

**NIH-Clinical Center  
Extramural Collaborations Committee**

**Sally J. Rockey, Ph.D. and John I. Gallin, M.D.  
Co-chairs**



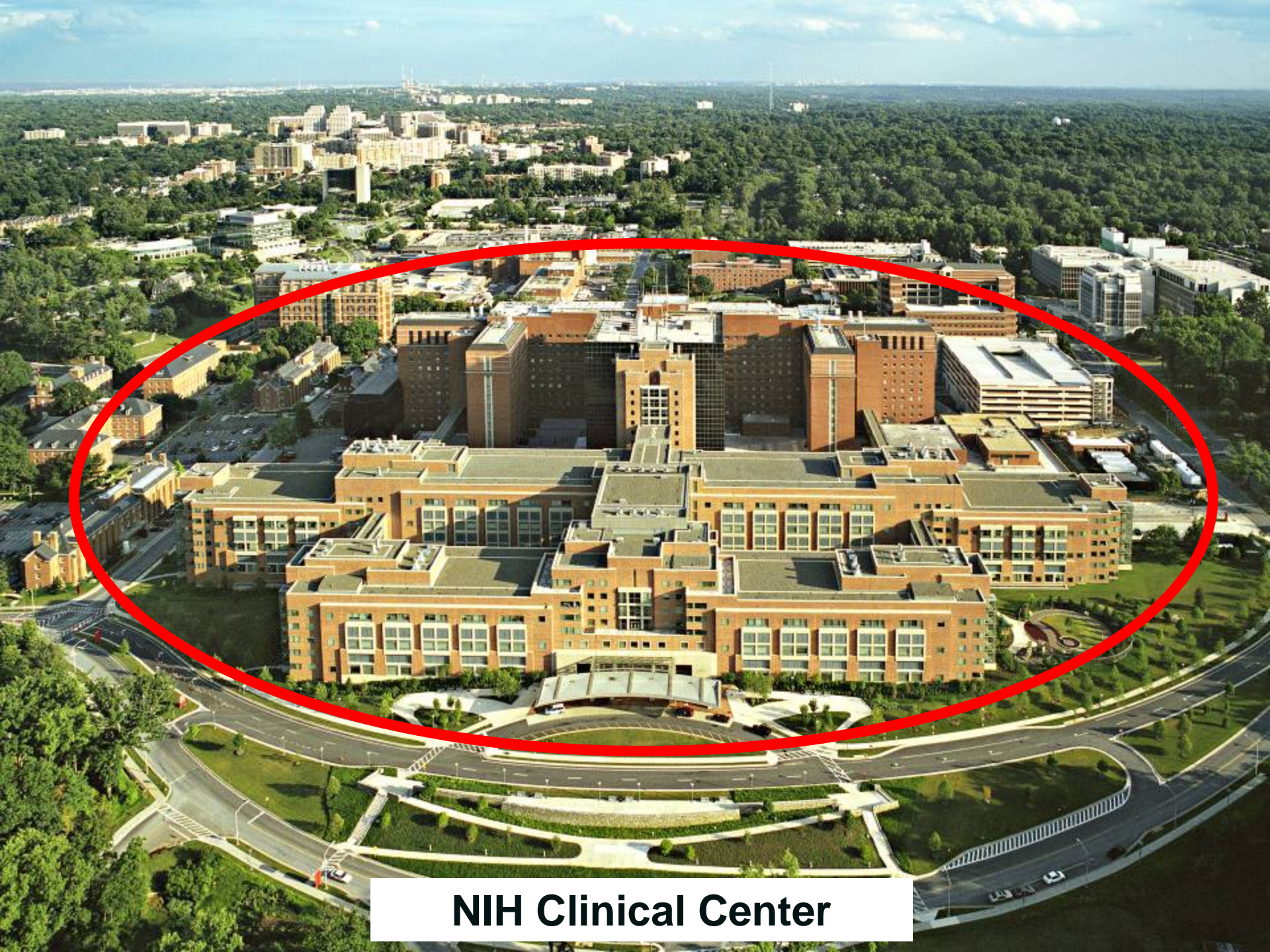
**June 10, 2011**



# Outline of Presentation

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- **Overview of NIH Clinical Center**
- **A new vision for the Clinical Center**



**NIH Clinical Center**

# Clinical Center Profile

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- More than 400,000 patients since opening in 1953
- 240 beds
- Hospital surrounded by research labs
- Every patient is on a research protocol
- Care is free
- Patient travel/housing provided as needed
- 2,250 CC employees + ~4,000 employees from 18 ICs that use hospital
- 1,255 credentialed physicians
- 1,443 active protocols
  - 49% natural history studies
  - 45% clinical trials  
(91% phase 1 and 2)



# Major Emphasis

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- **First in human with new therapeutics**
- **Study of patients with rare diseases**

# Current Rare Diseases at the NIH Clinical Center\*

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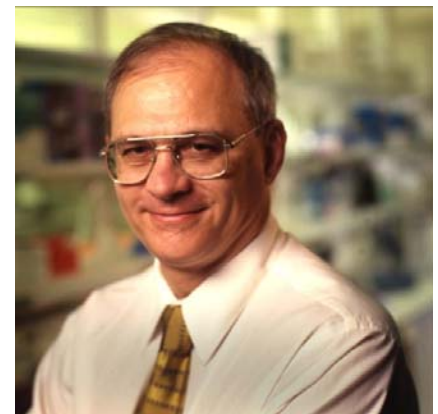
<b>Number of Rare Diseases</b>	<b>383</b>
<b>Number of Protocols</b>	<b>603</b>
• <b>Clinical Trials</b>	<b>325</b>
• <b>Natural History</b>	<b>253</b>
• <b>Other (training, screening, pharmacokinetics)</b>	<b>25</b>

\*May 26, 2011

# Undiagnosed Diseases Program (UDP)

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- A call for undiagnosed diseases with no phenotype restrictions
- A multi-disciplinary approach to each patient
- ~45 NIH senior consultants participate
- About 50% UDP patients have neurodegenerative diseases
- Total # of patients: ~4,000 screened; 350 admissions



William Gahl, MD, PhD  
Clinical Director, NHGRI

# Specialized Services and Facilities

- Phenotyping
  - Biomechanics laboratory
  - Metabolic chambers
- Cell Processing/GMP Facility





# Specialized Services and Facilities

## Imaging Capabilities

- **MRI Center**
- **PET Program**
  - **3 cyclotrons**
  - **Radiochemistry/GMP Facility**
  - **3 scanners**



# Specialized Services and Facilities

## Pharmaceutical Development Service GMP Facility

- Product formulation
- Analytical and quality control
- Pharmacokinetics
- Manufacturing capability (8 hour day)



- 75,000

- 150,000

- 220 liters

- 5,000

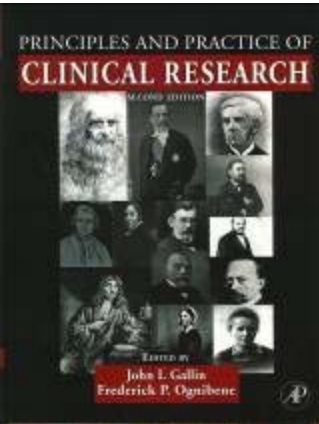


- **8,000 vials (includes vaccines and biologics)**

CC Pharmaceutical Development Section  
producing green tea capsules for a study

# NIH Curriculum In Clinical Research

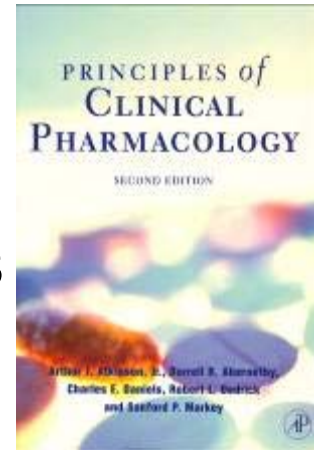
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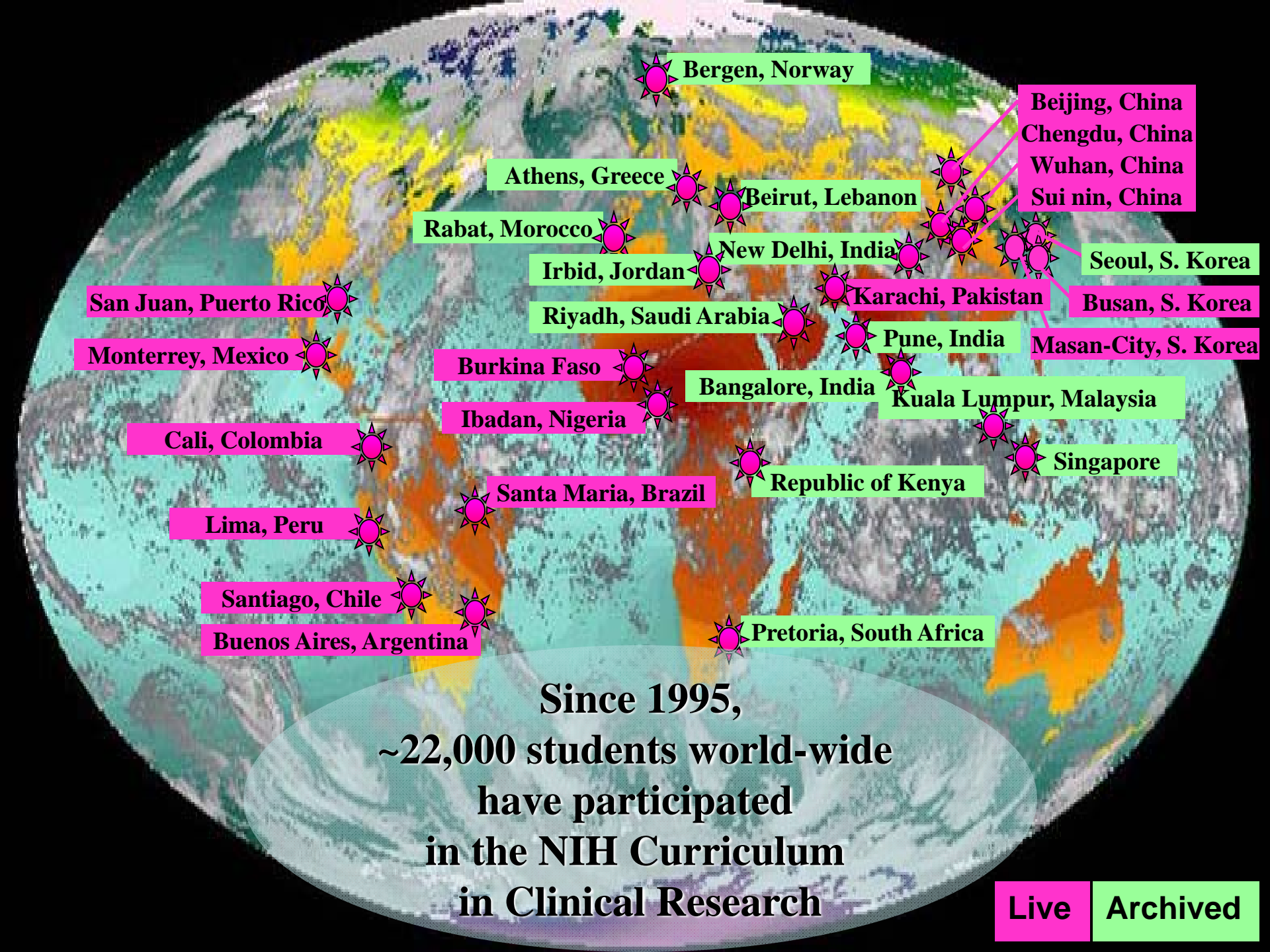
**Introduction to the Principles & Practice of Clinical Research**  
**>10,600 participants since course introduced in 1995**

## **Principles of Clinical Pharmacology**

**>6,600 registrants since course began in 1998**



**Ethical and Regulatory Aspects of Human Subjects Research**  
**>4,200 participants since course began in 1999**



Bergen, Norway

Beijing, China  
Chengdu, China  
Wuhan, China  
Sui nin, China

Athens, Greece

Beirut, Lebanon

Rabat, Morocco

New Delhi, India

Seoul, S. Korea

San Juan, Puerto Rico

Irbid, Jordan

Karachi, Pakistan

Busan, S. Korea

Monterrey, Mexico

Riyadh, Saudi Arabia

Pune, India

Masan-City, S. Korea

Cali, Colombia

Burkina Faso

Bangalore, India

Kuala Lumpur, Malaysia

Ibadan, Nigeria

Republic of Kenya

Singapore

Lima, Peru

Santa Maria, Brazil

Pretoria, South Africa

Santiago, Chile

Buenos Aires, Argentina

Since 1995,  
~22,000 students world-wide  
have participated  
in the NIH Curriculum  
in Clinical Research

Live Archived

**The Future**

**A New Vision  
for the Clinical Center**

# JAMA<sup>®</sup>

The Journal of the American Medical Association

**October 11, 1952**

## THE UNITED STATES PUBLIC HEALTH SERVICE'S CLINICAL CENTER FOR MEDICAL RESEARCH

*Norman H. Topping, M.D., Bethesda, Md.*

**Assistant Surgeon General, United States Public Health Service;  
Associate Director, National Institutes of Health.**

**...our facilities should be considered as a national resource, and not simply a Public Health Service laboratory. To carry out this principle we determined to invite outstanding persons from this country and abroad to work with us ...**

# NIH Scientific Management Review Board

SCIENTIFIC MANAGEMENT REVIEW BOARD  
REPORT ON THE NIH CLINICAL CENTER

DECEMBER, 2010



NATIONAL INSTITUTES OF HEALTH  
SCIENTIFIC MANAGEMENT REVIEW BOARD

**“The role of the NIH Clinical Center should be to serve as a state-of-the-art national resource, with resources optimally managed to enable both internal and external investigator use.”**

<http://smrb.od.nih.gov/>

December 2010

# NIH Clinical Center-Extramural Collaborations Committee

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- **Co-Chairs:** Sally J. Rockey, Ph.D. and John I. Gallin, M.D.

- **Members (32):**

Colleen Barros, OD  
Courtney Bell, CC  
Todd Cole, OD  
Virginia Hill Condon, CC  
Mitzi Diley, OD  
James Doroshov, NCI  
Joe Ellis, OD  
Diane Frasier, OD  
Zofia Gajdos, OD  
Maureen Gormley, CC  
Michael Gottesman, OD

Marcia Hahn, OD  
Della Hann, OD  
Alexander Hawkins, OD  
Lee Helman, NCI  
David Henderson, CC  
Holly Beckerman Jaffe, OD  
Nancy Jones, NIAID  
Maria Joyce, CC  
Daniel Kastner, NHGRI  
John Kim, OD  
Patricia Kvochak, OGC

Barbara McGarey, OGC  
John McGowan, NIAID  
Fred Ognibene, CC  
Pat Piringer, CC  
Carrie Pottker-Fishel, OGC  
Mark Rohrbaugh, CC  
Carl Roth, NHLBI  
Neil Shapiro, OD  
Lee West, OD  
Carol Wigglesworth, OD



# 2 Subgroups

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## NIH Clinical Center-Extramural Collaborations Committee

**Services and  
Training  
Workgroup**

**Extramural-  
Intramural  
Collaborations  
Workgroup**

# Services and Training Workgroup

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- **Chair:** Frederick P. Ognibene, CC

- **Members:**

Jodi Black, NHLBI  
Virginia Hill Condon, CC  
Robert DeChristoforo, CC  
Erin Dominick, CC  
Jerry Doyle, NINDS  
Chris Epinger, CC  
Diane Frasier, OD  
George Grimes, CC  
Della Hann, OD  
Peter Herscovitch, CC

Nancy Jones, NIAID  
Maria Joyce, CC  
Patricia Kvochak, OGC  
Lisa Marunycz, CC  
Barbara McGarey, OGC  
Colleen McGowan, CC  
John J. McGowan, NIAID  
Carrie Pottker-Fishel, OGC  
Dan Rinehuls, CC

# Services and Training Workgroup

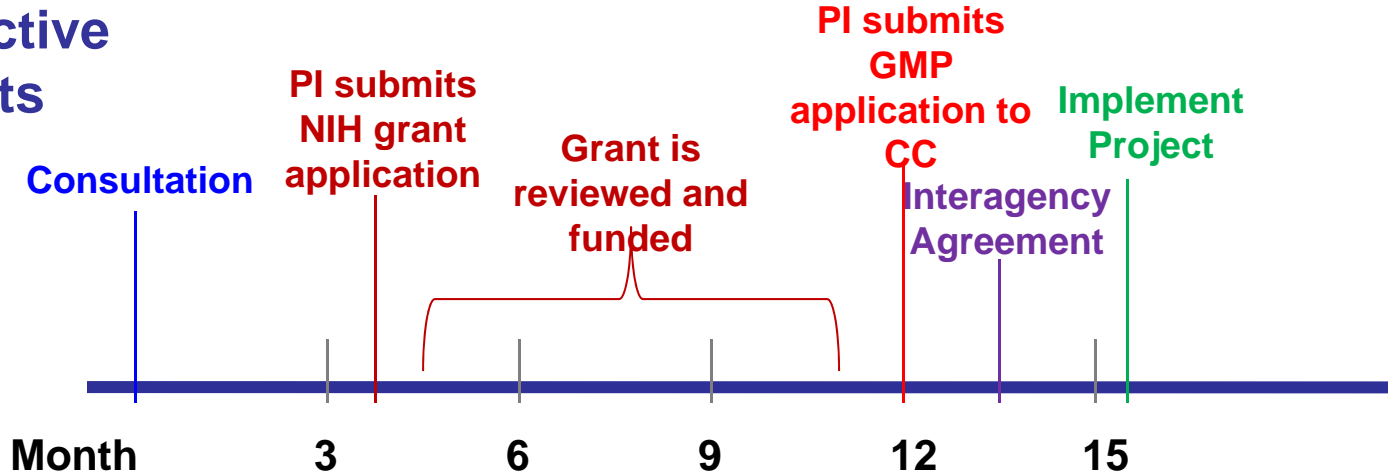
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**Initial focus on creating programs accessible to external investigators**

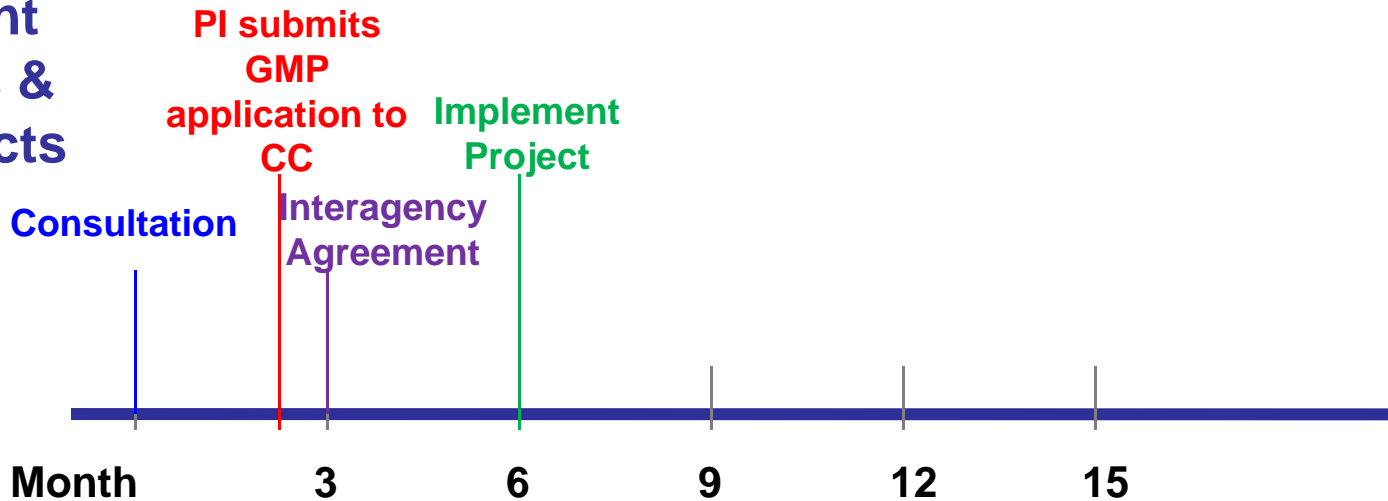
- 1. Pharmacy's Good Manufacturing Practices (GMP) Facility- service only ✓ *Program drafted***
  - **Currently available to prospective and current grantees and NIH R&D contracts**
  - **Access to foundation, industry, and academic partners to be developed**
- 2. Training in clinical research- access to existing core curricular courses**
- 3. Metabolic Unit- some patient activity**
- 4. Research PET- some patient activity**

# Projected Timelines for Access to GMP Facility

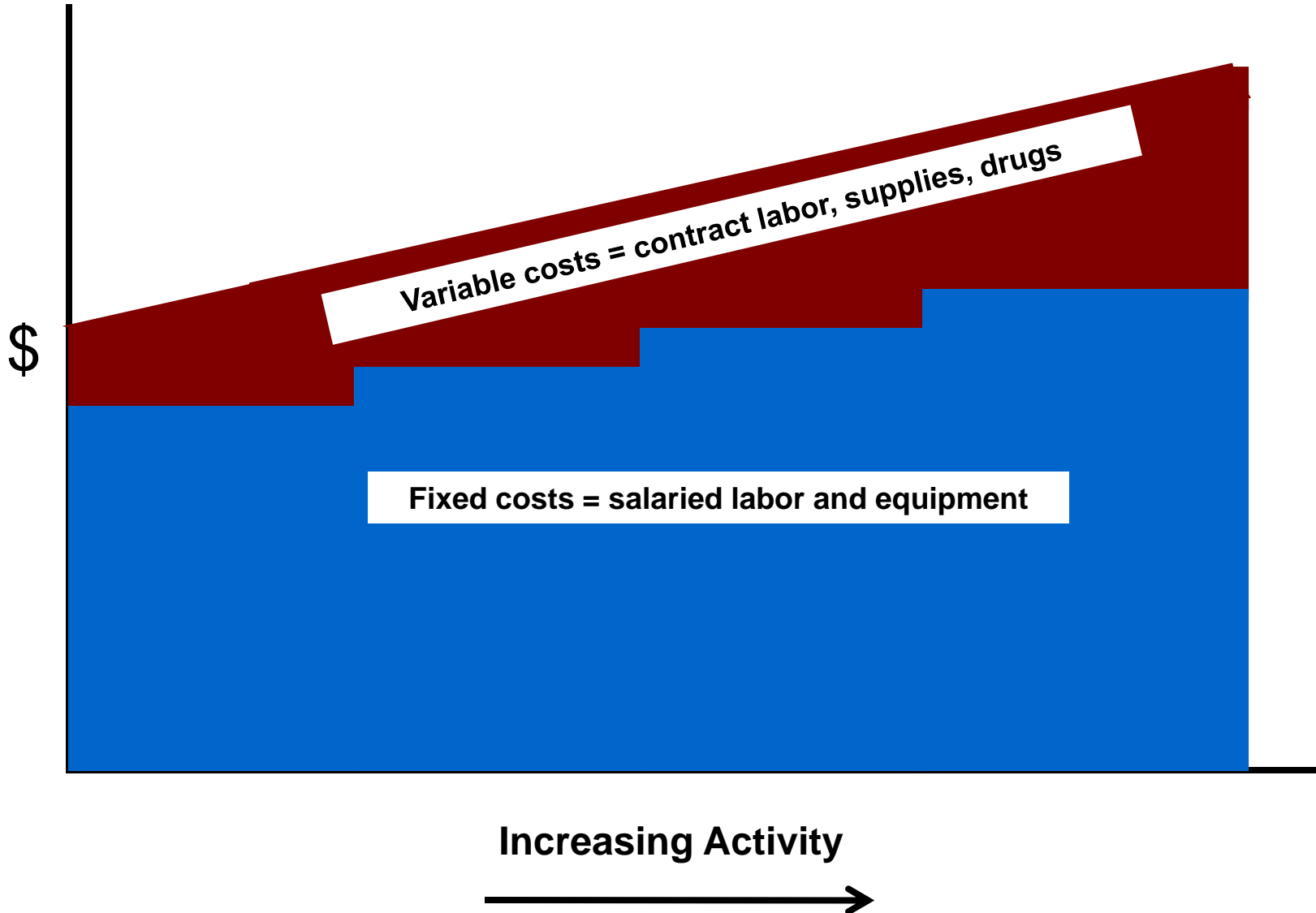
## Prospective Grants



## Current Grants & Contracts



# Cost Model



# Extramural-Intramural Collaborations Workgroup

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- **Chair:** Constantine Stratakis, NICHD

- **Members:**

Jeff Abrams, NCI

Courtney Bell, CC

Patricia Bennett, NIDDK

Todd Cole, OALM

Joe Ellis, OER

William Gahl, NHGRI

Greg Germino, NIDDK

Della Hann, OER

Petra Jacobs, NIDA

Nancy Jones, NIAID

Daniel Kastner, NHGRI

Walter Koroshetz, NINDS

Maria Koszalla, NIH/OD

Pat Kvochak, OGC

Anna Nicholson, NIAMS

Gail Pearson, NHLBI

Pat Piringer, CC

Forbes Porter, NICHD

Carrie Pottker-Fischel, OGC

Joel Sherrill, NIMH

Catherine Spong, NICHD

Robert Star, NIDDK

Anne Willoughby, NCRR

Sheila Zahm, NCI

Kathryn Zoon, NIAID

- **Focus:** Bench-to-Bedside Award Program (BTBAP) is  
*“low-hanging fruit”*

# Bench-to-Bedside Awards

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- A program to promote new partnerships between basic science and clinical investigators
- **Goals:**
  - Develop new clinical protocols
  - Discover new therapeutics and devices
  - Foster long-standing collaborations



# **Current Bench-to-Bedside Award Program**

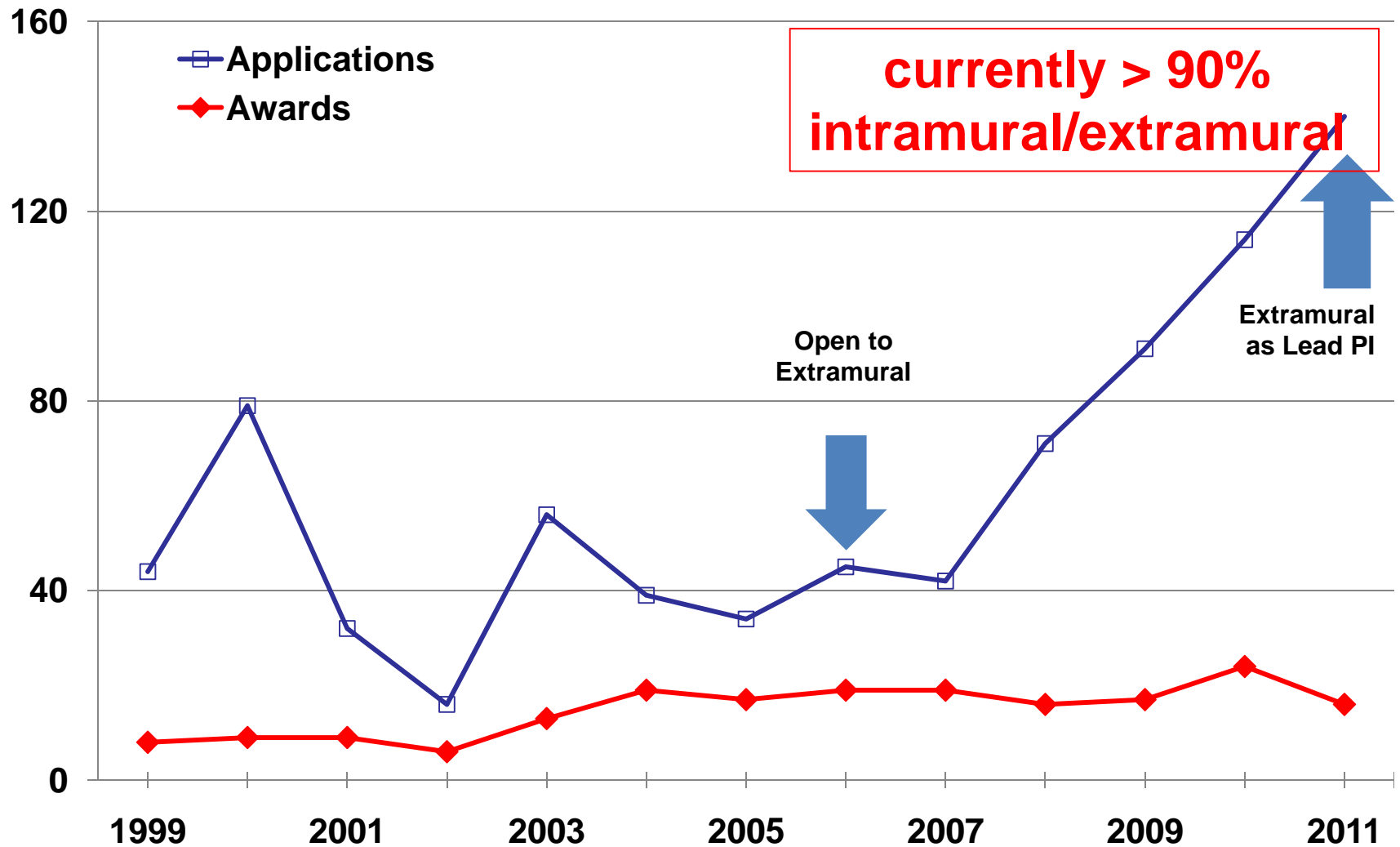
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- **Started in 1999**
- **192 projects funded to date; ~\$44M investment**
- **Today \$135K per year X 2 years**
- **In 2006 established intramural/extramural partnerships**

**<http://clinicalcenter.nih.gov/ccc/btb/index.html>**

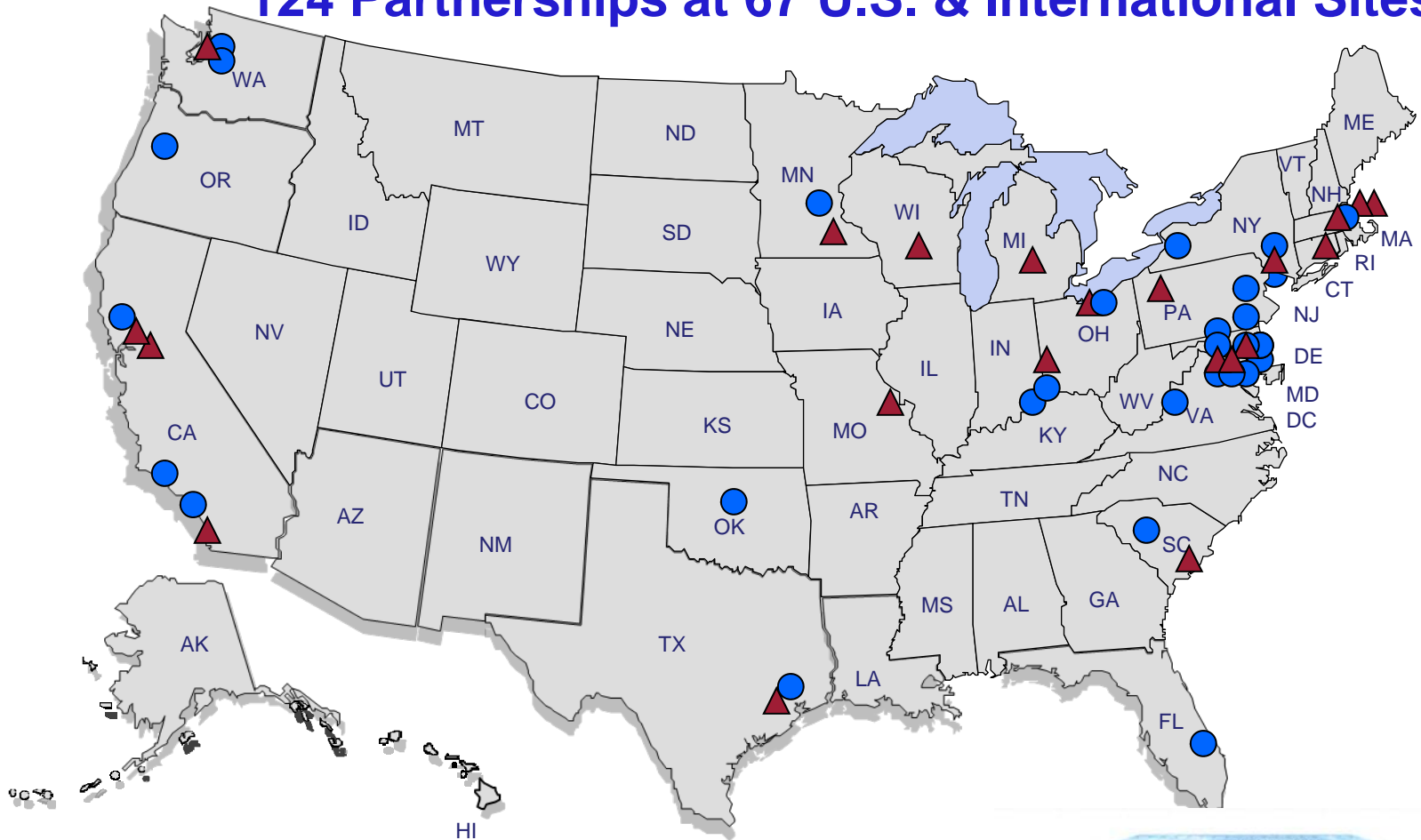


# Bench-to-Bedside Program Applications and Awards



# B2B Partnerships 2006 – 2011

## 124 Partnerships at 67 U.S. & International Sites



**Hospital A.C. Camargo, Brazil**  
**Hospital for Sick Children, Canada**  
**Imperial College, London**  
**Intl. Agency for Research on Cancer, France**  
**Makerere University, Uganda**  
**Sackler Sch. of Med, Israel**  
**University of Toronto, Canada**  
**University of Oxford, UK**  
**Zaria, Nigeria**



# Bench-to-Bedside Outcomes 1999 – 2009

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<b>Result</b>	<b>Number</b>
<b>Projects</b>	<b>152</b>
<b>Publications</b>	<b>162</b>
<b>New Protocols</b>	<b>92</b>
<b>Inventions/Patents Pending</b>	<b>32</b>
<b>Awarded Patents</b>	<b>5</b>



**Michael Iadarola, Ph.D., NIDCR**  
 2 Bench to Bedside Awards  
 in 1999 & 2001



**2001 project: "New Treatments for Intractable Pain"**

- **Partnerships:** NIDCR, NIAMS, NINDS, CC
- **Outcomes:**
  - Phase 1 clinical trial of a new pain-relieving drug (resiniferatoxin, RTX)
  - Patent pending (U.S. Patent #6,881,718)
  - License issued (Sherrington Pharmaceuticals)



**Joan Han, M.D., NICHD**

**Felicitas Lacbawan, M.D., F.C.A.P.,  
 SUNY Downstate Medical Center**



**2007 project: "WAGR Syndrome: Clinical Characterization and Correlation with Genotype"**

- **Partnerships:**
  - NICHD, NEI, NIDCR, NIMH, NIDDK
  - Georgetown U. Med. Ctr.
  - USUHS
- **Outcomes:**
  - CC protocol: 110 new patients
  - **Publication:** *Brain-derived neurotrophic factor and obesity in the WAGR syndrome.* Han et.al. *NEJM* 359: 918. 2008
  - **Partnerships:** addl awds 2010, 2011



**Manfred Boehm, M.D., NHLBI**

**Hal Dietz, M.D., Johns Hopkins**

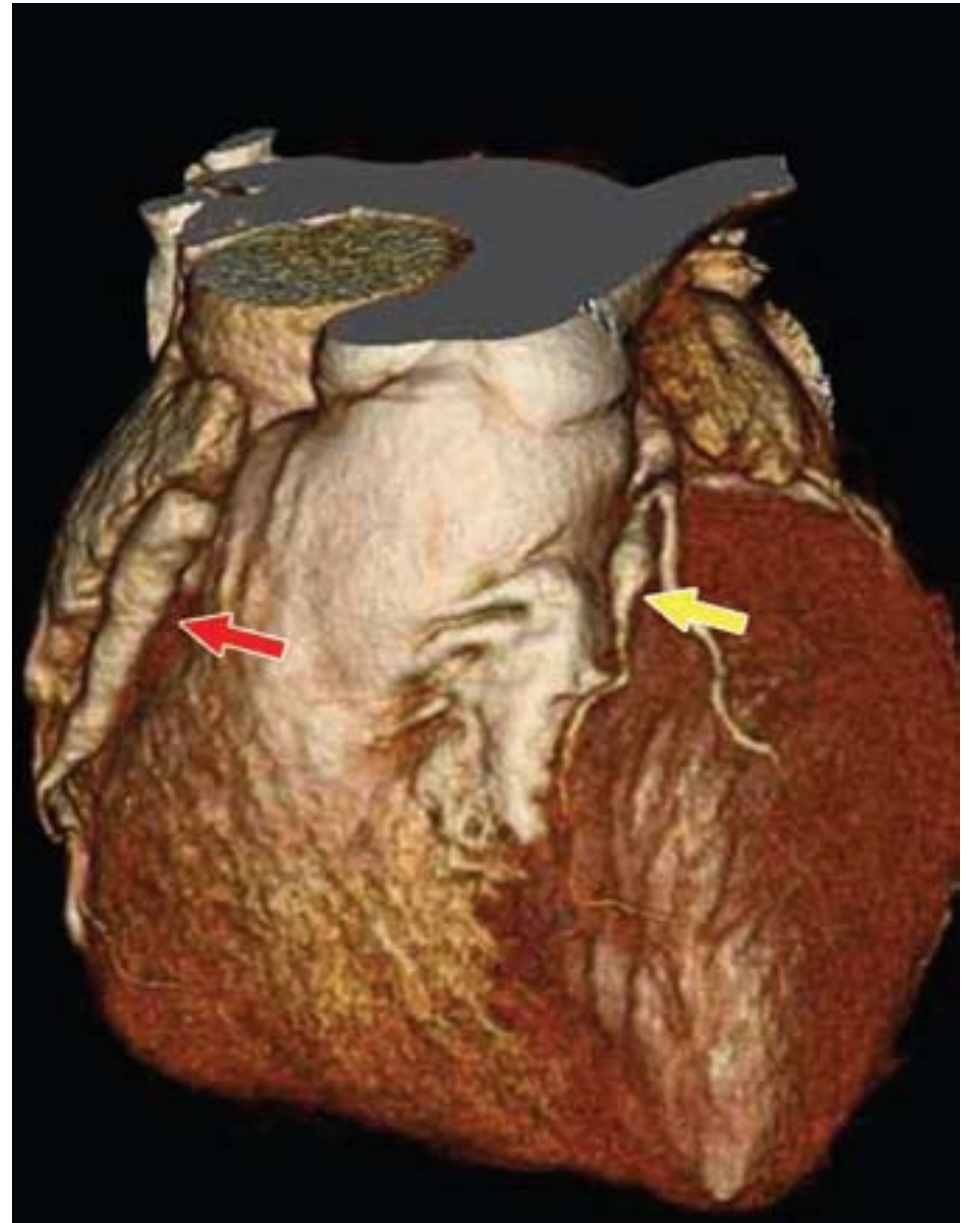


**Bench to Bedside Award in 2009**

**2009 project: "Aneurysm Formation in Patients with Mutations in STAT 3"**

- **Partnerships:**
  - NHLBI, NIAID, NIDDK, NHGRI
  - Johns Hopkins University
- **Outcomes:**
  - STAT 3 identified as a regulator in extracellular matrix remodeling and linked to aneurysm formation in HIE (Job's) Syndrome

# HIE (Job's) Syndrome



Grimbacher, et.al., NEJM 340; 692. 1999

Gharib, et.al., AJR 193; 478. 2009

# **Bench to Bedside Awards -The Problem-**

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- **Unstable funding**
- **Complex funding process**

# **SMRB Assessment of Bench-to-Bedside Award Program**

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**“...the successful Bench-to-Bedside Program, which creates partnerships between intramural and extramural investigators, would benefit from a stable funding model with increased resources.”**

# Recommendations

## Extramural-Intramural Collaborations Workgroup Bench-to-Bedside Awards

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### 1. Immediate: Stabilize program

- Funding as line within CC budget
- Allow for small number of 3 yr awards
- 2 funding cycles/yr
- Formalize program reviews

### 2. Future: Creation of bench-to-bedside grant mechanism fostering intramural/extramural partnerships



# **Proposed Bench-to-Bedside Grant Mechanism**

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- **Include first time investigators**
- **Allow established PI to initiate new B2B grants w/o limitation to administrative supplements**
- **Applications solicited by “Funding Opportunity Announcement”**
- **Applications submitted by extramural PI with funds to support both intramural and extramural investigators must include patients studied at the Clinical Center**
- **Grants.Gov would receive applications to be vetted through external review and IC councils**
- **To be piloted by limited number of ICs**