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# HUMAN MDC INJECTION INCREASES LEAK POINT PRESSURE IN A NUDE RAT MODEL OF STRESS URINARY INCONTINENCE

Hypothesis / aims of study
Prior studies have demonstrated that injection of muscle-derived cells (MDC) into periurethral muscle resulted in increased leak point pressures (LPP) in an animal model of stress urinary incontinence. Recently we have isolated and characterized human MDC. The objective of this study was to investigate the potential of human MDC for the treatment of urinary incontinence in a nude rat model.

Study design, materials and methods
A well-established stress urinary incontinence model, created through bilateral transection of the sciatic nerve, was utilized in the 8 week-old female, athymic nude rat (Hsd:RH-rnu, Harlan Laboratory). Human MDC (hMDC) were provided by Cook Myosite, Inc. (Pittsburgh,PA). Animals were divided into three experimental groups: (A) non-treated control; (B) sciatic nerve transection with periurethral sham-injection (20 µl saline) one week post-transection; and (C) sciatic nerve transection with periurethral injection of hMDC (1x $10^6$ cells/20 µl saline) one week post-transection (n=6 per group). LPP was measured 4 weeks following injection using the vertical tilt intravesical pressure clamp method. Cryosections of the urethra were labeled with H&E for general histology, and immunolabeled with lamins A/C to follow the fate of the injected hMDC.

Results
Bilateral sciatic transection resulted in a significantly lower LPP (28.5 ± 0.6 $cmH_2O$) compared to control group (43.6± 1.1 $cmH_2O$, $p<0.05$). LPP was restored to a significantly higher level following hMDC injection (37.9 ± 2.3 $cmH_2O$, $p<0.05$) vs. sham-injected. Importantly, no significant difference in hMDC and control group LPP was detected. Histologic evaluation demonstrated periurethral muscle atrophy in the sham injected group only. Human MDC were present in the nude rat's urethral 4 weeks after injection.

Interpretation of results
Treatment with hMDC led to restoration of LPP back to normal levels in an experimental model of stress urinary incontinence in the nude rat. We hypothesize that the injected hMDC differentiated into new muscle fibers and prevented periurethral muscle atrophy but the exact mechanisms of these actions are still being investigated.

Concluding message
Human MDC may now be considered as a therapy for stress urinary incontinence.