



NHLBI Gene Therapy Resources



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American Society of Gene and Cell Therapy
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Outline

1. Center for Fetal Monkey Gene Transfer for Heart, Lung and Blood Diseases.
2. Gene Therapy Resource Program for Heart, lung, and blood diseases.
3. Science Moving TowArds Research Translation and Therapy.

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

(Established in 2001)



Rhesus monkey (*Macaca mulatta*) image from Center
for Fetal Monkey Gene Transfer for Heart, Lung, and
Blood Diseases

Program Goals

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

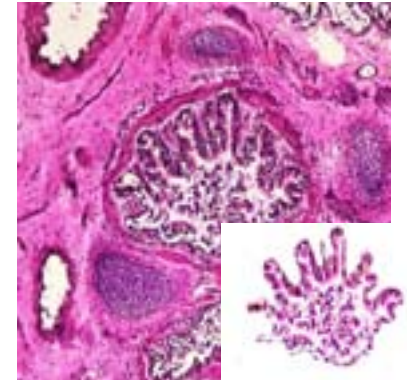
Provide NHLBI-funded investigators with essential expertise, services, and resources

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

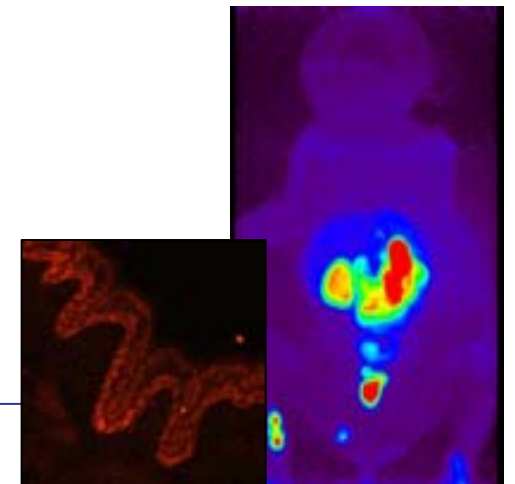
Services Offered to Grantees



- Study development and design
- Gene transfer (all age groups)
- Transplant models (autologous, allogeneic, xenogeneic)
- *In vivo* imaging (ultrasound, microPET, optical)



- Physiologic assessments
- Tissue harvests (collect, process, analyze)
- Laboratory (e.g., molecular, cellular including qRT-PCR, immunophenotyping, sorting, immunoselection, morphology, morphometry, laser capture)
- Assistance with study design



Access to Services

- **NHLBI-funded investigators**
- **Submit Letter of Intent (LOI) by June 30, 2011**
- **If LOI is approved, a full proposal template will be provided**

Look for annual calls for LOI submission in June issue of *Molecular Therapy* or check the website

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

Funded investigators may choose to:

- Provide their vectors for study, with all work completed by Center personnel
- Participate in analysis of samples collected
- Participate in the study as a visiting scientist

Contact Information

Visit the website:

www.CFMGT.ucdavis.edu

E-mail **Dr. Alice Tarantal** at:

aftarantal@primate.ucdavis.edu

Gene Therapy Resource Program

(Established in March 2007)

Gene Therapy Resource Program

History of Program

Major Research Challenges Identified by NHLBI Gene Therapy Working Group at June 2005 Meeting:

- Producing large scale, well-characterized viral vectors under current Good Manufacturing Practices for use in clinical trials
- Conducting pharmacology and toxicology studies in small and large animal models
- Meeting the regulatory requirements of the FDA, IBCs, IRBs, NIH RAC, and DSMB

The NHLBI responded to the recommendations of the Working Group by establishing the Gene Therapy Resource Program in March 2007

Gene Therapy Resource Program

Goals

Facilitate the translation of gene therapy research into clinical interventions

Provide resources for gene therapy research primarily in heart, lung, and blood diseases

Provide resources to investigators at other NIH institutes through transfer of funds

Gene Therapy Resource Program

Program Infrastructure

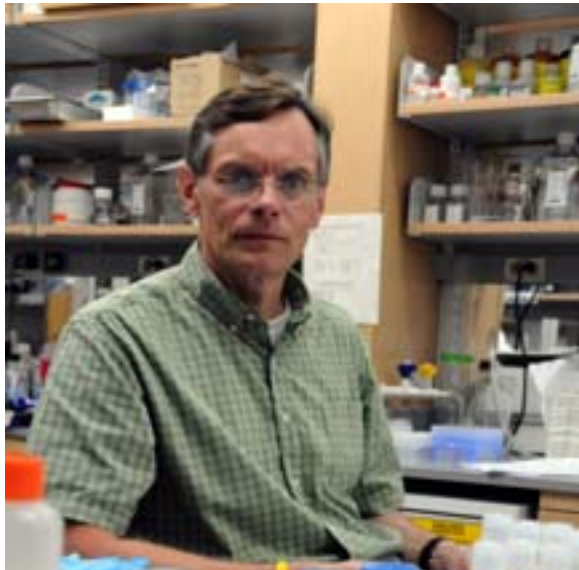
Clinical Coordinating Center
Social & Scientific Systems, Inc.
PI: Susan B. Sepelak, MS, MSM

Preclinical Vector Core
University of Pennsylvania
PI: James Wilson, MD, PhD

Clinical Lentivirus Vector Core
Indiana University
PI: Kenneth Cornetta, MD

Pharmacology/Toxicology Core
Lovelace Biomedical &
Environmental Institute
PI: Janet Benson, PhD

Clinical AAV Vector Core
The Children's Hospital of
Philadelphia
PI: Fraser Wright, PhD



Preclinical Vector Core University of Pennsylvania



Preclinical Vector Core

Produces large- and small-scale viral and non-viral vectors for studies in basic research directed toward clinical applications

Produces AAV (over 30 serotypes including 1, 2, 5, 6, 7, 8, 9, rh10), adenoviral, lentiviral (various pseudotypes) as well as plasmid-based vectors and provides extensive quality control testing for all vectors

Provides a variety of expression cassettes for both regulated expression and tissue-specific expression (e.g. heart, liver and lung)

Provides immunology testing services, including neutralizing antibody assays, interferon gamma ELISpot, and intracellular cytokine staining for adenoviral, lentiviral and AAV vector capsid and transgene products



Clinical-Grade AAV Vector Core Children's Hospital of Philadelphia

Clinical-Grade AAV Vector Core

Produces scalable clinical-grade adeno-associated virus (AAV) vectors for use in clinical studies

Produces GMP process-comparable AAV vectors for use in pharm/tox or other studies

Provides Chemistry, Manufacturing, and Controls (CMC) documentation and Certificate of Analysis (COA)

Assists in vector (cis) plasmid design to achieve optimal safety and productivity

Prepares certified components (plasmid DNA, HEK293 Master Cell Bank) and reagents required for clinical vector manufacture

Clinical-Grade Lentiviral Vector Core Indiana University



Clinical-Grade Lentivirus Vector Core

Produces scalable clinical-grade lentiviral vectors for use in clinical studies

Produces GMP process-comparable lentiviral vectors for use in pharm/tox or other studies

Evaluates and optimizes lentiviral vector constructs intended for clinical use

Provides pilot runs for pre-clinical evaluation prior to large-scale production

Assists in release testing to certify vectors for clinical use

Provides Chemistry, Manufacturing, and Controls (CMC) and Certificate of Analysis (COA)

Pharmacology /
Toxicology Core
Lovelace Biomedical and
Environmental Research
Institute



Pharmacology / Toxicology Core

Assists with pharmacology/toxicology study design, preparations of pre-IND materials, and in addressing FDA comments

Performs toxicology testing/efficacy and biodistribution studies of vectors in large and small animal models as a prerequisite for use in clinical studies

- Animal species available include rodents, rabbits, ferrets, beagle dogs, and non-human primates
- Facilities for cell culture/transduction, flow cytometry, animal surgery, necropsy, clinical pathology, histopathology, and assessment of vector biodistribution and transgene expression

Conducts studies according to Good Laboratory Practice Guidelines and prepares final study reports for inclusion in IND submissions



Clinical Coordinating Center Social & Scientific Systems, Inc.

Clinical Coordinating Center

Supports Program infrastructure including database, website, and MOP

Manages the RSA receipt, review, disposition, and tracking processes

Serves as liaison between Core labs & investigator in RSA development

Provides management support to the GTRP Steering Committee


Provides regulatory assistance to investigators; manages disbursement of clinical trial funds

Assures GTRP funded clinical studies are conducted in compliance with regulatory oversight bodies (OBA, FDA, DSMB, IRB, IBC)


Access to Program Resources

Step 1: Investigator Registration and Approval

Step 2: Submit RSA



Gene Therapy Resource Program

National Heart, Lung, and Blood Institute 

1 Investigator Registration **2** Request for Service Application (RSA) Core Laboratories Scientific Review Board Steering Committee NHLBI Gene Therapy Group

WHAT IS THE NHLBI GENE THERAPY RESOURCE PROGRAM?

The NHLBI Gene Therapy Resource Program (GTRP) facilitates the translation of gene therapy research into clinical interventions. The GTRP provides resources for gene therapy research primarily in heart, lung, and blood diseases as reflected in the NHLBI Mission (<http://www.nhlbi.nih.gov/about/org/mission.htm>). Requests for resources for gene therapy research that are consistent with the missions of other NIH Institutes may also be considered by the Program.

Resources are provided in the form of preclinical and clinical-grade vector production, pharmacology/toxicology testing, immunology testing, clinical trials funding assistance, and [regulatory support](#) at no cost to the investigator. Investigators must first receive approval of their Registration with the Program in order to request resources.

The GTRP, directed by the NHLBI Gene Therapy Group, consists of three vector production cores, a pharmacology/toxicology testing core, and a clinical coordinating center. A Scientific Review Board and Steering Committee review Request for Service Applications and make recommendations to the NHLBI Gene Therapy Group regarding the applications' scientific merit, feasibility, and compatibility with the Program's mission.

Preclinical Vector Core	Clinical-Grade AAV Vector Core	Clinical-Grade Lentivirus Vector Core	Pharmacology / Toxicology Core	Clinical Coordinating Center
University of Pennsylvania	The Children's Hospital of Philadelphia	Indiana University	Lovlace Biomedical and Environmental Research Institute	Social & Scientific Systems, Inc.
Produces large-	Produces scalable	Produces scalable	Performs toxicology	Coordinates RSA

HIGHLIGHTS

- » [Instructions for Submitting an RSA](#)
- » [RSA Review Process](#)

INFORMATION CENTER

- » [NHLBI Home](#)
- » [FAQ's](#)
- » [Regulatory Resources](#)
 - » [Regulatory Guidelines](#)
 - » [Fundamental Elements in Gene Vector Development](#)
- » [National Gene Vector Biorepository](#)
 - » [Article - April 2009](#)

Collaborations with Other NIH Institutes

National Eye Institute (NEI)

To support an intramural investigator requesting GMP process-comparable AAV vector production for use in pharmacology/toxicology studies related to retinoschisis.

The NIH-RAID Program and the National Institute of Neurologic Disorders and Stroke (NINDS)

To support an extramural investigator requesting GMP process-comparable AAV vector production for use in pharmacology/toxicology studies and clinical grade AAV vector production for use in a phase I clinical trial. Both studies are related to Parkinson's Disease.

The NIH-RAID Program

To support an extramural investigator requesting pharmacology/toxicology testing in studies related to osteoarthritis.

For More Information

Visit our website: www.gtrp.org

Visit our exhibit booth 408

E-mail the **Clinical Coordinating Center** at:

gtrpccc@s-3.com

SMARTT Program

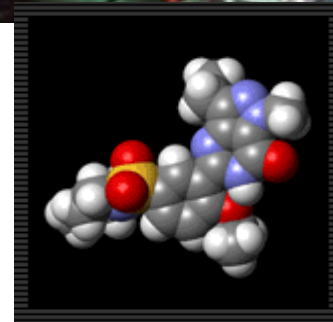
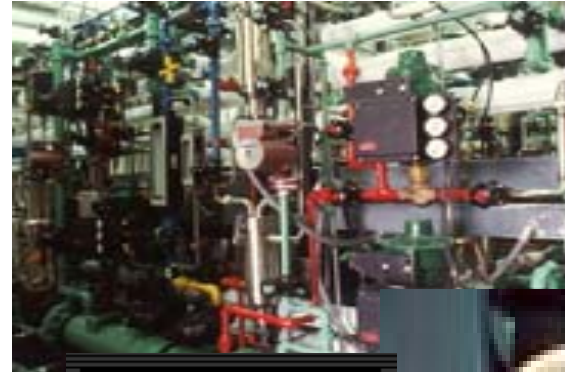


Goal:

Accelerate translation of research on diseases of the heart, lung, and blood from bench to bedside.

Approach:

Provide rapid, confidential services that support preclinical studies and regulatory submissions at no cost to investigators.



SMARTT Team

NHLBI SMARTT Committee

- Program Director: Sonia Skarlatos, PhD
Deputy Director, Division of Cardiovascular Diseases, NHLBI
- Steering Committee Chair: Terry Matsunaga, PhD
University of Arizona
- Representatives of each NHLBI division

Coordinating Center

- RTI International

Biologics Production Facility

- ABL, Inc.

Non-Biologics/Small Molecule Production Facility

- SRI International

Pharmacology/Toxicology Center

- SRI International

SMARTT Services

Biologics, Non-Biologics, and Small Molecule Production

- Production of non-GMP and cGMP test articles
- Cell line development and GMP cell banking
- Medicinal, synthetic, and analytical chemistry support
- Process development and scale-up
- Drug product fill and finish
- Pre-formulation testing and formulation development
- Stability and release testing

Pharmacology/Toxicology Testing

- Preclinical toxicology testing
- Safety pharmacology
- Drug metabolism and pharmacokinetics

Consulting

- Strategic planning for successful IND applications
- Preclinical and early phase clinical study support
- Assistance with IND applications

SMARTT Program Oversight

Steering Committee

- NHLBI and Facility representatives
- Independent Chair

Scientific Review Board

- Independent experts who evaluate Request for Service Applications

Program Evaluation Panel

- Independent experts who evaluate program performance

SMARTT Website

See <http://smartt.nhlbi.nih.gov> for more information and a complete list of services

National Heart Lung and Blood Institute
National Institutes of Health

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Log In

SMARTT

Getting Started
Register your interest with SMARTT
Submit a request for SMARTT services

TRANSLATION & THERAPY

REQUEST SERVICES

IMPLEMENT SERVICES

NHLBI APPROVAL

About this site

Our Goal

To accelerate translation of research from bench to bedside by providing services that support pre-clinical studies and regulatory submissions. These services are:

- Confidential
- Focused
- Performed at no cost to the investigator

Available Services

- Preclinical study planning & regulatory support
- Pharmacology & toxicology services
- Manufacturing of small molecules and non-biologics
- Manufacturing of biologics

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For More Information/Questions

E-mail **Sonia I. Skarlatos, Ph.D.** at:
skarlats@mail.nih.gov