Bioactive Gellan Gum Hydrogels with Immunomodulatory and Antibacterial Properties for Inflammatory Cartilage Regeneration

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Introduction

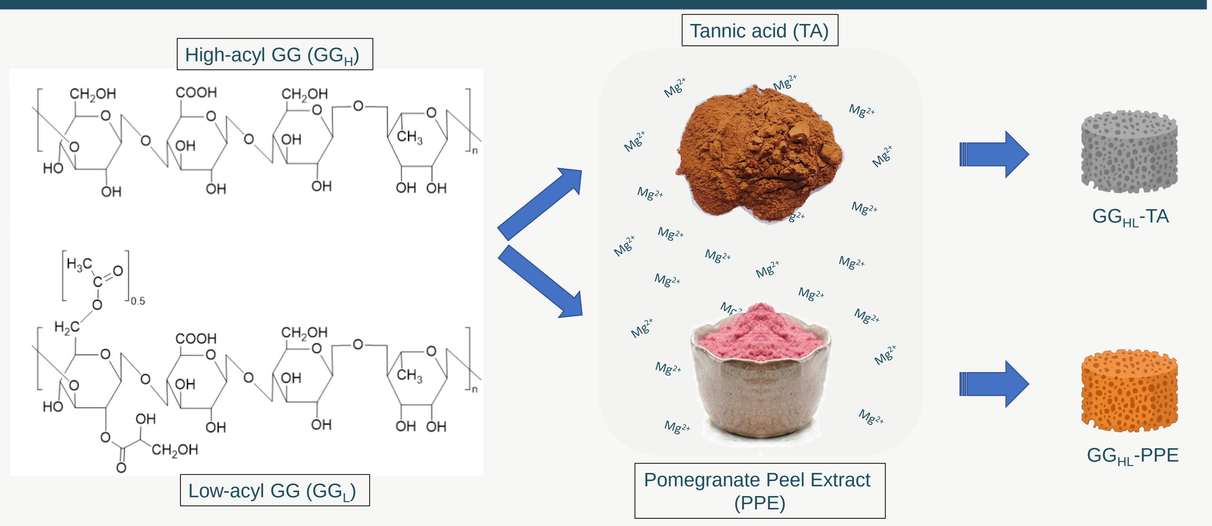
Cartilage regeneration remains a major challenge due to its **limited intrinsic repair capacity**

Natural-origin biomaterials are promising thanks to **biocompatibility and versatility**

Gellan gum (GG) is a bacterial polysaccharide with:

- Low cytotoxicity;
- High biocompatibility;
- Structural similarity to native cartilage;
- Tunable mechanical and biological properties;

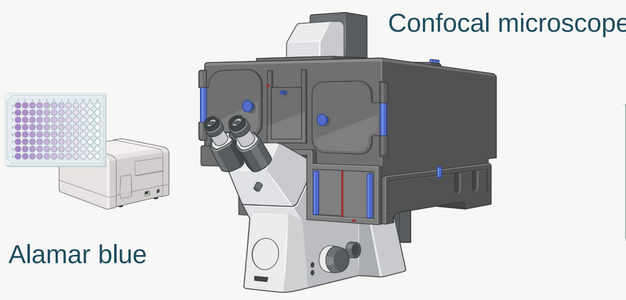
Materials and Methods



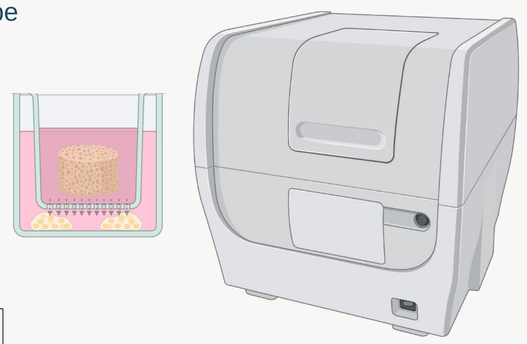
GG$_{HL}$-TA and **GG$_{HL}$-PPE** were physically and chemically characterized using:

- Attenuated Total Reflectance - Fourier Transform Infrared (**ATR-FTIR**) → Functionalization and crosslinking;
- Solid-State Nuclear Magnetic Resonance (**SS-NMR**) → Chemical structure and interactions;
- Scanning Electron Microscope (**SEM**) → Porosity;
- Static compression test → Stiffness;
- Antioxidant and Radical Scavenger Activity (**RSA**) → Intrinsic scavenging properties.

Afterwards, GG-based scaffolds were biologically characterized to verify their:

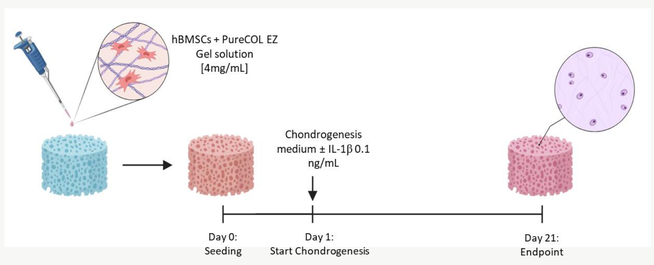


Cytocompatibility and ability to host cells (Human Mesenchymal stromal cells-hMSCs)



Real-time observation: Cytation 5

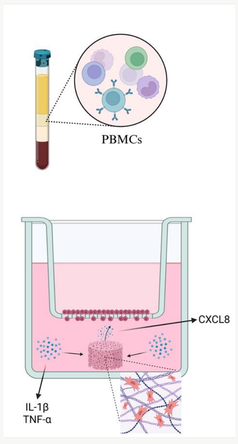
Antibacterial and antibiofilm activity (*S. aureus* and *E. coli*)



Chondrogenic potential under physiological and IL-1β/TNF-α inflammatory conditions (hMSCs)



qRT-PCR



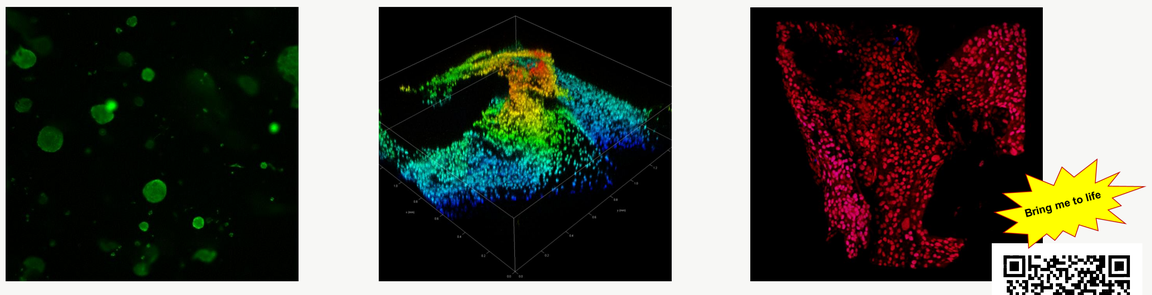
Anti-inflammatory and immunomodulatory activity (hMSCs; Peripheral Blood Mononuclear Cells-PBMCs)

Article GG$_{HL}$-TA

Article GG$_{HL}$-PPE

Results

TA and PPE, rich in –OH groups, provide favorable sites for **cell adhesion** and **scaffold colonization**.

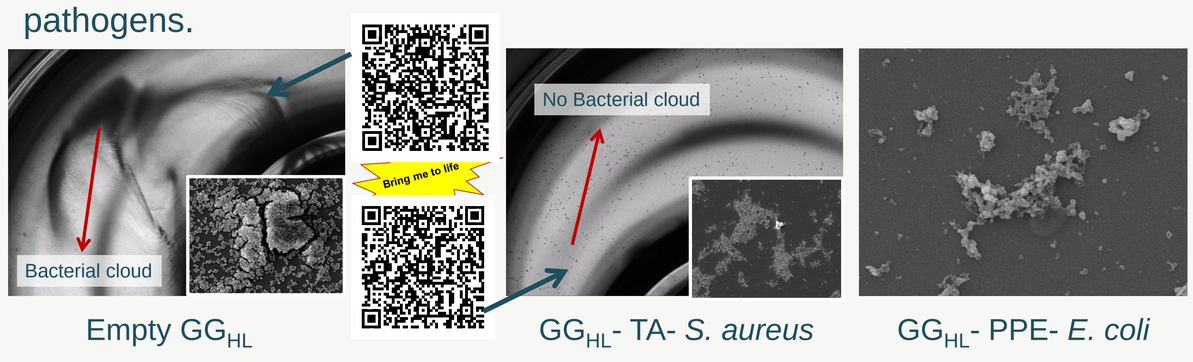


Empty GG$_{HL}$ no anchorage points

GG$_{HL}$- TA 3D spreading

GG$_{HL}$- PPE 3D spreading

TA and PPE **inhibit biofilm formation** and are active (**>90% eradication**) against both Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) pathogens.

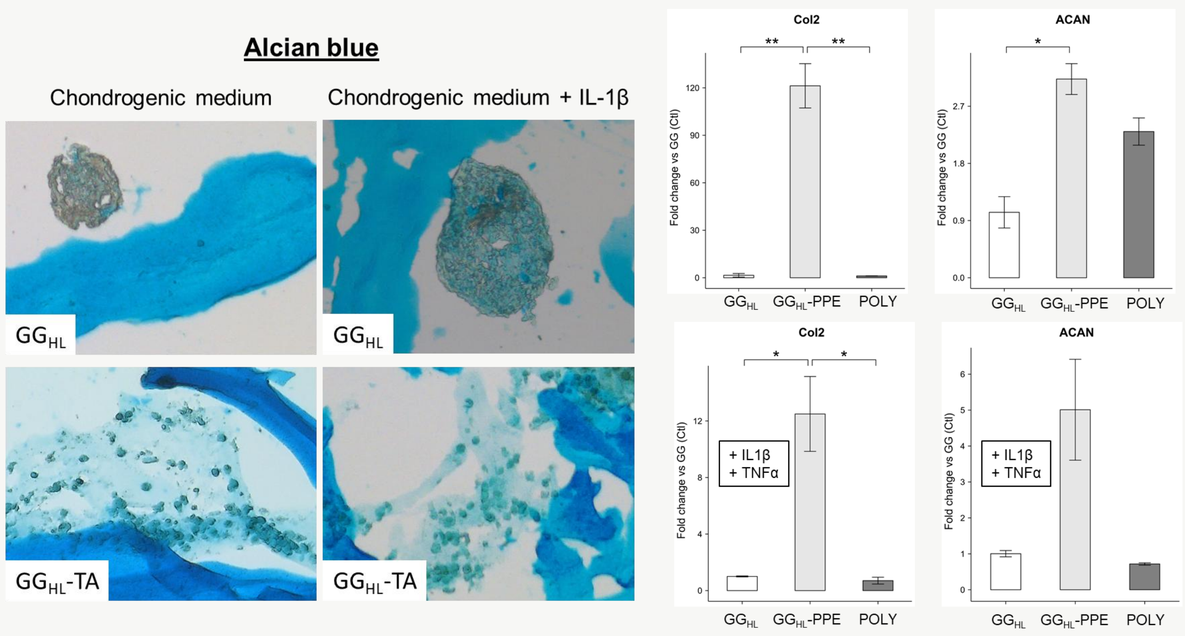


Empty GG$_{HL}$

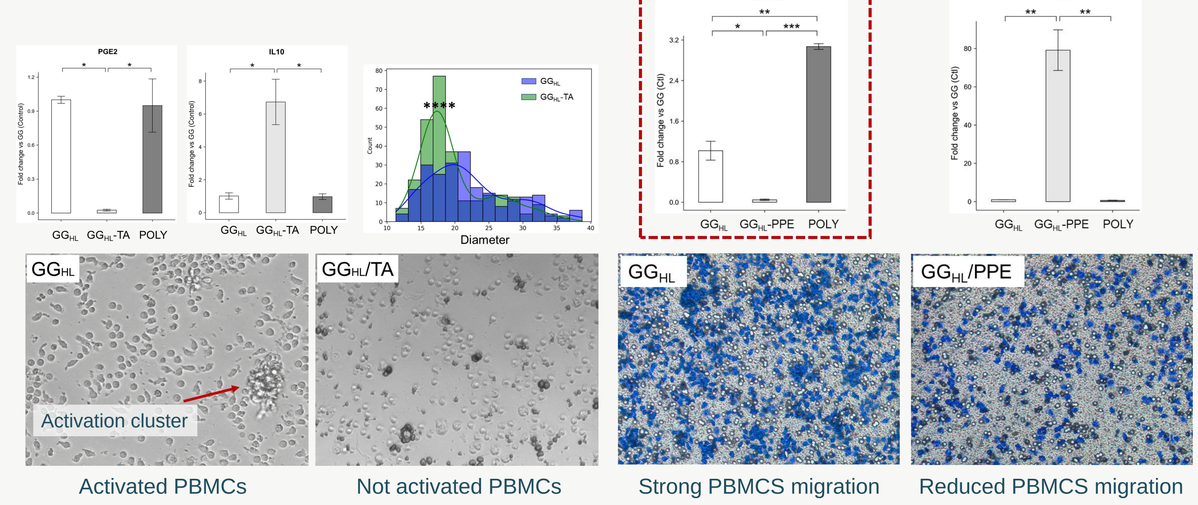
GG$_{HL}$- TA- *S. aureus*

GG$_{HL}$- PPE- *E. coli*

TA and PPE **promote chondrogenesis** and **enhance** GAGs and chondrogenic markers, **even under inflammatory conditions**.



TA and PPE **reduce inflammation, enhance anti-inflammatory responses**, and **limit** PBMCs **activation** and **migration**.



Activated PBMCs

Not activated PBMCs

Strong PBMCS migration

Reduced PBMCS migration

Conclusions

TA- and PPE-functionalized GG-based hydrogels

- Combine mechanical robustness + bioactivity
- Promote chondrogenesis (physiological/inflammatory)
- Inhibit biofilm formation & bacterial growth
- Modulate inflammatory response

These GG-based hydrogels represent promising scaffolds for cartilage repair