An emerging area of regenerative medicine is the engineering of synthetic extracellular matrices (ECM) that recapitulate biochemical and biophysical characteristics of native tissue environments to create an instructive microenvironment through a variety of biomaterials-based approaches. Hydrogels, highly hydrated cross-linked polymer networks, have emerged as powerful synthetic analogs of extracellular matrices for basic cell studies as well as promising biomaterials for regenerative medicine applications. A critical advantage of these synthetic matrices over natural networks is that bioactive functionalities, such as cell adhesive peptides and growth factors, can be incorporated in precise densities while the substrate mechanical properties are independently controlled. We have engineered poly(ethylene glycol)-maleimide hydrogels as stem cell niches for developmental studies and injectable vehicles for protein and cell therapeutic delivery. These synthetic hydrogels support the in vitro generation of organoids from human pluripotent stem cell-derived 3D spheroids without Matrigel encapsulation and promote their engraftment and reparative activities in vivo. Hydrogel mechanical properties, adhesive ligand type, and protease-dependent degradability are key parameters in engineering a synthetic ECM mimic that supports organoid viability, expansion and development. In addition, this synthetic hydrogel served as an injectable vehicle to deliver organoids to intestinal wounds via a colonoscope resulting in organoid survival, engraftment and wound repair. The modular design of this synthetic matrix and the ability to deliver it via endoscopic techniques support the translational potential of this delivery platform for regenerative medicine and overcomes limitations associated with the use of Matrigel for organoid technologies.