

## REGENERATIVE MEDICINE

## Advances in bladder tissue engineering

Two new studies highlight the ongoing progress in tissue engineering for bladder augmentation surgery, by showcasing the potential for novel cell types and culture conditions to enhance the growth and function of tissue-engineered grafts.

The first study, published in *Biomaterials*, demonstrates the possibility of using adipose tissue as a source of stem cells for bladder tissue engineering. Adipose-derived stem cells can be directed to differentiate into a range of lineages including functioning smooth muscle *in vitro*, and they offer the advantage of being both accessible and abundant.

The investigators obtained adipose stem cells from liposuction procedures and differentiated them into smooth muscle cells using inductive media. These cells were seeded onto synthetic bladder scaffolds, which were used to augment the bladders of adult female athymic rats that had undergone partial cystectomy to remove 50% of the urinary bladder. Other animals received augmentation with unseeded bladder scaffolds or suture closure with no augmentation.

By 12 weeks after surgery, implanted rats had organized urothelium covering the entire luminal surface of the scaffold, as well as evidence of differentiated and organized smooth muscle structures. The amount of smooth muscle was greatest in the rats with cell-seeded scaffolds, and these animals also demonstrated less

fibrosis and collagen deposition than the animals with acellular implants. After organ harvesting, the cell-seeded tissue demonstrated a weak contractile response to chemical stimulation. The authors conclude that adipose stem cells represent an attractive nonembryonic option for tissue engineering in the lower urinary tract.

The second study, from *Tissue Engineering Part A*, illustrates the importance of culture conditions in tissue engineering applications. Rather than use a synthetic scaffold, the investigators focused on cell-seeded small intestinal submucosa (SIS). “In our previous work, we observed that while adult stem cells changed the mechanical properties of the SIS, they did not penetrate into the tissue,” says Michael Sacks, corresponding author on the paper. “We thought that the best way to promote cellular penetration into the SIS was to use growth factors that were important in development of the bladder.” In fact, addition of the growth factors VEGF and FGF-2 resulted in significant penetration of rat bladder smooth muscle cells into SIS specimens.

The researchers also studied the effect of mechanical stimulation, which is important to the normal development of the bladder, on the bioengineered tissue. Their previous work had shown that *in vitro* stretching of rat bladders at non-physiologic frequency promoted



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profound changes in the extracellular matrix, particularly in elastin content. “We used this scheme on our engineered tissues once the cells had penetrated the matrix,” says Sacks. “We found that mechanical stimulation produced large amounts of elastin, which is important in bladder compliance.” Thus, control of elastin deposition by *in vitro* culture conditions and mechanical stimulation could be used to improve functional compliance in tissue engineered bladder wall.

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**Original articles** Jack, G. S. *et al.* Urinary bladder smooth muscle engineered from adipose stem cells and a three dimensional synthetic composite. *Biomaterials* 30, 3259–3270 (2009).

Long Heise, R. *et al.* Generating elastin-rich SIS-based smooth muscle constructs utilizing exogenous growth factors and cyclic mechanical stimulation. *Tissue Eng. Part A* doi:10.1089/ten.TEA.2009.0044