Supramolecular Hydrogel with Superior Dynamics for Enhanced Neurodifferentiation and Cell Adhesion

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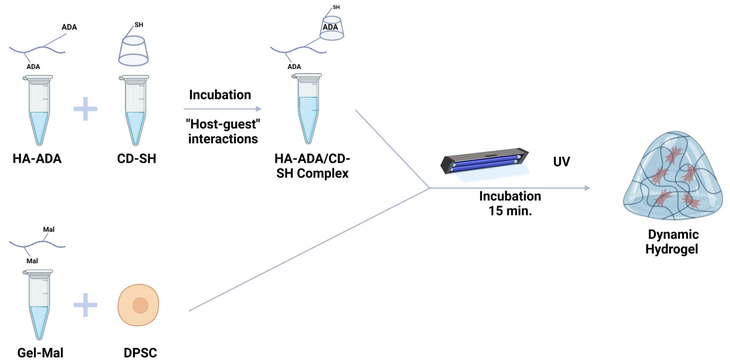
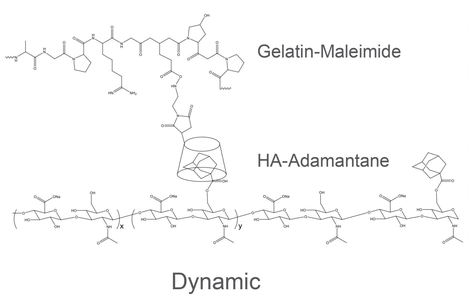
Introduction

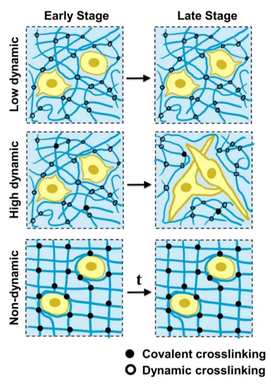
Spinal cord injuries (SCI) arise from damage to the central nervous system and are a major cause of permanent disabilities.[1] Over 500,000 people worldwide are impacted by SCI, indicating the need to refine therapeutic methods.[1] The primary treatment strategies currently available for nerve regeneration in SCI patients utilize autografts and nerve conduits, but both present their own challenges. Autografts have limited donor sites and result in donor-site morbidity while nerve conduits are expensive and lack biocompatibility and bioactivity.[2] To solve these drawbacks, dental pulp stem cells (DPSC) serve as a promising source of therapeutic cells for SCI treatment.[3] Direct DPSC transplantation, however, yields limited success prompting the use of a hydrogel to serve as a delivery vehicle.[3] Hydrogels provide structural stability, good cytocompatibility, and mimic the 3D biological microenvironment.[3] Therefore, we propose the use of a dynamic hydrogel encapsulated with DPSC to enhance neurogenesis and expedite nerve regeneration.

Materials & Methods

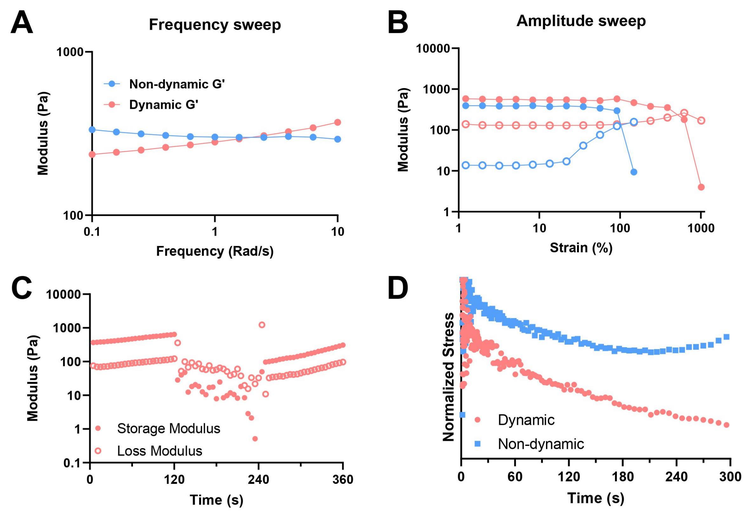


HA-ADA: Hyaluronan Adamantane
CD-SH: Cyclodextrin-Thiol
Gel-Mal: Gelatin-Maleimide

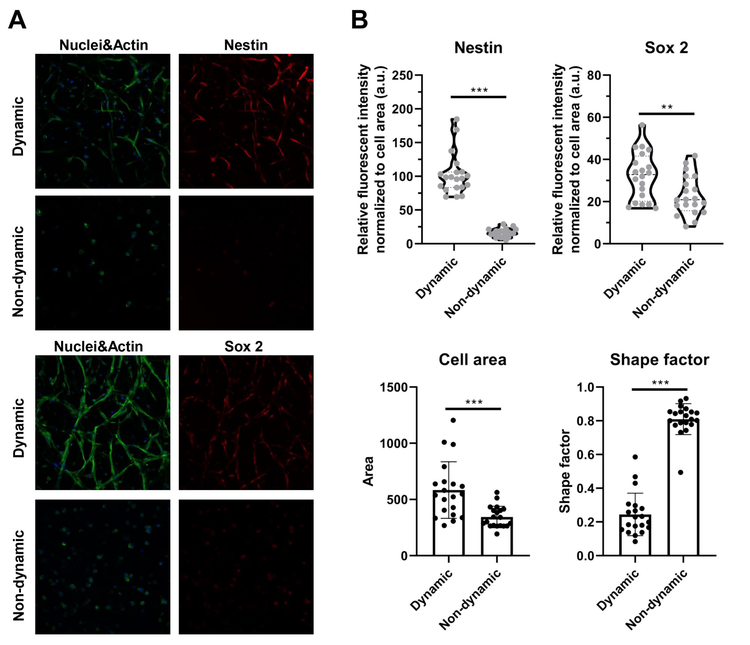




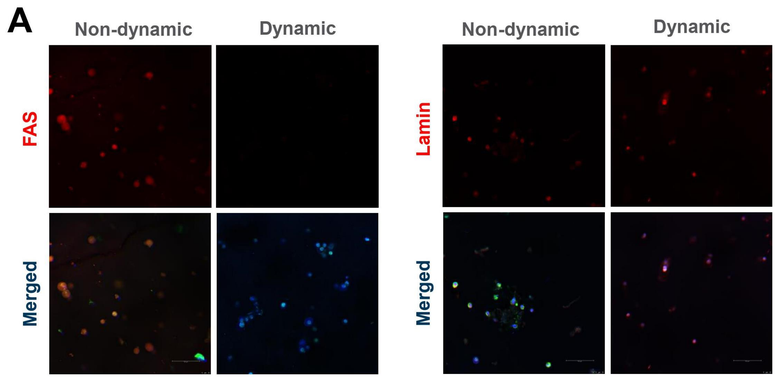
Results



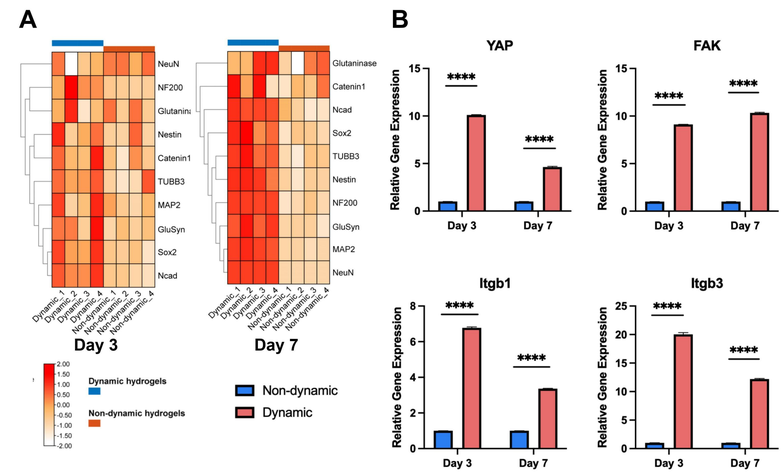
Rheological tests showed that our dynamic hydrogel has superior dynamics. (A) Frequency sweep and (B) amplitude sweep demonstrated that our dynamic hydrogel showed frequency responsiveness and super high fracture shear strain. (C) Step shear test with alternative high (1000%) and low (1%) shear strain exhibited good shear-thinning properties. (D) Stress relaxation test illustrated that our dynamic hydrogel has good matrix remodeling.



(A) Immunofluorescence imaging of neurostemness maintenance markers (Red: Nestin and Sox 2, Green: Cytoskeleton, Blue: Cell Nuclei) of DPSCs encapsulated in dynamic or nondynamic hydrogels. (B) Quantification of relative fluorescent intensity of Nestin and Sox 2, cell area spreading, and shape factor.



(A) Immunofluorescence imaging of inflammation (Red: FAS, Green: Cytoskeleton, Blue: Cell Nuclei) and cell adhesion (Red: Lamin, Green: Cytoskeleton, Blue: Cell Nuclei) of DPSCs encapsulated in dynamic or nondynamic hydrogels.



(A) Heat map of neurodifferentiation markers of DPSCs encapsulated in dynamic or nondynamic hydrogels after day 3 and day 7. (B) Quantitative PCR results of selective cell adhesion markers for cells cultured in dynamic or nondynamic hydrogels after day 3 and day 7.

Conclusion

Our dynamic hydrogel supports a more dynamic network and mechanical response allowing for greater cell adhesion and neurogenic differentiation. This shows potential for being a valuable resource in assisting nerve regeneration and treating nerve defects such as SCI.

References

1. Bennett, J., et al. (2020). Spinal cord injuries.
2. Liu, Y., et al. (2014). *J Mater Chem A*.
3. Luo, L., et al. (2018). *Stem Cells International.*