

# ERECTILE DYSFUNCTION (ED)

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## 1. ERECTILE DYSFUNCTION PROTOCOL

- A. **Clinical response:** Clinical response demonstrates a decrease in progression of disease and evidence of an improved repair process. In addition to physical examinations prior to stem cell graft and 6 months post-procedure, laboratory test results serve as evidence of repair process. Internationally recognized lab tests for monitoring erectile dysfunction (ED) include:
- Complete Blood Count
  - Liver enzymes o PT/aPTT
  - Prostate Specific Antigen (PSA)Adrenal hormone levels
  - Complete Metabolic Panel
  - HbA1c (Glycosylated hemoglobin)
  - Evaluation of vascular function of the penis with duplex ultrasonography
- B. **Objective:** To provide the patient with a treatment that stimulates his / her immune system, promote cellular regeneration and improve symptoms associated with Erectile Dysfunction. The direct injection in the corpus cavernosum of Ad-SVF Containing Adult Stem Cell Procedure should serve to compliment the patient's current treatment regimen or to promote healing when current treatment is not responding.

## 2. PRELIMINARIES

- A. **Background:** Erectile dysfunction (ED) is the inability to get and keep an erection firm enough for intercourse. Having erection trouble from time to time isn't necessarily a cause for concern, but if erectile dysfunction is an ongoing problem, it may cause stress, cause relationship problems or affect male self-confidence. Problems with erections may stem from medications, chronic illnesses, poor blood flow to the penis, drinking too much alcohol, or being too tired.
- B. **Causes of Erectile Dysfunction:** Often, the cause is multifactorial, but vascular causes are the most commonly implicated. Because the development and maintenance of a rigid erection depend on achieving a high intracavernosal pressure, it is not surprising that disorders affecting the peripheral arterial blood flow are strongly associated with erectile dysfunction. The vascular etiology of erectile dysfunction present in 60% of patients can be related to small vessel vascular diseases as in the case of diabetes and large vessel arteriosclerosis as in hypertension, which cause arterial insufficiency/erectile dysfunction.
- C. **Treatment Options:** Many treatment options are available for men with ED. Any underlying condition should be treated.
- **Phosphodiesterase (PDE) - 5 inhibitors:** This drug class consists of sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis), and avanafil (Stendra). Sildenafil was the first in this series of PDE inhibitors. Avanafil is the newest, approved by the FDA in April 2012. In one study of 390 men with diabetes and erectile

dysfunction, avanafil was found to be a safe and effective treatment as early as 15 minutes and more than 6 hours after dosing.

- ***Vasodilators***: These medications may be injected directly into the penis to exert their relaxant effect directly on the corpora cavernosal smooth muscle. They can be used as single agents or in combination. The most commonly used agents include alprostadil (prostaglandin E1 [PGE1]), papaverine, and phentolamine. The dose and most effective combination of these agents must be determined for each patient. These medications can be obtained commercially as Caverject and Edex or can be formulated according to the physician's request by compounding pharmacies.
- ***Androgens***: Treatment of ED in men with low levels of serum testosterone. Males with hypogonadism who desire a restoration of libido and who want to become sexually active, usually benefit from the exogenous supplementation of androgens. Androgens may be administered via injections, cutaneous application via gel or skin patches, or oral administration.
- ***Other treatments***: Include intraurethral pellet therapy / Medicated Urethral System for Erections (MUSE), vacuum devices, placement of prosthetic devices within the corpora, among other surgical treatments.

## 1. AD-SVF CONTAINING ADULT STEM CELLS TREATMENT OPTION

### A. Ad-SVF Containing Adult Stem Cells Procedure

- ***Initial patient evaluation***: A physician revises the medical information, lab work, and diagnostic imaging provided by the patient in order to determine the stage of the medical condition and any other secondary conditions. Application of the International Index of Erectile Function questionnaire (IIEF).
- ***Pre-op Evaluation / post-op medical consultation***: A medical specialist to the specific condition to be treated provides a medical consultation at the location where the procedure will be performed. During pre-op evaluation informed consent is obtained from all patients and medical records are updated, including patient's most recent physical exam, most up-to-date lab results and imaging studies. Physician then performs surgical risk assessment. Erectile dysfunction patients require in hospital pre-op evaluations by: endocrinologist, cardiologist and interventional radiologist. On the morning prior to procedure history and physical are performed by physician.
- ***Harvesting of adipose tissue***: Adipose tissue acquisition can be summarized as three step process:
  - ***Application of anesthetic / injection of tumescent solution***
  - ***Waiting time***

- **Acquisition of adipose tissue:** An area of the body with sufficient adipose tissue is selected; this is usually the periumbilical area. With the patient supine, the physician infiltrates a small amount of local anesthetic. A tissue sample is then obtained using 60 cc syringe(s) to aspirate 50 to 100 cc of adipose tissue. Immediately following lipo-aspiration, adipose tissue sample is processed (minimally manipulated) to separate stem cells for use as graft.
- **Preparation of Platelet Rich Plasma (PRP):** Using a standard phlebotomy technique the patient's own blood sample is obtained. After collection of whole blood, sample is centrifuged to obtain PRP aliquot. The regenerative potential of PRP is based on the release of growth factors / cytokines upon platelet rupture. PRP also enhances stem cell proliferation.
- **Autologous implant of Ad-SVF:** The stem cells obtained from the adipose tissue sample and the PRP are applied to the patient using appropriate protocol for their condition. Autologous Ad-SVF containing adult stem cells are infused via implant into the corpus cavernosum.
- **Procedure for Implant into Corpus Cavernosum:** Patient should take 50 mg of sildenafil (Viagra), immediately before surgeon begins mini-lipoaspiration. Evaluation of vascular function of the penis is performed the morning of the procedure, by Doppler ultrasound. The corpus cavernosum is infiltrated with 8 cc of 1% Lidocaine, allowing 10 minutes for expansion. 5 cc of SVF / stem cell concentrate is injected using a 1", 27 G needle into the innermost part of the penis and each side of the corpus cavernosum.

B. Post-op care for ed procedure:

- Patient remains under routine hospital care for 4 to 6 hours post-op
- Patient is observed for bleeding from catheter
- Urine sample checked for hematuria
- Post-op evaluation before discharge and 24 hours post-op
- Patient maintains pressure dressing for 24 hours post-op
- 500 mg ciprofloxacin po bid for 7 days
- In hospital urology consult if needed

C. Risks: There are possibilities for unwanted effects related to the local anesthesia, harvesting procedure, and injection of stem cells. Even with the most established protocol, adequate technique, and careful administration; a medical team may encounter uncontrollable events. Although there is no guarantee of perfect results, excellent results can be attained. The surgeon provides services in the most responsible, professional and diligent manner, always considering that surgeries imply risks. The risks of complications of adipose tissue harvesting and stem cell infusion are very low. Possible risks include but are not limited to:

- |                        |                    |
|------------------------|--------------------|
| ● Vascular spasm       | ● Pseudo-aneurysms |
| ● Vascular obstruction | ● Lymphadenopathy  |

- Bruising
- Nerve or muscle injury
- Allergic reaction
- Dizziness
- Nausea / Vomiting
- Allergic reaction
- Pain at site of injections
- Bleeding at injection site
- Malaise
- Low-grade fever
- Hot flashes
- Itching at injection site

D. Benefits: Stem cell therapy is an innovative therapeutic approach for erectile dysfunction. Stem cells have the innate ability to restore and renew damaged cells. Adipose derived Mesenchymal stem cells are particularly adept at restoring blood vessels and veins to a functioning state and can therefore be very useful in treating patients with Erectile Dysfunction. Studies have shown that the use of stem cell therapy for ED has proven to be the new and effective choice in ED treatment.

E. Follow-up Plan: Clinical response evaluated by use of International Index of Erectile Function, review of response to treatment and number of sexual attempts. The RigiScan is used to measure penile tumescence and rigidity continuously. International standards for follow-up:

- ***Pre-Ad-SVF implant:***
  - Patient follow-up with his urologist.
  - Clinical evaluation of symptoms
  - Use of International Index of Erectile Function questionnaire (IIEF)
- ***3 months after Ad-SVF implant:***
  - Patient follow-up with his urologist.
  - Clinical evaluation of symptoms
  - Use of International Index of Erectile Function questionnaire (IIEF)
- ***6 months after Ad-SVF implant:***
  - Patient follow-up with his urologist.
  - Clinical evaluation of symptoms
  - Use of International Index of Erectile Function questionnaire (IIEF)

## ED – Adult Stem Cells Schedule of Events

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**1. Initial Patient Evaluation:** A physician reviews the medical information, lab work, and diagnostic imaging provided by the patient in order to determine the stage of the medical condition and any other secondary conditions.

A. Pre-Examination:

- You will have a physical exam, which will include measuring your blood pressure, temperature and heart rate (vital signs).
- Your doctor will discuss your medical history and any medications that you are taking.
- Your doctor will assess how well you can perform your daily activities
- If needed, you will have a urine or blood pregnancy test.
- Blood will be taken.

B. Additional Tests: should be done during or soon after this visit

- Complete Blood Count
- Liver enzymes o PT/aPTT
- Prostate Specific Antigen (PSA)Adrenal hormone levels
- Complete Metabolic Panel
- HbA1c (Glycosylated hemoglobin)
- Evaluation of vascular function of the penis with duplex ultrasonography

C. Review Results: After your doctor has reviewed the results of these tests, he or she will assess whether you are a good candidate for stem cell therapy. If you decide to obtain this therapy you will sign a consent form. A medical specialist to the specific condition to be treated provides a medical consultation at the location where the procedure will be performed. During pre-op evaluation informed consent is obtained from all patients and medical records are updated, including patient's most recent physical exam, most up-to-date lab results and imaging studies. Physician then performs surgical risk assessment

**2. Pre-Operation / Stem Cell Procedure:**

A. Two Weeks Before Procedure:

- No Aspirin or medicines that contain aspirin or Ibuprofen since it interferes with normal blood clotting.
- You may take Tylenol or generic forms of this drug.
- Discuss with your primary physician to discontinue anticoagulant drugs at least 1 week before the procedure.
- Please discontinue all herbal medications as many have side effects that could complicate a surgical procedure by inhibiting blood clotting, affecting blood pressure, or interfering with anesthetics.
- Please discontinue all diet pills whether prescription, over-the-counter or herbal.
- NO SMOKING because nicotine reduces blood flow to the skin and can cause significant complications during healing.
- Purchase a compressive garment to wear after the lipoaspiration procedure.

B. Morning of the Procedure:

- Have a light breakfast.
- Take your regular prescribed medications
- Wear comfortable, loose-fitting clothes that do not have to be put on over your head.

3. **Stem Cell Procedure:**

A. Preparation & Harvesting of Adipose Tissue:

- *Application of anesthetic / injection of tumescent solution*
- *Waiting time (~15 – 20 minutes)*
- *Acquisition of blood sample*
- *Acquisition of adipose tissue:* An area of the body with sufficient adipose tissue is selected; this is usually the periumbilical area. With the patient supine, the physician infiltrates a small amount of local anesthetic. Immediately following lipo-aspiration, adipose tissue sample is processed (minimally manipulated) to separate stem cells for use as graft.

B. Preparation of Platelet Rich Plasma (PRP): Using a standard phlebotomy technique the patient's own blood sample is obtained. After collection of whole blood, sample is centrifuged to obtain PRP aliquot. The regenerative potential of PRP is based on the release of growth factors / cytokines upon platelet rupture. PRP also enhances stem cell proliferation.

C. Autologous implant of Ad-SVF: The stem cells obtained from the adipose tissue sample and the PRP are applied to the patient using appropriate protocol for their condition. Autologous Ad-SVF containing adult stem cells are infused via implant into the corpus cavernosum.

D. Procedure for Implant into Corpus Cavernosum: Patient should take 50 mg of sildenafil (Viagra), immediately before surgeon begins mini-lipoaspiration. Evaluation of vascular function of the penis is performed the morning of the procedure, by Doppler ultrasound. The corpus cavernosum is infiltrated with 8 cc of 1% Lidocaine, allowing 10 minutes for expansion. 5 cc of SVF / stem cell concentrate is injected using a 1", 27 G needle into the innermost part of the penis and each side of the corpus cavernosum.

#### 4. Recommended Post-Operation / Stem Cell Therapy Schedule:

##### A. Post-Op Medical Instruction - (Please follow these instructions closely!)

- **Post-op medication** will be given to you the day of your surgery. They will consist of an antibiotic and a painkiller:
  - **Antibiotic:** Cephalexin/Cipro, please take as directed beginning the day after surgery
  - **Painkiller:** Please take as directed and only as needed for pain
    - \* If you are unable to take any of these medications, please contact your patient coordinator so we can arrange for other medications.
- **Resume previous medication** as directed by the physician
- **Report any symptoms of feeling unwell:** fever, pain, etc. Patients should be seen promptly by an ophthalmologist for full evaluation should any of the above symptoms be encountered.
- It is recommended that the **patient have a companion stay with him or her** for at least 24 hours after discharge.
- You should **expect some of blood-tinged anesthetic solution to drain from the incision sites** during the first 24 to 48 hours. This will vary from patient to patient. Maxi-pads are recommended for bandages over your incision sites. You may take a shower 24 hours after the procedure.
- **Compressive garments should be worn** 24 hours a day for the first week and 12 hours a day for the second week.
- **Do not shower for the first 24 hours. Do not submerge yourself in any water** (i.e. taking a bath or swimming) for the 1<sup>st</sup> week.
- **If you experience nausea or vomiting it is probably due to the medication.** Please try to take it with food. If it persists, please contact our office.
- **Diet-meals are not restricted.**
- **Drink plenty of clear fluids.** We recommend 8 glasses of water or fruit juice every day.
- **Do not drink any alcohol** for 48 hours and limit alcohol intake for the first week.

B. Post-Op Medical Consultation Schedule: 1 month, 3 months, 6 month & 2 years

- ***Pre-Ad-SVF implant:***
  - Patient follow-up with his urologist
  - Review of medical history
  - Review of medication history
  - Review of any adverse events since the previous visit
  - Clinical evaluation of symptoms - use of International Index of Erectile Function questionnaire (IIEF)
- ***3 months after Ad-SVF implant:***
  - Patient follow-up with his urologist
  - Review of medical history
  - Review of medication history
  - Review of any adverse events since the previous visit
  - Clinical evaluation of symptoms - use of International Index of Erectile Function questionnaire (IIEF)
- ***6 months after Ad-SVF implant:***
  - Patient follow-up with his urologist
  - Review of medical history
  - Review of medication history
  - Review of any adverse events since the previous visit
  - Clinical evaluation of symptoms - use of International Index of Erectile Function questionnaire (IIEF)

*Your doctor will contact you by phone within the first week to follow up then future follow up visits will be arranged through your patient coordinator. If you need assistance before do not hesitate to contact us.*

# ERECTILE DYSFUNCTION – IIEF-5 Questionnaire

## The International Index of Erectile Function (IIEF-5) Questionnaire

From Macmillan Publishers Ltd: Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999 Dec;11(6):319-26. © 1999

<b>Over the past 6 months:</b>					
1. How do you rate your <b>confidence</b> that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, <b>how often</b> were your erections hard enough for penetration?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5
3. During sexual intercourse, <b>how often</b> were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5
4. During sexual intercourse, <b>how difficult</b> was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5. When you attempted sexual intercourse, <b>how often</b> was it satisfactory for you?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5

### IIEF-5 scoring:

The IIEF-5 score is the sum of the ordinal responses to the 5 items.

22-25: No erectile dysfunction

17-21: Mild erectile dysfunction

12-16: Mild to moderate erectile dysfunction

8-11: Moderate erectile dysfunction

5-7: Severe erectile dysfunction

# **ERECTILE DYSFUNCTION – Supporting Studies**

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Stem Cells Dev. 2012 Feb 10;21(3):343-51. doi: 10.1089/scd.2011.0303. Epub 2011 Sep 7.

## **Stem cell therapy for erectile dysfunction: a critical review.**

Lin CS, Xin ZC, Wang Z, Deng C, Huang YC, Lin G, Lue TF.

### **Source**

Department of Urology, School of Medicine, University of California, San Francisco, California 94143-0738, USA. clin@urology.ucsf.edu

### **Abstract**

Erectile dysfunction (ED) is a prevailing health problem that seriously impacts quality of life. Current treatment options are less effective for patients having cavernous nerve (CN) injury or diabetes mellitus-related ED. These 2 types of ED are thus the main focus of past and current stem cell (SC) therapy studies. In a total of 16 studies so far, rats were exclusively used as disease models and SCs were mostly derived from bone marrow, adipose tissue, or skeletal muscle. For tracking, SCs were labeled with LacZ, green fluorescent protein, 4',6-diamidino-2-phenylindole, DiI, bromodeoxyuridine, or 5-ethynyl-2-deoxyuridine, some of which might have led to data misinterpretation. SC transplantation was done exclusively by intracavernous (IC) injection, which has been recently shown to have systemic effects. Functional assessment was done exclusively by measuring increases of IC pressure during electrostimulation of CN. Histological assessment usually focused on endothelial, smooth muscle, and CN contents in the penis. In general, favorable outcomes have been obtained in all trials so far, although whether SCs had differentiated into specific cell lineages remains controversial. Recent studies have shown that intracavernously injected SCs rapidly escaped the penis and homed into bone marrow. This could perhaps explain why intracavernously injected SCs had systemic antidiabetic effects and prolonged anti-ED effects. These hypotheses and the differentiation-versus-paracrine debate require further investigation.

PMID: 21793654 [PubMed - indexed for MEDLINE] PMCID: PMC3272247

# ERECTILE DYSFUNCTION – Supporting Studies

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PLoS One. 2013 Aug 30;8(8):e72790. doi: 10.1371/journal.pone.0072790.

## **Correction of diabetic erectile dysfunction with adipose derived stem cells modified with the vascular endothelial growth factor gene in a rodent diabetic model.**

Liu G, Sun X, Bian J, Wu R, Guan X, Ouyang B, Huang Y, Xiao H, Luo D, Atala A, Zhang Y, Deng C.

### **Source**

Department of Urology, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, People's Republic of China ; Wake Forest Institute of Regenerative Medicine, Wake Forest University, Winston Salem, North Carolina, United States of America.

### **Abstract**

The aim of this study was to determine whether adipose derived stem cells (ADSCs) expressing vascular endothelial growth factor (VEGF) gene can improve endothelial function, recover the impaired VEGF signaling pathway and enhance smooth muscle contents in a rat diabetic erectile dysfunction (DED) model. DED rats were induced via intraperitoneal injection of streptozotocin (40 mg/kg), and then screened by apomorphine (100 µg/kg). Five groups were used (n=12/group)-Group 1 (G1): intracavernous injection of lentivirus-VEGF; G2: ADSCs injection; G3: VEGF-expressing ADSCs injection; G4: Phosphate buffered saline injection; G1-G4 were DED rats; G5: normal rats. The mean arterial pressure (MAP) and intracavernosal pressure (ICP) were measured at days 7 and 28 after the injections. The components of the VEGF system, endothelial, smooth muscle, pericytes markers in cavernosal tissue were assessed. On day 28 after injection, the group with intracavernosum injection of ADSCs expressing VEGF displayed more efficiently and significantly raised ICP and ICP/MAP ( $p<0.01$ ) than those with ADSCs or lentivirus-VEGF injection. Western blot and immunofluorescent analysis demonstrated that improved erectile function by ADSCs-VEGF was associated with increased expression of endothelial markers (VEGF, VEGF R1, VEGF R2, eNOS, CD31 and vWF), smooth muscle markers ( $\alpha$ -actin and smoothelin), and pericyte markers (CD146 and NG2). ADSCs expressing VEGF produced a therapeutic effect and restored erectile function in diabetic rats by enhancing VEGF-stimulated endothelial function and increasing the contents of smooth muscle and pericytes.

PMID: 24023647 [PubMed - in process] PMCID: PMC3758339

# **ERECTILE DYSFUNCTION – Supporting Studies**

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Asian J Androl. 2012 Jan;14(1):145-55. doi: 10.1038/aja.2011.79. Epub 2011 Oct 17.

## **Stem cells: novel players in the treatment of erectile dysfunction.**

Zhang H, Albersen M, Jin X, Lin G.

### **Source**

Minimally Invasive Urology Center, Provincial Hospital Affiliated to Shandong University, Jinan, China.

### **Abstract**

Stem cells are defined by their capacity for both self-renewal and directed differentiation; thus, they represent great promise for regenerative medicine. Historically, stem cells have been categorized as either embryonic stem cells (ESCs) or adult stem cells (ASCs). It was previously believed that only ESCs hold the ability to differentiate into any cell type, whereas ASCs have the capacity to give rise only to cells of a given germ layer. More recently, however, numerous studies demonstrated the ability of ASCs to differentiate into cell types beyond their tissue origin. The aim of this review was to summarize contemporary evidence regarding stem cell availability, differentiation, and more specifically, the potential of these cells in the diagnosis and treatment of erectile dysfunction (ED) in both animal models and human research. We performed a search on PubMed for articles related to definition, localisation and circulation of stem cells as well as the application of stem cells in both diagnosis and treatment of ED. Strong evidence supports the concept that stem cell therapy is potentially the next therapeutic approach for ED. To date, a large spectrum of stem cells, including bone marrow mesenchymal stem cells, adipose tissue-derived stem cells and muscle-derived stem cells, have been investigated for neural, vascular, endothelial or smooth muscle regeneration in animal models for ED. In addition, several subtypes of ASCs are localized in the penis, and circulating endogenous stem cells can be employed to predict the outcome of ED and ED-related cardiovascular diseases.

PMID: 22002437 [PubMed - indexed for MEDLINE] PMCID: PMC3735142

# **ERECTILE DYSFUNCTION – Supporting Studies**

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J Sex Med. 2009 Mar;6 Suppl 3:320-7. doi: 10.1111/j.1743-6109.2008.01190.x.

## **Potential of adipose-derived stem cells for treatment of erectile dysfunction.**

Lin G, Banie L, Ning H, Bella AJ, Lin CS, Lue TF.

### **Source**

School of Medicine, Department of Urology, University of California-Knuppe Molecular Urology Laboratory, San Francisco, CA 94143-0738, USA. glin@urology.ucsf.edu

### **Abstract**

#### INTRODUCTION:

Adipose-derived stem cells (ADSCs) are a somatic stem cell population contained in fat tissue that possess the ability for self-renewal, differentiation into one or more phenotypes, and functional regeneration of damaged tissue, which may benefit the recovery of erectile function by using a stem cell-based therapy.

#### AIM:

To review available evidence concerning ADSCs availability, differentiation into functional cells, and the potential of these cells for the treatment of erectile dysfunction (ED).

#### METHODS:

We examined the current data (from 1964 to 2008) associated with the definition, characterization, differentiation, and application of ADSCs, as well as other kinds of stem cells for the cell-based therapies of ED.

#### MAIN OUTCOME MEASURES:

There is strong evidence supporting the concept that ADSCs may be a potential stem cell therapy source in treating ED.

#### RESULTS:

The ADSCs are paravascularly localized in the adipose tissue. Under specific induction medium conditions, these cells differentiated into neuron-like cells, smooth muscle cells, and endothelium in vitro. The insulin-like growth factor/insulin-like growth factor receptor (IGF/IGFR) pathway participates in neuronal differentiation while the fibroblast growth factor 2 (FGF2) pathway is involved in endothelium differentiation. In a preliminary in vivo experiment, the ADSCs functionally recovered the damaged erectile function. However, the underlying mechanism needs to be further examined.

#### CONCLUSION:

The ADSCs are a potential source for stem cell-based therapies, which imply the possibility of an effective clinical therapy for ED in the near future.

PMID: 19267855 [PubMed - indexed for MEDLINE] PMID: PMC2895916

The treatments described in this manual are considered experimental and have not been evaluated or approved by the FDA.

# ERECTILE DYSFUNCTION – Supporting Studies

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J Sex Med. 2012 Jul;9(7):1834-41. doi: 10.1111/j.1743-6109.2012.02753.x. Epub 2012 Apr 30.

## **Effects of intravenous injection of adipose-derived stem cells in a rat model of radiation therapy-induced erectile dysfunction.**

Qiu X, Villalta J, Ferretti L, Fandel TM, Albersen M, Lin G, Dai Y, Lue TF, Lin CS.  
Source

Knuppe Molecular Urology Laboratory, Department of Urology, School of Medicine, University of California, San Francisco, CA 94143-0738, USA.

### **Abstract**

#### INTRODUCTION:

Radiation therapy (RT) for prostate cancer is frequently associated with posttreatment erectile dysfunction (ED).

#### AIM:

To investigate whether injection of adipose-derived stem cells (ADSCs) can ameliorate RT-associated ED.

#### METHODS:

Thirty male rats were divided into three groups. The control + phosphate-buffered saline (PBS) group received tail-vein injection of PBS. The radiation + PBS group received radiation over the prostate and tail-vein injection of PBS. The radiation + ADSC group received radiation over the prostate and tail-vein injection of ADSCs, which were labeled with 5-ethynyl-2-deoxyuridine (EdU). Seventeen weeks later, erectile function was evaluated by intracavernous pressure (ICP) in response to electrostimulation of cavernous nerves (CNs). Penile tissue and major pelvic ganglia (MPG) were examined by immunofluorescence (IF) and EdU staining.

#### MAIN OUTCOME MEASURES:

Erectile function was measured by ICP. Protein expression was examined by IF, followed by image analysis and quantification.

#### RESULTS:

Radiation over the prostate caused a significant decrease in erectile function and in the expression of neuronal nitric oxide synthase (nNOS) in penis and MPG. Cavernous smooth muscle (CSM) but not endothelial content was also reduced. Injection of ADSCs significantly restored erectile function, nNOS expression, and CSM content in the irradiated rats. EdU-positive cells were visible in MPG.

#### CONCLUSIONS:

Radiation appears to cause ED via CN injury. ADSC injection can restore erectile function via CN regeneration.

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The treatments described in this manual are considered experimental and have not been evaluated or approved by the FDA.

# **ERECTILE DYSFUNCTION – Supporting Studies**

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Nat Rev Urol. 2012 Jun 19. doi: 10.1038/nrurol.2012.111. [Epub ahead of print]

## **Stem cell therapy for voiding and erectile dysfunction.**

Vaegler M, Lenis AT, Daum L, Amend B, Stenzl A, Damaser MS, Sievert KD.

### **Source**

Department of Urology, University of Tuebingen, Hoppe-Seyler-Strasse 3, D72076 Tuebingen, Germany.

### **Abstract**

Voiding dysfunction comprises a variety of disorders, including stress urinary incontinence and overactive bladder, and affects millions of men and women worldwide. Erectile dysfunction (ED) also decreases quality of life for millions of men, as well as for their partners. Advanced age and diabetes are common comorbidities that can exacerbate and negatively impact upon the development of these disorders. Therapies that target the pathophysiology of these conditions to halt progression are not currently available. However, stem cell therapy could fill this therapeutic void. Stem cells can reduce inflammation, prevent fibrosis, promote angiogenesis, recruit endogenous progenitor cells, and differentiate to replace damaged cells. Adult multipotent stem cell therapy, in particular, has shown promise in case reports and preclinical animal studies. Stem cells also have a role in urological tissue engineering for ex vivo construction of bladder wall and urethral tissue (using a patient's own cells) prior to transplantation. More recent studies have focused on bioactive factor secretion and homing of stem cells. In the future, clinicians are likely to utilize allogeneic stem cell sources, intravenous systemic delivery, and ex vivo cell enhancement to treat voiding dysfunction and ED.

PMID: 22710667 [PubMed - as supplied by publisher] PMCID: PMC3769422

## ERECTILE DYSFUNCTION – References

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- [1] Causes of Diabetes. *National Diabetes Information Clearinghouse*. 2013. Web. 12/11/13
- [2] Davidson, J. *Clinical Diabetes Mellitus: A Problem-Oriented Approach*. Thieme medical Publishers, Inc: New York, 2000.
- [3] Chen, L. Jiang, X. Yang, L. “Differentiation of rat marrow mesenchymal stem cells into pancreatic islet beta-cells.” *World J Gas-troenterol* 2004; 10 (20): 3016-1020.
- [4] Fiorina, P. Jurewicz, M. Augello, A. Vergani, A. “Immunomodulatory Function of Bone Marrow-Derived Mesenchymal Stem Cells in Experimental Autoimmune Type 1 Diabetes.” *The Journal of Immunology*. 189 (2), 2009, 993-1004.
- [5] [www.clinicaltrials.gov](http://www.clinicaltrials.gov)