THE NDRI
INTERCHANGE
THE NATIONAL HUMAN TISSUE RESEARCH NETWORK –
Advancing the procurement, preservation, and distribution of human cells, tissues, and organs for research.
Volume 27, No. 1
November 2011

NDRI FACILITATES DRUG DISCOVERY IN CYSTIC FIBROSIS RESEARCH

New Drugs Promise Marked Improvement for CF Patients

Capri Faulk, a second-grader who took part in a VX-770 clinical trial at East Tennessee Children's Hospital in Knoxville, Tennessee.
(photo courtesy of the Cystic Fibrosis Foundation)

NDRI's collaboration with the Cystic Fibrosis Foundation to recover CF lungs for research has led to a major breakthrough in the development of two new drugs to combat the disease at its biological root. CF donor lungs recovered by NDRI were used by scientists at Vertex Pharmaceuticals, Inc. in the development of two compounds, Kalydeco™ (formerly VX-770; ivacaftor) and VX-809, which continue to show promising results in ongoing clinical trials. NDRI's capability to design a unique customized network for the recovery of diseased lungs is at the core of these discoveries.

"Our approach to the development of potential new medicines for CF is to target the root cause of the disease," says Eric Olson, Vertex Vice President and Cystic Fibrosis Franchise Leader. "In order to do this, we needed a relevant pharmacology model to assess our drugs. Airway cells derived from the native tissue provided by NDRI allowed us to better understand how Kalydeco and VX-809 might work in people with CF."

Outlook for CF patients improves with NDRI's help

NDRI's core competency in establishing and managing the design of transplant tissue networks for the recovery of explanted, diseased lungs for CF scientists has helped change the prognosis for patients with this disease. Currently over 100 donors have provided close to 160 diseased lungs and other tissues, including trachea, liver, lymph nodes, pancreas, skin and intestine, to researchers for CF drug discovery.

Eric Olson, Ph.D., Vice President and Franchise Leader, Vertex Pharmaceuticals Incorporated

NDRI recovers CF lungs when a healthy lung is transplanted by networking with the surgical teams at the nation's top transplant centers. In addition, NDRI's nationwide network of organ procurement organizations, hospitals and tissue banks enabled the collection of diseased lungs and other CF tissues consented *post mortem*. In partnership with the CF Foundation, NDRI continues to provide donated lungs and other biomaterials from CF patients to CF scientists for research studies.

Chris Penland, Ph.D., Director of Research, the Cystic Fibrosis Foundation

According to Chris Penland, Ph.D., Director of Research for the CF Foundation, "The most important contribution NDRI makes is their ability to reach out to the community to acquire tissues to help drug discovery efforts. If not for NDRI's efforts, it would have taken much longer for us to move to clinical trials."

CF researchers are developing targeted therapies focused on the root causes of disease that impact both the airways and the digestive system. Ongoing studies include those in the CF Foundation's drug development pipeline, focused on gene therapy, CFTR modulation, mucus alteration, anti-infective and anti-inflammatory agents, transplantation and nutrition.

Dr. Penland reports, "Airway epithelial cells isolated from CF lungs that NDRI has acquired are being used in several drug discovery projects within for-profit companies such as Pfizer and academic settings as well. Because responses from these cultured cells have been so predictive of the *in vivo* measurements of CFTR function," he says, "many groups recognize their value in the drug discovery and development process. These cells are also being put to use in experiments to understand what proteins influence CFTR folding and trafficking which is dysfunctional in CF."

"The most important contribution NDRI makes is their ability to reach out to the community to acquire tissues to help drug discovery efforts. If not for NDRI's efforts, it would have taken much longer for us to move to clinical trials."
— Chris Penland, Ph.D.

New drugs promise marked improvement for CF patients

"This year is going to be an exciting year for Vertex and our cystic fibrosis pipeline in particular," said Dr. Olson. Earlier this year, Vertex released promising results of Phase 3 clinical trials of Kalydeco in both adults and children who carry at least one copy of the G551D mutation of the CF gene. Patients who took the drug showed marked improvements in lung function (10%) and other key indicators of the disease, including sweat chloride levels, pulmonary complications and body weight.

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The NIH GTEx Project Moves Forward Exceeding Expectations

Goal is to Genotype Tissues and Organs of the Human Body

The National Institutes of Health, NIH, has funded $3.59 million to NDRI over 30 months in a subcontract overseen by SAIC-Frederick to provide human biospecimens for GTEx, the Genotype-Tissue Expression Project. This is the largest and first project of its kind where scientists aim to genotype tissues and organs of the human body to study gene expression. The resulting data promise to be a valuable resource for the study of gene expression and its relation to disease. The GTEx project is funded through the NIH Common Fund within the Office of the Director, in partnership with NHGRI, the National Human Genome Research Institute, NIMH, the National Institute of Mental Health, NCI, the National Cancer Institute, and NHLBI, the National Heart, Lung and Blood Institute.

NDRI's role in the GTEx project is to identify a large number of donors who meet the study criteria for genetic analysis. The challenge during the next 18 months is to consent 96 (110 total) donors with the goal of recovering a large number of tissues, 25-30, and some 35 tissue types, under six hours *post mortem* from each donor. NDRI's start date for recruitment of *post-mortem* donors was July 1, 2011, and, so far, has exceeded expectations; 24 donors have been recovered at a rate of about 6 per month, averaging three-to-four-hour *post-mortem* intervals, which is well under the 6-hour GTEx target. An additional 100 surgical donors will be recovered, an average of 10 tissues recovered per donor. *Post-mortem* tissues will total 7,600 biopecimens, while surgical specimens are projected to total 2,000. It is anticipated that by January 2013, NDRI will have recovered some 10,000 specimens from surgical and *post-mortem* donors. The NDRI GTEx team is led by Co-Principal Investigators John Lonsdale, Ph.D., NDRI Director of Research, and Jeff Thomas, Director of the NDRI Tissue Collection Center Networks.

Jeffery P. Struewing, M.D., M.S.
Epidemiologist, Office of Population Genomics
National Human Genome Research Institute

According to Jeff Struewing, M.D., M.S., GTEx Program Director at NHGRI, one of the major challenges is to collect samples from many different organs from the same donor, each of which has to be of excellent quality in order to perform state-of-the-art laboratory tests such as gene sequencing. He commented recently that solid organs collected by NDRI have yielded generally very high quality samples of RNA, and said he was very pleased with the results so far. RNA tissue quality is measured by a RIN (RNA Integrity Number) score. For the tissue provided by NDRI, the RIN score has been an average of 7, exceeding the GTEx target of 6. "Partnering with groups like NDRI, who have a wealth of experience working with families around the time of death to collect and process high-quality tissue samples for medical research, has been a real asset," Dr. Struewing adds. "We are off to a great start working with them and their Organ Procurement Organizations."

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>
> *—Jeff Struewing, M.D., M.S.*

NDRI GTEx Partners

Gary Walters, Senior Director of
Tissue Recovery and Kidney Perfusion,
LifeNet Health, Virginia

Fernando U. Garcia, M.D., Professor,
Department of Pathology and Laboratory Medicine,
Drexel University College of Medicine

Howard Nathan,
President & CEO,
Gift of Life Donor Program

The Gift of Life team partners with NDRI to recover surgical specimens for the GTEx project.

"NDRI is extremely well poised to be able to deliver exactly what is needed for this project, both in terms of timeliness and in terms of ultimate quality of the product."

— Carolyn Compton, M.D., Ph.D.

The NDRI partners for the GTEx project include, for *post-mortem* recovery, the Gift of Life Donor Program, Philadelphia, under the direction of Rick Hasz, Vice President of Clinical Services, and LifeNet Health, Virginia, under the supervision of Gary Walters, Senior Director of Tissue Recovery and Kidney Perfusion. Partnering for recovery of surgical tissues is Drexel University College of Medicine. Fernando U. Garcia, M.D., Professor Department of Pathology and Laboratory Medicine, supervises recovery of surgical specimens for comparative analyses with *post-mortem* tissues and organs. Further, NDRI is working with Laura Siminoff, Ph.D., Professor and Chair, Department of Social and Behavorial Health, Virginia Commonwealth University, to document ethical, legal and social considerations in the choices made to donate or not to donate tissues for research in general, and specifically, to the GTEx project.

Biospecimens recovered by NDRI are shipped to The Broad Institute at Harvard University and MIT for genetic analysis. Co-Principal investigators Wendy Winckler, Ph.D., and Kristin Ardlie, Ph.D., are responsible for the overall coordination of GTEx activities at Broad and the molecular and statistical analysis.

"This is an amazing opportunity for NDRI and for the scientific community," stated Lee Ducat, Founder and President of NDRI. "We are very excited about the early success of our effort and tremendously proud to be a part of this important, first time ever National Institutes of Health initiative to genotype the organs and tissues of the human body."

Carolyn Compton, M.D., Ph.D., Director of NCI's Office of Biorepositories and Biospecimen Research, and administrator of the Cancer Human Biobank (caHUB), a lead agency for the GTEx study, says, "Given their long record of successful tissue procurement for many challenging tissue areas and their established working relationship with donor sites of various sorts, NDRI is extremely well poised to be able to deliver exactly what is needed for this project, both in terms of timeliness and in terms of ultimate quality of the product." Knowledge gained studying these specimens, Dr. Compton says, will clarify the biology of how the genome is controlled on a tissue site specific level that will enormously impact our ability to understand how disease develops in specific organ sites. "It is my hope," she adds, "that this 'NIH Common Fund' initiative in partnership with private sector organizations like NDRI will focus awareness on the need for coordinated, multidisciplinary expertise to answer the next generation of scientific questions with a specific eye toward maintaining the requisite quality of biospecimens and associated donor data so they can be used in a way that will be transformative for medicine in the immediate future." ■

Carolyn Compton, M.D., Ph.D., Director, NCI Office of Biorepositories and Biospecimen Research, and Administrator, Cancer Human Biobank (caHUB)

The NDRI GTEx team with Co-Principal Investigators John Lonsdale, Ph.D., NDRI Director of Research, (left) and Jeff Thomas, (center) Director of the NDRI Tissue Collection Center Networks.

The NIH "FUSION" Study Collaboration – Mapping the Genetic Blueprint for Type 2 Diabetes

NIH Director Francis Collins, M.D., is leading a team of researchers at NHGRI, the National Human Genome Research Institute, who are participants in FUSION, the Finland-United States Investigation of Non-Insulin Dependent (Type 2) Diabetes Mellitus genetics study. The FUSION group is a 18-year collaboration that includes a statistical analysis group at the University of Michigan, researchers at the University of North Carolina, Cedars-Sinai Medical Center in Los Angeles, and the Finnish Health Ministry in Helsinki. The FUSION group participates in a broader international consortium that includes the diabetes genetics initiative of the Broad Institute at Harvard and MIT and the United Kingdom Type 2 Diabetes (UK T2D) Genetics Consortium. This U.S.-European collaboration of scientists aims to identify the genes associated with predisposition to Type 2 diabetes. Thus far, 42 distinct loci have been identified by the T2D research community in 34,000 patients.

The NHGRI group is intensely interested in learning how these identified disease associated genetic variants contribute to diabetes risk. Since many of these variants seem to affect levels of gene expression in the insulin-producing cells of the pancreas, isolated islets from human pancreas are critical to the work and are provided by NDRI from its national organ recovery network. Michael Erdos, Staff Scientist, a key member of the FUSION collaboration, explains. "We decided to use the genetic knowledge that we learned from the individuals in our study and take a look at how these variants associated in regions of the genome may affect the functionality of pancreatic islets." To do that, he needed human islets. "We can never have enough islets to study. NDRI has been a big help to us."

NDRI's collaboration with islet cell isolation laboratories makes it possible for approved researchers to obtain human pancreatic islet cells normal, Type 1 and Type 2. In the last decade, NDRI has collected pancreas for islet isolation and shipped more than seven million islet cell equivalents (IEQs) to 62 research laboratories around the country.

For the FUSION study Mike Erdos says, "We prefer islets that are 80% pure with greater than 90% viability, and generally, that is what we get from NDRI." Islets from both normal and T2D donors are shipped to the Collins Laboratory at NHGRI, enabling them to produce data from more than 120 islet cultures.

"We can never have enough islets to study. NDRI has been a big help to us...because we can't get islets from our living study cohort, these islets are critical surrogates to find the key genes associated with the disease and to learn how their effect is manifested."

— Mike Erdos, *NHGRI Staff Scientist*

The islets are subjected to a controlled set of experiments that include examining the mechanisms that regulate gene expression in the islets. The researchers are looking at the epigenomic structure of these islets under the influence of low versus high glucose, extracting and sequencing RNA and correlating these results by the presence or absence of DNA variations associated with diabetes risk. From this work they hope to gain insight into the pathway involved in the onset and development of Type 2 diabetes.

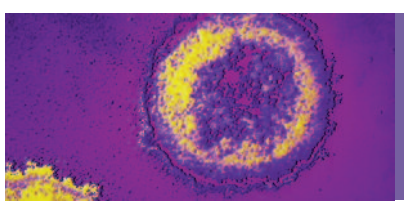
Francis Collins, M.D., Director of the National Institutes of Health
Leader, FUSION Study Collaboration

Their recent findings, some of which were published in *Cell Metabolism* (Nov 3, 2010), suggest that regulatory elements may be a key component to understanding the molecular defects that contribute to Type 2 diabetes. Dr. Collins' group focuses on several specific genes. Among those is MTNR1B, melatonin associated receptor 1B. They have found that the risk allele of MTNR1B is associated with Type 2 diabetes in patients with a disease onset of over 45 years of age. A variety of techniques have confirmed that the MTNR1B gene is actively expressed in human islets, and indeed is more highly expressed in patients carrying the higher risk form of the gene.

"We are hoping to discover what is different about T2D islets based on the genetic changes in the genomic regions we have identified in our study. Eventually, we hope to get to the point where we could develop an assay to investigate potential therapeutics for Type 2 diabetes."

— Mike Erdos

All of the islets that the group receives are genotyped and sorted into groups based on the type of disease gene alleles expressed in each. "Because we can't get islets from our living study cohort, these islets are critical surrogates to find the key genes associated with the disease and to learn how their effect is manifested." From these studies, he says, "We are hoping to discover what is different about T2D islets based on the genetic changes in the genomic regions we have identified in our study. Eventually, we hope to get to the point where we could develop an assay to investigate potential therapeutics for Type 2 diabetes." To complete the picture, the team is looking at doing a comprehensive genetic, epigenetic and metabolite study using muscle and fat biopsies from T2D subjects to match with the study of human islets. ■



For information about obtaining cells, tissues and organs (including rare disease specimens, bone marrow, cord blood and stem cell derivatives), call NDRI at 800-222-6374 or visit our website at www.ndriresource.org

Translational Research is the Focus of NDRI's 135 Published Works by Participating Scientists-2010

NDRI's collection of abstracts summarizing advances in science published in 2010, represent strategic collaborations with some 1,044 national and international authors at 112 distinguished research centers, institutes, companies, and universities. Translational research was a major focus in 90% of the 135 papers published by NDRI participating scientists in 75 peer reviewed journals.

Translational research advances were reported in major fields including drug and biomarker discovery, epigenetics, genetics and gene therapy, stem cell research, orthopedics, personalized medicine strategies, diagnostic methodologies, and mRNA-based therapeutic strategies. NDRI looks forward to expanding these collaborations and contributing on an even larger scale to the progress of translational research that directly benefits public health across a broad spectrum.

NDRI's collection of published papers reflects broad scope of research

As medical science and technology have advanced over the past several years, researcher study requests have become more complex and demanding. NDRI is successful in evolving systems that have kept pace with the challenges of complex dissection, lower *post-mortem* intervals to preservation, diverse processing techniques and delivery of quality tissues. NDRI is a "Researcher Responder" organization providing specimens in a customized, continuous way to scientists, who frequently say NDRI adds great value to their studies by facilitating research that otherwise might not be possible. NDRI serves over 500 researchers each year with about 15,000 specimens from the 40,000 offered through NDRI's national network of 240 tissue collection centers. The 135 publications resulting from NDRI's service cover the gamut of biomedical research in some 54 different diseases. These include common diseases such as arthritis, Alzheimer's, cancer, cardiovascular disease, diabetes and its complications, eye diseases, including age-related cataracts, macular degeneration and diabetic retinopathy, neurodegenerative diseases, infectious diseases including herpes simplex and HIV, and respiratory and rare diseases. Publications of rare disease research focus on amyotrophic lateral sclerosis, polycystic kidney disease, cystic fibrosis, idiopathic dilated cardiomyopathy, Leber congenital amaurosis, LAM, myotonic dystrophy, cardiac amyloidosis, renal angiomyolipoma, tuberous sclerosis complex and von Hippel-Landau disease. These publications underscore the importance of NDRI efforts to provide human biospecimens to translational research, bringing the promise of future clinical and patient improvements in multiple areas of public health.

Translational Highlights from 135 Publications Based on NDRI Service to Scientists

Stuart Schreiber, et al., at Harvard publish findings that point to a potential way of increasing beta cell mass and islet cell production. In their publication entitled, "Small-molecule inducers of insulin expression in pancreatic alpha-cells," the authors demonstrate an important first step on a new pathway to treatment for diabetes. Using the small molecule, BRD7389, which they identified through screening, the investigators were able to induce pancreatic alpha cells to produce a low level of insulin, something alpha cells do not normally do. Their findings point to a potential way of increasing beta cell mass and consequently, insulin production, by converting other cell types into functioning beta cells. This work could eventually lead to a new drug to treat diabetes that bypasses several key limitations associated with stem cell or islet cell transplants.

William Balch, Ph.D., et al., at The Scripps Research Institute publish on a potential new CF treatment. Dr. Balch and co-authors describe a new therapeutic approach for restoring partial function to lung cells in patients with acute cystic fibrosis in their paper entitled, "Reduced histone deacetylase 7 activity restores function to misfolded CFTR in cystic fibrosis." The authors showed that a compound called suberoylanilide hydroxamic acid (SAHA), used to treat lymphoma, can restore about 28 percent of normal function to lung surface cells with the most common, yet severe, mutation in the cystic fibrosis gene. The CFTR or Cystic Fibrosis Transmembrane Conductance regulator protein is normally found at the cell surface and regulates movement of sodium and chloride in and out of cells, which is necessary for proper hydration of the lung, intestine, and pancreas. Although more than 1,400 different mutations can lead to defects in CFTR protein, the mutation that causes a severe form of the disease is responsible for more than 90 percent of cystic fibrosis cases worldwide and results in complete loss-of-function in the patients with two copies of the mutated gene – one from each parent. The authors believe the added degree of function enabled by SAHA or a similar compound could make a huge difference to patients with an acute form of CF. Their discovery may open the way to a new class of therapies for CF and potentially many other chronic diseases.

Joseph Hollyfield, Ph.D., and team at the Cleveland Clinic Foundation offer potential drug discovery targets for AMD. In their publication entitled, "Quantitative Proteomics: Comparison of the Macular Bruch Membrane/Choroid Complex from Age-related Macular Degeneration and Normal Eyes," the team sheds new insights into the development of AMD, age-related macular degeneration. The results of their proteomic analysis endorse inflammatory processes at work in both early and advanced AMD pathology and implicate different pathways of progression to advanced dry and wet AMD, and provide new potential drug discovery targets for AMD, a leading cause of blindness worldwide.■

For copies of NDRI published abstracts, contact NDRI Research Director John Lonsdale, Ph.D. at jlonsdale@ndriresearch.org

Photo: Digital rendition of a triple-labeled section of human retina, courtesy of Lauren C. Liets, Ph.D., University of California, Davis, CA

NIH Researchers Unveil New Class of Dual-Targeted Drugs Against HIV-1 and Herpes Simplex Virus-2

Researchers at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) at NIH, using human cervical tissues from NDRI, have discovered a new strategy to suppress the human immunodeficiency virus, HIV-1, by modifying a drug developed decades ago to treat genital herpes infections. Herpes simplex virus type 2 (HSV-2) is commonly associated with HIV-1 infection and is known to facilitate HIV-1 transmission and progression. The NIH team published the results of their work to modify the antiherpetic drug, Acyclovir, which could spell double trouble for both diseases.

According to Leonid Margolis, Ph.D., Head, Section on Intercellular Interactions and senior author on the paper, "The tissues from NDRI are indispensible not only for this particular drug development work but for our work in general." Human tissue samples maintain cell architecture and more faithfully represent the pathogenesis of disease including HIV that cannot be replicated in cell cultures," he explains. "NDRI provides an excellent source of tissues which are essential for us."

> ***"Human tissue samples maintain cell architecture and more faithfully represent the pathogenesis of disease including HIV that cannot be replicated in cell cultures. "NDRI provides an excellent source of tissues which are essential for us."***
>
> *— Leonid Margolis, Ph.D.*

Working with human tissues in the lab, the NIH scientists replicated what doctors were seeing in their HIV patients. Namely, that when given Acyclovir (ACV) to control genital herpes, their HIV symptoms also improved. "To our surprise," reports Dr. Margolis, "we found that ACV suppresses HIV in singularly infected tissues, those only infected with HIV." Lead author Christophe Vanpouille, Ph.D., explains that other forms of the herpes virus are present in most people's tissues. These viruses carry an enzyme that phosphorylates or activates ACV to attack HIV-1.

> ***"To have one drug that can fight two viruses that are so linked to each other is the big advantage of these kind of drugs."***
>
> *— Christophe Vanpouille, Ph.D.*

Their experiments on human cervical and other tissues enabled the team to develop compounds called Acyclovir ProTides. This is the first in a new class of dual antiviral drugs that suppresses both HIV-1 and HSV-2 by directly and independently blocking the key replicative enzymes of both viruses. According to Dr. Vanpouille, "To have one drug that can fight two viruses that are so linked to each other is the big advantage of these kind of drugs."

Leonid Margolis, Ph.D., Head, Section on Intercellular Interactions, Eunice Kennedy Shriver National Institute of Child Health and Human Development at NIH

In collaboration with a British lab headed by Chris McGuigan, Ph.D. and a Belgian lab led by Jan Balzarini, Ph.D., the team succeeded in designing a chemically phosphorylated ACV, which suppresses HIV-1, and they are now fine-tuning the drug to more efficiently stop HIV-1.

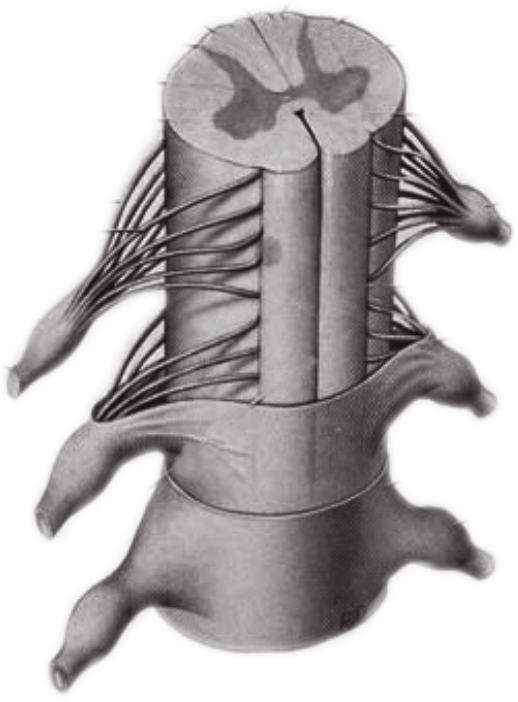
"To develop a new drug takes decades and hundreds of millions of dollars," says Dr. Margolis. "We should be investigating which of the currently approved drugs could be repurposed to treat other infections. The drug we have developed is one example of such an approach." The antiviral developed with ACV and delivered cell-to-cell by the ProTide strategy could be the answer to new and more effective anti-HIV drug cocktails.

NIH team uses cervical tissues from NDRI for other projects

The NIH team is also using human cervical tissues from NDRI for a variety of other projects including modeling for HIV transmission toward the development of effective topical microbicides and other preventive strategies. "Cervical tissue from NDRI replicates *in vitro* a system which mimics sexual transmission of HIV from men to women," explains Dr. Margolis.

The team has found that a well known anti-HIV drug called Tenofovir works against herpes as well in very high concentrations. They have begun work to "supersize" this drug as a potential dual-action antimicrobial agent with potential therapeutic as well as prophylactic applications. ■

NDRI Recovers DRGs - Dorsal Root Ganglia for Chronic Pain and Other Studies



NDRI has achieved a significant logistical and technical breakthrough in the ability to recover dorsal root ganglia (DRGs) for neurological studies. DRGs are neurons located along the vertebral column. These neurons enable the body to detect and transmit pain and other sensory signals through the central nervous system. DRGs are important for the study of chronic pain caused by neuropathies, traumatic injury, cancer and other illnesses. Research models using human DRG neurons are shedding light on pain mechanisms and hold the promise of finding the next generation of safe and effective treatments for debilitating, chronic pain.

The recovery of DRGs is extremely complex. NDRI's experienced procurement team designed protocols for DRG recovery and then selected appropriate partners from within its national network of Tissue Collection Centers to train in the recovery of DRGs from cervical, thoracic and lumbar regions of the spine. High quality DRGs are now being recovered within 4 hours *post-mortem* for a variety of studies including electrophysiology, live cell imaging, in situ hybridization and microarray analysis. DRG samples are shipped fresh at four degrees centigrade, snap-frozen or fixed. Accompanied by detailed medical history information for each donor. NDRI designed collection kits facilitate appropriate preservation and shipping of recovered DRGs to the research laboratory on time, viable and according to protocol. NDRI also provides other customized neurological tissues for research including central and peripheral nervous system tissues, whole brain and brain sections, whole spinal cord, and spinal cord sections. ■

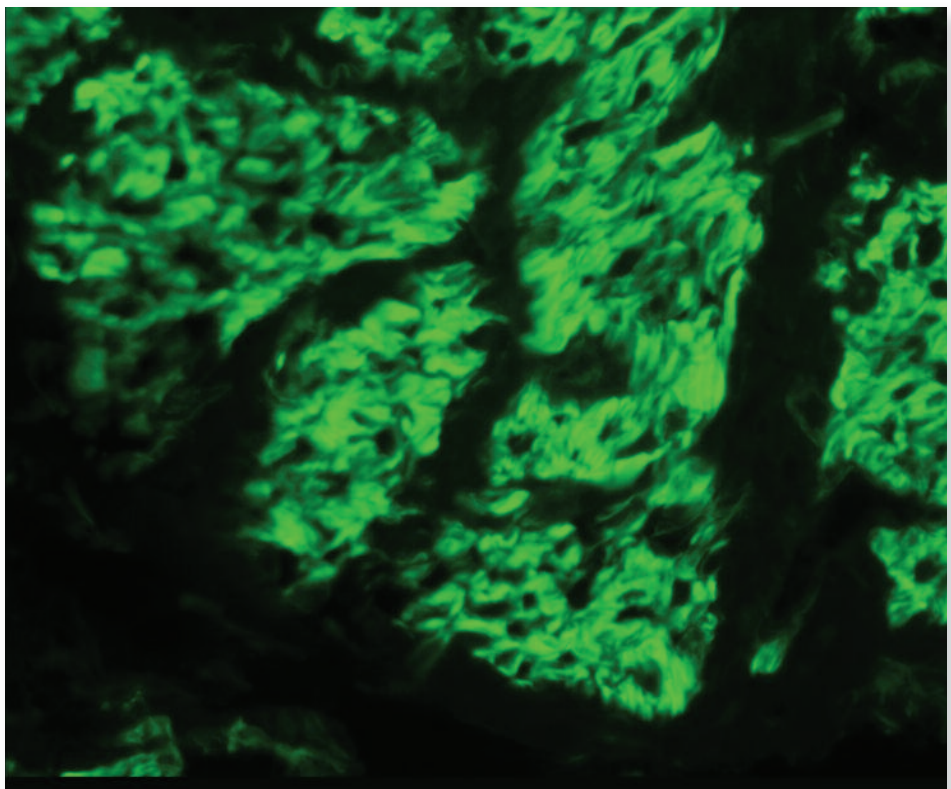
Researchers wanting to apply for Dorsal Root Ganglia or with any questions, contact Thomas Bell, Ph.D., at tbell@ndriresource.org.

A New Drug Combination Shows Promise as An Effective Treatment for LAM Patients

New hope for women fighting LAM may one day come in the form of a one-two punch. University of Pennsylvania researchers led by Vera Krymskaya, Ph.D., Associate Professor of Medicine, discovered in laboratory testing that combining the cholesterol lowering drug, Simvastatin, with an drug already used to treat LAM patients in clinical trials, produces a supercharged combination that appears to knock out existing tumors as well as stops new tumor growth in the lab.

LAM (lymphangioleiomyomatosis) is a multi–system disease that primarily affects women of childbearing age and is often fatal. The disease is characterized by an unusual type of muscle cell growth and the formation of cysts that progressively destroy healthy lung tissue and lead to respiratory failure.

Previously, with the opportunity to study "LAM cells" derived from explanted lungs recovered by NDRI, Dr. Krymskaya and her team identified a key cell growth-controlling pathway disrupted in LAM tumor cells, a major advance toward understanding the disease. She was able to restore the signaling pathway to normal and shrink existing tumors using an immunosuppressant drug called rapamycin. Her discovery led to clinical trials. "The Rapamycin trials were very promising," Dr. Krymskaya reports. "Rapamycin may now buy some patients additional time living with their disease."



LAM lung tissue samples from the NDRI show LAM cells (green).
(photo courtesy of the University of Pennsylvania)

Vera Krymskaya, Ph.D., Associate Professor of Medicine, University of Pennsylvania

Study combines Simvastatin with Rapamycin

Simvastatin is one of a class of drugs called statins, some but not all of which have been shown to synergize with Rapamycin to induce cell death and control proliferation in various cancers as well as in animal smooth muscle cells. In her laboratory tests with mice, Dr. Krymskaya found that the combination of Simvastatin and Rapamycin inhibited LAM tumor cell growth and improved long-term, tumor-free survival. "Initially, the 'LAM cells' were critical to test our hypothesis before moving to animal models," she says. "We also need human tissue to show that what we find in our mouse models can be validated in pathologically relevant human cells. The tissue NDRI sends us is a great resource."

So far Dr. Krymskaya says their data in support of the new drug combination are very promising and one day could signal an effective treatment for LAM patients. Next steps are to test the combination therapy directly on lung tissues in a LAM animal model that her team has developed, the results of which have not yet been published.

The good news, she said, was that Rapamycin did indeed attack and reduce the size of existing LAM tumors in some patients treated in the study group. The bad news was that in some patients who responded to treatment, when Rapamycin therapy was stopped the disease progressed again to pre-treatment levels.

Back at the lab, once again using LAM cells from tissue provided by NDRI, Dr. Krymskaya's team was able to further define key cellular and molecular mechanisms that regulate LAM tumor cell processes. (*Molecular and Cell Biology,* June 2011). "To have human cells derived from human tissue was a key factor in validating our novel molecular treatment targets," Dr. Krymskaya explains.

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>
> *—Vera Krymskaya, Ph.D.*

Amy Farber, Chief Executive, LAM Treatment Alliance

Amy Farber, Chief Executive, LAM Treatment Alliance, is hopeful these latest findings will move research closer to a viable treatment for LAM, but acknowledges there is more work to be done before offering this combination therapy to patients in clinical trials. "The results from the earlier Rapamycin trial, although encouraging, showed the critical need for increasing both the efficacy as well as identification of the types of patients who will likely respond to this intervention," she says. "Dr. Krymskaya's work is a very welcome contribution among the many other options now being considered. We commend her and the NDRI and encourage rapid translation and maturation of current concepts to clinical implementation." ■

NDRI Partnership Critical to Joslin "Medalist Study" Reporting Long-Term Type 1 Patients Still Produce Insulin

NDRI is collaborating with George King, M.D., Senior Vice President and Chief Scientific Officer at the Joslin Diabetes Center, and team members Susan Bonner-Weir, Ph.D., Senior Investigator, and Research Associate and Principal Investigator Hillary Keenan, Ph.D. , on the landmark Joslin Medalist Study of patients who have lived with Type 1 diabetes for 50 years or more. "Our study has examined over 600 Medalists at Joslin Diabetes Center for the presence of eye, kidney, nerve and heart diseases," Dr. King explains. "These studies have shown that significant numbers of Medalists have minimal complications and many still produce insulin. This is a surprise since the Medalists have had diabetes for such a long time." The Joslin study represents the first comprehensive analysis of beta cell function in a large group of insulin-dependent patients. Findings are providing early clues to potential treatments for preserving and even restoring islet cells.

> ***"NDRI has been a key partner to help us in the procurement of the donated tissues from the Medalists."***
>
> *— George King, M.D.*

NDRI's role is to coordinate *post-mortem* recovery of tissues and organs nationally, for the Joslin Study and to create a "Medalist Donor Registry." The NDRI Medalist Registry contains 380 registered medalists who have consented to donate some 2,136 biospecimens for study. NDRI staff stay in close contact with the Medalists through the registration and consent process, building relationships, person to person. Medalists complete a questionnaire of some 120 data points of donor medical and family history, which can be made available to scientists participating in the study.

"The Medalists are a group of wonderful people who not only contributed their time for this study but also are willing to donate their organs after death in order for us to positively evaluate the eyes, kidney, pancreas and blood vessels for protective factors, explains Dr. King. "NDRI has been a key partner to help us in the procurement of the donated tissues from the Medalists."

Hilary Keenan, Ph.D., Principal Investigator

NDRI's "Private Donor Program" has the unique ability to coordinate *post-mortem* recovery from the Medalists wherever they live throughout the country. Consented Medalists reside in 46 states, including Alaska and Hawaii. Through its national network of 62 recovery professionals, NDRI coordinates *post-mortem* recovery of donated specimens at the time and place of death. NDRI has designed and tested the systems and recovery protocols, so that when the time comes, tissues can be recovered from Medalists, processed under 12 hours *post mortem* and delivered in a viable state to Joslin research laboratories.

For the Joslin Study, NDRI has coordinated 22 *post-mortem* recoveries from Medalists in 17 different states of the U.S., a total of 249 tissues which have been studied by Joslin scientists who have published their findings. Currently, Medalists' donations have enabled the study of pancreas, kidney, spleen, lymph nodes, eyes, skin, heart, aorta and blood.

> ***"The Joslin families are powerfully passionate about helping science find a cure for diabetes. Our charge is to make sure the families' wishes to donate to research are fulfilled.***
>
> *— Lee Ducat*

Feedback to families and loved ones is important. NDRI is in touch with next of kin to assure that all went well with the recovery of their loved ones' donations. "The Joslin families are powerfully passionate about helping science find a cure for diabetes. Our charge is to make sure the families' wishes to donate to research are fulfilled," says NDRI President Lee Ducat.

Hilary Keenan, Ph.D., PI on the project, works closely with NDRI staff to coordinate the interface with the Joslin Medalists. "There are many steps which must occur for a successful donation and successful study to take place," she says. "The sensitivity and experience of the NDRI staff, allows them to answer any questions our participants have to help them understand what will happen when their organs are donated. My staff has a wonderful rapport with the NDRI staff, study participants are comfortable discussing end-of-life decisions with the coordinators, and we have published scientifically valuable results based on tissues recovered by NDRI."

George King, M.D., Senior Vice President and Chief Scientific Officer, Joslin Diabetes Center and Co-Principal Investigator, Joslin Diabetes Program's Medalist Study

> ***"My staff has a wonderful rapport with the NDRI staff, study participants are comfortable discussing end-of-life decisions with the coordinators, and we have published scientifically valuable results based on tissues recovered by NDRI."***
>
> *— Hilary Keenan, Ph.D.*

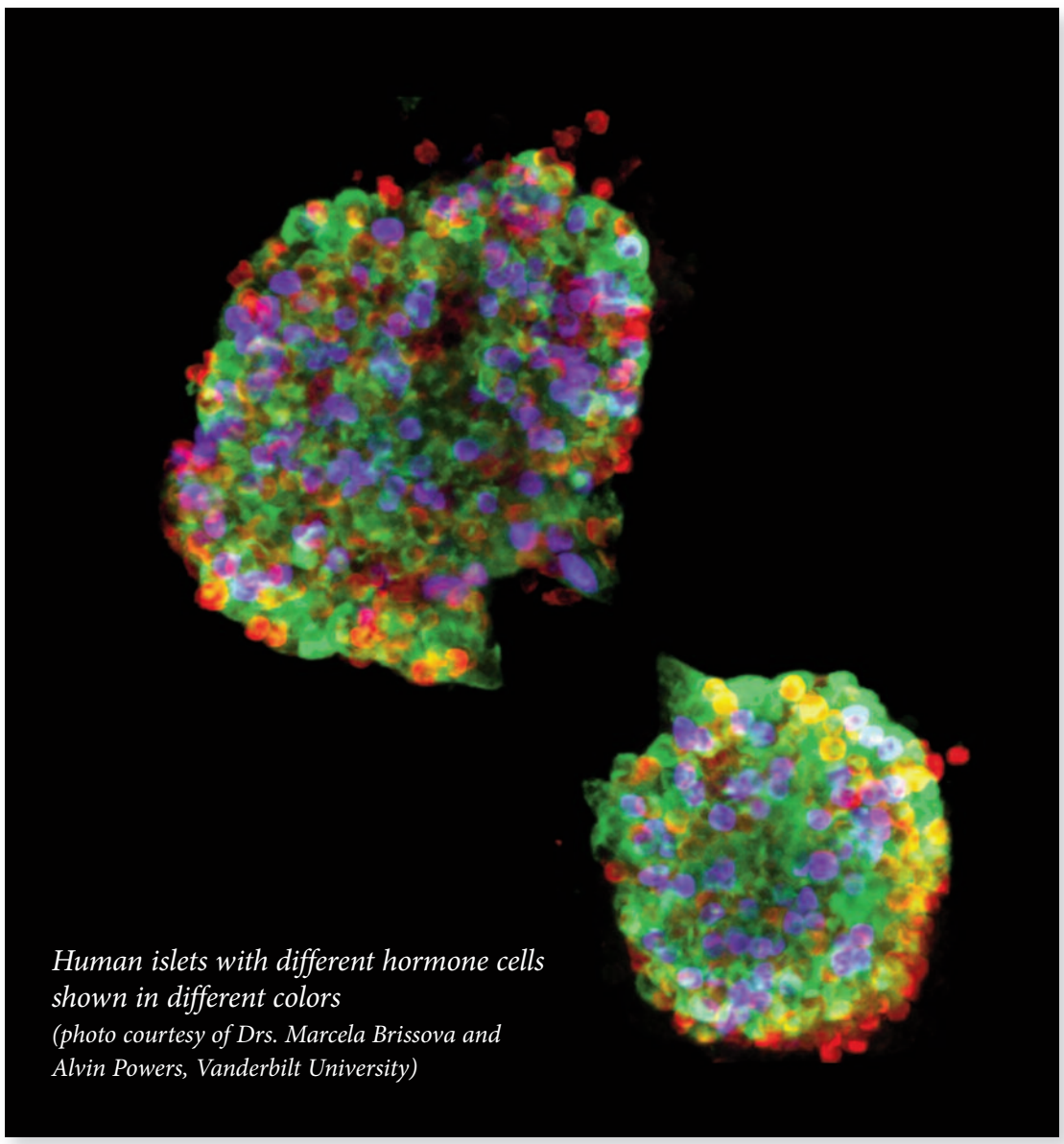
Publications based on Medalist study show findings

The Joslin team have published results of their work in *Diabetes* November 2010 and in *Diabetes Care* in April 2011. These publications based on *post-mortem* tissues recovered from Medalists report that most Medalists have clinical and laboratory findings consistent with "typical" Type 1 diabetes. This includes genetic factors as well as other clinical characteristics, such as weight and cholesterol levels. Further, examination of tissues from the Medalists *post mortem* has confirmed active insulin-producing beta cells, and most strikingly, some of the beta cells showed signs of cell proliferation, cell death and autoimmune attack. Susan Bonner-Weir, Ph.D., reports, "Through the generosity of the Medalists who have consented to donate their organs after death for correlation with *pre-mortem* clinical assessments, we have been able to document that even those without detectable C-peptide still have some insulin-positive beta cells in their pancreas." Everyone so far has had some insulin positive cells. This is exciting because it suggests that there may be on-going turnover of insulin-producing cells even after so many years of Type 1 diabetes," she adds. "Perhaps eventually we will be able to harness the autoimmunity and stimulate the endogenous replacement of the beta cells."

According to Dr. King, the kidneys examined from some of the Medalists *post mortem* are also fairly normal. This offers important confirmation of findings from kidney function tests which were performed while these Medalists were alive. The tissues are needed, he says, to confirm the presence of the protective factors that could be therapeutic agents.

Dr. Bonner-Weir agrees. "NDRI's role in this is critical. Since the Medalists in this study live across the United States, having NDRI organize the *post-mortem* organ donations makes it possible for us to add this important component to the overall study." ■

Studies at Vanderbilt Focus on Pancreatic Islet Cell Regeneration



Human islets with different hormone cells shown in different colors
(photo courtesy of Drs. Marcela Brissova and Alvin Powers, Vanderbilt University)

Much remains to be learned about Type 1 diabetes and how it develops. There is a significant need to continue studying human pancreas from donors with the disease; and young, normal donors, in particular, may provide new insights into the disease process as well as how islet cells develop and proliferate. To aid this effort, NDRI is collaborating with scientists who are part of the Beta Cell Biology Consortium (BCBC). As a team science initiative, funded by the National Institute of Diabetes and Digestive and Kidney Diseases, the BCBC is working to build on existing knowledge of how pancreatic islet cells grow and function to develop new cell-based therapies for insulin delivery. Currently the BCBC consists of 50 research laboratories around the world.

A Coordinating Center located at Vanderbilt University provides the organizational infrastructure for the BCBC. Alvin Powers, M.D., Professor of Medicine and Director of the Vanderbilt Diabetes Center, leads a group of BCBC scientists from Vanderbilt, the University of Massachusetts, Stanford University and the University of Geneva, who are working to understand how human beta cells (insulin-producing cells of the pancreas) grow and proliferate with the ultimate goal of developing ways to stimulate the regeneration of beta cells in individuals with Type 1 and Type 2 diabetes.

In one area of their research, Dr. Powers and Professor Seung Kim, M.D., Ph.D., Howard Hughes Medical Institute, Stanford University, are partnering with NDRI to recover pancreas from normal donors under 10 years of age for islet isolation and study. "Based on studies in mice and very limited human data, we wanted to test the idea that young human beta cells are more capable of proliferating than those from adults," Dr. Powers explains. "However, human islets from young individuals were not available for study, and under existing systems, not routinely identified as pancreas donors. NDRI is a critical component in making our studies possible." From this work, the scientists hope to understand how beta cells from young individuals proliferate and then possibly translate this information into new therapies for Type 1 and Type 2 diabetes.

Seung Kim, M.D., Ph.D.

In a related area of study, to assist Seung Kim's research, NDRI succeeded in providing pancreas and associated tissues (blood, spleen and lymph nodes) from donors who were pregnant or of childbearing age. "By comparing molecular signatures from islets of juvenile and adult donors, we have improved our understanding of the pathways controlling islet cell growth and maturation," Dr. Kim reports. Previous studies in his lab showed that a protein called menin plays a role in controlling pancreatic beta cell mass. Excessive amounts of menin prevents beta cells from growing and proliferating.

During pregnancy, too much menin decreases beta cell mass and can lead to gestational diabetes. A hormone called prolactin produced in high amounts during pregnancy helps beta cell mass to expand so enough insulin is produced for the woman and her growing fetus. Dr. Kim's group found that by administering prolactin to pregnant mice in the lab, menin levels decreased while beta cell mass increased. Besides illustrating menin's role in causing gestational diabetes, the researchers proposed that prolactin may be a potential therapy for reversing the disease.

The clinical collaborations between Alvin Powers, Seung Kim and scientists in the BCBC are paving the way to possible development of islet regeneration therapies for Type 1 diabetes as well as improved treatments to mitigate or prevent Type 2 diabetes. ■

"Human islets from young individuals were not available for study, and under existing systems, not routinely identified as pancreas donors. NDRI is a critical component in making our studies possible."

***— Alvin Powers, M.D.,** Professor of Medicine and Director of the Vanderbilt Diabetes Center*

For information about NDRI biospecimens and services, contact us at 800-222-6374 or visit our website at www.ndriresource.org

NDRI Founder Transformed Biomedical Research by Opening Pathways to Human Biomaterials - *What's Next?*

NDRI Founder and President Lee Ducat changed history when she provided scientists with access in a continual way to human biomaterials for their research projects, customized for their studies. For the last three decades she has led the organization to become one of the largest private, non-profit national networks recovering human cells, tissues, and organs for research. She also founded the Juvenile Diabetes Research Foundation in 1970 and in 1988, Human Biological Data Interchange, a worldwide Type 1 diabetes registry of patients available for genetic research. Now, Lee Ducat is transitioning to a new role in 2012. She plans to reduce to half time her day-to-day responsibilities with the NDRI organization and devote her energy and talents to the international expansion of NDRI's human tissue and researcher networks and to lead initiatives in both translational research and environmental science. She will step down as NDRI President and CEO, but will remain a member of the NDRI Board of Directors.

"Throughout this journey I've tried to help where I could to fill the gaps in medical science so that research on human diseases could move forward faster," she says. "I see new opportunities and new gaps to fill, and I am looking forward to the challenges ahead."

Where it all began

Lee Ducat wasn't always interested in medical research. In her twenties she put aside a career in radio and television to become a wife and homemaker. She enjoyed a typical middle-class lifestyle, raising three children with her husband in the Philadelphia suburbs. Things changed drastically almost overnight when her nine-year-old son, Larry, was diagnosed with juvenile diabetes.

"In those days, very few people knew children came down with diabetes. I certainly didn't know it," she recalls. "One day you have a perfectly normal healthy kid, the next day you find out he has a chronic disease that changes his life forever. For the longest time I walked around in a blur, I could hardly see through the tears."

Lee didn't wait too long before she decided to do something to help her son. With help from his doctor, Robert Kaye, M.D. and a few close friends, she started a grassroots effort that would rock the world of diabetes research on it's axis. In May 1970, the Juvenile Diabetes Foundation was born. Lee spearheaded early fundraising and championed efforts to build a strong and widespread legislative campaign in Washington to increase awareness about juvenile diabetes and secure government funding. She recruited Senator Richard Schweiker (R-PA) as a major advocate along with many celebrity spokespersons who helped bring national focus to the organization's efforts. Their hard work led to the creation of the National Diabetes Commission and then the passage of the National Diabetes Act in 1972, gaining funding support from the National Institutes of Health and NIDDK, the National Institute for Diabetes, Digestive and Kidney Diseases. The diabetes effort became a prototype for legislatively constructing a research effort across all NIH institutes, the CDC and other federal agencies.

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Arthur Rubenstein Returns to the NDRI Board of Directors

Arthur Rubenstein, MBBCh, returns to the NDRI Board of Directors, having served as a founding member in the 1980s. Dr. Rubenstein supported the design of the NDRI prototype for a national system of human tissue recovery for scientists to support their mission to study the human model and to corroborate animal studies in man. "The role of the NDRI Board of Directors has been invaluable over the past three decades," he says. "The provision of a variety of human tissues to investigators was a visionary concept, which has been remarkably valuable and productive.'" He notes that today NDRI provides a unique service to investigators all over the world and has become indispensible to many research projects. Its spectacular success exceeds even our most optimistic expectations and is a tribute to the foresight, drive and vision of Lee Ducat, its founder."

"As personalized medicine becomes a reality during the next decade, the combination of human tissue from well characterized donors will become increasingly crucial for diagnostic, therapeutic and research purposes. The importance of the NDRI will undoubtedly increase in the years ahead."

— Arthur Rubenstein, MBBCh

"As personalized medicine becomes a reality during the next decade, the combination of human tissue from well characterized donors will become increasingly crucial for diagnostic, therapeutic and research purposes," he adds. "The importance of the NDRI will undoubtedly increase in the years ahead."

Arthur Rubenstein is recognized for a decade of leadership as Executive Vice President of the University of Pennsylvania for the Health System and Dean of the School of Medicine until his retirement, July 2011. He remains Professor of Medicine, within the Department of Medicine Division of Endocrinology, Diabetes and Metabolism at U Penn.

Dr. Rubenstein is credited with stabilizing the school's financial position while strengthening research, educational and clinical programs during his tenure and working to build an infrastructure for translational research, strengthened by many interdisciplinary research institutes, including the Institute for Translational Medicine and Therapeutics. The Perelman Center for Advanced Medicine and the Roberts Proton Therapy Center were built under his leadership. He led the school to its highest rankings ever in the annual survey of graduate and professional schools by *U.S. News & World Report.* He is also credited with enacting strict ethics policies to reduce physician conflicts of interest.

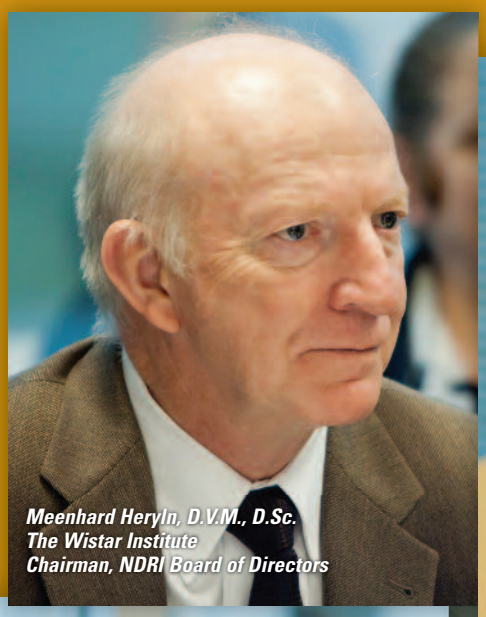
Arthur Rubenstein, MBBCh, Professor of Medicine Division of Endocrinology, Diabetes and Medicine, U Penn

In recognition of his contribution to education and research while at U Penn, in 2009, the Association of American Medical Colleges awarded him their top honor, the Abraham Flexner Award for Distinguished Service to Medical Education. In presenting the award, the AAMC described him as "the complete academic medicine physician leader."

Before joining U Penn, Dr. Rubenstein served as Chair of the Department of Medicine at the University of Chicago and was honored as the Coggeshall Distinguished Service Professor of Medical Sciences at the University's Pritzker School of Medicine. He was also formerly Dean and Gustave L. Levy Distinguished Professor of Mount Sinai School of Medicine in New York City.

The author of more than 350 publications, Dr. Rubenstein has held editorial advisory positions with several respected journals, including the *Annals of Internal Medicine,* and the *Journal of Diabetes and Its Complications.* He is a Fellow of the College of Medicine of South Africa and of the Royal College of Physicians of London and a Master of the American College of Physicians. He received his medical degree from the University of the Witwatersrand in Johannesburg. In 2001, his alma mater conferred upon him the honorary degree of Doctor of Science in Medicine. ■

NDRI Board of Directors Meeting With Strategic Partners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The Wistar Institute
Chairman, NDRI Board of Directors


Michael White
JDRF Board Member
NDRI Board Member


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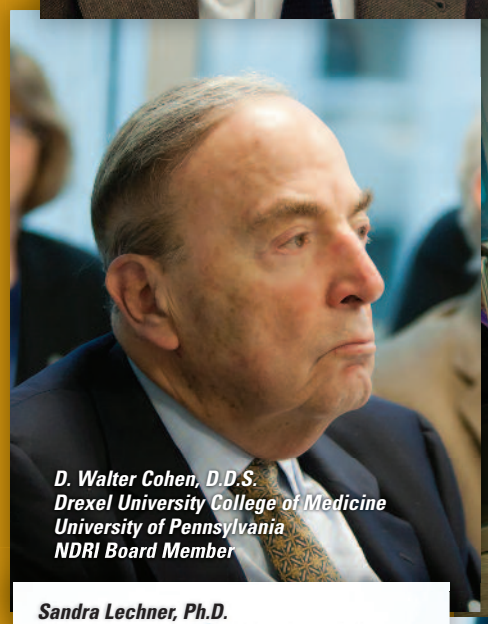
University of Pennsylvania
NDRI Board Member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Drexel University College of Medicine
University of Pennsylvania
NDRI Board Member


Lou Philipson, M.D., Ph.D., FACP
University of Chicago
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Beverly Mayhew
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Lee Ducat
NDRI President and Board Member


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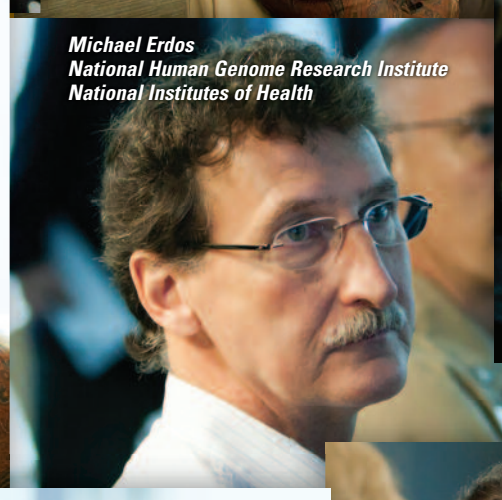
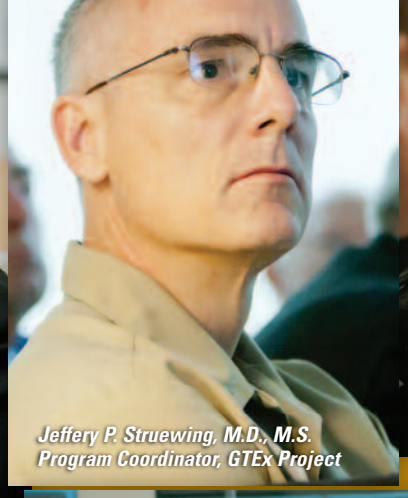
Vertex Pharmaceuticals Incorporated


Michael Erdos
National Human Genome Research Institute
National Institutes of Health


Chris Pentand, Ph.D.
Cystic Fibrosis Foundation


Michael Gaba, Esq.
NDRI Counsel


Yaffa Rubinstein, Ph.D.
Office of Rare Diseases Research, National Institutes of Health


Jeffery P. Struewing, M.D., M.S.
Program Coordinator, GTEx Project


Lois Jovanovič, M.D.
Sansum Diabetes Research Institute


Fernando Garcia, M.D.
Drexel University College of Medicine


Gary Walters
LifeNet Health


Howard Nathan
Gift of Life


Karen Ball
The Sturge-Webber Foundation


Lee Ducat, President and Board Member, presenting the Distinguished Service Award to Lois Jovanovič, M.D., Sansum Diabetes Research Institute

Continued from cover

NDRI Facilitates Drug Discovery in Cystic Fibrosis Research

Kalydeco is designed to increase the function of a defective CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) protein in the lungs of people with the G551D mutation. NDRI helped the CF community move over the early but critical hurdles in the development of these drugs. The defective CFTR protein functions like a locked gateway on the cell surface. Kalydeco helps unlock the gate enabling chloride to pass through, as it would in healthy cells. This restores a proper flow of salt and fluids on the surface of the lung. Based on their promising Phase 3 clinical trial results, Vertex has taken the next step and applied for U.S. Food and Drug Administration approval to make Kalydeco available to CF patients with at least one G551D mutation.

The compound VX-809 was developed to correct the most common mutation in the CFTR gene. In people with this F508del mutation, CFTR proteins do not reach the cell surface in normal amounts. VX-809, known as a CFTR corrector, aims to increase CFTR function by increasing the trafficking or movement of CFTR to the cell surface. Vertex is currently conducting a Phase 2 study that is evaluating combinations of Kalydeco and VX-809 in people with the F508del mutation. Combination therapy, if successful, would be beneficial for between 50–90% of the CF population. Recently, Dr. Penland presented experimental data from work conducted using NDRI-recovered tissues that showed combination therapy produced a six-fold improvement of normal CFTR function up to about 30%. Preliminary results from the current Phase 2 trial are promising, suggesting that combining VX-809 and Kalydeco does improve CFTR function in CF patients. Further testing is planned.

The CF Foundation recently announced their continued collaboration with Vertex to develop a second "corrector" drug, also aimed at helping the 90% of patients who have the more common mutations.

"We are extremely pleased that efforts to develop drugs that target the fundamental physiological problem in CF are moving forward rapidly," says Dr. Penland. "We in the cystic fibrosis community are keeping our collective fingers crossed that these agents will change the course of disease for many who have relied solely on symptomatic therapies." ■

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NDRI Founder Transformed Biomedical Research by Opening Pathways to Human Biomaterials - *What's Next?*

One of the JDF's biggest early achievements was to build a network of chapters across the United States and around the world to raise money to power up research toward discovery. Today in more than 100 locations worldwide the Juvenile Diabetes Research Foundation (JDRF) members are the living force carrying on Lee Ducat's dream to fund research to find a cure. JDRF leads the world in supporting Type 1 diabetes science with funding at well over $100 million a year, bringing its total research funding to more than $1.5 billion since Lee founded the organization in 1970. Billions more research dollars were added with the government effort Lee started and led to support diabetes research.

Founding NDRI

By the close of the seventies, Lee had become well known to many of the leading diabetes researchers. She had served by appointment from President Gerald Ford on the National Diabetes Commission and the National Diabetes Advisory Board, and was subsequently appointed by President Ronald Reagan and Secretary of Health Richard Schweiker to the second National Diabetes Advisory Board, where she served as vice chair and as chair of the Board's International Symposium.

Prominent among the leading diabetes researchers of the time was Paul Lacy, M.D., Ph.D., at Washington University in St. Louis. a renowned pioneer in islet cell transplant research who became a life-long friend and advocate. Dr. Lacy's research on animals was ready to move to the next stage and for that he needed human pancreas. At the time, there was no system in place that could provide pancreas or any other kinds of human tissues for that matter in the quantities and quality required for diabetes research. Dr. Lacy challenged Lee to solve the problem, and in 1980, she founded NDRI, the National Diabetes Research Interchange, with help from a $3 million grant from Pew Memorial Trust, Philadelphia.

NDRI staff and advisors worked with organ procurement organizations around the country to target pancreas from organ donors for islet isolation and transplant research initiated by Paul Lacy, M.D., Ph.D., and David Scharp, M.D., at Washington University in St. Louis, whose seminal research to isolate and transplant human islets led to the first clinical trials in humans and forged a new pathway to treatment. This work would not have been possible without NDRI, which continues to support islet transplantation research at multiple institutions around the world. Dr. Lacy, who became NDRI's first Board Chairman, once commented, "NDRI has transformed the attitude of medical scientists from ignoring the use of human tissue in research to one of requiring these tissues for the study of human disease. New and important findings would not have been made in the absence of this unique organization."

"NDRI has transformed the attitude of medical scientists from ignoring the use of human tissue in research to one of requiring these tissues for the study of human disease. New and important findings would not have been made in the absence of this unique organization."

— Paul Lacy, M.D., Ph.D.

Throughout NDRI's 31-year history, Lee has looked for ways to increase the availability of the kinds and quality of human biomaterials researchers need to move science forward to cure both common and rare diseases. The National Disease Research Interchange became the prototype for national recovery of human biomaterials for scientists. Today, more than 40,000 human biomaterials of all types are offered through NDRI each year and are matched to the protocols of some 500 researchers at close to 250 research centers. Some 15,000 biospecimens are projected to be placed in 2011. In the last year, 135 publications documented scientific advances using human biomaterials from NDRI, including the discovery of two new drugs which will improve the lives of people with cystic fibrosis. Specialized initiatives include collaborations in support of diabetes research, a targeted rare disease initiative, providing short-hours *post-mortem* tissues, support for HIV/AIDS research, cancer, cystic fibrosis, islet cell research, stem cell research and more. Literally NDRI serves research in just about every disease. NDRI was first to create one of the worlds largest registry of some 7,000 families for genetic research. The HBDI – the genetics division of NDRI provides extensive family history data, cell lines, sera, and DNA for both Type 1 and Type 2 diabetes research as well as other diseases. NDRI is now one of the lead agencies funded by the Office of the Director, NIH to provide human tissues to the GTEx project which aims to genotype all the tissues and organs of the human body.

Helping to make research happen

Lee Ducat is a pioneer in the effort to provide the resources scientists need for laboratory research in human diseases. She has worked tirelessly to facilitate scientific exchange to move research forward. In 1988, she initiated the "Search for the Diabetes Genes" on Capital Hill to increase funding for diabetes research. Through NDRI in collaboration with top NIH leaders including current NIH Director Francis Collins, M.D., Lee has initiated several groundbreaking scientific conferences on "The Genetics of Rare and Common Diseases," "The Discovery of Diabetes Subtypes," and "The Genetics of Rare Disease."

Accolades for her lifetime achievements in support of diabetes and all disease research come from industry and academia, the U.S. Congress, Presidential Task Forces, the Joslin Diabetes Center, the Diabetes Research Institute, the American Diabetes Association, and an Honorary Doctorate from Women's Medical College. Her home state of Pennsylvania honored her as a "Distinguished Daughter," in 2007 and most recently, JDRF honored her in Philadelphia at their 40th anniversary celebration in June 2010. ■

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Editorial Committee Chairman: Lee Ducat, President of NDRI
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Questions or requests for additional information about articles in the NDRI newsletter are welcome. Core support for NDRI comes from NCRR, NEI, NIAID, NIDDK, NIAM.S., NHLBI, and ORDR at the National Institutes of Health, and the State of Pennsylvania. Additional sources of support include the NDRI Partners Program, voluntary health organizations and private donations. NDRI is a 501c 3 non-profit organization for which contributions for various initiatives are welcome and may be sent to NDRI.