Cell-free HA-MA/PLGA scaffolds with radially oriented pores for *in situ* inductive regeneration of full thickness cartilage defects

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For *in situ* inductive cartilage regeneration, a scaffold with special architecture and bioactivity to induce cell infiltration and chondrogenesis is of great importance. Methacrylated hyaluronic acid/PLGA scaffolds with radially oriented pores are fabricated by thermally induced phase separation. The macro-porous scaffolds are implanted into the full thickness articular cartilage defects in rabbit model to realize the *in situ* inductive cartilage regeneration without employment of any extraneous cells or chondrogenetic growth factors.

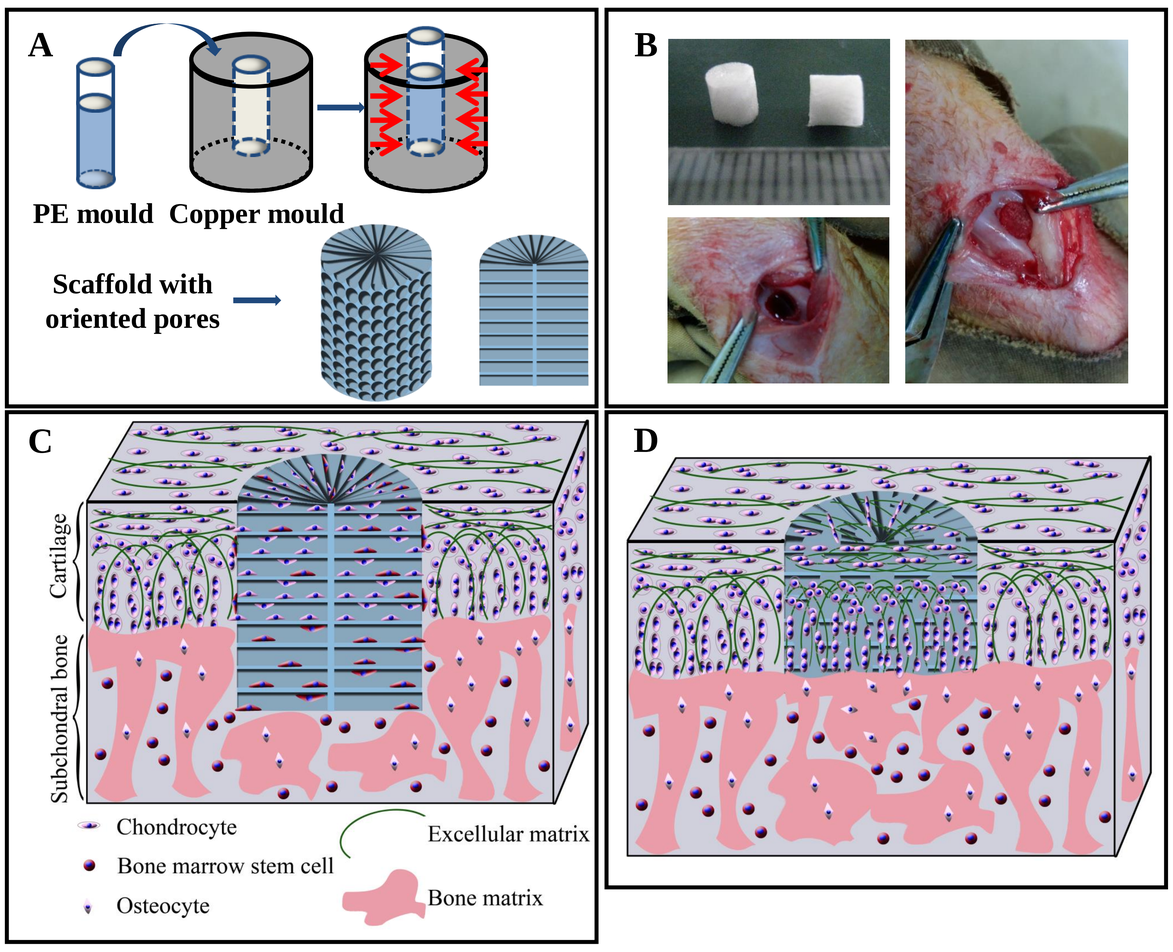

Figure 1. (A) Schematic illustration to show the preparation procedures of oriented porous O-HA-MA/PLGA scaffold by thermally induced phase separation (TIPS) in radial direction. Low right cartoons show the 3D and side view of the structured scaffold. (B) Grow view of scaffolds and surgical procedure in rabbit knee joint. (C) Schematic illustration of cell migration into the oriented scaffold after transplantation *in vivo*, and (D) regeneration of the full thickness defect along with deposition of extracellular matrices and degradation of the scaffold.

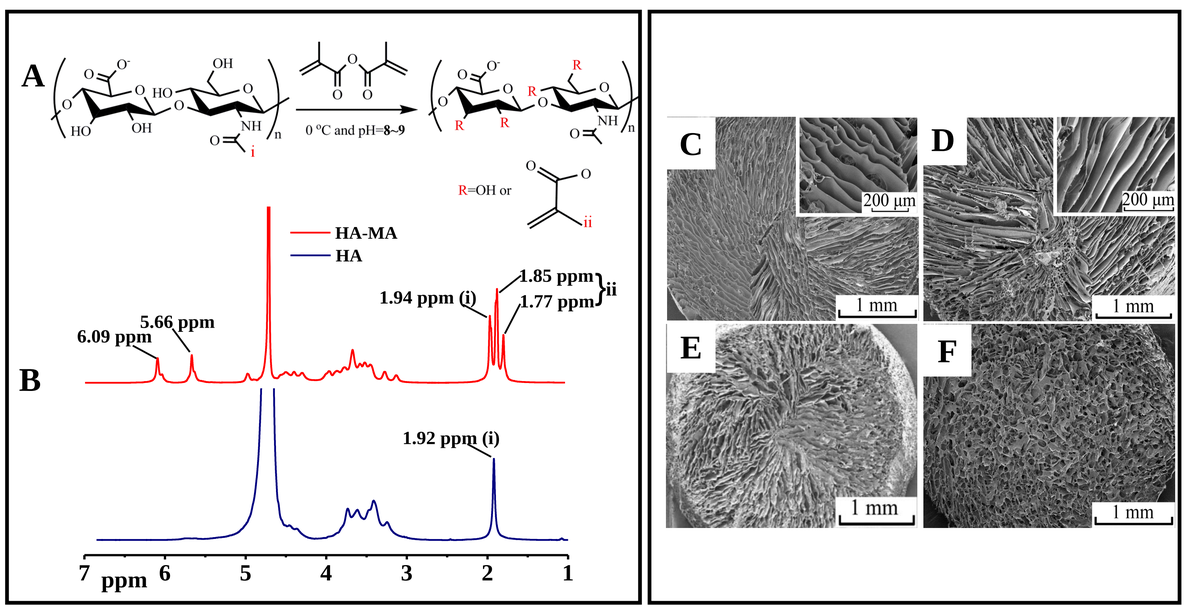

Figure 2. (A) Schematic of transesterification reaction between MA and HA. (B) ^{1}H NMR spectra of HA and HA-MA. (C-F) SEM images of (C) the as-prepared and (D) rehydrated and freeze-dried O-HA-MA scaffold, (E) hybrid O-MA-HA/PLGA scaffold, and (F) hybrid R-HA-MA/PLGA scaffold (control). Insets are higher magnification images.

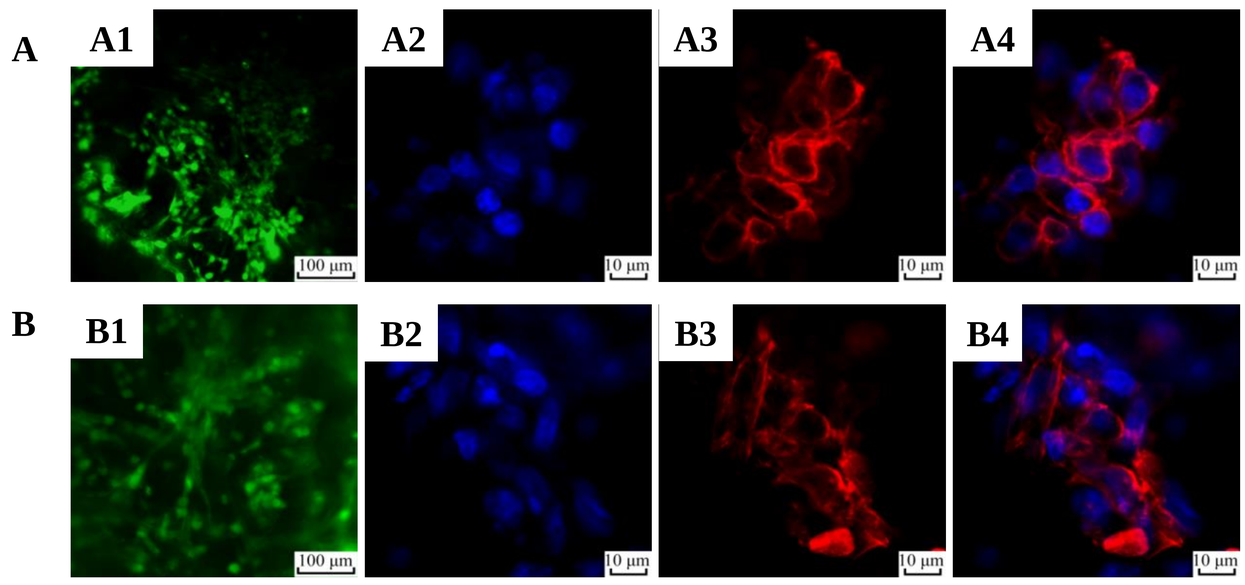

Figure 3. Fluorescent (A1, B1) and CLSM images (A2-A4 and B2-B4) of BMSCs in (A) O-HA-MA/PLGA and (B) R-HA-MA/PLGA scaffolds. (A1, B1) viable BMSCs stained by FDA (green), (A2, B2) nucleus stained by DAPI (blue), (A3, B3) cytoskeleton stained by rhodamine-conjugated phalloidin (red), and (A4) and (B4) merged images of (A2) and (A3), and (B2) and (B3), respectively.

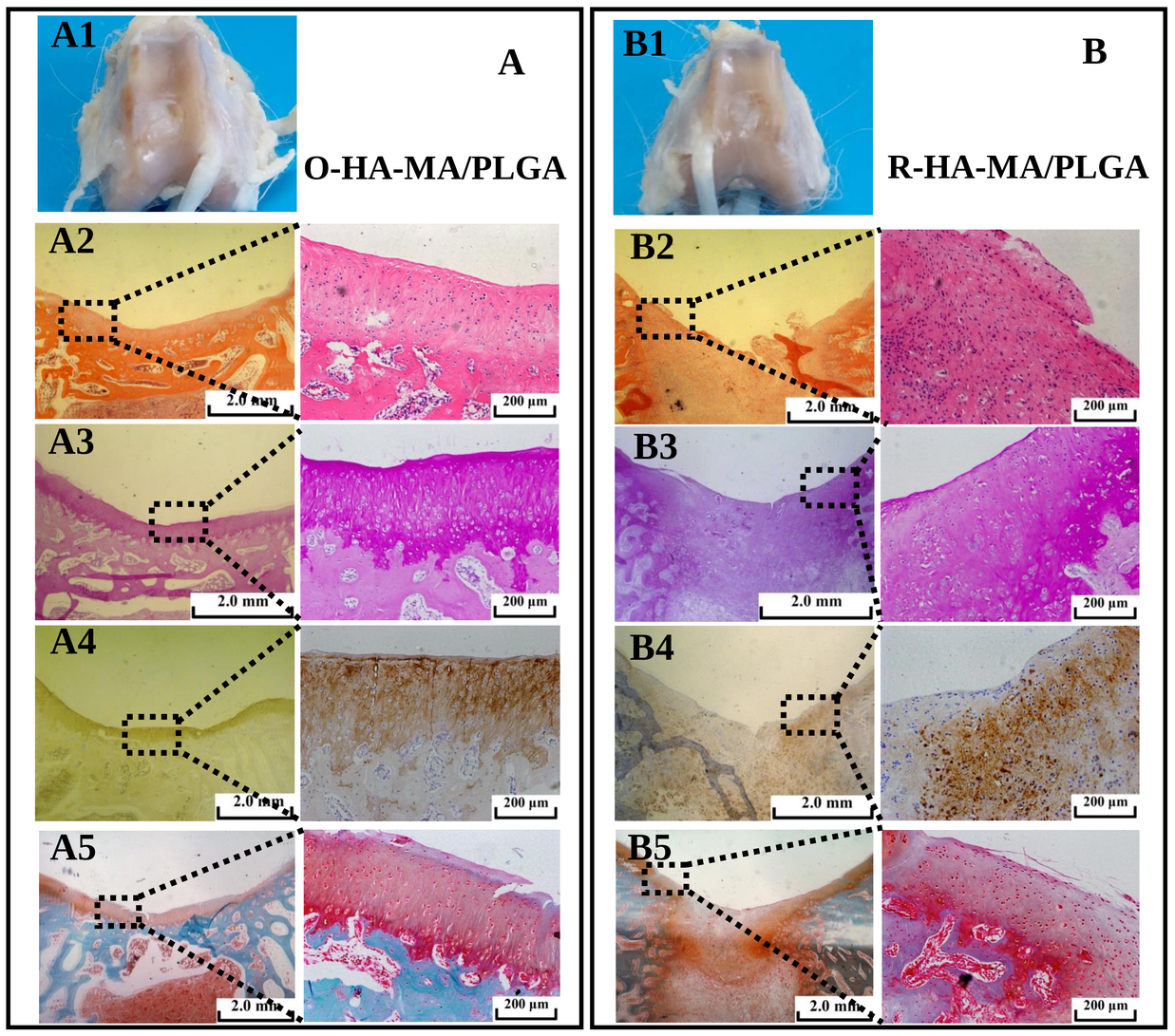

Figure 4. Histological analysis of the neo-cartilages after the full thickness cartilage defects (4 mm in diameter, and 4 mm in depth) were repaired by (A) O-HA-MA/PLGA and (B) R-HA-MA/PLGA for 12 w, respectively. (A1, B1) Gross view, (A2, B2) H&E staining, (A3, B3) PAS staining of GAGs, (A4, B4) immunohistochemical staining of type II collagen, and (A5, B5) safranine O and fast green staining of cartilage (red) and bone (green), respectively.

Conclusion

A macro-porous hybrid O-HA-MA/PLGA scaffold with oriented pores arranging along the radial direction, stable porous structure against re-hydration, and larger compression modulus was prepared. After transplantation of the cell-free O-HA-MA/PLGA scaffold in rabbit knee for 12 w, the cartilage defects and subchondral bone were both well regenerated with obvious tide marks. The neo tissues in the O-HA-MA/PLGA group integrated well with the surrounding tissues, and preserved much more regular distribution of cells and ECMs, which are similar to the native cartilage. Moreover, both of the cartilage and subchondral bone were better regenerated, and integrated well with each other.

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References

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