304

Lee J N[1], Lee H[2], Chun S Y[2], Kim B S[1], Kim H T[1], Kim T[1], Seo Y J[3], Kim D Y[4], Yoo E S[1], Kwon T G[1], Chung S K[1], Kim B W[1]

1. *School of Medicine, Kyungpook National University,* ***2.*** *BioMedical Research Institute, Kyungpook National University Hospital,* ***3.*** *College of Medicine, Dongguk University,* ***4.*** *Catholic University of Daegu School of Medicine*

HUMAN URINE-DERIVED STEM CELLS SEEDED SURFACE MODIFIED COMPOSITE SCAFFOLD GRAFTS FOR BLADDER RECONSTRUCTION IN A RAT MODEL

Hypothesis / aims of study

The aim of this study was to investigate the synergistic effect of human urine-derived stem cells (USCs) and a heparin-immobilized basic fibroblast growth factor (bFGF)-loaded scaffold (composed of Polycaprolactone/Pluronic F127/3 wt% bladder submucosa matrix) for regeneration of the bladder smooth muscle and urothelial layers in a rat model.

Study design, materials and methods

The scaffold containing endogenous amine groups was fabricated using an immersion precipitation method, and heparin was immobilized on the surface via covalent conjugation. bFGF was loaded onto the heparin-immobilized scaffold by a simple dipping method. The surface modified scaffold (scaffold$^{heparin\text{-}bFGF}$) was analyzed for heparin immobilization efficiency, amount of released bFGF, biocompatibility, and differentiation rate into smooth muscle and urothelial cells using urine-derived stem cells (USCs) *in vitro*. For *in vivo* evaluation, the following groups were tested: partial bladder wall cystectomy (about 40%) group, unmodified scaffold implanted after partial cystectomy group, scaffold$^{heparin\text{-}bFGF}$ implanted group, and USCs combined with the scaffold$^{heparin\text{-}bFGF}$ group. At 8 weeks post-operation, the bladder capacity and compliance of the grafts were measured and histological and immunohistochemical analysis was performed.

Results

The scaffold$^{heparin\text{-}bFGF}$ exhibited evenly immobilized heparin, high affinity and sustained released of bFGF, an open-porous structure, and significant biocompatibility. The amount of heparin immobilized to the scaffold was 0.72 ± 0.11 μg/6 mm^2. The bFGF affinity for the heparin-immobilized scaffold was about 1.4 times higher than that of the unmodified scaffold, and heparin-immobilized scaffold showed sustained release of bFGF for 14 days. Evaluation of cells cultured on the scaffold$^{heparin\text{-}bFGF}$ indicated significantly high biocompatibility compared to the unmodified scaffold. The differentiation rates, indicated by detection of α-SM actin, Caponin I, pan-CK, and CK19 markers at day 14 with FACS, were 96.71, 70.13, 77.87, and 76.66%, respectively. Real-time analysis showed that stem cell markers expression decreased at day 14, while smooth muscle and urothelial cell markers were increased. Results of the *in vivo* study showed that the USC-scaffold$^{heparin\text{-}bFGF}$ group exhibited significantly increased bladder capacity and compliance compared to the other groups, and the values were similar to normal bladders. Histological and immunohistochemical analysis showed regeneration of smooth muscle tissue, a multi-layered urothelium, a condensed submucosa layer, and no aggregation of host CD8 lymphocytes in the USC-scaffold$^{heparin\text{-}bFGF}$ group.

Interpretation of results

The scaffold$^{heparin\text{-}bFGF}$ supported significant heparin immobilization and bFGF loading, resulting in enhanced biocompatibility and cell differentiation rates *in vitro*. The USCs combined with the scaffold$^{heparin\text{-}bFGF}$ induced a synergistic effect, as indicated by increased bladder capacity, compliance, histological reconstruction, and reduced inflammation in a partial cystectomy rat model.

Concluding message

We proposed that USC-scaffold$^{heparin\text{-}bFGF}$ could be an effective strategy for bladder reconstruction.

Disclosures

Funding: no **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Ethics Committee of Kyungpook National University School of Medicine