Welcome to the Duke CTSA Virtual Town Hall

You are muted upon entry into WebEx. Use Chat Function to ask questions or add comments. Click on the microphone by your name to mute or unmute your phone. (You are muted on entry.) Click here to see Participants and Chat Function.
Your host:
Ebony Boulware, MD, MPH
Contact PI, Duke CTSA

Reminder: This WebEx conversation is being recorded. It will be posted on the CTSA website for future reference.
Duke CTSA Virtual Town Hall

A quarterly WebEx conversation with the opportunity to...

• Learn about what the CTSA offers
• Meet the people who are providing services and resources
• Learn how to access these resources
• Ask questions of CTSA leadership
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Duke CTSA – Supporting Translational Medicine

• The CTSA is the NIH’s largest single investment in biomedical research. Over 60 CTSA programs now exist in the U.S.

• Goal: to develop and implement national standards and best practices for
  • accelerating the process of translating laboratory discoveries into treatments
  • training a new generation of clinical and translational researchers, and
  • engaging communities in clinical research efforts.

• In October 2013, the NIH renewed Duke’s CTSA grant, committing to $47 million over five years.
Where We Are on the CTSA Timetable

CTSA 1.0

Bridge Funding

CTSA 2.0

Competing Renewal Due May 2017
Today's Focus

Programs/Areas Supported by the Duke CTSA
Follow the Funding

CTSA Funding Distribution

- Biostatistics, 3%
- Clinical Trials and Outcomes, 2%
- Community Engagement, 3%
- DOCR, 8%
- Translation Acceleration, 18%
- Research Resources, 13%
- Oversight and Management, 9%
- Education, 20%
- Biomedical Informatics, 25%

Funding for Regulatory Affairs included in this category.
Next on the Agenda

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Initially funded by Clinical Translational Science Award (CTSA)

The Regulatory Affairs Group offers regulatory advice to investigators in all aspects of research from preclinical requirements to first-in-human studies and beyond

Free of charge
Scope of Work

- Regulatory Guidance and Support
  - Regulatory Consultation
  - Preclinical Testing and GMP Manufacturing
  - Regulatory Submissions and Maintenance

- Regulatory Education
  - Regulatory Training Programs
  - Regulatory Publications
During 2015, RA group provided regulatory guidance and support to over 200 PIs

- Regulatory consultation with the PIs
- Facilitating meetings with the FDA
- Review of all PI initiated protocols prior to the IRB review (over 500 new and over 400 renewals)

Providing support and guidance on current Good Manufacturing Practices (cGMP) and Quality System Regulations (QSR)

- On-campus - CT2, DHVI, and the MSRB1 manufacturing suites
- Off-campus - BARDA funded projects, Stanford, UNC
Support in preparation and submission of over 600 various regulatory documents

- Initial INDs - 90
- Pre-IND Meetings - 19
- Original IDEs - 8
- Pre-Submissions - 11
- Initial ITPs - 3
- BLA Submissions - 86
- All other FDA submissions – 383

Capability of electronic submissions

- 36 electronic submissions during the last year with more coming in the near future
Collaboration with other CTSA and Non-CTSA Institutions

Providing regulatory support outside of Duke University

- Duke-NUS
- University of North Carolina
- Stanford University
- Boston University
- Harvard School of Medicine
- Texas Children's Hospital
- University of Arizona
- Wake Forest University
- Miami School of Medicine
- University of Southwestern
Regulatory Training Programs

- 313 participants attended General Regulatory Affairs Training
- 64 participants attended Medical Device Regulatory Affairs Training
Supporting the development of regulatory training at John Hopkins, Duke-NUS and University of Arizona

Developed 14 GMP Training Modules

3 hours long IND/IDE Workshops

(Duke, UNC, Boston University)

Chairing national IND/IDE Workgroup of over 70 participants across CTSA institutions

In collaboration with the University of Michigan, developed training modules on the FDA electronic submission requirements

Published 7 papers
Development of CN-105, a first-in class neuroprotectant

Daniel Laskowitz, MD, MHS
Duke University Medical Center
Slow progress in neurological therapeutic development

Successes:
- Acute Stroke Treatment
- Disease Modifying therapies for MS
- Mechanical/Endovascular Devices

Slow, incremental benefit in
- Neurodegenerative disorders
- Extrapyramidal disorders
- Seizure disorders
Unmet needs in acute brain injury
Establishing translational lab

Animal Modeling of:
- Traumatic Brain Injury
- Subarachnoid Hemorrhage
- Middle Cerebral Artery Occlusion
- Intracranial Hemorrhage

Principles:
- Recapitulate clinical disease
- Clinically relevant histology
- Focus on short and long term functional endpoints
- Advance understanding of basic biology
- Emphasis on novel therapeutic approaches
Fostering Translational Neuroscience: Role of Academic Departments

- Unmet clinical need
- Disease pathophysiology and treatment
- Mechanistic Studies
- Proof of Principle Clinical Studies
- Phase I
- Regulatory process
- Animal modeling
From gene to Drug:

Development of apoE based therapy for acute brain injury
APOE4 Increases Age-Specific Prevalence of Alzheimer’s Disease.
Linearized apoE peptides are neuroprotective

Linearized peptides model the helical face involved in receptor binding interactions
Summary of apoE peptide

**In Vitro:**
Blocks microglial activation: in BV2 cells, human microglial cell line, primary culture
Blocks NMDA excitotoxicity

**In Vivo:**
- TBI (Laskowitz et al., *J Neurotrauma*, 2007)
- Stroke/MCAO (Wang et al., *Exp Neurol*, 2013)
- Intracranial hemorrhage (James et al., *Stroke*, 2009)
- Subarachnoid hemorrhage (Gao et al., *Neurocrit Care*, 2006)
- Multiple sclerosis (Li et al., *JPET*, 2010)
Development of CN-105

- Pre-IND meeting (11/13)
- Granted Orphan Drug status by FDA (1/15)
- IND clinical hold lifted 10/15
- IND approved (11/15)
- Phase 1 study initiated in (12/15) at DCRU
- Initial therapeutic outlet in ICH
Thank You
Received **PhD and MS** in Molecular Biology in December of 2007 and July of 2004, respectively

My dissertation research focused on signaling pathways in cancer, particularly the growth factor receptor-bound protein-7 (GRB7) signaling pathway
First postdoctoral fellowship at the University of North Carolina at Chapel Hill (UNC)

Breast cancer translational research

Discovery of molecular mechanisms of novel tumor endothelial markers, a discovery which is now showing promising results for breast cancer therapy
Duke postdoc projects

- Second postdoctoral fellowship at Duke
- NIH/NCI R25 postdoctoral training fellowship
- Research Project #1: Imaging and Molecular Profiling in LABC and IBC
  
  The overall objective: to identify biomarkers that can be used to improve the standard of care in LABC/IBC patients

- Research Project #2: Differential expression of angiogenic genes in invasive high grade serous ovarian carcinomas
  
  The overall objective: to establish quantifiable and reproducible biomarkers that can aid in prognosis, predict treatment outcome, and serve as therapeutic targets in ovarian cancer.
Current position at Duke

Research Scientist, responsible for:

- Managing and supervising two of the DCI’s research labs’ translational research projects.
- Developing of new projects and protocols (including IRB protocols)
- Writing grant proposals (e.g. NCI, DoD)
- Communicating the results to the supervisors
- Providing directions to lab members

- Attended two of the Regulatory Affair internship trainings at Duke University’s DTMI
The DTMI Regulatory Affairs Internship

- According to the DTMI website, the RA internship program is designed for “anyone who either wishes to explore this as a potential career or to broaden their knowledge base.”

- Online training vs. classroom training
  - Jelena Petrovic Berglund, PhD, RAC
    Director of Regulatory Affairs, Head of Regulatory Training
The DTMI Regulatory Affairs Internship

- I have taken the:
  - The General Regulatory Affairs Training Program
    Investigational New Drug Application (IND)
  - The Medical Device Regulatory Training Program
    Investigational device exemption (IDE)

Training on: the IND/IDE submissions, practiced completing INDs and IDEs, went over the FDA requirements for the submission and review process of INDs, IDEs, IND exemption requests, IND Amendments, study determination requests, pre-IND meeting briefing packets, etc.
The Critical Role of Regulatory and the QSU in Cellular Therapies and Transplantation

Joanne Kurtzberg, MD
Duke University Medical Center
January 12, 2016
Programs Supported

- CT2
  - CCBB
  - GMP cell manufacturing laboratory
- Adult and Pediatric PBMT Programs
- Stem Cell Transplant Laboratory
HSCT Programs – Historical Perspective

- ABMT, established 1980
- PBMT, established 1990
- Stem Cell Transplant Laboratory, established ~1995
- Full service, in and out patient programs
- Multiple research programs, INDs, clinical protocols
  - Industry sponsored studies
  - NIH sponsored studies
- Federally mandated outcomes reporting
  - Auditing
  - SAE, AE
  - Engraftment, Survival, GvHD, Relapse, TRM
- Requirement for FACT accreditation
Carolinas Cord Blood Bank - History

- Established 1997 through COBLT/NHLBI contract (IND)
- Current inventory~25,000 (Duke) + ~6,000 (CORD:USE)
- 10 collection sites with access to >55,000 births/year
- Staff, hybrid and kit collection models
- Units listed and distributed through NMDP
- ARC bank 1999-2001 (IND)
- NMDP Member bank 2004-present (IND)
- FACT accreditation 2005-present
- FDA Masterfile 3/2005-closed at licensure
- HRSA: NCBI Bank 2006-present (cohorts 1 and 5)
- Netcord Bank 2007-present
- CAP Accreditation/CLIA Certified 2010 - present
- BLA received October 4, 2012
Quality Management and Data Systems

- Quality Systems Unit
  - Reports to Regulatory Affairs in SOM
    - Bruce Burnett
    - Director Amanda Parrish
    - Staff of 10

- QSU
  - Overall
  - Collection sites
  - Processing Laboratory
  - STCL
  - ABMT/PBMT
  - Master Control
  - Support Functions
QSU – Support Functions

- Personnel/Training
- Facilities
- Environmental Monitoring
- Equipment Management
- Inventory Control/Supply Management
- Product Release
- Quality Investigations
- Internal Audits
- Inspection Support (FDA, FACT, CLIA, CAP, NIH, Industry Sponsors)
QSU – Support Functions, cont

- **Document Control**
  - Master Control
  - SOPs
  - Change Control
  - Event Management
    - Deviations
    - Adverse Events
    - Complaints
    - CAPAs
    - OOS
Pathway for the development of DUOC-01

- Hypothesis based on observations in the clinic
- GMP Manufacturing – optimization and validation
- IND - enabling, Preclinical studies
  - Safety - tumorigenicity
  - Mechanisms of action
  - Biodistribution (brain and CSF after IT injection)
- Release criteria for IT injection
- Stability in final formulation, release of product for administration
- Clinical protocol development
- IND submission, responses to clinical holds, maintenance
- IRB submission including review by the SCRO
- Study monitoring and data analysis
THE DEVELOPMENTAL PATHWAY FOR DUOC-01 2007-2015

OUTCOMES

Day 0 IV

Day 28 IT

Begin D7
• Thanks to Bruce and Amanda and their teams.

• We couldn’t survive or thrive without you!
• Reminder: To ask a question, please type it in the Chat Box in the right-hand panel. Send it to “Everyone”.

• If you are asked to speak, please unmute your phone (behind your name in the participant list)
Congratulations to our 3 newest KL2 Scholars:

- Kathryn Dickerson, PhD, from the Department of Psychiatry
- Michael Cary, PhD, from the School of Nursing
- Rasheeda Hall, MD, MBA, from the Department of Medicine

New Funding Opportunities


- **Duke-Coulter Award** – Up to $700,000 for several teams of co-investigators from Biomedical Engineering and the School of Medicine. Summary applications encouraged by Jan. 31, 2016. Final proposals due by March 9, 2016.

NEXT CTSA VIRTUAL TOWN HALL

APRIL 28, 2016
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