

#### Regenerative Medicine From the Lab to the Clinic; How Close are we? Workshop 25 Tuesday, August 24 2010, 09:00 – 10:30

Time	Time	Торіс	Speaker
09:00	09:30	Tissue Engineering and Regenerative Medicine	George Christ
09:30	10:00	Urinary Incontinence: PreClinical Studies for	James Yoo
		Translation	
10:00	10:30	Role of Strategic Regulatory and Program	Kevin B. Johnson
		Management in Setting Up Regenerative Program	
10:30		Conclude	

#### Aims of course/workshop

To bring an understanding to the audience about what regenerative medicine is; where the lab and clinical fields of stem cell world come together and how to navigate the regulatory and organizational challenges.

#### **Educational Objectives**

Participants will be able to have a basic understanding of regenerative medicine and its application in current urology

...... Will have an understanding of cell growth and how cell therapy may help restore function to urologic conditions

...... Will identify and recognize obstacles and paths to successful implementation of a regenerative program







WAKE FOREST		Cell Types Grown
Trach Kidne Esop Bladd Sm/S Cartil Ureth Vess Saliv	nea Agus Aagus der k Muscle lage ara els ary glands	Bone Breast Lung Retina Uterus Heart Nerve Liver Pancreas
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Multidisciplinary studies of bladder regeneration *in vivo* 

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WARE FOREST

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	Avera	ge cystom	etric par	ameter esti	mates	
	Bcap (mL)	MV (mL)	RV (mL)	BP (cm H <sub>2</sub> O)	TP (cm H <sub>2</sub> O)	MP (cm H <sub>2</sub> O)
Controls n=16	0.96 ± .05	0.90 ± .05	0.05 ± .01	$12.92 \pm 0.89$	28.1 ± 1.7	49.2 ± 3.7
2 weeks n=10	0.46 ± .02 *	0.42 ± .03*	0.05 ± .02	11.17 ± 2.48	22.36 ± 3.7	30.5 ± 5.9*
4 weeks n=9	$0.72 \pm .05*$	0.67 ± 0.1*	0.06 ± .03	$14.01 \pm 2.64$	27.1 ± 3.28	38.2 ± 5.0
8 weeks n=8	0.82 ± .09	$0.69 \pm .1^{*}$	0.10 ± .04	$10.61 \pm 1.27$	26.74 ± 2.5	37.3 ± 3.3



















WAKE FOREST			r	Smooth muscle IH								НС	
	<u>1 WEEK</u>		<u>K 2 WEEKS</u>		<u>4 WEEKS</u>		<u>8 WEEKS</u>						
BASE/ DOME	A	В	С	A	В	С	A	В	С	A	В	С	
SMA	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	
DES	+/+	+/-	+/-	+/+	+/+	+/-	+/+	+/+	+/+	+/+	+/+	+/+	
мнс	-/-	-/-	-/-	-/-	+/-	+/-	-/-	+/-	+/+	+/+	+/+	+/+	
										Ins	stitute for	Regenera	tive N





















Aged animals show normalization by the 4 week time point

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Regenerative Medicine: Lab to the Clinic How Close are we?

Urinary Incontinence: Preclinical Studies for Translation

#### James J. Yoo

Wake Forest Institute for Regenerative Medicine and Department of Urology Wake Forest University Health Sciences Winston-Salem, NC, USA Wake Forest Institute for REGENERATIVE MEDICINE



#### Urinary Incontinence

- Bladder Pressure >> Sphincter Pressure
- Sphincter Insufficiency: Myofiber loss, Dennervation, Hormonal Changes
- Treatment Options: Surgery: Sling operations Injection Therapy: Bulking agents

>No current treatment is able to functionally restore the damaged sphincter muscle !

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#### **Objectives**

- To determine whether regenerative medicine approaches could provide a solution for urinary incontinence
- To determine whether muscle cell therapy could restore damaged sphincter function in preclinical models
- The achieve a refined muscle cell therapy system that would facilitate a rapid clinical translation



#### **Muscle Precursor Cells (MPC)**

- Pool of satellite cells (SC): Heterogeneous
  Cultured cells that express muscle specific markers
  - Ability to form new myotubes
  - Long term survival
  - Formation of new motor units
  - Growth arrest after maturation into myofibers

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Autologous muscle precursor cells are able to restore otherwise irreversibly damaged sphincter function in preclinical models

The injected cells are able to survive and form mature tissue within the damaged sphincter region

The refined culture system for human muscle cells may facilitate a rapid clinical translation

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SCHOOL of MEDICINE

### **Institute for Regenerative Medicine**

Role of Strategic Regulatory and Program Management in the Clinical Translation of Regenerative Medicine Technologies

> Kevin B. Johnson, PhD MBA Director of Regulatory Affairs



# Improve patients lives by developing regenerative medicine therapies and support technologies



### **Multi-Disciplinary and Cross-Functional Core Programs**





# **Support Infrastructure**





### Academic / Research mindset

- Smaller scale
- Exploratory and mechanism-focused science
- Incremental, sequential, 'just fast enough'
- Science for science sake; 'pure'
- Regulatory requirements less of a focus (if at all)
- Goal: publish and get grants

### Development / Translational mindset

- Product consistency, scaled manufacturing
- Focused, pragmatic and streamlined science
- Equipment, reagent, other choices critical
- Regulatory requirements critical
- Goal: Reproducibly manufacture solutions for patients



# **Project Development Teams**





- "Begin with the end in mind"
- Regulatory not just rules and regulations; helps build the body of evidence
- Building the case, the messages, the story for FDA
- Clinical safety and efficacy endpoints mirrored by preclinical studies/results



- Documentation, documentation, documentation...
- Regulatory environment and precedents change over time
- Early regulatory consultation and integration within project team is key to successful development
- Saves time, effort and \$\$



#### FDA Interactions for Regenerative Medicine Development Projects





### Portfolio Management

- Target Product Profile (TPP)
- Stage-gate decision process (Go/No Go)
- Timeline and budget management
- Program and Project Risk Assessment
- Financial analysis (not yet...)

### Program / Project Management

- Microsoft Project
- Development Team meetings

### Educational programs

- Regulatory Compliance and Submissions
- Intellectual Property
- Commercialization
- Fundraising and Business Development