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Institution: Department of Urology, Pharmacology and Orthopedic Surgery
Title: FUNCTIONAL RESTORATION OF DENERVATED EXTERNAL URETHRAL SPHINCTER AFTER MUSCLE DERIVED STEM CELL INJECTION IN MALE RAT

Aims of Study:

Our previous study showed the long term survival of autologous muscle derived cell into the urethra and bladder wall[1-2]. In this study, we determined whether allogenic muscle derived stem cells (MDSC) can survive and restore function in denervated male rat urethral sphincters.

Methods:

MDSC were isolated from normal 6 weeks SD rats via preplating technique were used. Late preplating MDSC were first transduced with retrovirus carrying the expression of the β-galactosidase reporter gene. A midline incision was made and 1~1.5x10^6 MDSC were injected into allogenic denervated proximal urethral sphincters. After two weeks, urethral muscle strips were prepared from normal, denervated, and denervated+MDSC injected rats. Fast twitch muscle contractions were recorded after electrical field stimulation (60V, 2.5Hz)[3]. The tissue was then sectioned, assayed for β-galactosidase activity and then counterstained with H+E.

Results:

Denervated sphincters produced a decrease in fast twitch muscle contraction amplitude (5.95±3.24% of the normal sphincter contraction), while denervated+MDSC injected sphincters showed an improvement of the fast twitch muscle contraction amplitude (88.81±36.72% of the normal sphincter contraction). Histologic evaluation demonstrated new skeletal muscle fiber formation at the injection site of the urethral sphincter.

Conclusions:

Deficient External urethral sphincter muscle function was restored through stem cell tissue engineering. MDSC-mediated myoplasty warrants further investigation as a new method to treat stress urinary incontinence.

References:

(1) 2001 Persistence and survival of autologous muscle derived cells versus bovine collagen as potential treatment of stress urinary incontinence J Urol 165:271-276

(2) 2000 Preliminary results of myoblast injection into the urethra and bladder wall. Neurourol Urodyn 19:279-283

(3) Parlani et al. 1992 The rat external urethral sphincter An in vitro model to evaluate the activity of drugs on the smooth and striated components of the urinary bladder outlet. J Pharmacol Methods 28(2):85-90

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