Hyaluronic acid and recombinant collagen creates a biomimetic extra-cellular matrix environment with synergistic potential for regenerative medicine

HTL Biotechnology, 7 Rue Alfred Kastler, 35133 Javené (France)
Gabriele Pitingolo, Monique de Leeuw, Lixin Dai, Anne-Laure Gaudry*
**gpitingolo@htlbiotech.com*

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.
- **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.



HTL's HA in the unique form of fiber

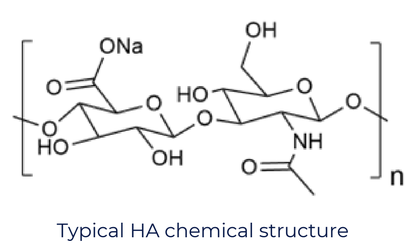


Innovative biopolymers at HTL addressing today's and tomorrow's **unmet medical needs**

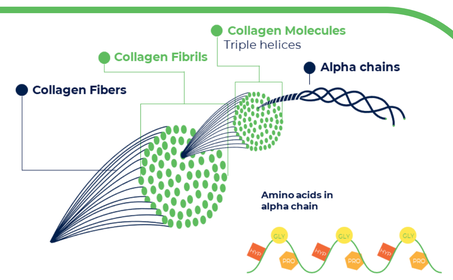
Introduction

- **Hyaluronic acid (HA)** and **collagen** are key constituents of **the extracellular matrix** (ECM), contributing to tissue hydration, mechanical integrity, and cellular activity. Collagen supports cell adhesion, migration, and matrix remodeling, whereas HA plays a central role in maintaining hydration, volume, and viscoelastic properties. The combination of these two biomolecules can recreate a biomimetic ECM-like microenvironment with significant potential for applications in regenerative medicine and aesthetic therapies.

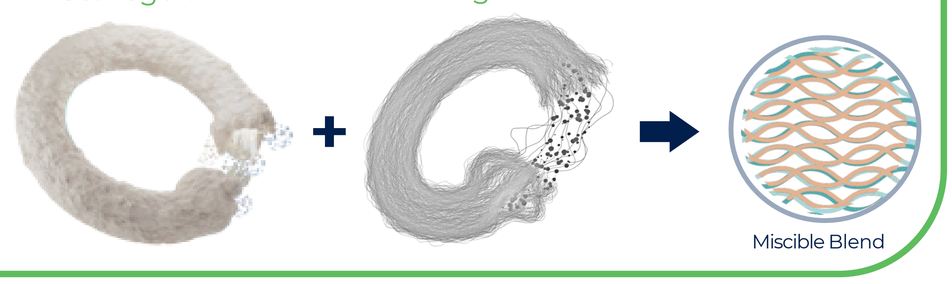
- Traditionally, formulations combining animal-derived collagen and hyaluronic acid have faced technical limitations, often requiring crosslinking or chemical modification to achieve sufficient stability and compatibility. Advances in recombinant protein technologies now open new opportunities for innovation. By producing both pharmaceutical-grade **hyaluronic acid (HA Signature)** and **recombinant collagen (ColRegen*)** , it is possible to design highly compatible systems where the two biopolymers exhibit improved miscibility and functional synergy.



Typical HA chemical structure



Recombinant human protein design



Methods

HA Signature and ColRegen* are highly miscible

Solution preparation:

- 50 kDa HA and ColRegen* were individually dissolved in Milli-Q water at 5% (w/w).
- The solutions were mixed 1:1 (v/v) to obtain a final concentration of 2.5% (w/w) of each component.
- The mixture was left overnight at room temperature before transparency evaluation.

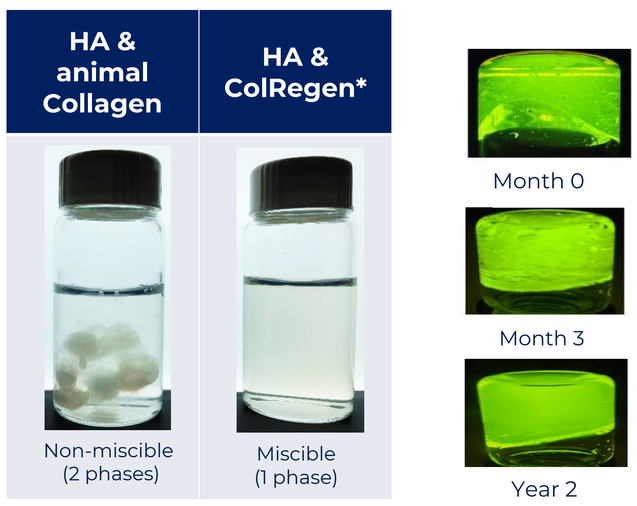


Figure 1. Animal collagen tends to be not miscible with Hyaluronic acid, instead HA and recombinant collagen are very miscible. In addition, HA and ColRegen* remain miscible over a period of at least two years.

Material Characterization and ECM Stimulation

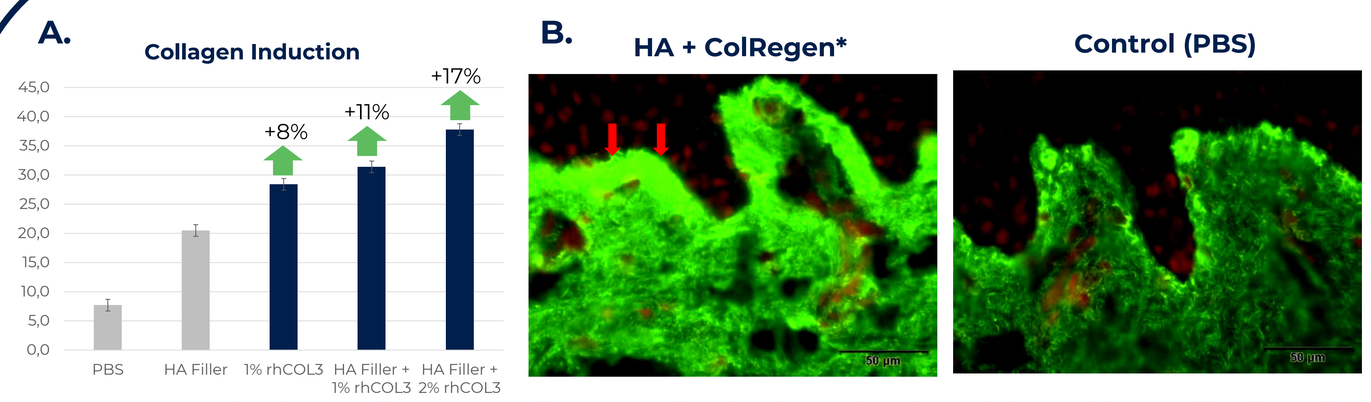


Figure 2. HA and ColRegen* increase collagen production in *ex vivo* dermal tissue (A). Specifically, Collagen I production increases in *ex vivo* dermal tissue (B), red arrow indicates collagen immunostaining.

HA combined with ColRegen* is a biocompatible biostimulator and has anti-inflammatory properties

Figure 3. (A) HA+ColRegen* decreases AP-1 in macrophages, (B) Colregen* treatment displays little to no inflammation at 28 days post intradermal injections.

Conclusion & perspectives

- The **extracellular matrix** components, such as HA and collagen, are vital for cellular function and tissue hydration. Here, the combination of these two components demonstrated **miscible properties** (Figure 1) and promotes the **biostimulation** of key ECM components, such collagen (Figures 2 and 3) and elastin (data not shown).

- Furthermore, the **ColRegen*:HA** combination releases collagen. Together, these findings highlight the **synergistic combination** of collagen type III with HA could represent a unique and innovative approach in regenerative medicine.

References and collaborators

- Eurofins Laboratoire BIO-EC
- DaVINCI Biomedical Research Products Inc.
- Rutgers University, Research Pathology Services

* Recombinant human collagen type 3