Muscle Precursor Cells (MPCs) and Adipose-derived Stem Cells (ADSCs) for the Treatment of Bladder Voiding Dysfunction
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Introduction
Bladder voiding dysfunction (BVD) in the elderly is commonly due to bladder outflow obstruction (benign prostatic hyperplasia, BPH) with 30% of men at the age of 65 affected. Currently there is no treatment modality that reverses the underlying cause, the decreased bladder contractility. Muscle Precursor Cells (MPCs) and adipose-derived stem cells (ADSCs) are envisioned as promising cell sources with the capability to regenerate muscle fibers.1,2 The goal of this research was to evaluate the use of adult stem cells for the treatment of bladder voiding dysfunction due to decrease muscle contractility.

Materials and Methods
Infravesical obstruction was performed in 66 male Lewis rat (6-8 weeks old), six weeks later, eight rats were evaluated as a positive control by cystometry and later by organ bath analysis. In addition, morphological (histomorphometry, Western-Blotting, RT-PCR) bladder tissue changes were analysed. MPCs from the soleus muscle and ADSC from the inguinal region of adult male Lewis rats were expanded in culture. Both cell types were characterized by FACS analysis and immuno-cytochemistry (CD 34, CD29, CD44, Desmin, MyHC, Actinin). In sixteen rats, stem cell injection with an insulin syringe (1.5 x 10^6 cells) into the bladder wall and deligation was performed six weeks after the obstruction. Target cells were labelled with PKH-67. 4 and 8 weeks after stem cell injection, morphological and functional changes were assessed. Healthy, age matched rats served as a control.

Results
MPCs and ADSCs used were positively characterised by FACS. Obstructed rats had a greater bladder weight, lower threshold pressure, maximum bladder pressure and lower contractility on Electrical Field Stimulation (EFS) at 80V and 32Hz than age matched rats (Figure 1A). Histomorphometric analysis showed a higher connective tissue-to-smooth muscle ratio between the animals with obstruction and controls (Figure 1B & C). After stem cell injection, we were able to track the cells by PKH67. Organ bath analysis and urodynamic studies showed an improved contraction on EFS (3516 ± 233.7mg per 100mg tissue for the MPCs and 1755 ± 565mg per 100mg tissue for the ADSCs) and higher intermicturition pressure after cell treatment (Figure 2 A). The same trend was seen by RT-PCR and Western-Blotting where gene expression and protein translation of smoothelin and caldesmon after stem cell therapy was closer to normal (Figure 2 B).

Discussion and Conclusions
In our study, we were able to establish a model of hypocontractile bladder in a small animal and demonstrated that MPCs and ADSCs can support the restoration of bladder voiding dysfunction. Our results show improved contractility, voiding pressures and molecular expression after cell therapy.

References

Acknowledgements
The project was funded by the Max and Hedwig Niedermaier-Stiftung and Fonds für Medizinische Forschung

Disclosures
The authors have nothing to disclose