



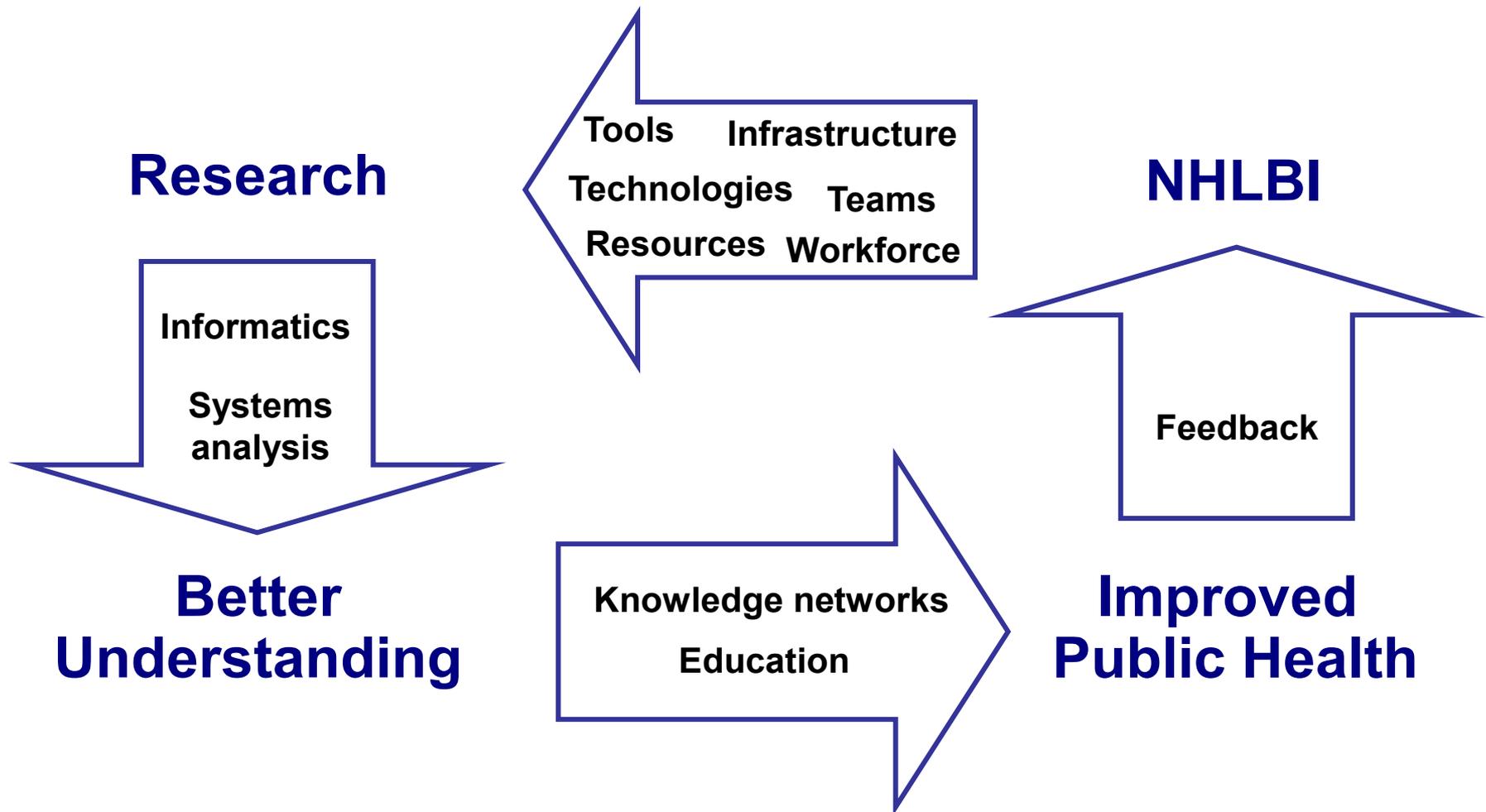
NHLBI Strategic Plan: Future Opportunities for Cardiovascular Research



National Heart, Lung, and Blood Institute



NHLBI's Strategic Plan Promotes Advances in Research Approaches



Planning Principals



NHLBI Strategic Plan Objectives

Develop a scientific blueprint for the next decade.

- A living, working plan from an inclusive and participatory process.
- Identify strategic priorities where NHLBI:
 - Initiates – does not happen unless the Institute takes a lead
 - Catalyzes – Institute facilitates the outcome
 - Supports – investigator-initiated research

NHLBI Strategic Plan Goals

Goal 1

Improve understanding of the molecular and physiologic basis of health and disease. Use that understanding to develop improved approaches to disease prevention, diagnosis and treatment. *Form → Function*

Goal 2

To develop personalized preventive and therapeutic regimens for cardiovascular, lung, and blood diseases. *Function → Cause*

Goal 3

Generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery. *Cause → Cures*

NHLBI Strategic Plan Leads Toward Personalized / Pre-emptive Medicine



Need to Transform Medical Research in the 21st Century

20th Century

**Treat disease
when symptoms appear and
normal function is lost**

**Did not understand the
molecular and cellular
events that lead to disease**

**Expensive in financial and
disability costs**

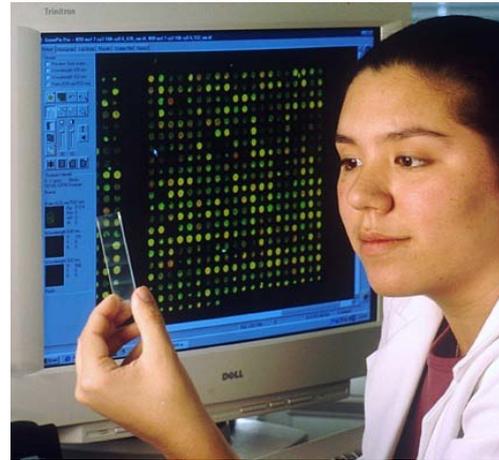
21st Century

**Intervene before symptoms
appear and preserve normal
function for as long as possible**

**Understanding preclinical
molecular events and ability to
detect patients at risk**

**Orders of magnitude more
effective**

The Future Paradigm: Transform Medicine from Curative to Preemptive

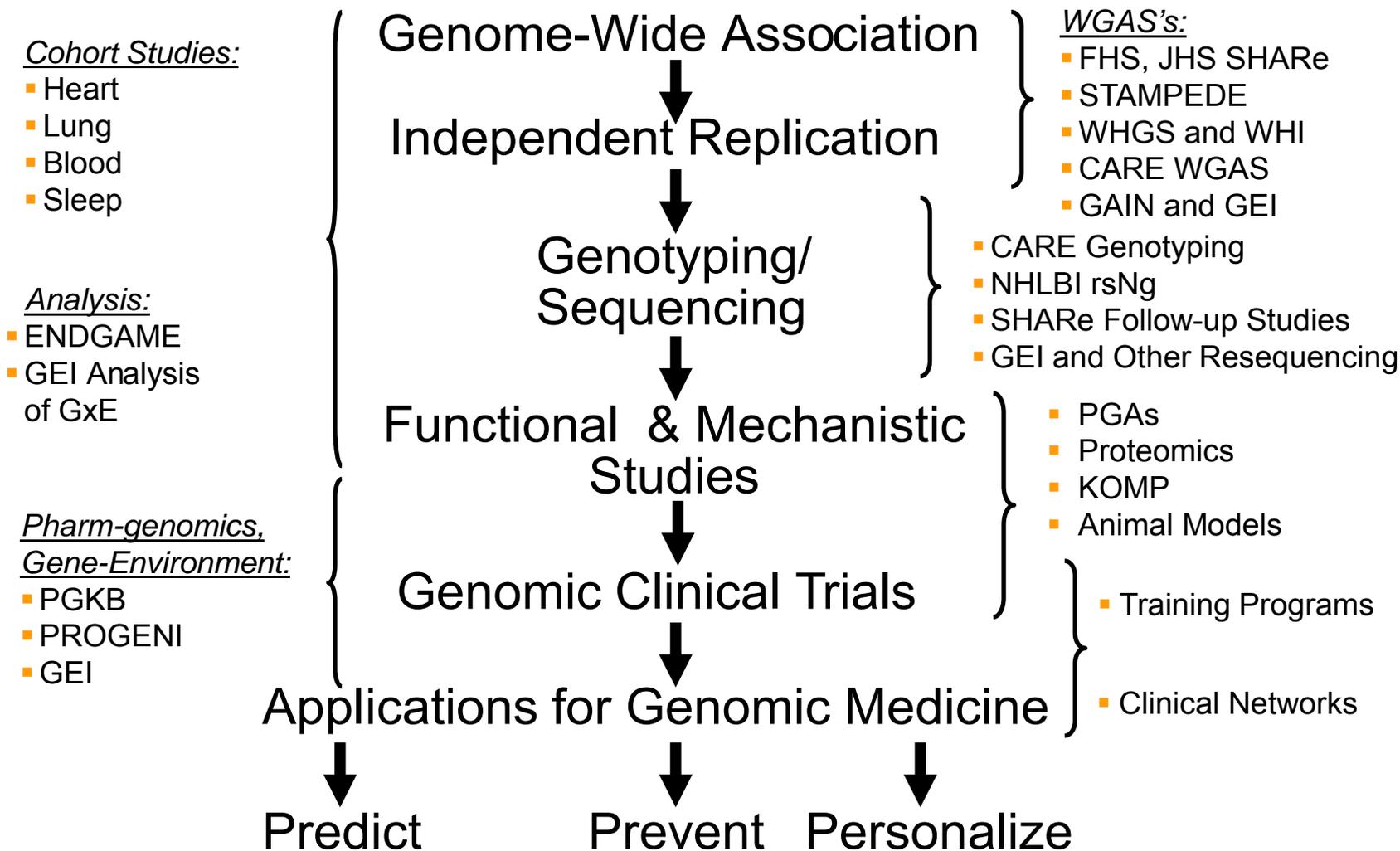


Predictive ↔ Personalized ↔ Preemptive



Participatory

NHLBI Strategic Plan Goals



NHLBI Strategic Plan Goals

Goal 1

Improve understanding of the molecular and physiologic basis of health and disease. Use that understanding to develop improved approaches to disease prevention, diagnosis and treatment. *Form → Function*

Goal 2

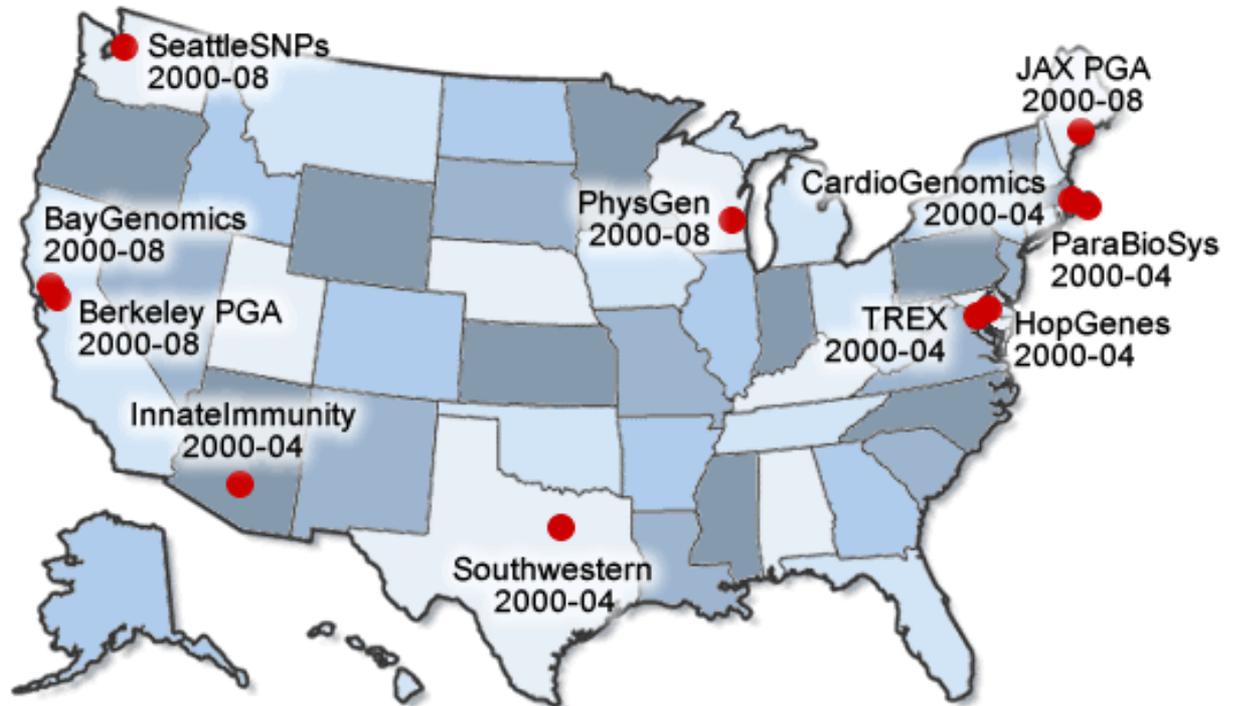
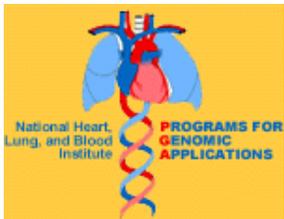
To develop personalized preventive and therapeutic regimens for cardiovascular, lung, and blood diseases. *Function → Cause*

Goal 3

Generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery. *Cause → Cures*

Programs of Genomic Applications

To develop information, tools, and resources to link genes to biological function on a genomic scale. To provide workshops, courses, and visiting scientist programs to facilitate the training of researchers in the use of the data and related technologies developed by the PGAs.



PGA Web Sites

The image displays four overlapping web browser windows, each showing a different genetic research website:

- PhysGen Homepage (http://pga.mcw.edu/):** Features a navigation menu with categories like Data, General Info, Tools, Support, Quick Links, and About. It lists various genomic resources such as Consomic, ENU Mutant, and Genotype.
- SeattleSNPs (http://pga.mbt.washington.edu/):** A "Variation Discovery Resource" with a search bar and sections for Home, Sequencing Resources, and Welcome to SeattleSNPs. It mentions funding from the National Heart Lung and Blood Institute's (NHLBI) Programs for Genomic Applications (PGA).
- BayGenomics Home Page (http://baygenomics.ucsf.edu/):** Features a central image of a mouse and a navigation menu including Overview, People, Data Access, Workshops, and What's new?. It displays a DNA sequence:


```

      GGACCCATAGATTACAGGATTAATAGGATATTAGATTAC
      GCAAATGGTAACAGAATACCAATTAGATTGAGATTACC
      TCATCAGGGTGGTGATGTAATGATAGGATAGGATTAG
      
```
- Berkeley PGA (http://pga.lbl.gov/):** A page from the National Heart Lung and Blood Institute's Programs for Genomic Applications. It includes a section titled "Do you need your BACs to be sequenced? Do you have clinical samples and need us?" and a "VISTA" section describing a suite of programs for genomic sequences.

NHLBI Resequencing and Genotyping Service

<http://rsng.nhlbi.nih.gov/scripts/index.cfm>

The screenshot shows a Mozilla Firefox browser window displaying the NHLBI Resequencing and Genotyping Service website. The browser's address bar shows the URL <http://rsng.nhlbi.nih.gov/scripts/index.cfm>. The website header includes the National Heart Lung and Blood Institute logo and the text "NHLBI Resequencing & Genotyping Service". A navigation menu contains links for Home, How to Apply, Resources & Links, FAQ, About Us, and Contact Us. The main content area features a "Register | Sign In" link, a "RS&G News" section with links to "Application Templates", "See Us at Upcoming Conferences", and "Spring Applications are Due on Tuesday, May 1, 2007", and an "Application Deadlines" section stating that applications are due May 1 and November 1 of each year through May 1, 2009. The "Selected RS&G Projects" section lists "Completed projects". A central text block explains that the NHLBI has funded the RS&G Service to provide DNA resequencing and genotyping services at no charge to qualifying investigators. It notes that the service only considers investigations using human DNA and that preference is given to researchers investigating the genetic components involved in the cause, variable outcome, and progression of heart, lung, blood, and sleep diseases and disorders. Interested investigators are directed to [apply through this Web site](#) for the service, which is provided free of charge to qualifying applicants. An "Application Information" section includes "Application Guidelines" (visit [Application Guidelines](#)), "How to Apply" (visit [How to Apply](#)), and contact information for issues related to the application process: nhlbi_rsng@nhlbi.nih.gov. The browser's status bar at the bottom shows "Done" and "National Heart, Lung, and Blood Institute".

NIH Knockout Mouse Project

<http://www.knockoutmouse.org/>



Knockout Mouse Project (KOMP)
Data Coordination Center

Search KOMP Gene List
Enter gene symbols (Use "*" for wildcards) or gene ID:
 Search
e.g., Adam9, Pax7, MG2, 81814

Browse KOMP Gene List by
[Gene Symbol](#) [Chromosome](#)

Hub [What is the KOMP Gene List?](#)

What is KOMP?

KOMP is a trans-NIH initiative to generate a public resource of mouse embryonic stem (ES) cells containing a null mutation in every gene in the mouse genome. Two groups have been funded by this program to generate knockout mouse lines: [Regeneron Pharmaceuticals, Inc.](#) and a collaborative team at the Children's Hospital Oakland Research Institute (CHORI), the University of California at Davis [School of Veterinary Medicine](#), and the Wellcome Trust [Sanger Institute](#). Groups at the [University of Pennsylvania](#), the [Samuel Lunenfeld Research Institute](#) of Mount Sinai Hospital, and at [Regeneron Pharmaceuticals, Inc.](#) have been funded to develop methods to improve the efficiency of creating knockout C57BL/6 ES cell lines.

For more details see [NIH KOMP Home Page](#).

Recent News

- [KOMP Gene List V0.7 is available](#) (16 May 2007)
- [KOMP Gene List V0.6 is available](#) (11 Apr 2007)
- [KOMP Gene List V0.5 is available](#) (20 Mar 2007)
- [Search or browse the KOMP Gene List](#) (13 Mar 2007)
- [KOMP Gene List V0.4 is available](#) (30 Jan 2007)
- [Commentary in Cell: A Mouse for All Reasons](#) (12 Jan 2007)
- [Call for KOMP Gene Nominations](#) (12 Jan 2007)
- [KOMP Initiative NIH Press Release](#) (7 Sept 2006)

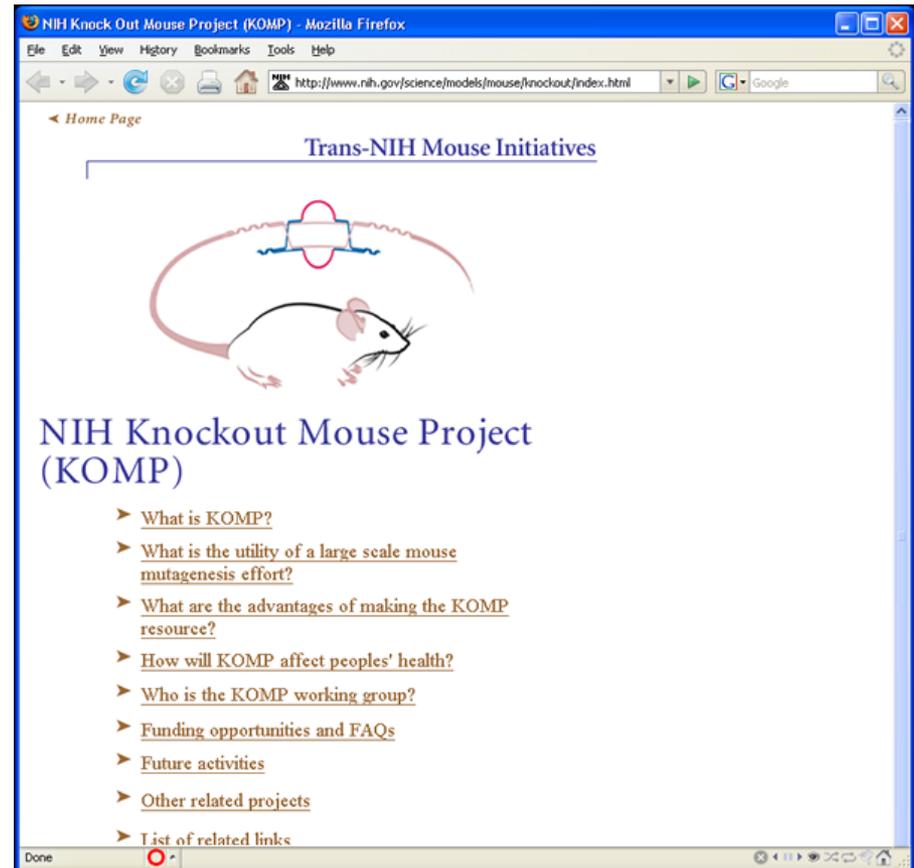
What is the KOMP Data Coordination Center (DCC)?

To support the mission of the KOMP initiative, the Data Coordination Center will

- serve as a central clearinghouse of information about the progress of the KOMP project.
- provide the scientific community with comprehensive information about all publicly available mouse knockout mutants.
- [More details.](#)

KOMP Resources and Information

- [KOMP Gene List](#)
- [Nominable genes](#) to be knocked out by the KOMP project.



NIH Knock Out Mouse Project (KOMP) - Mozilla Firefox

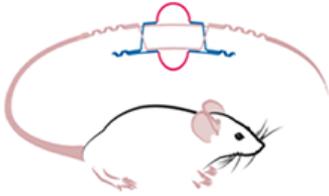
File Edit View History Bookmarks Tools Help

http://www.nih.gov/science/models/mouse/knockout/index.html

Google

Home Page

Trans-NIH Mouse Initiatives



NIH Knockout Mouse Project (KOMP)

- [What is KOMP?](#)
- [What is the utility of a large scale mouse mutagenesis effort?](#)
- [What are the advantages of making the KOMP resource?](#)
- [How will KOMP affect peoples' health?](#)
- [Who is the KOMP working group?](#)
- [Funding opportunities and FAQs](#)
- [Future activities](#)
- [Other related projects](#)
- [List of related links](#)

Done

<http://www.nih.gov/science/models/mouse/knockout/index.html>

Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases

- Evaluate the safety and efficiency of gene transfer strategies as they emerge
- Use established monkey models to explore fetal approaches for heart, lung, and blood diseases
- Provide NHLBI-funded investigators with essential expertise and resources - *annual call for proposals for studies with monkeys at no cost*

www.CFMGT.ucdavis.edu

(also linked from NHLBI web site:

www.nhlbi.nih.gov/resources/resources.htm)



Macaca mulatta image from Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases

NHLBI Proteomics Initiative

<http://www.nhlbi-proteomics.org/>

Login SEARCH GO

NHLBI PROTEOMICS

Home | The Centers | News & Events | Publications | Resources & Tools | Links | Contact Us

Discussions
NewsSpots
Help


National Heart Lung and Blood Institute


National Institutes of Health


Department of Health and Human Services

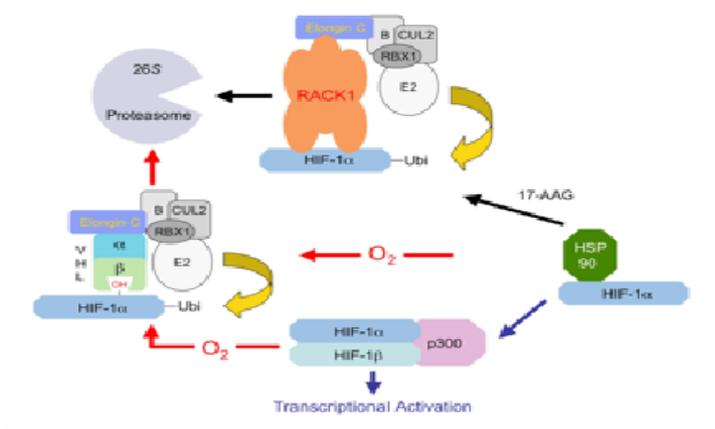
Welcome

The National Institute of Heart Lung and Blood has established a consortium of 10 highly interactive, multi-disciplinary Proteomic Centers to enhance and develop innovative proteomic technologies and apply them to relevant biological questions that will advance our knowledge of heart, lung, blood, and sleep health and disease.

This NHLBI Proteomics Initiative is intended to complement and enhance the NHLBI's ongoing research programs, which include a substantial investment in clinical research, genomic research, basic biology, technologies, and training and education programs.

"Visit the ProteomicsPortal!"

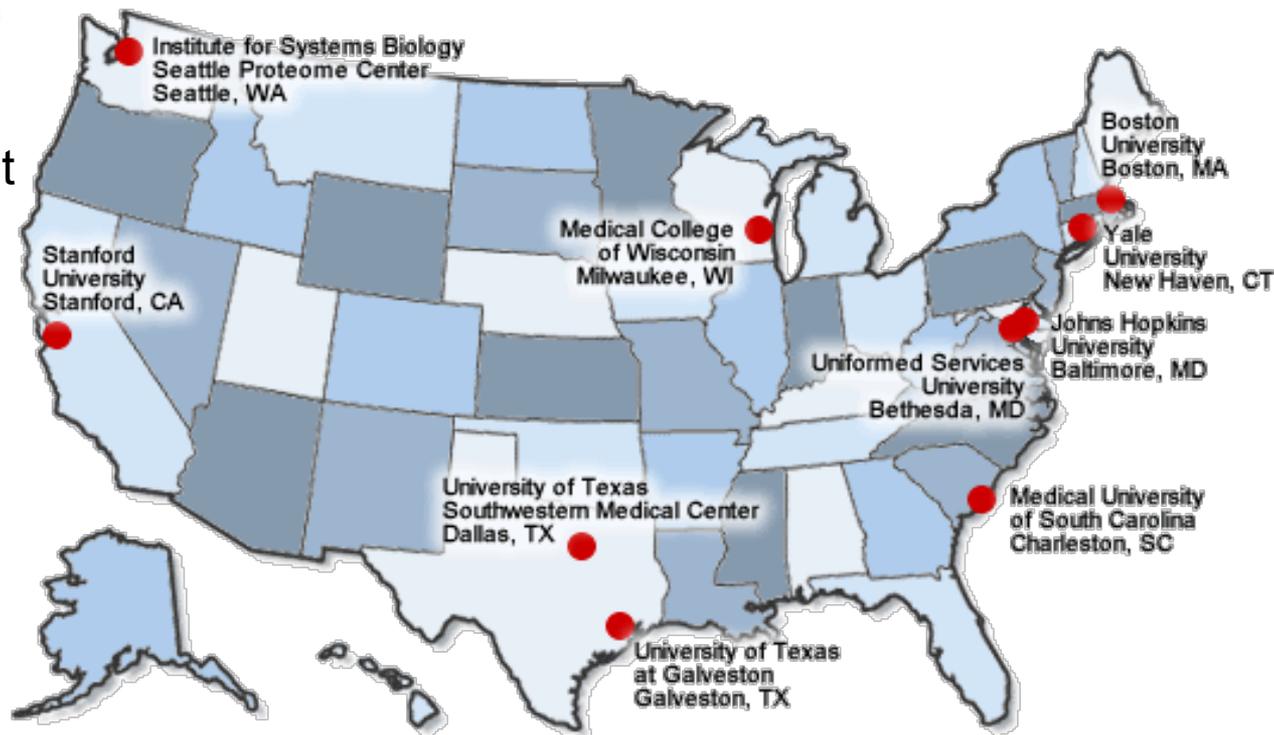
 Read about Dr. Semenza's lab at Johns Hopkins NHLBI Proteomics Center identifying role for RACK1 in oxygen-independent regulation of HIF-1 α [Spring 2007 NewsSpots](#)



The diagram illustrates the regulation of HIF-1 α by RACK1. In the presence of oxygen (O₂), HIF-1 α is ubiquitinated (Ubi) by a complex consisting of E2, RBX1, and CUL2, and is targeted to a 26S Proteasome for degradation. In the absence of oxygen, HIF-1 α forms a complex with HIF-1 β and p300, leading to transcriptional activation. HSP 90 is shown to stabilize HIF-1 α , and 17 β AAG is involved in the ubiquitination process.

NHLBI Proteomics Initiative

Highly interactive, multi-disciplinary Proteomic Centers to enhance and develop innovative proteomic technologies and apply them to relevant biological questions.



NHLBI Clinical Proteomics Program

Goals of the Clinical Proteomics Program

- Facilitate validation of protein panels that can be used to predict disease susceptibility
- To assist in differential diagnosis, disease staging, selection of individualized therapies, and monitoring of treatment responses
- To establish a high quality education and skills development program
- Design panels of candidate proteins for disease areas
- Develop high throughput analytic methodologies
- Assess predict value of proteomic measurements using biological and clinical information
- Establish procedures and standards for quality control

NHLBI Clinical PROTEOMICS Programs

- Home
- The Denver Children's Hospital Clinical Proteomics Program
- The Mayo Clinic Rochester
- Massachusetts General Hospital
- Vanderbilt University Medical Center
- Steering Committee
- Education

Home

The NHLBI Clinical Proteomics Programs were established in July, 2005 to promote systematic, comprehensive, large-scale validation of existing and new candidate protein markers that are appropriate for routine use in the diagnosis and management of heart, lung, blood, and sleep diseases. The goal of this program is to facilitate validation of protein panels that can be used to predict disease susceptibility, to assist in differential diagnosis, disease staging, selection of individualized therapies, and monitoring of treatment responses. An additional goal is to establish a high quality education and skills development program to encourage and ensure that scientists develop competencies and expertise needed to address the complex, multifaceted challenges in clinical proteomics.

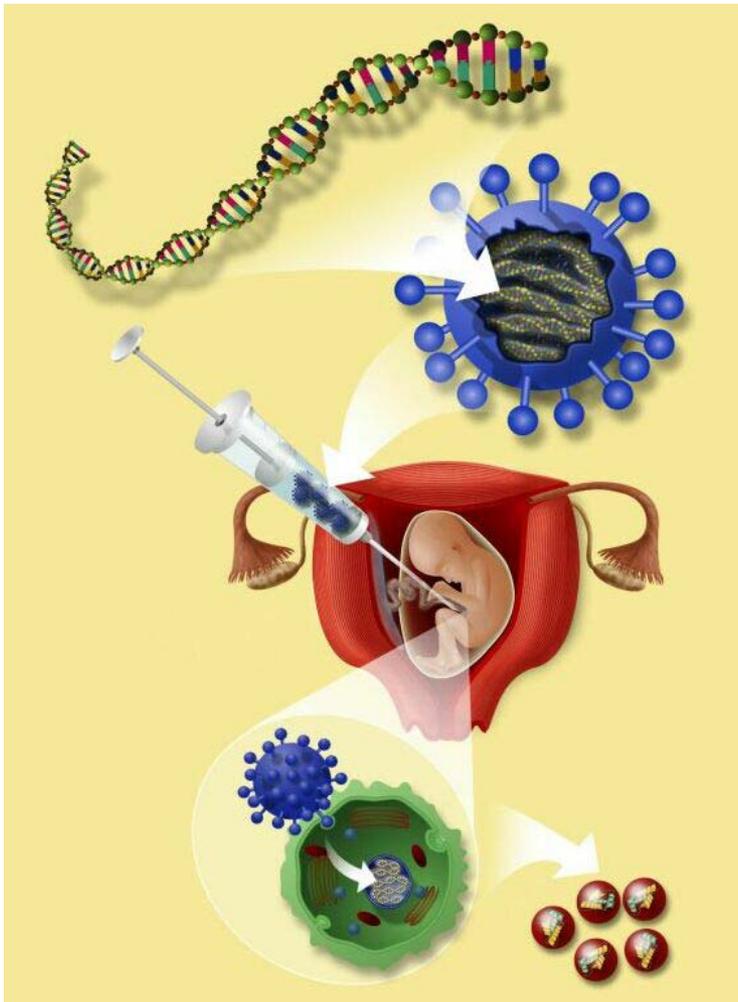
The specific goals of the Clinical Proteomics Program are to:

- (1) design panels of candidate proteins for disease areas,
- (2) develop high throughput analytic methods
- (3) assess the predictive value of these proteomic measurements using biological specimens and clinical data from existing study populations
- (4) establish procedures and standards for quality control.

Logos: NHLBI, Colorado University of Colorado at Boulder, MAYO CLINIC

<http://www.mc.vanderbilt.edu/root/vumc.php?site=proteomics>

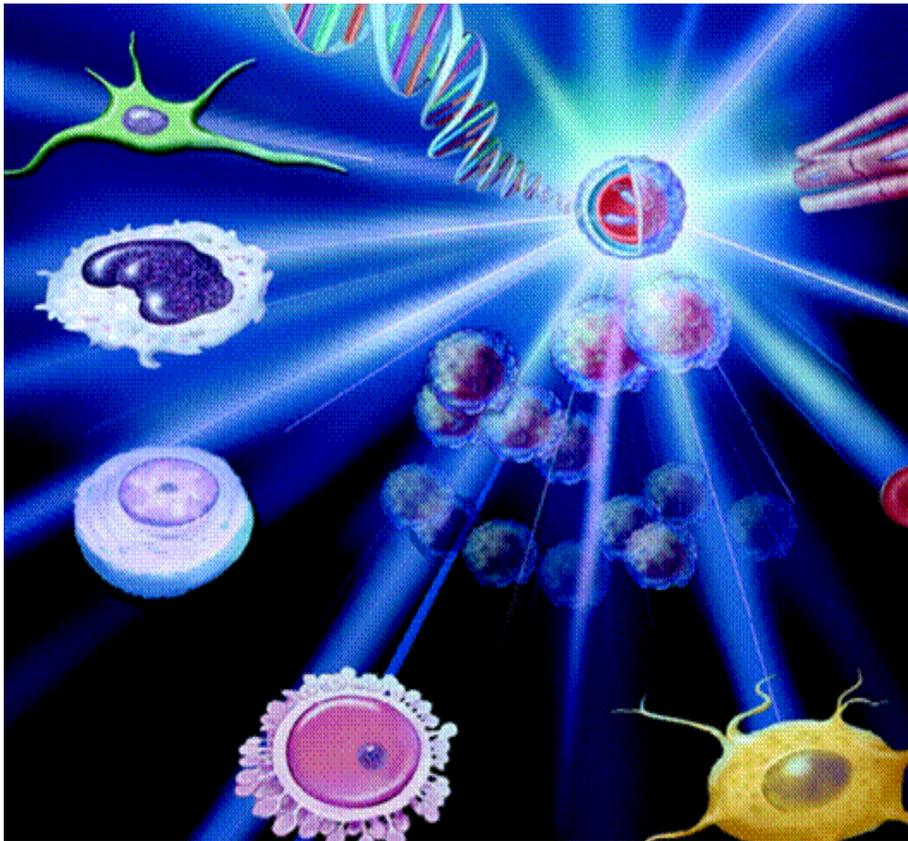
NHLBI Gene Therapy Resource Program (GTRP)



- Facilitate the translation of basic research in gene therapy to clinical application in heart, lung and blood diseases
- Provide the resources needed for gene therapy trials
- Provide support for gene therapy clinical protocols and assistance on regulatory issues

Gene Therapy image from Nikolaus Fiebiger Center of Molecular Medicine, University Erlangen-Nuernberg

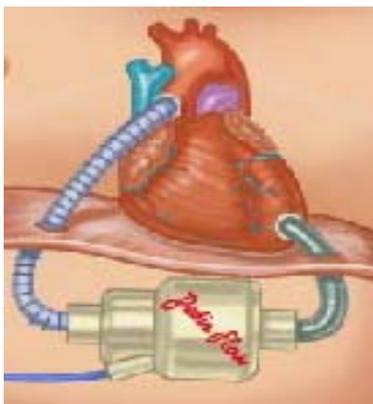
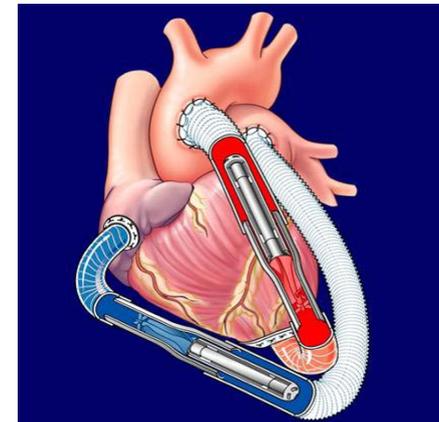
NHLBI Production Assistance for Cellular Therapies (PACT)



- Manufacture a clinical grade product for PIs lacking a cGMP facility
- Work closely with FDA to facilitate translation to clinical studies
- Three Cell Processing Centers:
 - Baylor College of Medicine
 - University of Minnesota
 - University of Pittsburgh
- Application and Information at: <http://www.pactgroup.net/>

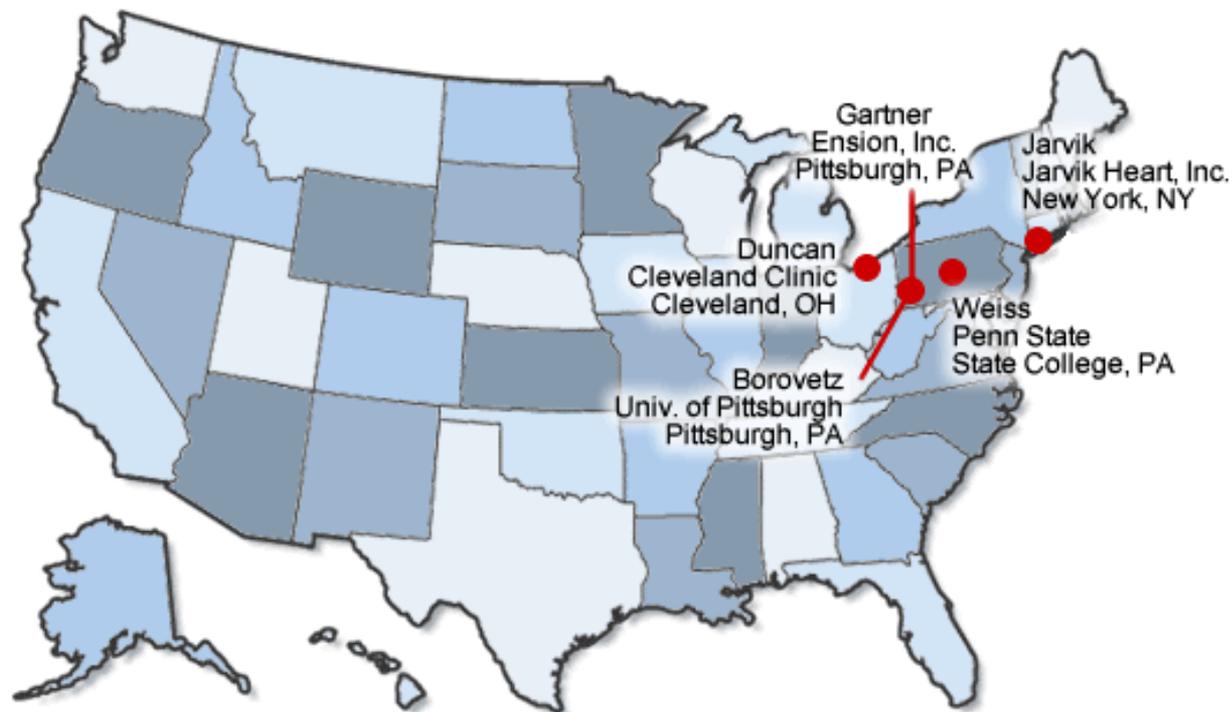
The NHLBI Pediatric Circulatory Support Program

The goal of the Pediatric Circulatory Support program is to develop novel circulatory assist devices or other bioengineered systems for infants and children with congenital and acquired cardiovascular disease who experience cardiopulmonary failure and circulatory collapse.

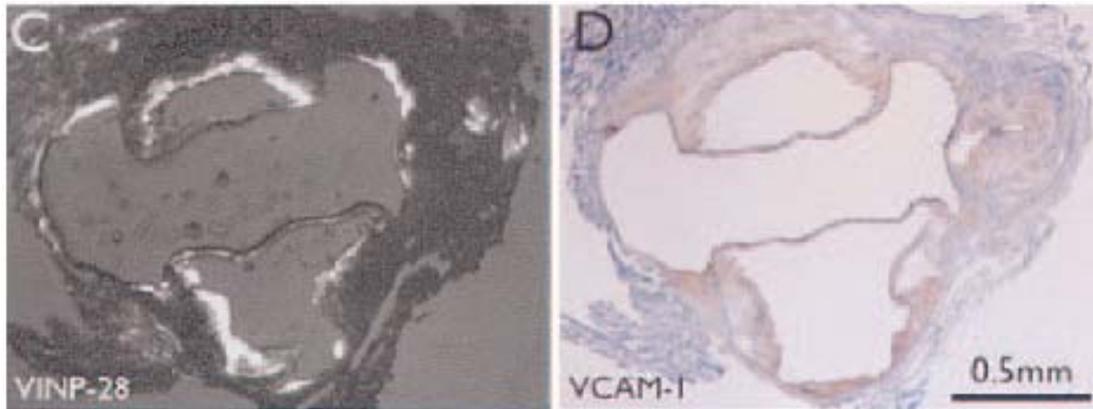


NHLBI Pediatric Circulatory Support Program

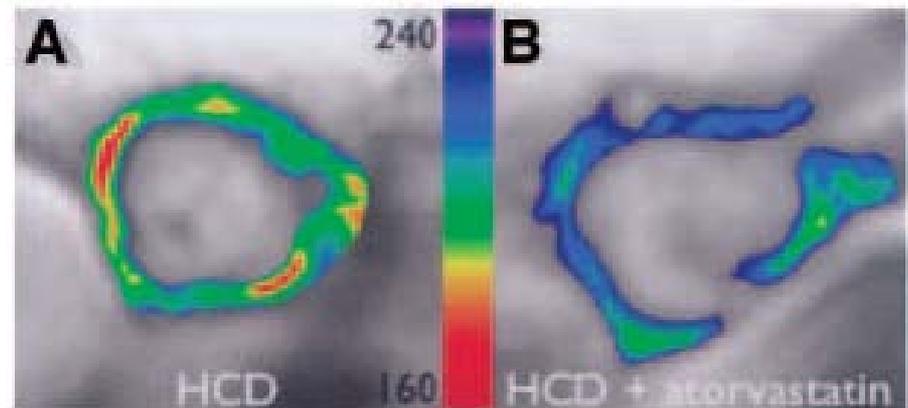
The goal of the Pediatric Circulatory Support program is to develop novel circulatory assist devices or other bioengineered systems for infants and children with congenital and acquired cardiovascular disease who experience cardiopulmonary failure and circulatory collapse.



Imaging Plaque Using Nanotechnology



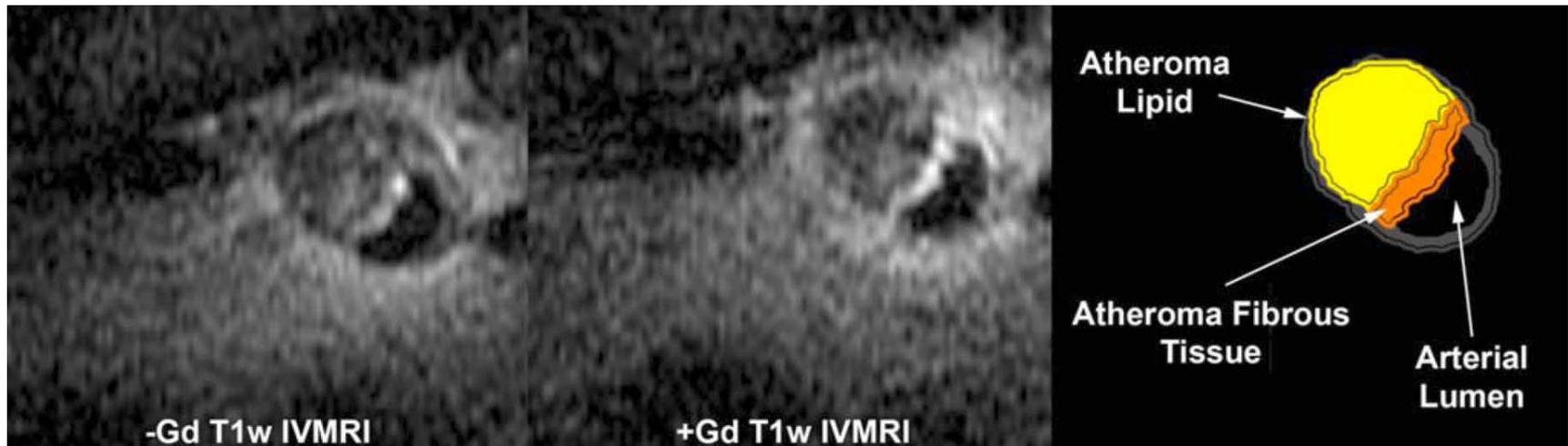
Target validation



Plaque regression in vivo

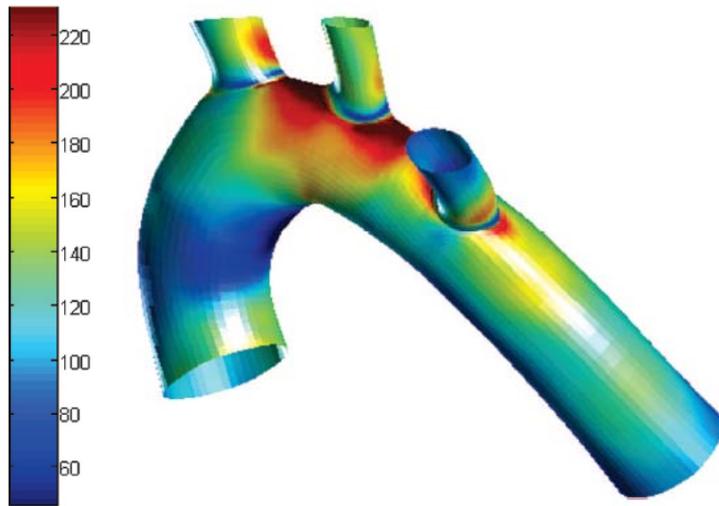
Circulation 114:1504, 2006 Nahrendorf et al

Improved Characterization of Atherosclerotic Plaques during Intravascular Magnetic Resonance Imaging of Human Arteries

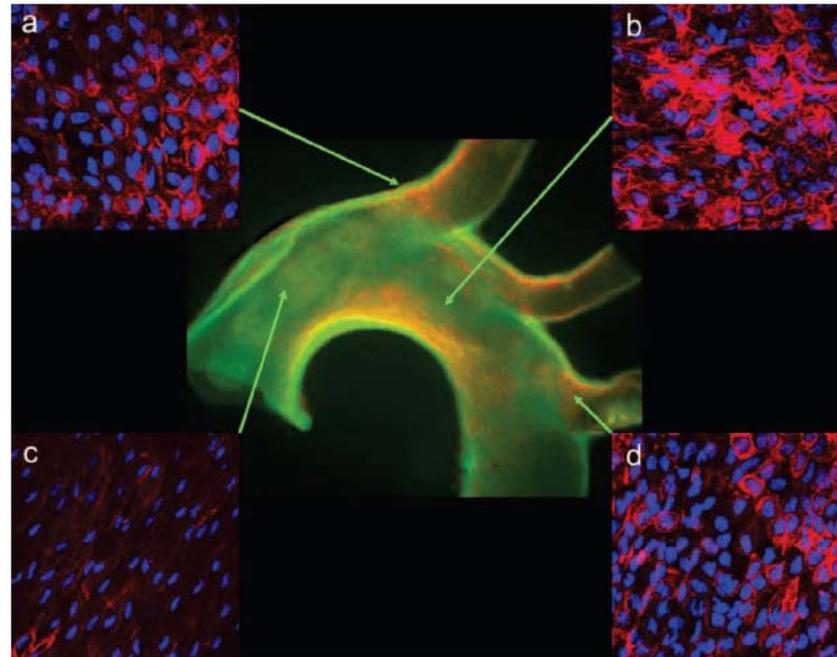


Developments of tools to reliably diagnose high risk atherosclerotic plaques that may cause clinical events at an early stage are critical. A multidisciplinary approach that combines state-of-the-art imaging technologies with a fundamental understanding of the cellular and molecular architecture of animal and human atherosclerotic plaques was used to detect and provide information on plaque pathology and the nature of its content. For the first time, high resolution imaging of atherosclerotic plaque components using intravascular magnetic resonance imaging (IVMRI) has been accomplished in humans. Improvement is shown in the next slide.

Shear Stress and Atherogenesis



Wall shear stress



Pro-atherogenic marker expression

Arterioscler Thromb Vasc Biol 2006 27:346 Suo et al

Marfan Syndrome: Bedside to Bench



A mouse engineered to harbor a Marfan-associated mutation in the fibrillin-1 gene recapitulates the human phenotype

	Bone Overgrowth	Emphysema	MVP	Myopathy	Aneurysm
Nml					
MFS					

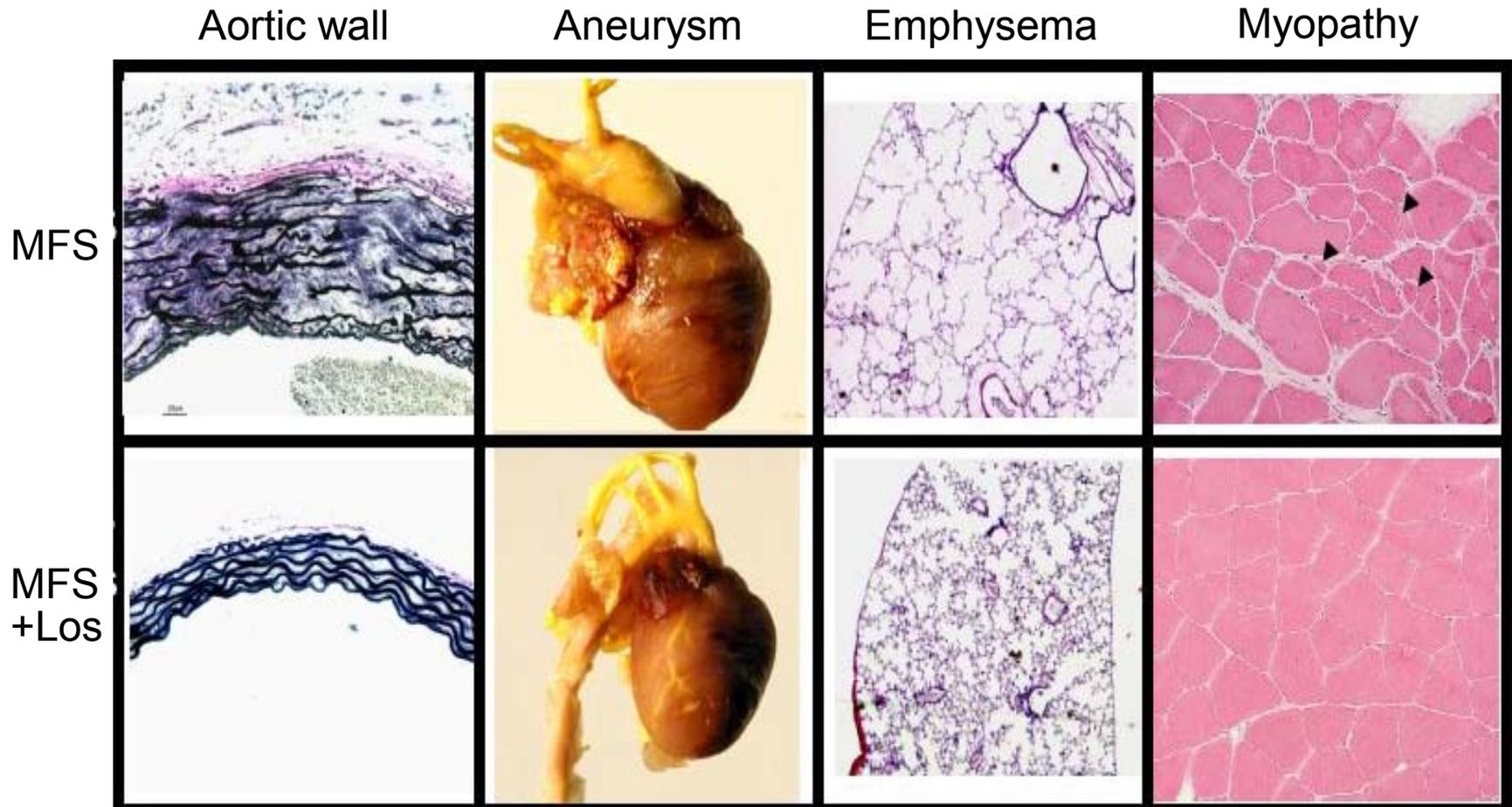
Neptune...and Dietz, *Nature Genetics*, 2003

Judge...and Dietz, *JCI*, 2004

Habashi...and Dietz, *Science*, 2006

Cohn...and Dietz, *Nature Medicine*, 2007

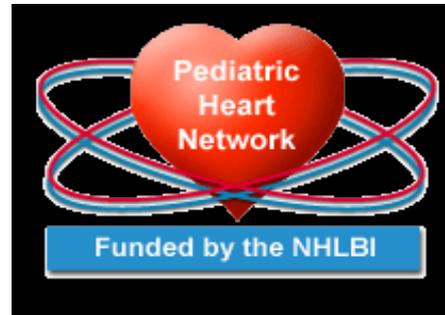
Losartan Prevents Aortic Aneurysm and Attenuates Other Phenotypes in a Mouse Model of Marfan Syndrome



Habashi...and Dietz, *Science*, 2006
Cohn...and Dietz, *Nature Medicine*, 2007

Marfan Syndrome: Bench to Bedside

- Pilot data in two children showed dramatic arrest of aortic root growth with Losartan
- NHLBI able to take advantage of Pediatric Heart Network (www.PediatricHeartNetwork.com)
- Randomized trial of losartan vs. atenolol in 600 patients 6 mos – 25 years old launched February 2007
- Reinventing the clinical research enterprise: unique partnership with National Marfan Foundation, FDA's Orphan Drug Program, Merck, Novopharm
- Unique opportunity for pediatric translational research



The Extended Opportunity...

The TGF β Arteriopathies

Loeys-Dietz Syndrome

Loeys...and Dietz, *Nature Genetics*, 2005
Loeys...and Dietz, *NEJM*, 2006

Arterial Tortuosity Syndrome

Coucke et al, *Nature Genetics*, 2006

Cutis Laxa

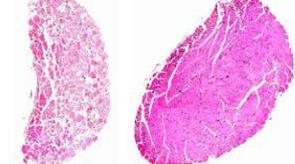
Huchtagowder et al., *AJHG*, 2006
Hanada et al., *Circ Res*, 2007

Vascular Ehlers-Danlos Syndrome

Loeys...and Dietz, *NEJM*, 2006
Cooper...and Dietz (unpublished)

Duchenne Muscular Dystrophy

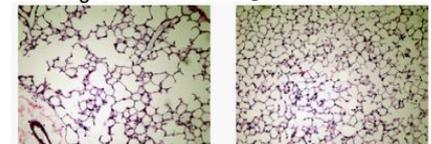
DMD DMD +losartan



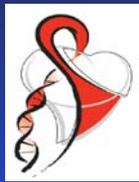
Cohn...and Dietz, *Nature Medicine*, 2007

Smoking-induced Emphysema

Cig Smoke Cig Smoke + losartan



Neptune...and Dietz, unpublished



National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Associated Cardiovascular Conditions

- *To facilitate research to improve diagnosis and management of genetically induced thoracic aortic aneurysms*
- *Includes syndromes such as Marfan, Ehlers-Danlos, Loeys-Dietz, and Turner Syndromes*
- *Will collect genetic and medical data, biospecimens, and DNA*
- *Will make data, biospecimens, and DNA available to investigators for research*

Basic and Translational Research in Peripheral Arterial Disease (PAD)

Pathophysiology--genetic determinants, biomarkers, roles of inflammation, insulin resistance, and endothelial dysfunction.

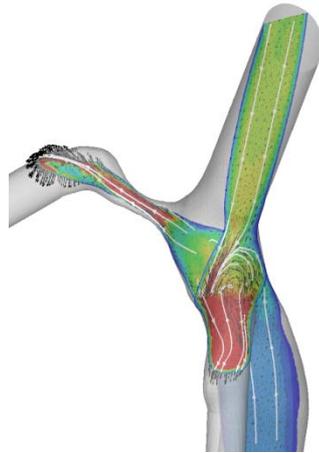
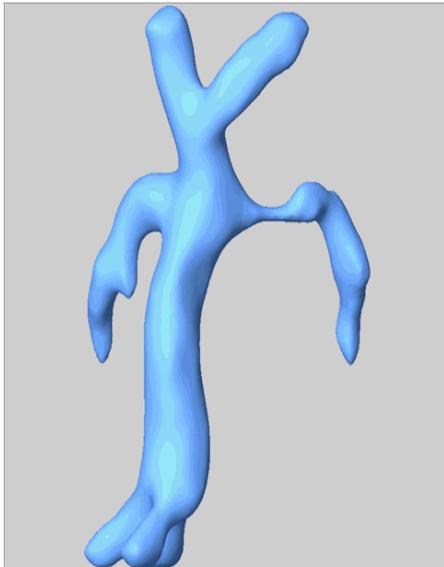
Clinical studies--of exercise, endovascular intervention and lipid modification in PAD. Endpoints range from functional activity level to volume of arterial atherosclerotic plaque burden.

Imaging--development of noninvasive Magnetic Resonance, Intravascular Ultrasound, and hyperspectral technologies for diagnostic and serial follow-up applications in PAD.

Personalized Medicine for HLBS

Total Cavopulmonary Connection Flow With Functional Left Pulmonary Artery Stenosis Angioplasty and Fenestration In Vitro

Kerem Pekkan, PhD; Hiroumi D. Kitajima, MSc; Diane de Zelicourt, MSc; Joseph M. Forbess, MD; W. James Parks, MD; Mark A. Fogel, MD; Shiva Sharma, MD; Kirk R. Kanter, MD; David Frakes, PhD; Ajit P. Yoganathan, PhD



Yoganathan and colleagues

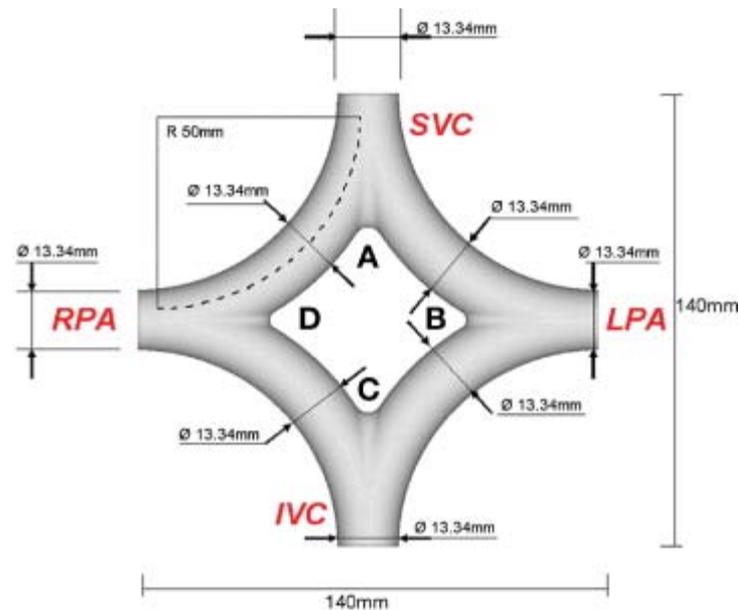
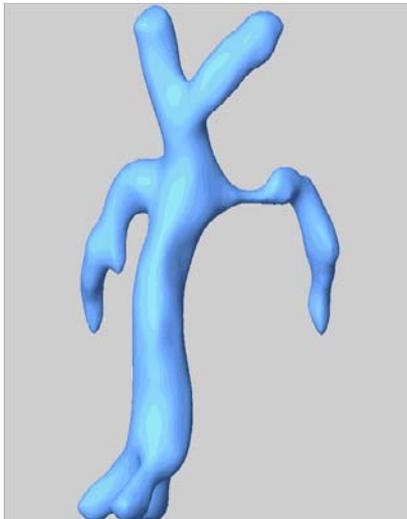
- Use MRI to define total cavopulmonary connection (TCPC) anatomy in individual patients
- Use computational fluid dynamics to evaluate and predict resulting flow
- Goal of individualized surgical planning

Generalized Medicine for HLBS

Introduction of a New Optimized Total Cavopulmonary Connection

Dennis D. Soerensen, MS, Kerem Pekkan, PhD, Diane de Zelicourt, MS, Shiva Sharma, MD, Kirk Kanter, MD, Mark Fogel, MD, and Ajit P. Yoganathan, PhD

Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, Georgia; Carnegie Mellon University, Pittsburgh, Pennsylvania; Pediatric Cardiology Associates, Department of Surgery, Emory University, Atlanta, Georgia; and Division of Cardiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania



Yoganathan and colleagues

The individualized studies suggest a new design for the total cavopulmonary connection (TCPC)

Improve understanding of the molecular and physiologic basis of health and disease:

Form → Function → Cause

- Using new molecular and genetic approaches, the cause of high cholesterol levels in hypercholesterolemics was discovered as due to defects in the LDL receptor gene responsible for clearing cholesterol from plasma
- The extensive basic science knowledge gained led to the discovery of “statins” which inhibits the activity of a key enzyme in the biosynthetic pathway of cholesterol, and to the discovery of Ezetimibe that acts via a complementary pathway to statins.
- Molecular genetic studies in humans identified a proprotein (PCSK9) that reduces the number of LDL receptors (LDLR) and lowered risk of developing atherosclerosis in affected individuals.
- PCSK9 could be considered as a biological marker that can regulate the levels of LDL receptors.
- Targeting PCSK9 in the bloodstream has the potential to control plasma cholesterol levels and could be explored for the treatment of hypercholesterolemia.

NHLBI Strategic Plan Goals

Goal 1

Improve understanding of the molecular and physiologic basis of health and disease. Use that understanding to develop improved approaches to disease prevention, diagnosis and treatment. *Form* → *Function*

Goal 2

To develop personalized preventive and therapeutic regimens for cardiovascular, lung, and blood diseases. *Function* → *Cause*

Goal 3

Generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery. *Cause* → *Cures*

NHLBI GWAS Related Programs

- SNP Health Association Resource (**SHARe**)
- Candidate Gene Association Resource (**CARE**)
- SNP Typing for Association with Multiple Phenotypes from Existing Epidemiologic Data (**STAMPEED**)
- Enhancing Development of Genome-wide Association Methods (**ENDGAME**)
- Genetic Analysis Information Network (**GAIN**)

NHLBI Genome Wide Association Studies (GWAS): Driving Principle

The greatest public benefit will be realized if data from GWAS are made available, under terms and conditions consistent with the informed consent provided by individual participants, in a timely manner to the largest possible number of investigators.

NCBI My NCBI
Welcome mmailman. [Sign Out](#)

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search **WGA** for all[sb] Go Clear [Save Search](#)

Limits Preview/Index History Clipboard Details

Display Browse studies Show 20 Send to

All: 5941

Browse WGA

By Studies **By Diseases** Advanced Search

Disease	Studies	Variables	Documents	Participants	Type of Study	Status
macular degeneration	1	-	-	-		
Age-Related Eye Disease Study (AREDS)	-	182	23	600	case-control	

NCBI My NCBI
Welcome mmailman. [Sign Out](#)

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search **WGA** for all[sb] Go Clear [Save Search](#)

Limits Preview/Index History Clipboard Details

Display Browse studies Show 20 Send to

All: 5941

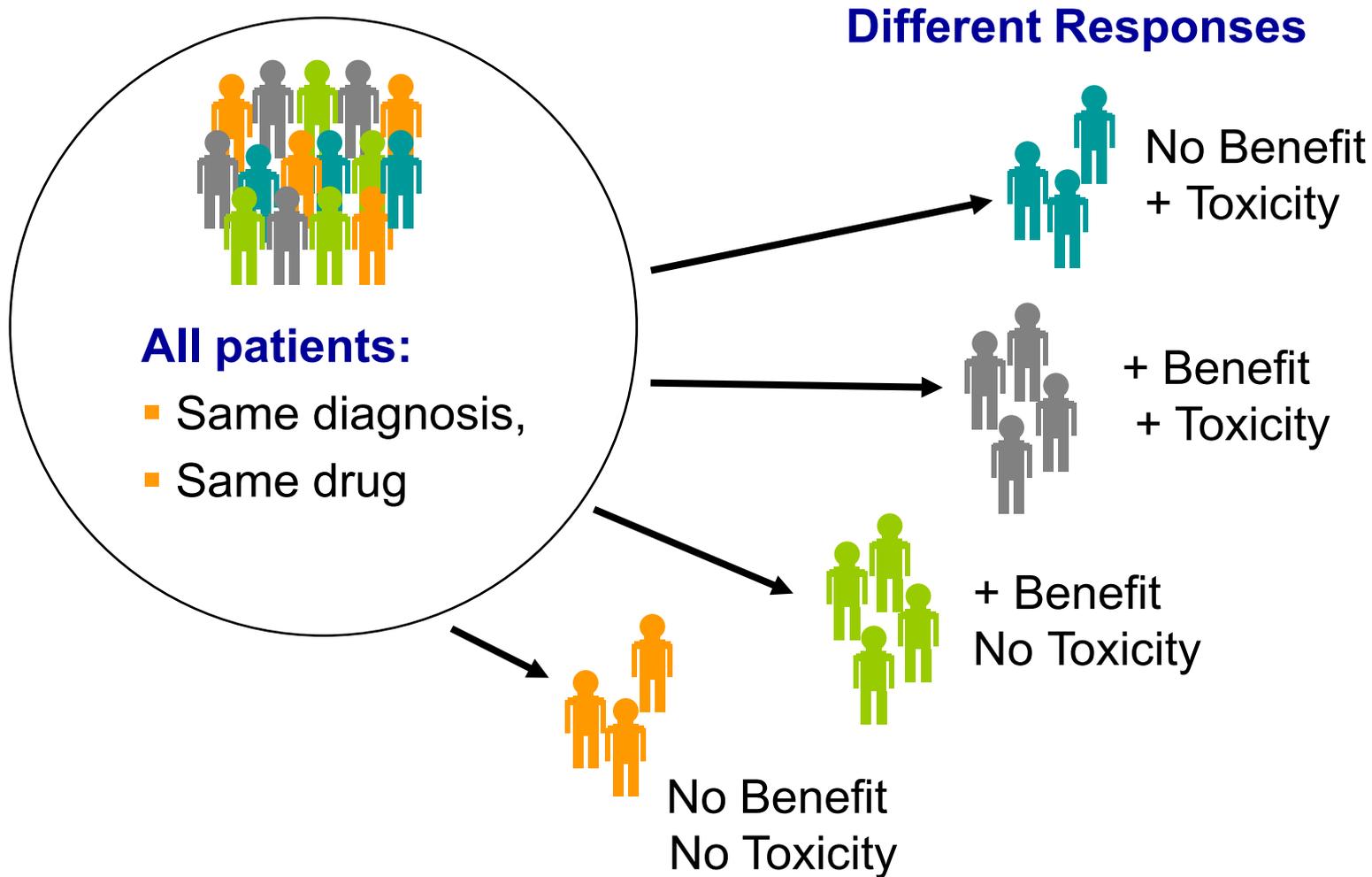
Browse WGA

By Studies By Diseases Advanced Search

Study	Sub-Studies	Variables	Documents	Participants	Type of Study	Status
Age-Related Eye Disease Study (AREDS)	-	182	23	600	case-control	
NINDS Parkinsonism Study	2	100	-	2573		
NINDS Parkinsonism Study - Cases	-	40	-	1498		
NINDS Parkinsonism Study - Controls	-	60	-	1075		

Display Browse studies Show 20 Send to

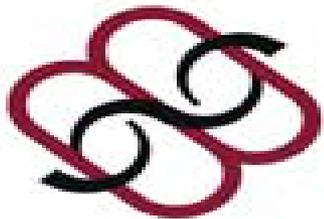
Variations in Drug Response



Pharmacogenetics and Gene-Environment Interactions

NHLBI Ancillary Pharmacogenetic Studies

<https://www.pharmgkb.org/views/loadNhlbiMembers.action>



PGRN

Pharmacogenetics Research Network

<http://www.nigms.nih.gov/pharmacogenetics>

PROGENI Network

NHLBI GxE Interaction Studies

<http://www.biostat.wustl.edu/progeni/>

Randomized Trial of Genotype-Guided Dosing of Warfarin Therapy

Large, multicenter, double-blind, randomized trial comparing three possible approaches to guiding warfarin therapy initiation:

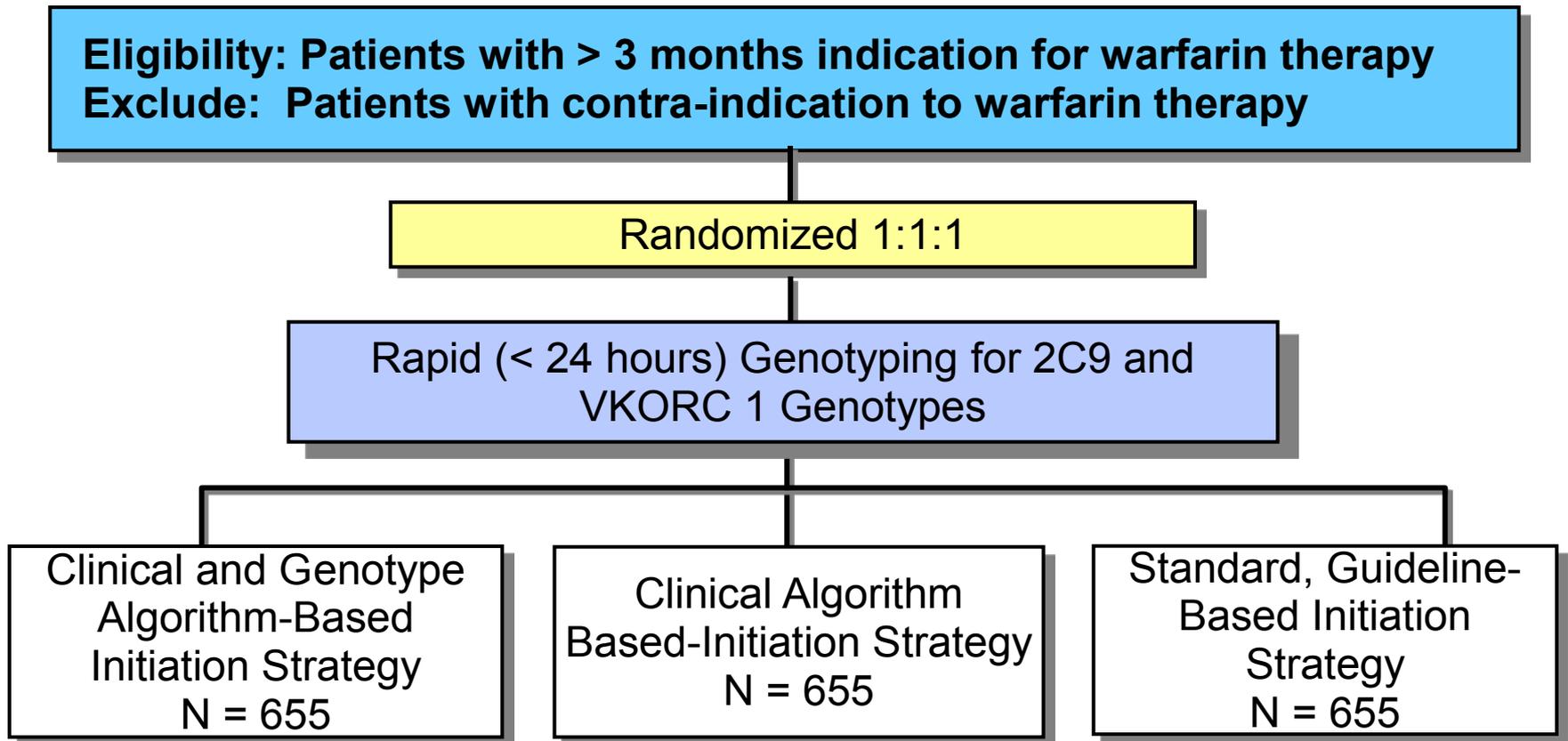
- initiation of warfarin therapy based on an algorithm using clinical information and the individual's genotype relative to two genes known to influence warfarin metabolism (CYP2C9 and VKORC1 genes)
- initiation of warfarin therapy based on an algorithm using only clinical information
- standard, guideline-based initiation strategy

NHLBI-HV-08-03

Response Date: June 20, 2007

<http://www.fbo.gov/spg/HHS/NIH/NHLBI/NHLBI%2DHV%2D08%2D03/listing.html>

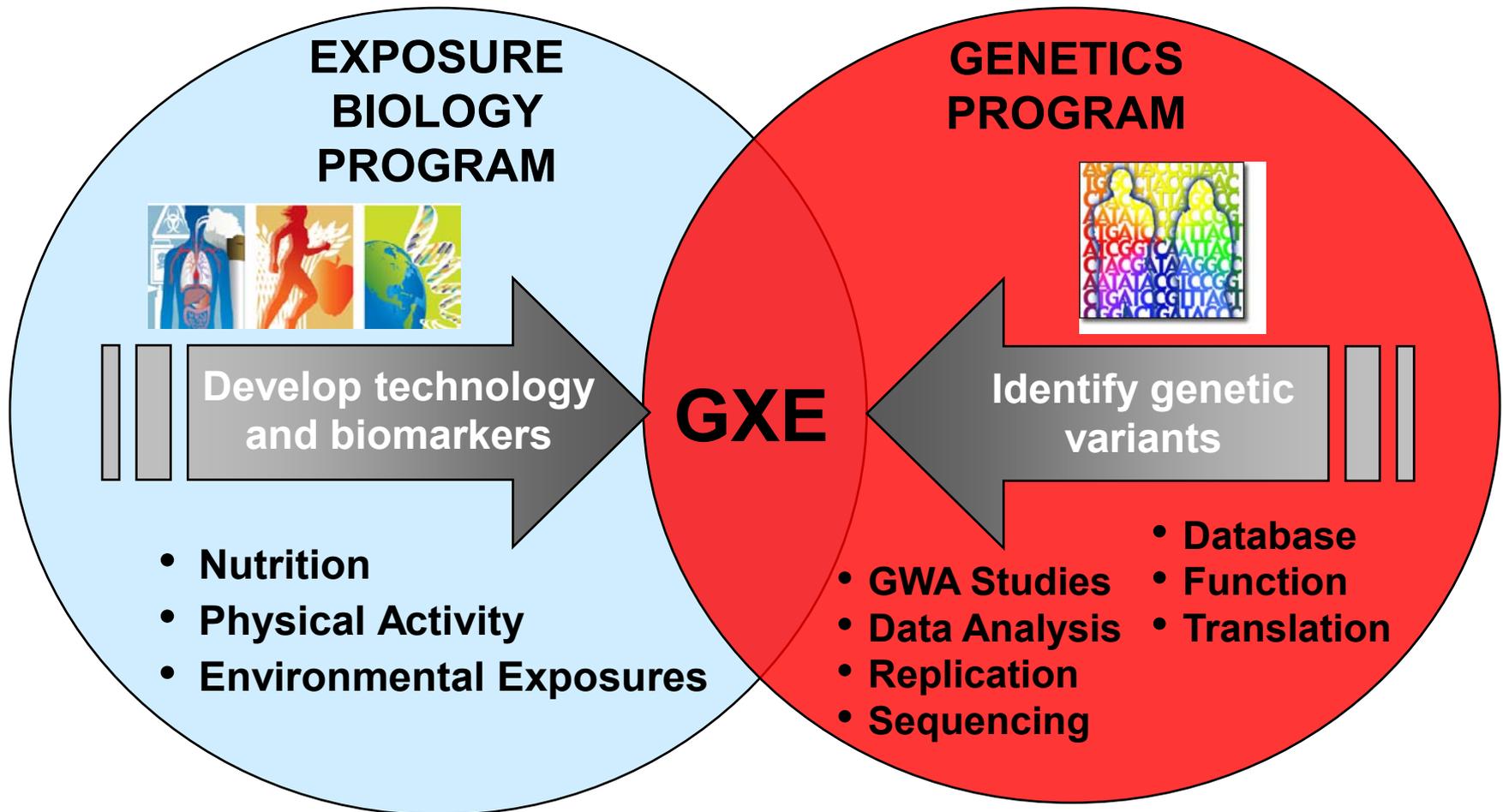
Randomized Trial of Genotype-Guided Dosing of Warfarin Therapy *Draft Flowchart*



Subsequent doses adjustments based on INR response to the initial doses with dosage increments or decrements relative to first dose following a standardized protocol

Genes and Environment Initiative

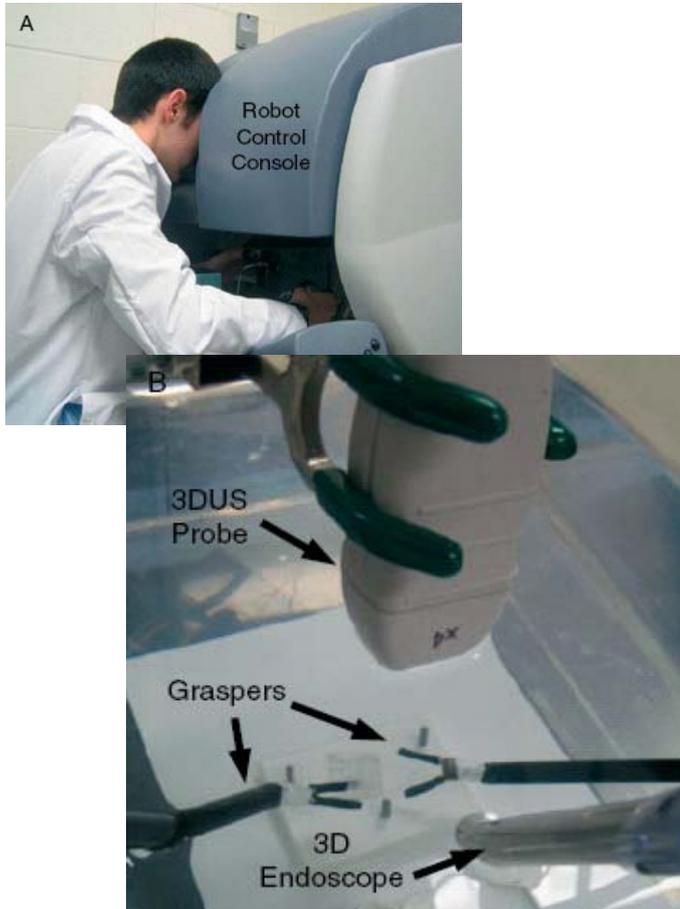
<http://genesandenvironment.nih.gov/>



Improvements in Image-Guided Surgery

3D ultrasound in robotic surgery: performance evaluation with stereo displays

Paul M. Novotny¹
Stephen K. Jacobsen¹
Nikolay V. Vasilyev²
Daniel T. Kettler¹
Ivan S. Salgo³
Pierre E. Dupont⁴
Pedro J. Del Nido²
Robert D. Howe¹



Del Nido and colleagues

Improved techniques in image-guided surgery reduce collateral trauma and enable earlier intervention before symptoms become established.

Improvements in Image-Guided Surgery

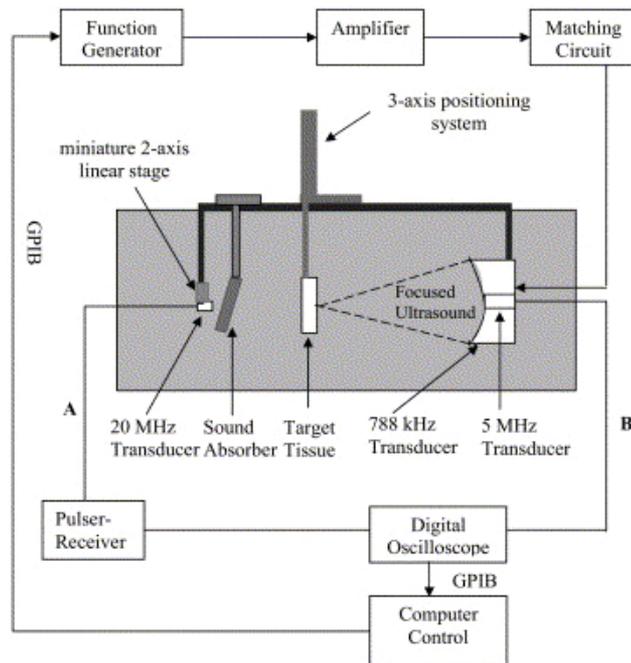
(continued)

Investigation of Intensity Thresholds for Ultrasound Tissue Erosion

Zhen Xu,* J. Brian Fowlkes,**† Achi Ludomirsky,‡ and Charles A. Cain*

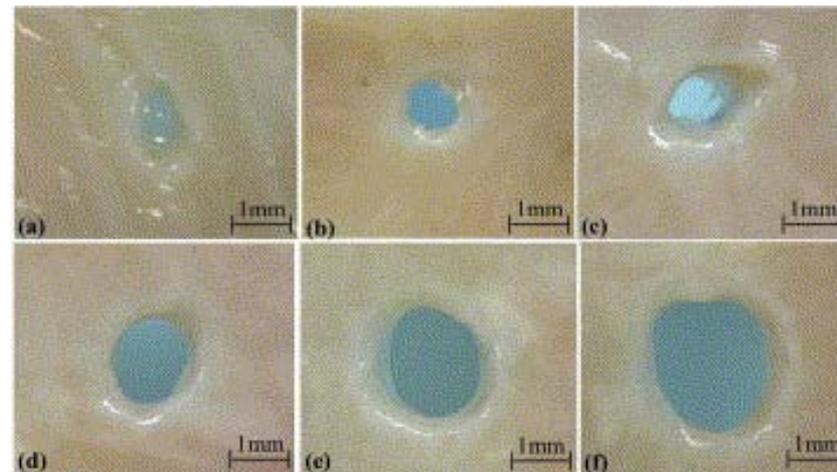
*Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, USA;

†Department of Radiology, University of Michigan, Ann Arbor, MI, USA; ‡Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, USA

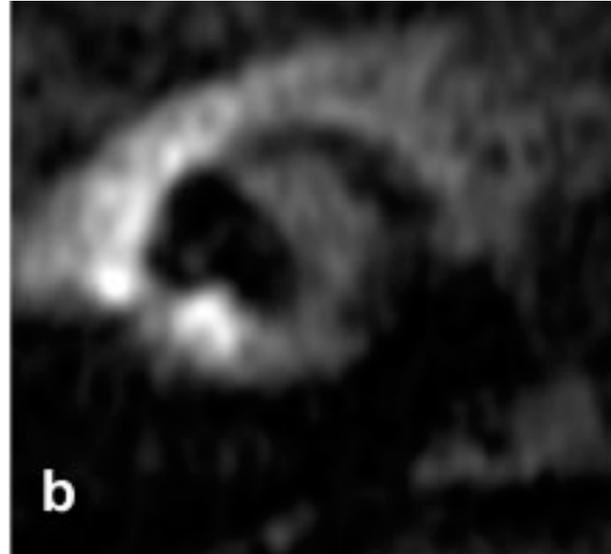


Cain and colleagues

Image-guided surgery can be performed using ultrasound directly to create tissue perforations, thus bypassing the need for even minimally-invasive surgical procedures.



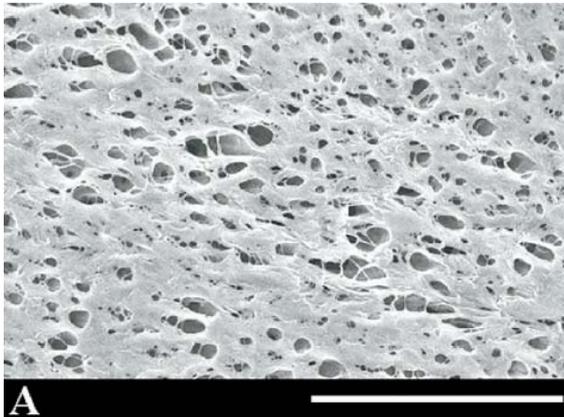
Generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery. Cause → Cures



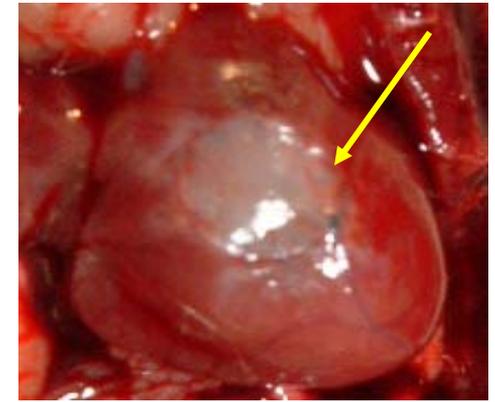
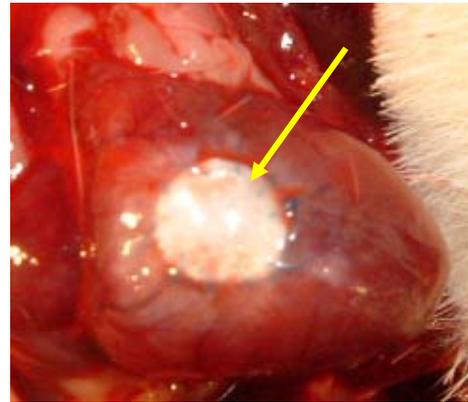
Intravascular magnetic resonance imaging (IVMRI) permitted the characterization of the fine structure and composition of arteries in the legs (iliac arteries) of human subjects. The individual components of the plaques were identified with adequate sensitivity and specificity to the extent that when a contrasting agent was used, the microvascular density and capillary permeability relative to surrounding tissues could be detected.

This represents an important advance in the field of atherosclerosis, with both clinical and research implications particularly for the assessment of plaque-stabilizing therapies and ultimately for reducing cardiovascular events.

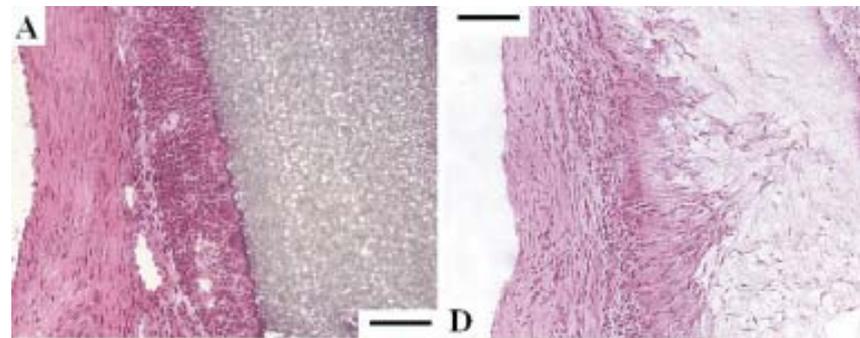
Patch Replacement of Heart Muscle



PEUU scaffold



RVOT repair with PTFE or PEUU



Integration of tissue with PEUU

Ann Thorac Surg 83:648, 2007 Fujimoto et al

Thoracic Aortic Aneurysms Bedside to Bench

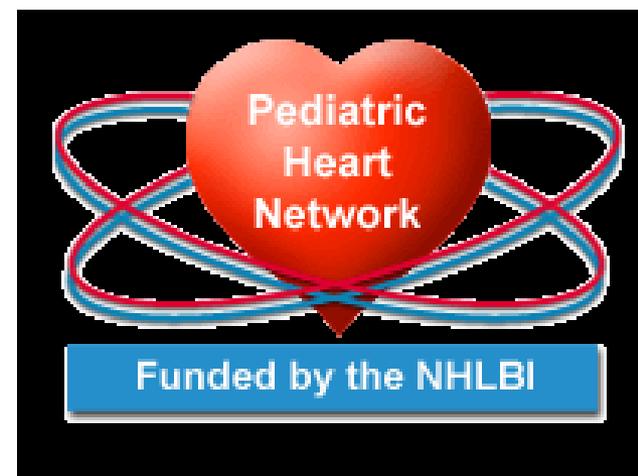


GenTAC

National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Associated Cardiovascular Conditions

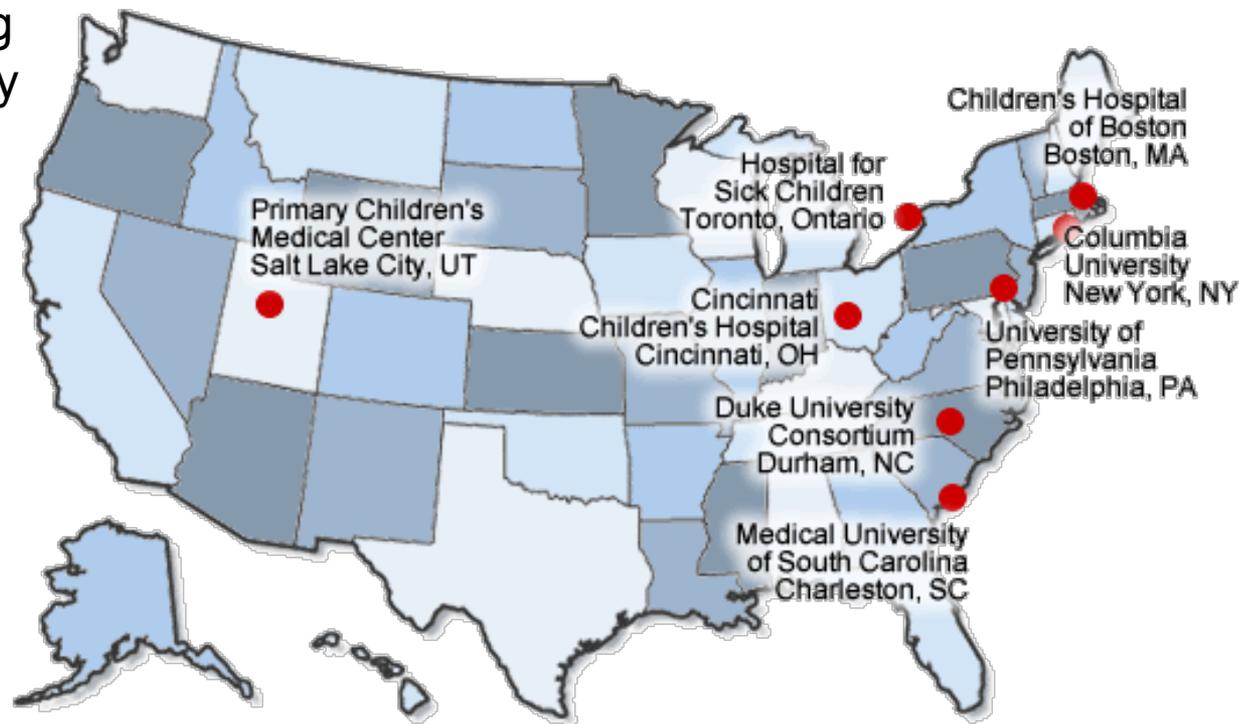
- *To facilitate research to improve diagnosis and management of genetically induced thoracic aortic aneurysms*
- *Includes syndromes such as Marfan, Ehlers-Danlos, Loeys-Dietz, and Turner Syndromes*
- *Will collect genetic and medical data, biospecimens, and DNA*
- *Will make data, biospecimens, and DNA available to investigators for research*

DCVD Clinical Research Networks Excel in Translational Research



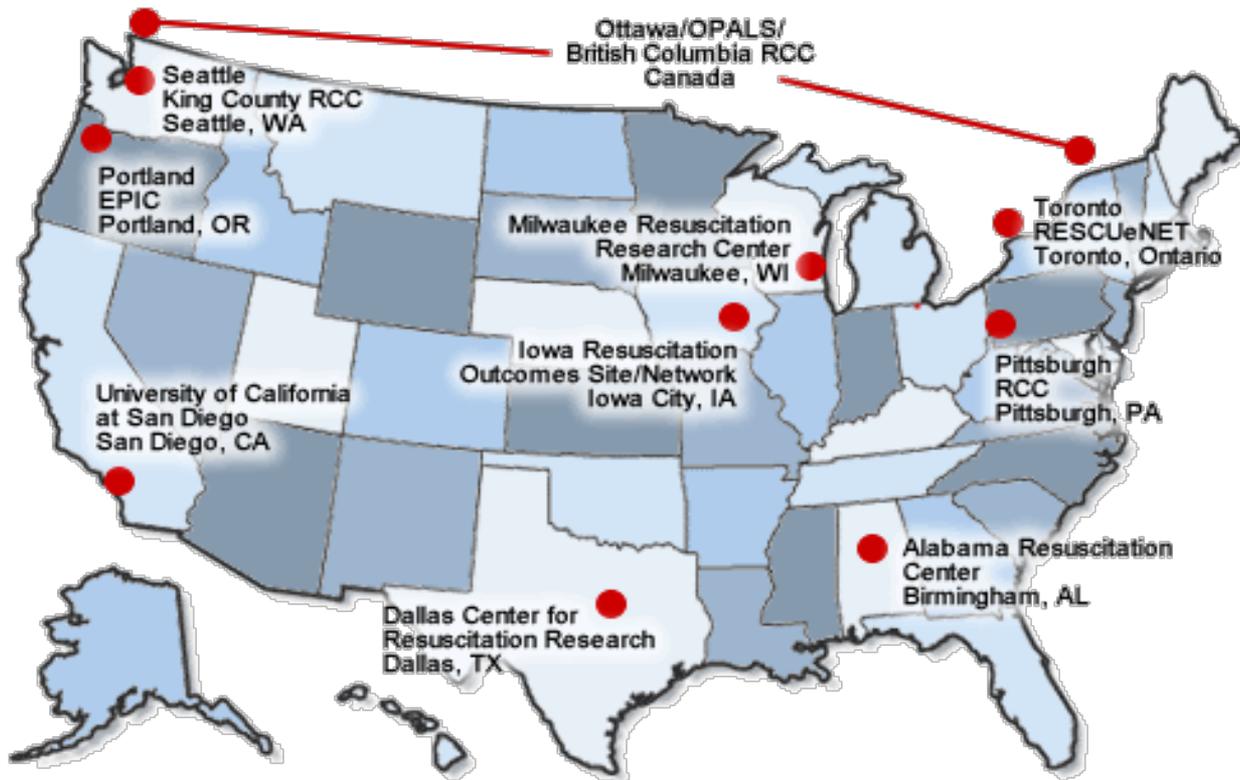
Pediatric Heart Network

To help parents, patients, and healthcare professionals consider many aspects of joining a pediatric clinical study



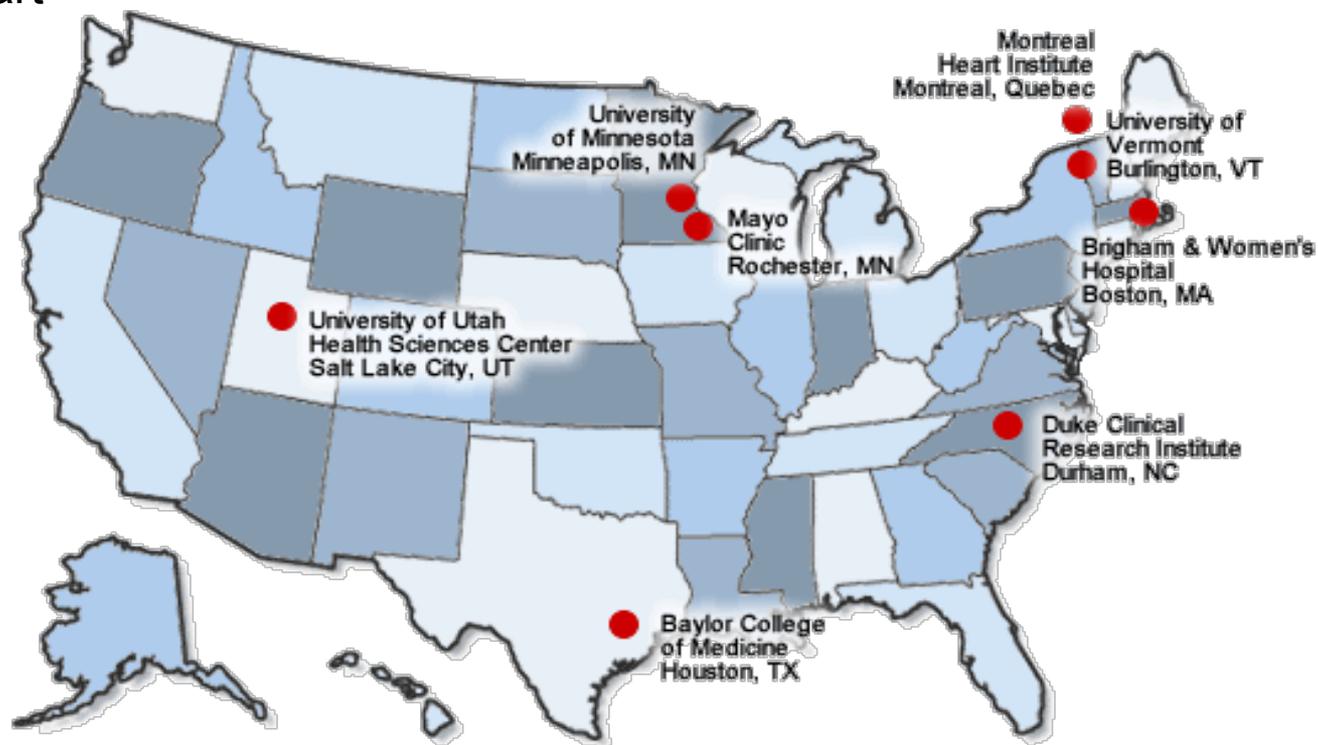
Resuscitation Outcomes Consortium

To conduct clinical research
in out-of-hospital
cardiopulmonary arrest &
life-threatening trauma



Heart Failure Research Network

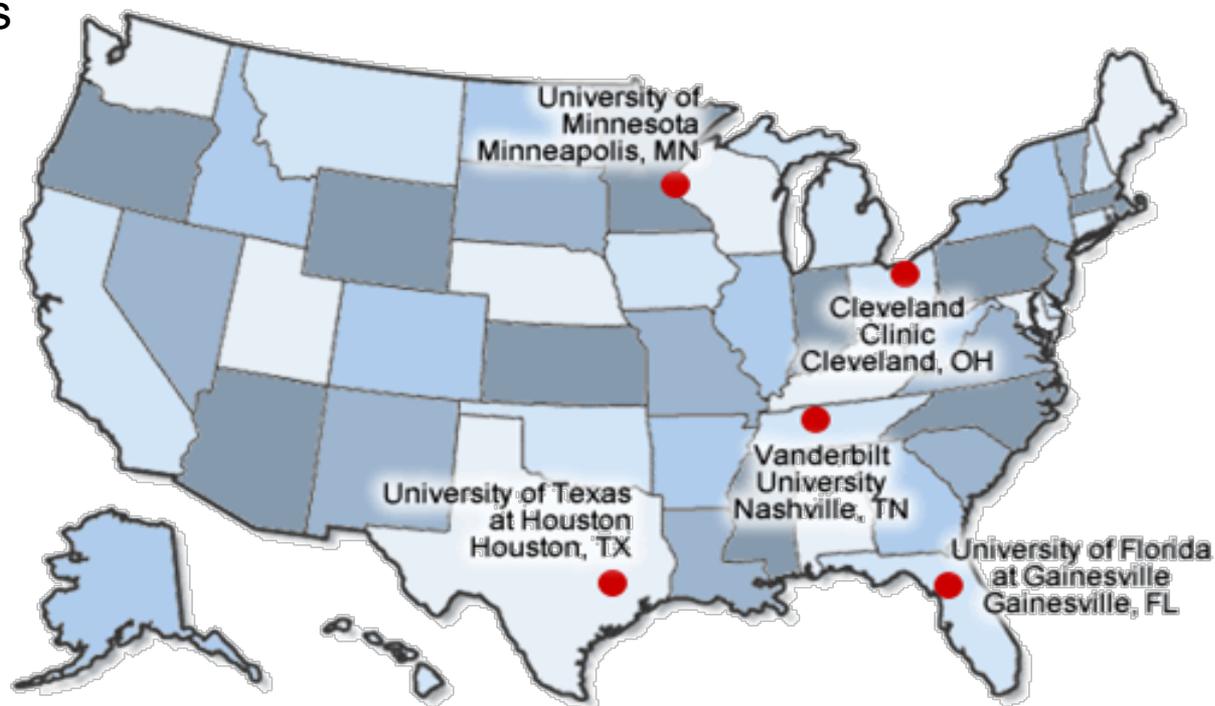
To expedite clinical research to evaluate the diagnosis, management, and treatment of heart failure



**HEART
FAILURE** NETWORK

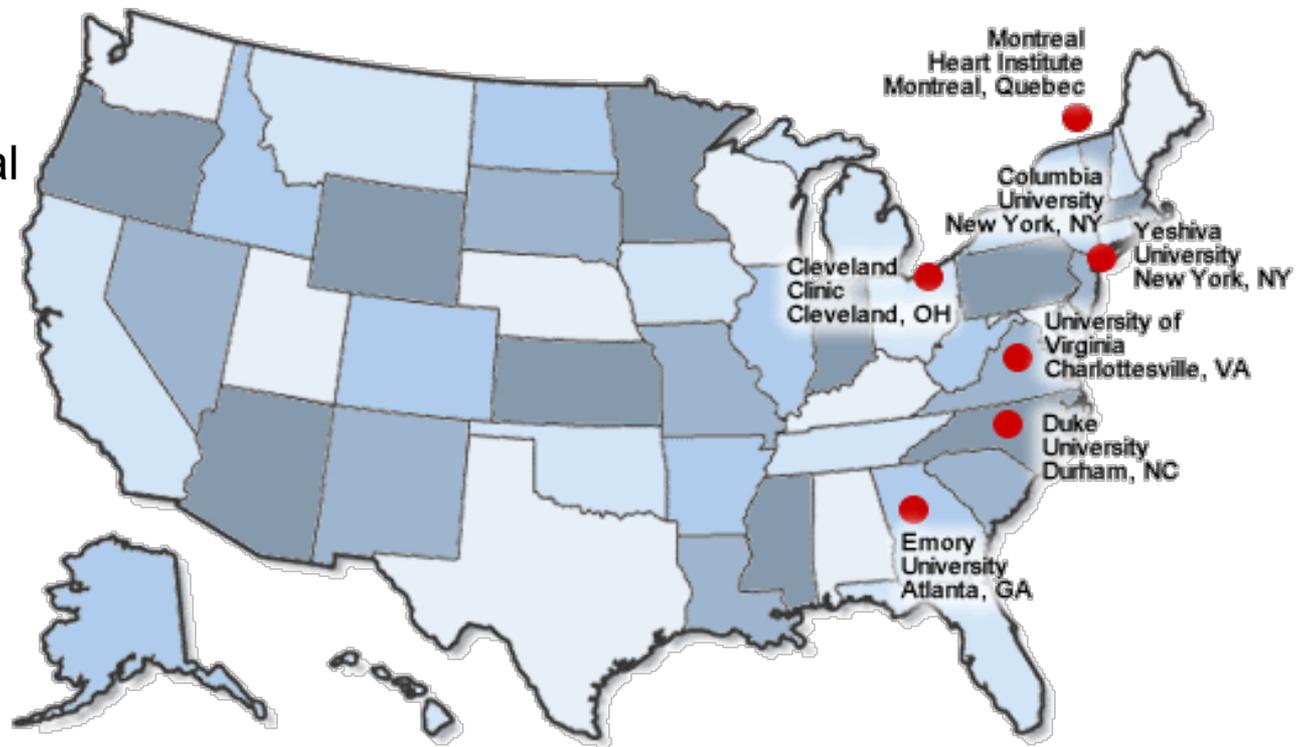
Cardiovascular Cell Therapy Research Network (CCTRN)

To promote and accelerate clinical research in the evaluation of novel cell therapy treatment strategies for individuals with cardiovascular disease



Cardiothoracic Surgical Network

The goal is to inform the use of new interventions in surgical practice by moving promising therapies and techniques from the laboratory into clinical use



Cardiovascular Trials of Revascularization

Trial	Condition	Treatment
BARI 2D	Type 2 Diabetes + CAD	CABG/PCI
CLEVER	Femoral Artery Stenosis	Femoral Artery Stent
CORAL	Renal Artery Stenosis + Hypertension	Renal artery stent
FREEDOM	Type 2 Diabetes + CAD	PCI versus CABG
STICH	Ischemic HF	CABG ± Surgical Ventricular Restoration

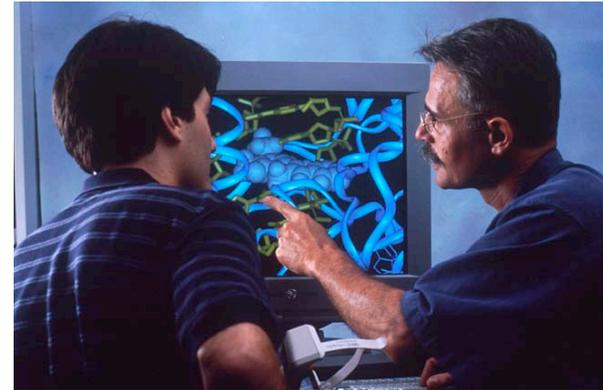
Trials in Chronic CV Disease

Trial	Condition	Treatment
AIM-HIGH	CHD + Atherogenic Dyslipidemia	Extended release niacin + statin vs statin
BARI 2D	Type 2 Diabetes + CAD	Insulin Sensitizing vs Insulin Providing
SANDS	Native Americans with Type 2 Diabetes	Intensive treatment of CV risk factors vs UC
TACT	CAD	Chelation Therapy (EDTA)
TOPCAT	HF with Preserved cardiac Function	Spirinolactone

Trials in Acute CAD

Trial	Condition	Treatment
IMMEDIATE	Acute Coronary Syndrome or MI	Glucose-Insulin-Potassium (GIK) Infusion
PACE-MI	Acute MI	Pacemaker-Facilitated Beta Blocker Therapy

Training of New Clinical Investigators

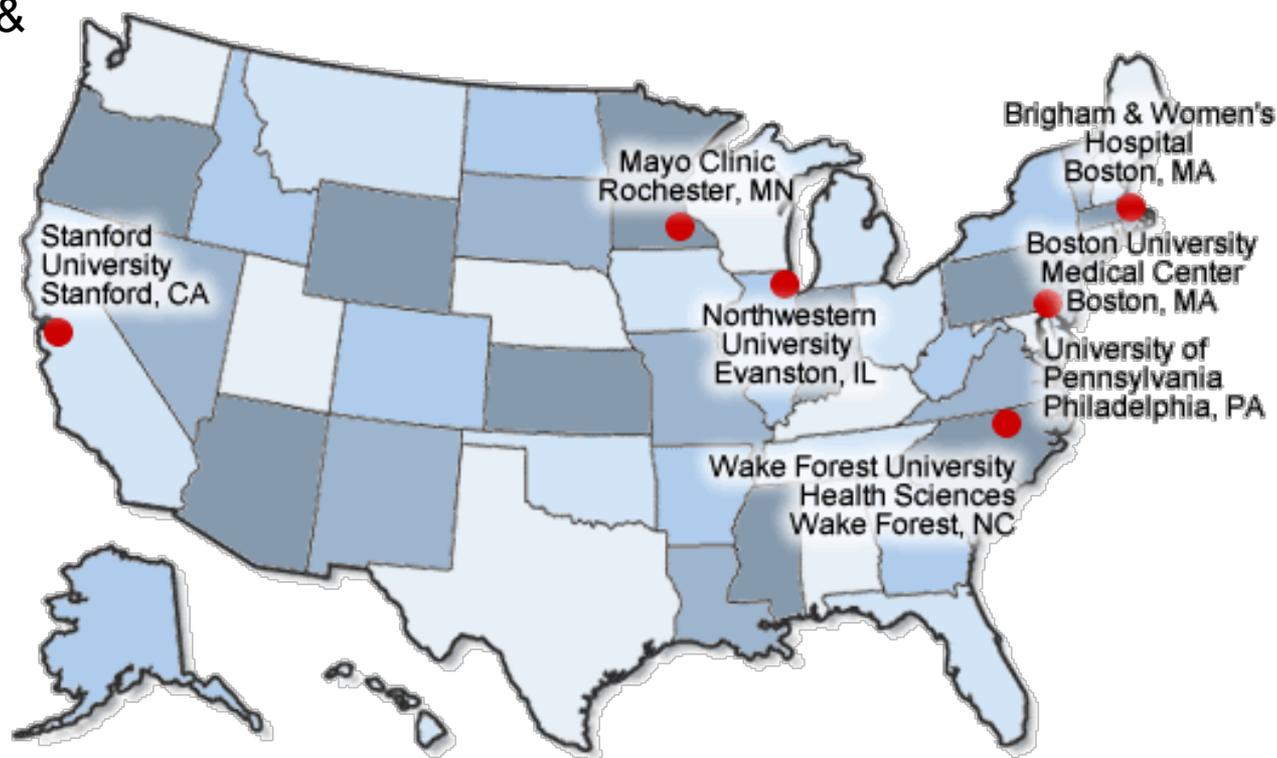


Clinical Research Training Awards

- T32 Institutional pre- & post-doctoral training
- T35 Institutional short-term training
- K12 Institutional mentored clinical scientist program in vascular medicine (2007)
- NIH K99/ R00 Pathway to Independence award (2007)
- K08 Mentored early career clinical scientist award
- K23 Mentored early career patient-oriented research award
- K24 Mentored mid-career patient oriented research award
- K02 Independent scientist award
- K01 Mentored career development to promote diversity
- K07 Cultural competence & health disparities award

Research Career Development Programs in Vascular Medicine (K12)

The goal is to offer comprehensive clinical research training for physicians wanting to specialize in the new & evolving discipline of vascular medicine



NHLBI Strategic Plan Goals

Goal 1

Improve understanding of the molecular and physiologic basis of health and disease. Use that understanding to develop improved approaches to disease prevention, diagnosis and treatment. *Form → Function*

Goal 2

To develop personalized preventive and therapeutic regimens for cardiovascular, lung, and blood diseases. *Function → Cause*

Goal 3

Generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery. *Cause → Cures*

Partnering to Enhance Success



Partnering: Clinical Trials in Organ Transplantation (CTOT)



National Institute of Diabetes
& Digestive & Kidney
Diseases



National Institute of Allergy and Infectious Diseases
National Institutes of Health

NIAID, NHLBI and NIDDK-sponsored Cooperative Research Network to conduct clinical and mechanistic studies with the goal of improving outcomes for recipients of solid organ transplants – heart, lung, kidney, liver

Participatory Research

Pediatric Heart Network
Department of Health and Human Services - National Institutes of Health

Home About the Site Glossary Contact Us

Clinical Trial Child Participation Current Studies Information for Practitioners Completed Studies Future Studies

Deciding whether a child will participate in a clinical study can be especially difficult. This site was developed to help parents, patients and healthcare professionals consider many aspects of joining a pediatric clinical study. The site was created and is maintained by the Pediatric Heart Network (PHN), which was established in 2001 by the National Heart, Lung, and Blood Institute to improve outcomes and quality of life in children who acquire or are born with heart disease.

- For Parents
- For Health Care Providers
- Current Studies
- Future and Completed Studies
- Participating Hospitals
- Helpful Resources
- Publications

Department of Health and Human Services National Institutes of Health National Heart, Lung, and Blood Institute

www.PediatricHeartNetwork.com



Clinical trials have resulted in the everyday use of treatments and medication, often curing disease and making the management of healthcare conditions safer and more effective. Pediatric research is imperative to evaluate drugs and treatments in developing minds and bodies.

A Video For Parents

- The most important thing parents can do, when asked to participate in clinical research, is to get informed.
- Know all there is to know...about the child's condition, the treatments available, the potential outcomes, the people involved, the risks and benefits...
- The answers are there – the questions just need to be asked. The more you know, the more you can feel good about your decision, whatever you decide.

Stay-in-Circulation Campaign

Peripheral Arterial Disease

The first national awareness campaign to increase public and health care provider awareness of PAD and its association with other cardiovascular diseases



NIH Core Strategic Vision

- Transform medicine and health from a Curative to a Preemptive paradigm
- Support basic research to identify the earliest molecular stages of disease in complex biological systems
- Accelerate translation of findings from the bench to the bedside to the community
- Provide the evidence and knowledge base to allow for a rational transformation of our healthcare system

Future Directions

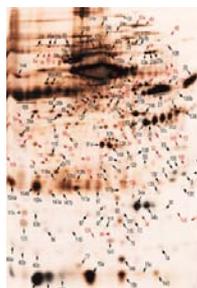
Basic Discovery

Clinical

Communication



Genomics



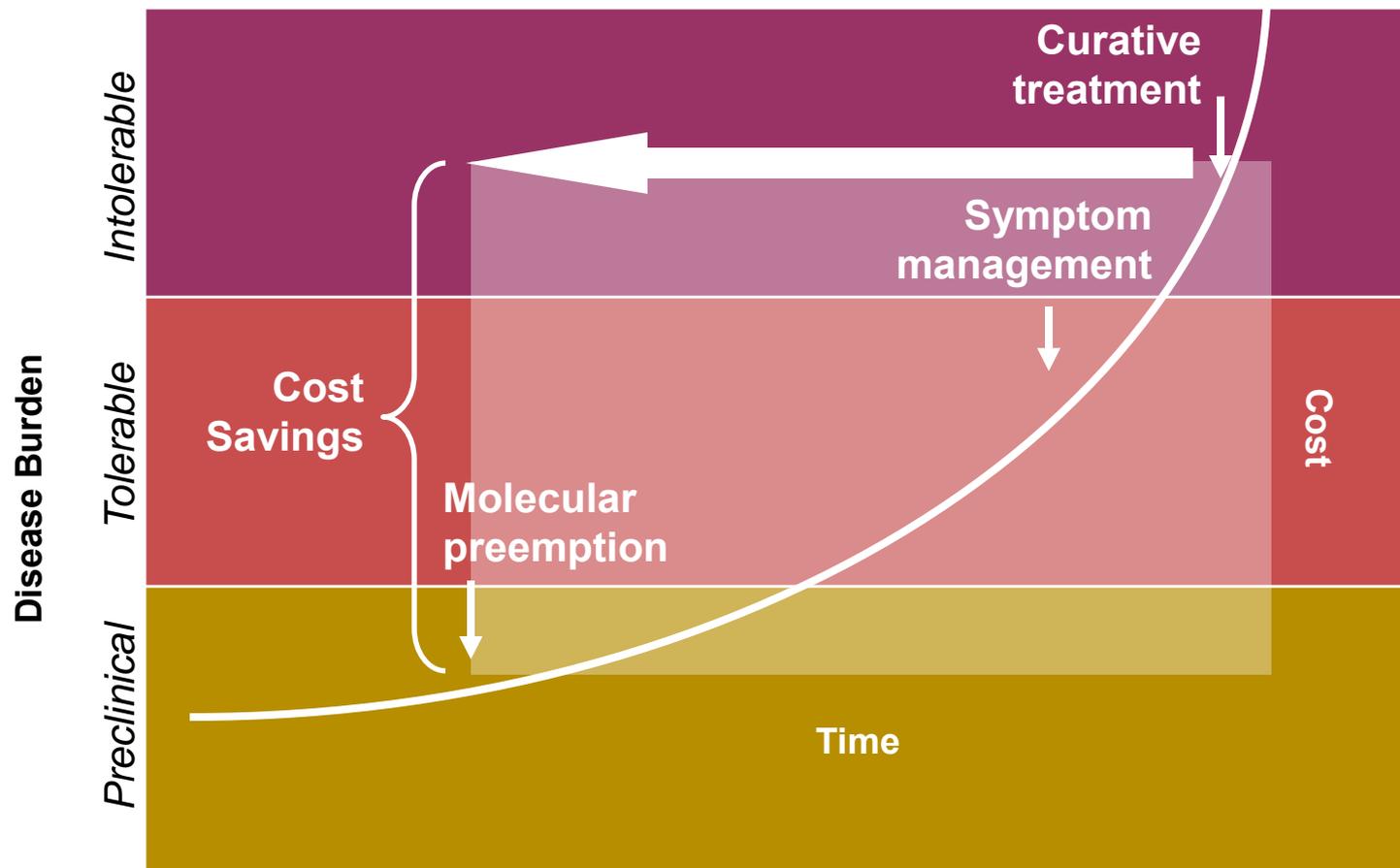
Proteomics



Stem Cell Research
Tissueogenesis

Cell Imaging
Translational

The Future Paradigm: Preempt Disease



Goal One: Form to Function

Goal 1: To improve understanding of the molecular and physiological basis of health and disease and use that understanding to develop improved approaches to disease diagnosis, treatment, and prevention.

Challenge 1.1

To delineate mechanisms that relate molecular events to health and disease.

- 1.1.a** Develop a detailed understanding of the molecular, cellular, and physiological mechanisms that maintain health from embryonic development to the end of the human lifespan.
- 1.1.b** Identify intracellular targets of key signaling and transcriptional pathways in normal and pathologic states.
- 1.1.c** Determine key genetic variants that are associated with specific diseases and delineate the molecular mechanisms that account for susceptibility or resistance to disease.
- 1.1.d** Define molecular, cellular, and organ-specific responses to environmental challenges, and the mechanisms by which heritable and non-genetic factors interact in disease initiation and progression and in therapeutic response.
- 1.1.e** Determine the role of systemic pathological processes, such as inflammation, immunity, and infection, in the development and evolution of disease.

Goal One: Form to Function (continued)

Challenge 1.2

To discover biomarkers that differentiate clinically relevant disease subtypes and that identify new molecular targets for application to prevention, diagnosis – including imaging, and therapy.

- 1.2.a** Identify molecular signatures that allow complex disease phenotypes to be stratified into clinically relevant categories.
- 1.2.b** Develop in vivo molecular imaging methods and probes for investigating the biology of disease processes.

Goal Two: Function to Causes

Goal 2: To improve understanding of the clinical mechanisms of disease and thereby enable better prevention, diagnosis and treatment.

Challenge 2.1

To accelerate translation of basic research findings into clinical studies and trials and to promote the translation of clinical research findings back to the laboratory.

- 2.1.a** Integrate advances in regenerative biology to develop clinically feasible applications.
- 2.1.b** Apply discoveries in nanotechnology to the development of new diagnostic and therapeutic strategies.
- 2.1.c** Integrate, analyze, and share extant and emerging genotypic and phenotypic data.

Challenge 2.2

To enable early and accurate risk stratification and diagnosis of cardiovascular, lung, and blood disorders.

- 2.2.a** Exploit noninvasive imaging methods to detect and quantify subclinical disease.
- 2.2.b** Apply new discoveries in biomarkers to improve risk assessment, diagnosis, prognosis, and prediction of response to therapy.

Goal Two: Function to Causes (continued)

Challenge 2.3

To develop personalized preventive and therapeutic regimens for cardiovascular, lung, and blood diseases.

- 2.3.a** Improve the understanding of the interactions between genetic and environmental factors that influence disease development and progression and response to therapy.
- 2.3.b** Identify and evaluate interventions to promote health and treat disease in genetically defined patient subgroups by altering developmental or environmental exposures including drugs, diet and exercise, sleep duration and quality, and infectious agents and allergens.

Challenge 2.4

To enhance the evidence available to guide the practice of medicine, and improve public health.

Goal Three: Causes to Cures

Goal 3: To generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery.

Challenge 3.1

To complement bench discoveries and clinical trial results with focused behavioral and social science research.

- 3.1.a** Develop and evaluate new approaches to implement proven preventive and lifestyle interventions.
- 3.1.b** Develop and evaluate policy, environmental, and other approaches for use in community settings to encourage and support lifestyle changes.
- 3.1.c** Develop and evaluate interventions to improve patient, provider, and health system behavior and performance in order to enhance quality of care and health outcomes.

Goal Three: Causes to Cures (continued)

Challenge 3.2

To identify cost-effective approaches for prevention, diagnosis, and treatment.

- 3.2.a** Evaluate the risks, benefits, and costs of diagnostic tests and treatments in representative populations and settings.
- 3.2.b** Develop research designs, outcome measures, and analytical methods to assess prevention and treatment programs in community and health-care settings across populations and lifespan.

Challenge 3.3

To promote the development and implementation of evidence-based guidelines in partnership with individuals, professional and patient communities, and health care systems and to communicate research advances effectively to the public.

- 3.3.a** Establish evidence-based guidelines for prevention, diagnosis, and treatment and identify gaps in knowledge.
- 3.3.b** Develop personalized and community- and health care system-oriented approaches to increase the use of evidence-based guidelines by individuals, communities, health care providers, public institutions, and, especially, by populations that experience a disproportionate disease burden.
- 3.3.c** Communicate research advances effectively to the public.