Growth Factor Release from a Chemically Modified Elastomeric Poly(diol citrate) Scaffold Promotes Angiogenesis in vivo

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Attempts to regenerate functional urinary bladder tissue have been hampered by obstacles including appropriate scaffold choice and poor vascularization of developing tissue. The elastomeric properties of poly(1,8-octanediol-co-citrate) (POC) scaffolds have recently been shown to aid in urinary bladder regeneration when seeded with epitope defined, human mesenchymal stem cells in the context of a nude rat urinary bladder augmentation model.[1] In order to further promote increased tissue growth and development, we sought to create heparan sulfate binding POC (POC-HS) scaffolds that would allow for the binding and extended release of growth factors conducive to localized angiogenesis. POC scaffolds were prepared as previously described.[1] POC-HS were created by activating the POC in MES buffer [2-(N-morpholino)ethanesulfonic acid], containing 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and N-Hydroxysuccinimide. Scaffolds were incubated in MES buffer containing PEG-diamine. Heparan sulfate was activated. POC scaffolds were incubated in the activated heparan sulfate solution. Scaffolds were stored in PBS. Subsequently, human growth factors (GF) vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and insulin-like growth factor (IGF-1) were individually mixed into a PBS solution containing BSA and added to POC-HS scaffolds. Scaffolds were removed, rinsed in PBS and underwent GF release and quantification with the appropriate enzyme-linked immunosorbent assay (ELISA) Assay. Control samples consisted of POC scaffolds without heparan sulfate that were loaded with GFs under identical incubation conditions and processed accordingly. Athymic nude rats underwent subcutaneous implantation with either Condition **A**)POC scaffold alone, **B**)POC-VEGF, or **C**)POC-HS-VEGF. Animals were sacrificed at 4 weeks post-implantation. In vitro cumulative GF release from POC-HS based scaffolds demonstrated an extended GF release profile compared to POC-GF control samples. Gross subcutaneous specimens of Conditions **A-C** demonstrated increased vascularity with POC-HS-VEGF. Data demonstrate that POC can be chemically modified to release pro-angiogenic GFs over time and promote localized angiogenesis.

References: 1. Sharma AK. Biomaterials 2010;31(24):6207-6217.