

# TRANSLATIONAL SCIENCE PROGRAMS: AN UPDATE

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# OVERVIEW

- ◉ Translational Science: Definition
- ◉ Highlights of Best Practice at Northwestern:
  - Dermatology Tissue Acquisition and Biorepository
    - ◉ *Acquire tissue and deliver to the SDRC*
  - Skin Disease Research Center (SDRC)
    - ◉ *Administrative Core*
    - ◉ *Skin Tissue Engineering Core*
    - ◉ *Phenotyping and Morphology Core*
    - ◉ *DNA/RNA Delivery Core*
  - Collaborative clinics
  - Northwestern University Clinical and Translational Science (NUCATS) Institute
    - ◉ *Finance and budgeting*

# TRANSLATIONAL MEDICINE OR SCIENCE

- ◉ An *interdisciplinary branch of the biomedical field supported by three pillars:*

- 1. *Benchside,*
- 2. *Bedside,*
- 3. *Community.*<sup>1</sup>

- ◉ “*Process of translating discoveries in the laboratory into clinical interventions for:*

- *diagnosis*
- *treatment*
- *prognosis*
- *or prevention of disease*

*with a direct benefit to human health*”<sup>2</sup>



<sup>1</sup>Cohrs. Et al. *New Horizons in Translational Medicine*. 2 (3): 86-88. 2015

<sup>2</sup>Minna et al. *Nature Med*. 2, 974-975. 1996

## “BENCH-TO-BEDSIDE”

- Harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients
- Ensuring that new treatments and research knowledge actually reach the patients or populations for whom they are intended and are implemented correctly
- End point: Production of a new drug

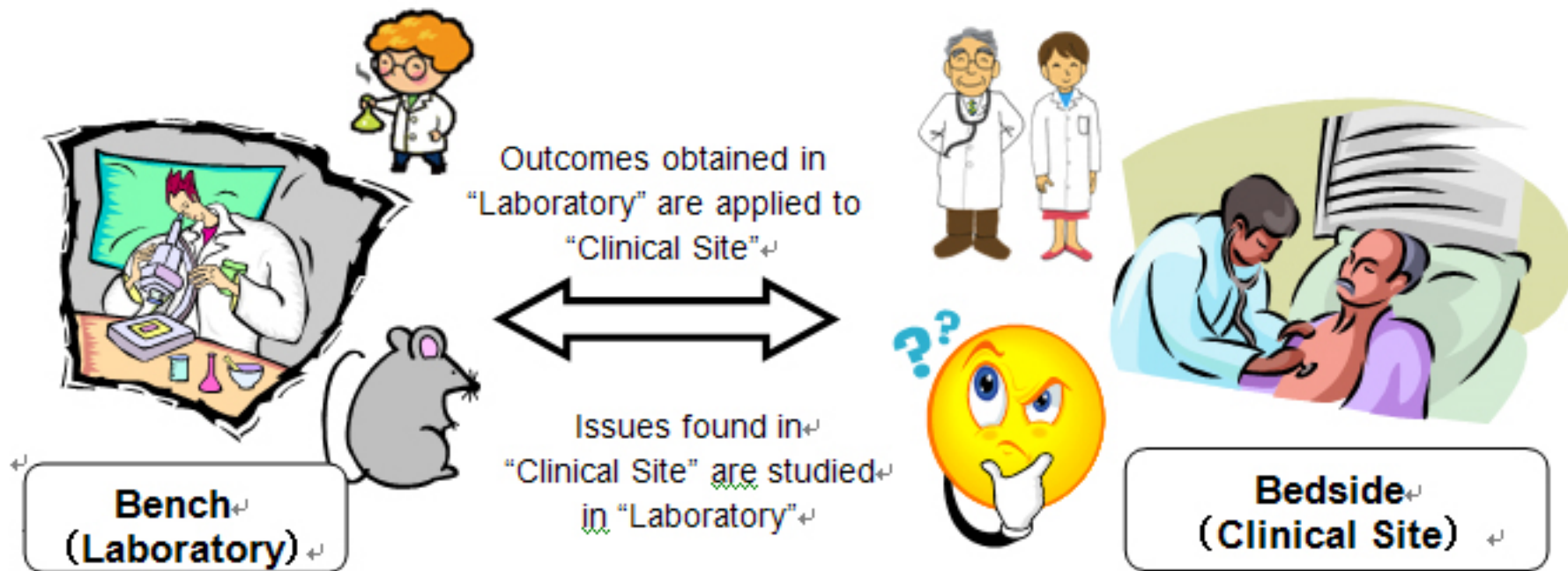
# TRANSLATIONAL SCIENCE

- ◉ Two-way traffic between basic research and the clinic
- ◉ According to Coleman and Harris, the “bridge must be crossed in both directions, bringing concepts from the laboratory into the clinic and taking observations from the clinic to the laboratory”<sup>1</sup>

<sup>1</sup>Coleman et al. Radiation Res. 1998;150:125-133.

# TRANSLATIONAL SCIENCE

## Translational Research





# TRANSLATIONAL RESEARCH CENTER

- ◉ The goal is to combine disciplines, resources, expertise, and techniques within these pillars to promote enhancements in prevention, diagnosis, and therapies.
- ◉ Highly interdisciplinary and collaborative field, the primary goal of which is to coalesce assets of various natures within the individual pillars in order to improve the global healthcare system significantly

# WHAT MAKES NORTHWESTERN RESEARCH SUCCESSFUL:

## \*\*BEST PRACTICES AT OUR UNIVERSITY\*\*

Resources available to support Dermatology &  
Non-Dermatology Investigators at Northwestern

### 1. Dermatology Tissue Acquisition and Biorepository

- *Principal Investigator: Dennis P. West, PhD*

### 2. Skin Disease Research Center

### 3. Northwestern University Clinical and Translational Science Institute (NUCATS)



# DERMATOLOGY TISSUE ACQUISITION AND BIOREPOSITORY

- ◉ What is it?
- ◉ A repository or storage of in vitro cell cultures from patient skin samples
- ◉ Dennis P. West, PhD (PI)
- ◉ The biorepository is available for any Northwestern University investigator who requests either fresh or archived tissue for his/her research (Dermatology or other Departments)
- ◉ >100,000 tissue samples in the archived repository

# BIOREPOSITORY

- ◉ Genetics data and health information is de-identified and stored in the biorepository
- ◉ De-identified data/samples are available for any research question:
  - What causes certain diseases
  - How to develop new scientific methods

# DERMATOLOGY TISSUE ACQUISITION AND BIOREPOSITORY

## Principal Investigator:

- **Dennis P. West, PhD**
- Vincent W. Foglia Family Research Professor of Dermatology
- Professor of Department of Dermatology and Department of Pediatrics
- Director of Dermatopharmacology Program
- Director of Dermatology Translational Core



# BIOREPOSITORIES AT NU

- ◉ Purpose: take fresh OR archived patient tissues and make them available for researchers
- ◉ NU Dermatology has two federally-compliant, IRB-approved tissue and cell biorepositories to support research activities
  - **FRESH TISSUE**
  - Faculty, for ex. Dr. Paller, who wants fresh research tissue, fills out a fresh tissue request form. For ex., she can say: “We need skin from the bottom of a foot of someone who has diabetes.” So then, fresh tissue, discarded during procedures such leg amputation of a diabetic person, is then taken directly by our coordinator and brought to Dr. Paller’s Lab.
  - **ARCHIVED TISSUE**
  - We have a fulltime coordinator who retrieves archived tissues upon researchers’ requests.
    - ◉ Intellipath (more recent archive) - PI will ask for scalp skin of ex for a 37 year old with alopecia areata.
    - ◉ ABC Lab (all specimens here are older than 10 years).
- ◉ The Pathology Department at Northwestern has had its own Biorepository for ages, however, as of 8 years ago, DermPath has created its own Biorepository called Intellipath

# OBJECTIVES OF THE BIOREPOSITORY

1. To expand the amount of biological material available for diagnostic purposes

2. To give investigators the opportunity to study how patient cells behave and respond to potential treatments in a safe, invitro environment

3. To help determine how genetic markers can be used to diagnose and treat disease

◉ For example:

◉ If a researcher is doing a mouse model of psoriasis, he or she can design a protocol to screen dermatology clinics and obtain tissue samples from psoriasis patients in the clinic

# TISSUE REQUESTS

- All specimen requests are reviewed and filled by the Northwestern Dermatology Clinical Trials Repository Fellow and dispensed without identification to the Research PI
- Investigator has to sign an agreement that the tissue will not be sold
- <http://skinresearch.northwestern.edu/research/Fresh%20tissue-request-form%20HTML1.html>

Clear

Please provide a summary of your research project. Include objectives and aims as necessary. \*

Specify Tissue Type: \*

☐ Skin Tissue

☐ Skin Swab

☐ Buccal Swab

☐ Blood

☐ Mucous Membrane Swab

☐ Saliva

☐ Other

Indicate Quantity for each specimen, Diagnosis if applicable, and Specific Parameters (gender, age, race, and ethnicity). Please also include step-by-step specimen transport instructions: \*

Tissue is provided with the following information: diagnosis, age of patient at the time of tissue collection, gender, lesional or non-lesional tissue, and anatomic site. Any requested medical record data extraction must be specified below: \*

# TISSUE REQUEST FORMS

- ◉ Fresh tissue request form:

- ◉ <http://skinresearch-dev.fsm.northwestern.edu/research/Fresh%20tissue-request-form%20HTML1.html>

- ◉ Archived tissue request form:

- ◉ <http://skinresearch-dev.fsm.northwestern.edu/research/Archived%20tissue-request-form%20html.html>



# DERMATOLOGY TISSUE ACQUISITION AND BIOREPOSITORY

- ◉ Examples of tissues that we collect:

- skin,
- hair,
- nail,
- saliva,
- urine,
- buccal swabs,
- mucous membranes,
- stool (coming soon)
- and other tissues

# LOG KEPT BY THE TRANSLATIONAL CORE COORDINATOR

- ◉ Subject ID number (assigned sequentially)
- ◉ Type of dermatological disorder/diagnosis (confirmed or presumed)
- ◉ Subject age at the time of the visit (not DOB)
- ◉ Subject gender
- ◉ Subject race
- ◉ Subject ethnicity
- ◉ Tissue site location (anatomic site) and lesional or non-lesional
- ◉ Date of sample collection
- ◉ Additional non-identifiable information as requested by researcher per requisition
- ◉ Date of sample release from Translational Core to Skin Disease Research Center Morphology and Phenotyping Core

# STUDY SITES FOR THE BIOREPOSITORY:

- ◉ Northwestern Memorial Hospital (NMH)
- ◉ Ann & Robert H. Lurie Children's Hospital of Chicago
- ◉ Northwestern Medicine Lake Forest Hospital
- ◉ Northwestern Medical Group Satellite Clinics
  - Glenview
- ◉ Greater Chicagoland population
  - 9.73 million

# BIOREPOSITORY: INCLUSION CRITERIA OF THE PROTOCOL

- ◉ Male or female age 0 to 70 years old
- ◉ Subjects with peripheral blood, saliva, and/or tissue removed for standard of care OR following informed consent
- ◉ Newborn males undergoing routine circumcision where the tissue is intended to be discarded per institutional policy
- ◉ Subjects include viable neonates; (nonviable neonates and neonates of uncertain viability if samples were collected for non-research purposes)

# NORTHWESTERN INNOVATIVE APPROACH

- ◉ Recognized for being very good at acquiring tissue
- ◉ Specimen acquisition is through the biorepository (for which an IRB approval and IRB-approved consent already exists)
- ◉ When a researcher requests specific de-identified tissue, the researcher does not need to create a new IRB submission since the biorepository is already under the IRB approval

# DERMATOLOGY TISSUE ACQUISITION AND BIOREPOSITORY

## End Goals of the Biorepository:

1. An understanding of the molecular and cellular basis for skin disease or disease physiology
2. Development of novel therapeutic strategies in the clinic
3. Better patient management

# SKIN DISEASE RESEARCH CENTER

- ◉ The Clinical Research Unit (CRU) extensively interfaces with the Northwestern University - Skin Disease Research Center (NU-SDRC)
- ◉ NU-SDRC is comprised of 60 collaborating cutaneous bench biologists and 13 skin-focused clinical research members from 25 departments across NU
- ◉ In addition to the Administrative Core, the SDRC is comprised of 3 distinct research service cores:
  - Skin Tissue Engineering Core
  - Morphology and Phenotyping Core
  - DNA/RNA Delivery Core
- ◉ Each Core has full time, dedicated, well-trained staff members



# SKIN DISEASE RESEARCH CENTERS

- ◉ Funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
- ◉ The first federally funded research centers in dermatology and began in 1988
- ◉ Provide resources for a number of established investigators as well as young junior investigators, often from different disciplines, to adopt a multidisciplinary approach to common research problems

## SDRC CONTINUED...

- ◉ SDRCs take advantage of the strengths of both basic and clinical researchers
- ◉ Promote research collaborations that enhance productivity
- ◉ Core units are established that provide **shared** facilities, equipment, and technical services



# STUDY COORDINATORS/STAFF

- ◉ One dedicated full-time study coordinator/research fellow
- ◉ Every other study coordinator/ research fellow is a back up to the main one and is trained to consent the patients for the Biorepository

# SDRC: RESEARCHERS REQUESTING SLIDES

- ◉ If researchers indeed would like to request identified data, there is one rule:  
They need to write a new IRB-approved protocol.



# EXAMPLES OF PHYSICIANS WHO USE THE BIOREPOSITORY FOR THEIR RESEARCH

- ◉ 1. Dr. Tom Hope/ Dr. Gianguido Cianci (Penile Biopsies)
- ◉ 2. Dr. Jaehyuk Choi (CTCL)
- ◉ 3. Dr. Amy Paller (Biomarkers)
- ◉ 4. Dr. Jonathan Silverberg (Atopic Dermatitis)
- ◉ 5. Dr. Stavonnie Patterson (Alopecia Areata)



# PHYSICIAN SCIENTISTS AT NORTHWESTERN DERMATOLOGY

## ◉ Jaehyuk Choi, MD/PhD

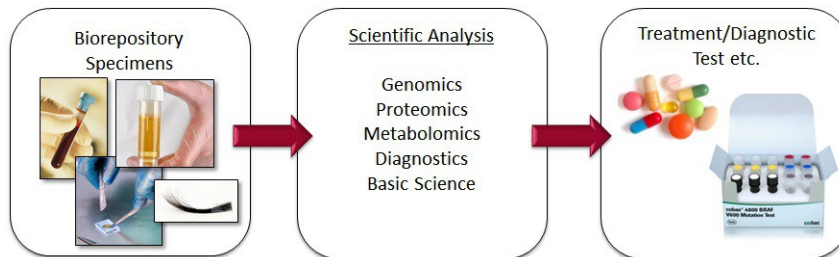
- Ruth K. Freinkel, MD, Research Professor in Dermatology
- His lab identifies the genetic basis of inherited and acquired immunological disorders and skin cancer
  - Ex.: recently identified genes and mutations underlying cutaneous T cell lymphoma
  - Employ a comprehensive approach with human tissues and animal models to investigate the functions of these genes
  - Utilizes the biorepository in order to elucidate the pathophysiology of the lymphoma and lead to identification of novel therapeutic targets



# BIOBANKING

**Jonathan Silverberg, MD, MPH, PhD**

- He collects biomarkers and genetic information (skin, blood, urine, saliva, buccal mucosa) in patients with atopic dermatitis and analyzes how the biomarkers correlate with clinical improvement, severity of disease, response to treatment, and quality of life (from surveys filled out by the patients)





# CLINIC WORK FLOW

How will you integrate this into workflow?

1. Patients come in for regular standard of care visit
2. At the end of the visit, the PI asks the patient if he/she is willing to participate in the biobanking study
3. Team of coordinators is ready to take the patient to the venipuncture unit
4. Meanwhile, the physician is not losing any of the time
5. Clinic workflow is not interrupted

# BIOBANKING - WORKFLOW



Patient is asked to provide tissue for research - Informed Consent



Blood and tissue collected in the operating room or by the pathologist



Tissue is frozen



Blood is processed into whole blood, serum and plasma



Store samples and associated clinical data



Sample distribution



Provide tissue or blood to researchers for their research projects

# BIOMARKERS

- ◉ Amy Paller, MD
- ◉ Collaborative project of Dr. Paller's:
  - collect blood, skin samples, transepidermal water loss tape strips
  - send the samples to the Rockefeller University for analysis



# RECENT PRESS RELEASE

- ◉ September 23, 2016
- ◉ “Pediatric Atopic Dermatitis May Benefit From Early Immune Intervention”
- ◉ Published in the Journal of Allergy and Clinical Immunology
- ◉ 2 collaborative centers:
  - Northwestern University
  - Mount Sinai, NYC/Rockefeller University
- ◉ From skin biopsies in infants, they found that non-lesional, normal appearing skin in infants with atopic dermatitis is already highly abnormal with significant immune activation, which means that early immune intervention may help infants with eczema

# VARIOUS COLLABORATIONS AT NORTHWESTERN DERMATOLOGY

- ◉ Multidisciplinary Lymphoma Clinic
  - Dermatologist (Dr. Joan Guitart)
  - Oncologist
- ◉ Multidisciplinary Eczema Clinic
  - Dermatologist (Dr. Jonathan Silverberg)
  - Allergist/immunologist
- ◉ Multidisciplinary Psoriasis Clinic
  - Dermatologist (Dr. Kenneth Gordon)
  - Rheumatologist (Dr. Eric Rutterman)

# NUCATS

(NORTHWESTERN UNIVERSITY CLINICAL AND TRANSLATIONAL  
SCIENCE INSTITUTE)

## ◉ Centers at NUCATS

- 1. Center for Translational Innovation
- 2. Center for Clinical Research (CCR)
- 3. Center for Community Health
- 4. Center for Data Science and Informatics  
(Dermatology is the biggest user of this aspect, 8  
million+ patients; most advanced in the US for  
datamining)
- 5. Center for Educations and Career  
Development
- 6. Galter Health Science Library

# CENTER FOR CLINICAL RESEARCH: COMPONENTS

- ◉ 1. Regulatory Unit
  - 20~ regulatory coordinators
  - IRB communications
- ◉ 2. Coordinator Unit
  - Full time study coordinators available
- ◉ 3. Recruitment Unit
  - 5~ recruitment coordinators
  - Recruitment campaigns, calling patients, marketing
- ◉ 4. Financial Unit
  - Available for financing of industry trials
  - Negotiate budgets with sponsors



# ADDITIONAL SUPPORT FOR OUR RESEARCH CENTER

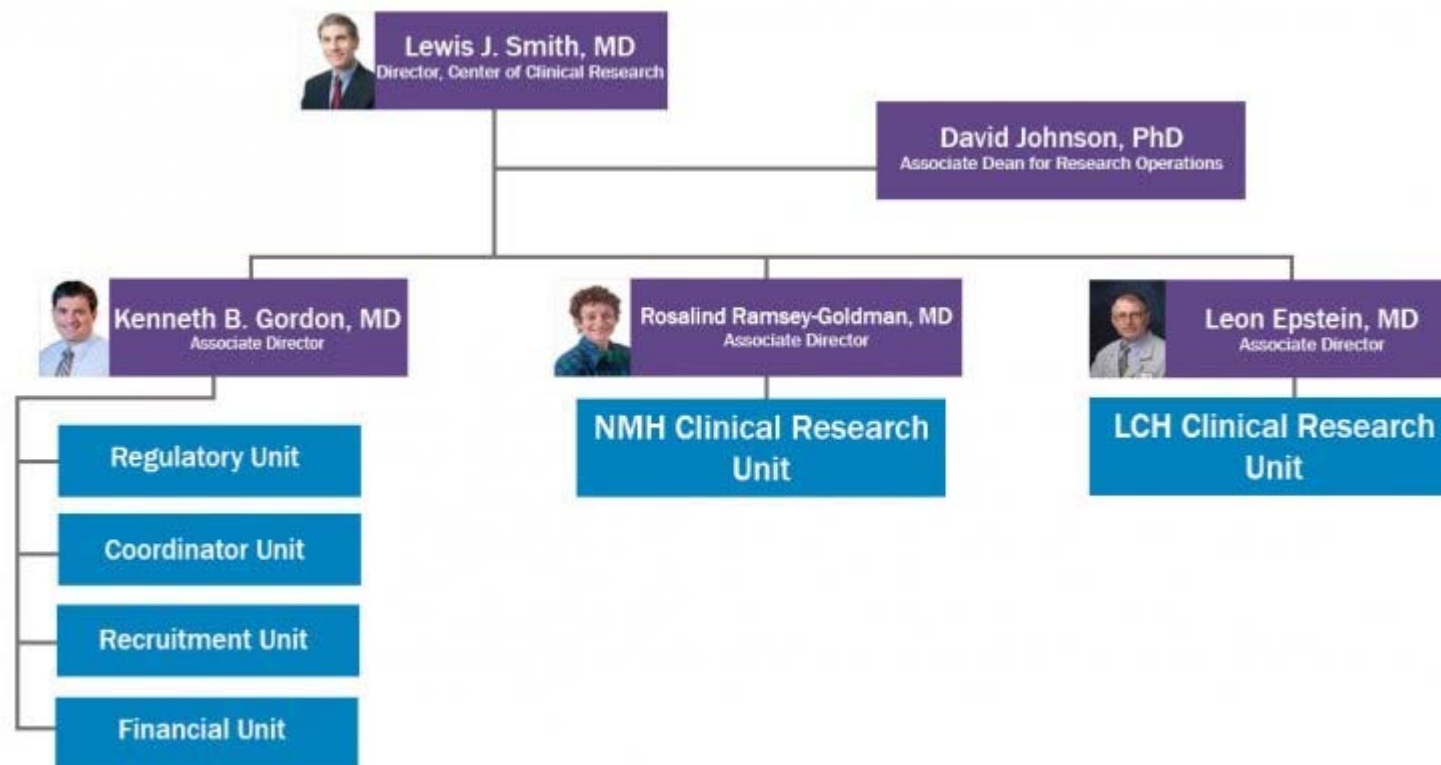
- ◉ Diagnostic Testing Center (DTC) Unit
  - 10~ Phlebotomists
  - EKG technicians
  - CXR technicians
- ◉ Investigational Pharmacy
- ◉ Clinical Research Core Lab Unit
  - Process blood and urine and ship samples
  - 24-hour clinical nurses for infusions, PK sampling, and close monitoring



# FINANCES

- ◉ Federally mandated charge back mechanisms are complex -many steps in the process
- ◉ We charged for:
  - Staff time to obtain informed consent
  - Staff time to collect the tissue
  - Staff time to process the tissue (if needed)
  - Depending on who/where the tissue is being stored there may be fees for the storage

# CENTER FOR CLINICAL RESEARCH: LEADERSHIP



# PROGRAMS AT NUCATS

- ◉ 1. Biostatistics, Epidemiology, and Research Design
- ◉ 2. Evaluation and Continuous Improvement Program
- ◉ 3. Pilot Translational and Clinical Studies Program
- ◉ 4. Collaboration and Team Science Program

# SUMMARY

What you need to do to set this up at your institution:

- ◉ Money/grants
  - Industry
  - Government
- ◉ Innovative, motivated investigators
- ◉ Protocols
- ◉ Facilities
- ◉ NUCATS
- ◉ Compliance/safety - Drs. Dennis West and Stephanie Rangel