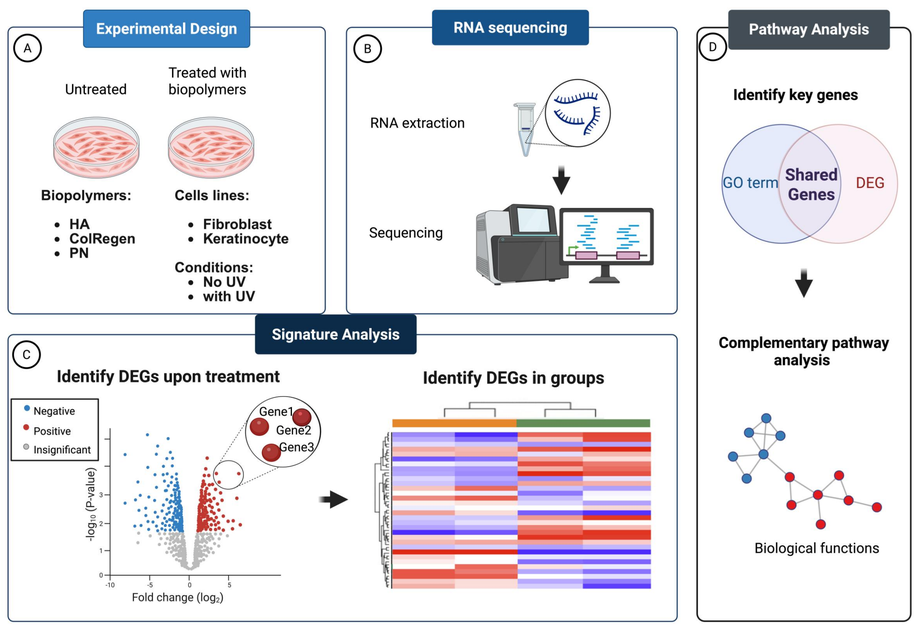

Figure 2. Experimental outline. (A) Three HTL biopolymers (HA, ColRegen* and PN[1]) were applied to monolayer 2D culture of human primary fibroblast and human primary keratinocyte under normal and UV conditions. (B) Total RNA was extracted 48 hours after treatment and performed RNA-sequencing (C) Individual differentially expressed genes (against untreated control) were plotted with a threshold of $Log_2 < -1$ and $Log_2 > 1$ $p < 0.05$. (D) Significantly expressed GO term pathways related to skin functions were analyzed.

Results

UV Treatment

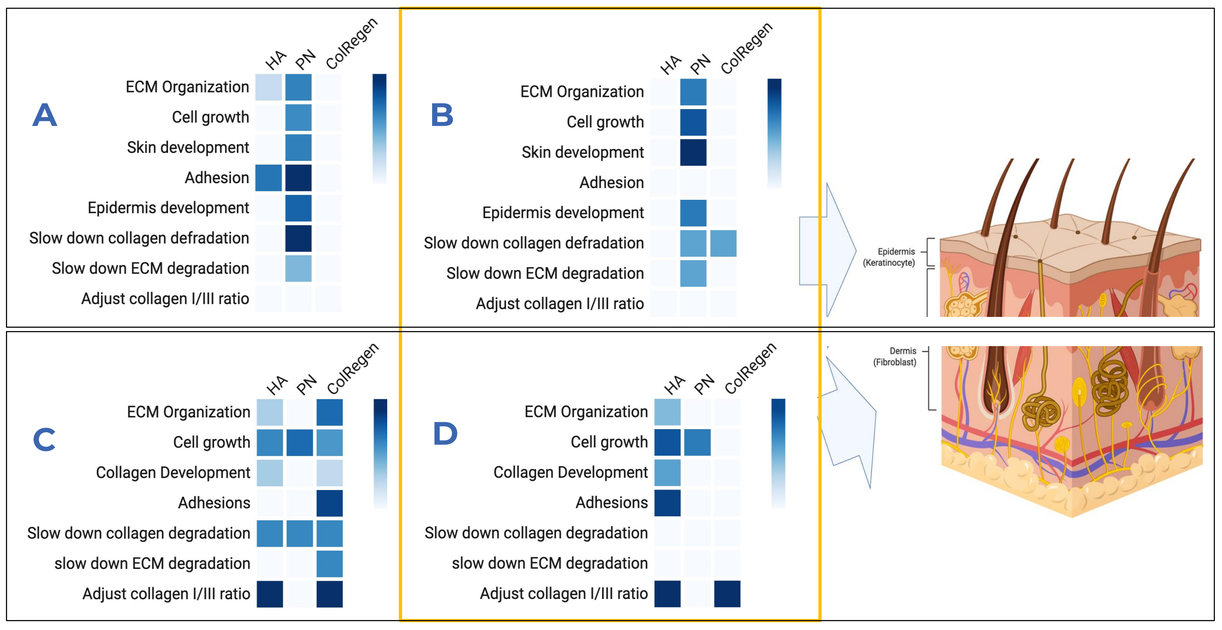

Figure 3. RNA-sequencing results for biological pathways related to skin functions. Heatmaps were generated according GO term pathway enrichment. The darkest color represent the most enriched function in the individual subgroup, and the lightest color represents the least enriched function in the individual subgroup. (A) GO term pathway enrichment of biopolymers with human keratinocytes under normal condition (B) GO term pathway enrichment of biopolymers with human keratinocytes under stressed condition (UV) (C) GO term pathway enrichment of biopolymers with human fibroblast under normal condition (D) GO term pathway enrichment of biopolymers with human fibroblast under stressed (UV) condition.

Conclusion & perspectives

- To acquire a comprehensive understanding of HTL Biopolymers on skin regeneration and anti-aging functions, we performed **an RNA-sequencing based experiment** with two different cell types (fibroblast and keratinocytes) under normal and stressed (UV) conditions. Interestingly HTL biopolymers exhibited significant and complimentary potentials on many skin related pathways with different layers of skin structure. For example, **PN[1]** showed functions on keratinocytes (epidermis); **HA** and **ColRegen*** showed significant activities on fibroblast (dermis).
- This data will direct us to further validate the findings in more advanced models and potential synergistic combination of different HTL biopolymers for skin regeneration.

References & collaborators

- Toby Chin, Xin Er Lee, Pei Yi Ng, Yaelim Lee, Oliver Dreesen, The role of cellular senescence in skin aging and age-related skin pathologies. *Front Physiol*, 2023
- BioInnovation
- StratiCELL
- Novogene

* Recombinant human collagen type 3
[1] Polynucleotide with high and low Molecular Weight