Amniotic membrane-derived multichannel hydrogels for neural tissue repair

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Neural tissue regeneration demands advanced biomaterials that recapitulate the structural, mechanical, and biochemical characteristics of native neural environments. In this work, we introduce multichannel 3D hydrogels derived from human amniotic membrane methacryloyl (AMMA), designed to support neural stem cell (NSC) functions and promote directional tissue regeneration. AMMA was synthesized from decellularized human amniotic membrane and photopolymerized into scaffolds with ~250 µm channels using a custom 3D-printed mold. These hydrogels exhibit low stiffness (~5 kPa), mimicking central nervous system (CNS) mechanical properties, and high-water content, supporting their application as soft tissue analogs.

Under 2D conditions, AMMA hydrogels enabled uncoated NSC adhesion, proliferation, and neuronal differentiation, confirmed by TUJ-1 and GFAP expression. In 3D cultures, cells organized into neurospheres and longitudinal columns within the channels, establishing extensive neuronal networks. Synaptophysin staining confirmed the presence of synaptic vesicles, indicating functional connectivity. Importantly, the hydrogel structure allowed for efficient cell infiltration and neurite extension along channel axes, supporting both scaffold integration and guided regeneration.

Entirely human-derived, AMMA offers an ethical, bioactive, and highly customizable platform that overcomes limitations associated with animal- or synthetic-based scaffolds. These scaffolds can transport cells or therapeutic agents and be adapted to lesion-specific geometries, enhancing their clinical relevance. This study highlights the translational promise of AMMA as a next-generation biomimetic scaffold for CNS and peripheral nerve repair, bridging the gap between fundamental research and clinical application.

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