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Injecting RNA interference lentiviruses targeting the muscarinic 3 receptor gene into the bladder wall inhibits neurogenic detrusor overactivity in rats with spinal cord injury

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Introduction & Objectives: To investigate the effects of injecting RNA interference (RNAi) lentiviruses targeting the muscarinic 3 (M_3)receptor gene into the bladder wall on bladder activity in rats with spinal cord injury (SCI).

Materials & Methods: Four M_3 RNAi lentiviruses were constructed and used to infect primary cultured bladder smooth muscle cells (BSMCs). Western blotting and quantitative reverse transcription polymerase chain reaction (qRT-PCR) were performed to determine the optimal RNAi lentivirus with the highest interference efficiency. Female Wistar rats were subjected spinal cord transection at T9-10 and randomly divided into three groups (n = 8), namely, blank control, negative control, and experimental groups, and injected into the bladder wall with saline, negative control shRNA and M_3 RNAi lentiviruses, respectively, one week after spinal cord transection. The normal rats were used as normal control group. Urodynamic parameters and bladder tissues were evaluated in the different groups.

Results: An M_3 RNAi lentivirus with the highest interference efficiency (78.9%) was constructed and identified. Three weeks after injecting M_3 RNAi lentiviruses into the bladder wall, western blotting and qRT-PCR showed that the M_3 receptor was significantly down regulated in the experimental group. Cystometric evaluation suggested that down regulating M_3 receptor expression could substantially decrease basal pressure, residual volume and non-voiding contraction number, increase intercontraction interval, and significantly improve bladder compliance in rats with SCI.

Conclusions: Injecting RNAi lentiviruses targeting the M_3 receptor gene into the bladder wall could effectively inhibit neurogenic detrusor overactivity (NDO) due to SCI. Thus, this approach may be a potential treatment for NDO in SCI.