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Injectable polypeptide hydrogels via methionine modification for neural stem cell delivery

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Abstract:

Injectable hydrogels with tunable physiochemical and biological properties are potential tools for improving neural stem/progenitor cell (NSPC) transplantation to treat central nervous system (CNS) injury and disease. Here, we developed injectable diblock copolypeptide hydrogels (DCH) for NSPC transplantation that contain hydrophilic segments of modified L-methionine (Met). Multiple Met-based DCH were fabricated by post-polymerization modification of Met to various functional derivatives, and incorporation of different amino acid comonomers into hydrophilic segments. Met-based DCH assembled into self-healing hydrogels with concentration and composition dependent mechanical properties. Mechanical properties of non-ionic Met-sulfoxide formulations (DCH_{MO}) were stable across diverse aqueous media while cationic formulations showed salt ion dependent stiffness reduction. Murine NSPC survival in DCH_{MO} was equivalent to that of standard culture conditions, and sulfoxide functionality imparted cell non-fouling character. Within serum rich environments *in vitro,* DCH_{MO} was superior at preserving NSPC stemness and multipotency compared to cell adhesive materials. NSPC in DCH_{MO} injected into uninjured forebrain remained local and, after 4 weeks, exhibited an immature astroglial phenotype that integrated with host neural