undergoing TA incision and grafting with SIS (n=8); and (4) the same procedure with syngeneic stem cell-seeded SIS (n=8). Eight weeks after first stage surgery, all rats underwent, cavernosal pressure measurement in response to nerve stimulation, penile morphometric analysis and tissue collection for further histological evaluation, real time-PCR, Westen blot and immunostaining analysis for gene and protein expression.

RESULTS: Erectile function evaluation 8 weeks after surgery showed that seeding ADSCs on SIS grafts resulted in a significant restoration of erectile response compared to the group with SIS grafting alone. Cross sectional measurement of rat penis with SIS graft with or without seeded ADSCs demonstrated 38.2%~41.0% and 29.5%~30% increase in mean diameter respectively, compared to the sham group. Masson's trichrome staining showed only mild fibrosis around the graft in the ADSCs-seeded SIS graft group, with moderate fibrosis in the SIS graft alone group. eNOS, nNOS and VEGF expression decreased significantly. Conversely, iNOS and TGFβ1 increased in the SIS graft group, but seeded ADSCs SIS grafts had a significant restoration of eNOS, sNOS and VEGF expression.

CONCLUSIONS: Rats undergoing TA incision and grafting procedures with autologous ADSCs-seeded SIS grafts maintained better erectile function compared to animals grafted with SIS without ADSCs seeding ($p<0.001$). The present study suggests ADSC seeded SIS grafting materials can be exploited clinically for TA reconstruction in Peyronie's disease to better maintain erectile dysfunction.

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UPREGULATION OF A DISTINCT SET OF CHEMOKINES FOLLOWING CAVERNOUS NERVE INJURY IS RESPONSIBLE FOR RECRUITMENT OF ADIPOSE TISSUE-DERIVED STEM CELLS TOWARDS THE MAJOR PELVIC GANGLION.

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INTRODUCTION AND OBJECTIVES: We have recently demonstrated the essential role of adipose tissue-derived stem cell (ADSC) recruitment towards the major pelvic ganglion (MPG) in rats following cavernous nerve injury (CNI). The interaction between chemokines and their receptors plays a major role in this process. The objectives of this study were to examine chemokine-expression in neuro-inflammation of the rat MPG following cavernous nerve injury (CNI), and to match these chemokines to genomic, structural and functional expression of chemokine receptors (CRs) in human ADSC.

METHODS: (MPG) Six male 12 weeks old Sprague Dawley rats underwent laparotomy and bilateral crush injury of the cavernous nerves. Six rats served as sham controls (laparotomy and periprostatic dissection only). Twenty-four hours after CNI, the MPGs were harvested; RNA was isolated and subjected to qPCR analysis in triplicate. (ADSC) Human ADSC were isolated from subcutaneous adipose tissue of 5 consenting donors. Cells were subjected to qPCR for all 21 known CRs. These results were validated by FACS and intracellular FACS. Migration of ADSC towards gradients of CCL2,19,28; CX3CL1, CXCL12 and XCL1 was assessed in-vitro in a chemotaxis assay.

RESULTS: (MPG) Twenty-four hours following CNI, neuro-inflammation was present in the rat MPG as illustrated by significant upregulation of TNFA. Crush injury further resulted in significant upregulation of the chemokines CCL2,28, CXCL12, CX3CL1 and XCL1. (ADSC) RNA for CRs CCR1,3,4,10; CX3CR1; CXCR4,6,7; XCR1; CCRL1,2 was detected by qPCR of ADSC. Validation by FACS at p5 showed low membranous CR expression, however, intracellular FACS indicated high expression of CCR4,10, CX3CR1 and XCR1 at p5, and modest expression of of all other qPCR-detected CRs except CCRL1 and 2. Functional activation by calcium imaging was present for CCL2 (binds to CCR4), CCL28 (CCR10), CX3CL1 (CX3CR1) and XCL1 (XCR1). Cells migrated towards gradients of CCL2,28, XCL1 and CX3CL1, but not towards CCL19. The number of cells migrated towards CXCL12 was low.

CONCLUSIONS: CNI-related neuro-inflammation is accompanied by the expression of various chemokines. We identified the ligand-CR pairs CCL2-CCR4, CCL28-CCR10, CX3CL1-CX3CR1 and XCL1-XCR1 as potentially responsible for ADSC homing towards the MPG following CNI. Surprisingly, CXCR4/7-SDF1(CXCL12), is not likely a major homing factor for ADSC, as previously proposed. Modification of expression of these receptors in ADSC could improve homing and thus treatment efficacy.

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SYNERGISTIC EFFECT OF MESCENCHYMAL STEM CELLS AND MATRIXEN ON THE ERECTILE FUNCTION IN THE RAT MODEL WITH BILATERAL CAVERNOUS NERVE CRUSHING INJURY

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INTRODUCTION AND OBJECTIVES: There have been several studies about the effect of mescenchymal stem cells (MSCs) in various diseases. Moreover, the treatment effect of MSCs has been observed in the animal model of erectile dysfunction caused by cavernous nerve injury. However, some difficulties appeared in stem cell therapy in spite of their therapeutic effect. For example, stem cells seemed to easily spread-out into the adjacent tissue after administration. Therefore, we are not able to get anticipating results from the stem cell therapy, in addition, this may cause unexpected and unfavorable events. As a result, we used Matrixen, which is a collagen based biocompatible polymer, to enhance the implantation ability of MSCs and compared the effect of MSCs and MSCs mixed with Matrixen in the rats of cavernous nerve crushing injury.

METHODS: Rats were divided into 4 groups: control group (n=5), Bilateral cavernous nerve crushing group (BCNC group, n=5), BCNC administered with MSCs group (n=10,1×106 in 20 μl) and BCNC administered with MSCs/Matrixen group (n=10, 1×106 in 20 μl). Before administration, MSCs were labeled with PKH26. After 4 weeks, intracavernosal pressure (ICP) /mean arterial pressure (MAP) ratio was measured by cavernous nerve electrical stimulation. The major pelvic ganglion (MPG) and penile tissue were collected from each group after Functional assessment. Immunofluorescent staining of MPG was performed with PKH26 and Tuj1. Masson's trichrome staining and western blot analysis of endothelial nitric oxide synthase (eNOS) and neuronal nitric oxide synthase (nNOS) were done in corpus cavernosum.

RESULTS: ICP/MAP ratios of BCNC with MSCs and MSCs/Matrixen groups were significantly increased compared with BCNC group. Moreover, ICP/MAP ratios of MSCs/Matrixen group was significantly increased compared with BCNC with MSCs group. In MPG, the more implantation of MSCs and increased expression of nerve cells were observed in MSCs/Matrixen group. More restoration of smooth muscle was also observed in BCNC with MSCs/Matrixen group. Significant increase expression of nNOS was noted in BCNC with MSCs/Matrixen group.

CONCLUSIONS: From these results, Matrixen is supposed to enhance the implantation of MSCs and differentiate to neural cells in MPG and we considered that the use of transplant cell carrier such as Matrixen may help the implantation of MSCs and improve the therapeutic effect of MSCs.

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