Take Home Messages: Basic Science

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BPH: Current Issues in Basic Science
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• A leading hypothesis:
  
  • Inflammation is involved in the etiology of BPH and promotes BPH progression
  
  • Inflammation can lead to the development and progression of BPH through a number of proposed mechanisms.
  
  • They include immunological and structural mechanisms or the observed link with metabolic syndrome.
Among 38 SNPs associated with CaP risk, several associated with aspects of a well-characterized LUTS phenotype.

Confirmed a prior association between 5p15 and BPH interventions (Icelandic men)

SNPs on chromosome Xp11, 9q33, 8q24 and 7q21 may predict severe LUTS

Can genetic tests predict which men are at greatest risk for severity of LUTS and bother?
Reconstruction
Objectives:
- To compare a novel molded collagen type I scaffold’s mechanical and biological properties with conventional biological-sourced materials decellularized human epicardium (DHE) and decellularized porcine small intestinal submucosa (SIS)

Materials and Methods:
- Stress and strain were measured for DHE, SIS, porous molded collagen (PMC) and cross-linked molded collagen (CMC).
- All four materials were implanted subcutaneously in rats and harvested 3d, 7d, 14d, and 28d and evaluated for persistence, gross appearance in situ, and cellular infiltration assessed by immunohistochemistry (IHC) and quantitative polymerase chain reaction (qPCR).
Study design

Impant Material Subcutaneously

Collect Tissues
- 3 day
- 7 day
- 14 day
- 28 day

Stress Strain Testing
Scanning Electron Microscopy

Cellular Infiltration/Inflammation
Profile Tissue Response

Sprague-Dawley

Tut SIS CPC CLC
PCR characterization of graft cellularization – 28 Days

- TGFb
- CD68
- ITGB2
- CD3e
- VEGF

Legend:
- Tut
- SIS
- CPC
- CLC
Histology
28-Days Post-Implantation
Transplantation
Penile Transplantation – The Science of Rejection and Erection
N. Sopka, T. Bivalacqua
The Johns Hopkins School of Medicine

Control
Autograft
Allograft
Allograft + Immunosuppression
EFS – Electrical Field Stimulation

A. EFS - Contraction

- Effect of Rejection: $P = 0.0095$
- Effect of Frequency: $P = 0.049$
- Interaction of Rejection and Frequency: $P = 0.8652$

B. EFS - Relaxation

- Effect of Rejection: $P = 0.0148$
- Effect of Frequency: $P = 0.0426$
- Interaction of Rejection and Frequency: $P = 0.9487$
**EFS** – Electrical Field Stimulation

### A: EFS Contraction

- **Graph**: Shows the effect of EFS on contraction/tissue weight across different frequencies for Allo and CsA groups.
- **Data**:
  - Effect of Rejection $P = 0.1460$
  - Effect of Frequency $P = 0.0134$
  - Interaction of Rejection and Frequency $P = 0.8890$

### B: EFS Relaxation

- **Graph**: Shows the effect of EFS on relaxation (% Max PE) across different frequencies for Allo and CsA groups.
- **Data**: 
  - Effect of Rejection $P = 0.0254$
  - Effect of Frequency $P = 0.0136$
  - Interaction of Rejection and Frequency $P = 0.4412$
C

EFS Contraction

Effect of Treatment $P = 0.3841$
Effect of Frequency $P < 0.0001$
Interaction of Treatment and Frequency $P = 0.7805$

D

EFS Relaxation

Effect of Treatment $P = 0.0053$
Effect of Frequency $P = 0.3186$
Interaction of Treatment and Frequency $P = 0.9525$
Erectile dysfunction
• **Objectives:**
  – Angiotensin-II is a known mediator of smooth muscle vasoconstriction and fibrosis after bilateral cavernosal nerve injury (CNI). Sacubitril-valsartan is a new oral drug combination for the treatment of symptomatic chronic heart failure in adults with reduced ejection fraction.
  – To compare the combined effects of sacubitril/valsartan and valsartan/ sildenafil on bilateral CNI-induced functional changes in rat cavernosal tissue.

• **Materials and Methods:**
  – Bilateral CNI were produced in anesthetized male rats and cavernosal tissue was removed 2 weeks after CNI.
  – Organ-bath relaxant responses were performed on CC strips.
  – After phenylephrine-induced contraction (Phe, 10 µM), dose-response curves were evaluated.
  – Electrical field stimulation of the cavernosal autonomic nerves was accomplished by the use of platinum electrodes positioned on the either side of the tissue strip in the absence and presence of these drugs.
069. NO-independent and Purinergic-dependent NANC-mediated Relaxation in the Proximal vs Distal Internal Pudendal Artery
Odom, MR
East Carolina University, USA

• **Objective:**
  – Morphological and signaling pathway differences exist between proximal and distal rat IPA resulting in disproportionate regulation of vascular tone.
  – To identify and characterize mechanisms responsible for regulation of vascular tone in the proximal and distal rat IPA

• **Materials and methods:**
  – Evaluate endothelial and smooth muscle function with concentration response curves to phenylephrine, acetylcholine, and nitric oxide (NO) donor
  – Stimulate neurotransmitter release using electric field stimulation (EFS)
  – Assess non-adrenergic, non-cholinergic (NANC) pathways during EFS
Distal IPA has greater vascular resistance than the proximal IPA
Increased EFS mediated contraction and NANC relaxation in distal IPA
Purinergic inhibition improves NANC relaxation in distal IPA
Conclusions

• Distal IPA vasodilation is dependent on NO, but proximal IPA vasodilation is unaffected by NO inhibition
• Greater EFS-mediated adrenergic contraction and NANC relaxation in distal IPA
• IPA is responsive to purinergic stimulus
• Purinergic inhibition improves EFS mediated NANC relaxation in distal IPA

*Identification of novel signaling pathways in the IPA may lead to novel therapeutic targets to treat ED by increasing blood flow to the penis*
• **Objective:**
  - Sonic hedgehog (SHH) protein delivered by nanoparticle based peptide amphiphile (PA) hydrogels to the penis suppress apoptosis in a rat cavernous nerve (CN) resection model.
  - To examine the hypothesis that SHH PA will suppress morphology changes in the penis in a CN crush model that more readily reflects injury observed in prostatectomy patients

• **Materials & Methods:**
  - Bilateral CN crush was performed on Sprague Dawley rats (n=48) and SHH or mouse serum albumin (MSA, control) protein was delivered by PA injected into the corpora cavernosa. Rats were sacrificed after 4 and 9 days. 2X SHH protein was also assayed at 4 days and a second SHH PA injection at 5 days occurred prior to sacrifice at 9 days. TUNEL and hydroxyproline assay were performed.
Deliver SHH protein to the penis and CN at time of surgery

27% decrease in apoptotic index (p=0.0001)
Deliver SHH protein to the penis and CN at time of surgery