NDRI Research Brief

News from National Disease Research Interchange

May 2006

Welcome to the first issue of the NDRI Research Brief, an update on developments in the use of tissues and organs for research. In this issue you'll learn about the growing need for donated skin, efforts to understand osteoarthritis, and important work in AIDS research. In future issues we'll share best practice examples for research recoveries and stories about the people who are helped by biomedical research. In addition, you have the chance to win a $25 Amazon.com gift certificate by participating in the "Mystery Microscopy" contest. I hope you find Research Brief helpful and will share the newsletter with your associates. Please don't hesitate to call me at 800-222-NDRI if have any questions about providing tissues or organs for research.

Jeff Thomas, NDRI Director of Donor Services

NDRI Board Members Arthur Caplan, Ph.D., D. Walter Cohen, D.D.S., Hal Broxmeyer, Ph.D., and David Bodine, Ph.D., blow out the candles on a cake at a recent anniversary celebration.

NDRI Turns 25

A Quarter Century of Support for Research

The year 1980 was a heady time for diabetes researchers. Advances in pancreas islet cell transplants in animals offered hope that a cure for Type 1 diabetes might be possible.

Dr. Paul Lacy and his colleagues at Washington University had shown that islet cells transplanted from the pancreas produced insulin and could cure animals of their diabetes. The next step was to perfect the techniques used to remove islet cells from human pancreata and to transplant them into people with Type 1 diabetes.

Patients and parents of children with insulin-dependent diabetes waited anxiously for this research to be carried out.

But there was a severe shortage of donated human pancreata that prevented this work from being accomplished. Often, donated pancreata unsuitable for whole-organ transplant, yet still valuable for research purposes, were not recovered from donors or were simply discarded.

Lee Ducat, founder of the Juvenile Diabetes Foundation and mother of a diabetic child, was quick to act on the need for pancreata. In 1980, with a grant from the Pew Memorial Trust, she collaborated with Dr. Lacy to establish the National Diabetes Research Interchange (NDRI), a non-profit organization to find and deliver to investigators human tissues needed for diabetes research.

"We were the first and only organization to make human tissue available to

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FEATURED RESEARCH

In Search of a Cure for Osteoarthritis

Many of us have parents or grandparents with deformed fingers, stiff joints, and other hallmarks of osteoarthritis. Indeed, more than half of the population aged 65 or older has some x-ray evidence of osteoarthritis in at least one joint, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Long thought to be an inevitable result of the wear and tear of aging, physicians treat arthritis by relieving symptoms and there are no medicines that cure or prevent the condition.

But in the last decade, research has shown that there is more to osteoarthritis than aging alone. Investigators have discovered that the production, maintenance,

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Dr. Robert Terkeltaub

▶ *In Search for a Cure for Osteoarthritis continued*

and breakdown of cartilage, as well as bone changes, stem from a complicated biochemical cascade of events. Many researchers are trying to pinpoint what things go wrong in that cascade with the hope of developing treatments that target the triggering factors.

Rheumatologist Dr. Robert Terkeltaub of the San Diego VA Hospital and the University of California San Diego is one of the researchers who hopes to uncover the key biochemical culprits that cause osteoarthritis. Dr. Terkeltaub already has a few suspects—components of the immune system, enzymes, and other compounds that seem to work together to cause osteoarthritis. But to solve this case, he needs firm evidence—a tight link between the appearance of these suspect chemicals in joint tissue and the development of arthritis.

The best way for him to collect that evidence is via the human joint cartilage that is often discarded from donors of musculoskeletal tissue used for bone transplants. He isolates cartilage cells from normal and osteoarthritic human knee cartilage, as well as knee cartilage damaged by a sports or other injury. He then grades them for their degree of arthritis and assesses the amounts of his suspect molecules in the cartilage to see if the same chemicals repeatedly show up as cartilage progresses from being normal to arthritic.

Dr. Terkeltaub's research depends on regular access to human cartilage tissue, including normal cartilage from young donors as well as cartilage from people with sports injuries.

To serve the needs of osteoarthritis researchers, NDRI can receive shavings of cartilage totaling 5 grams or more from musculoskeletal donors. To learn more about how you can help advance research into osteoarthritis, call NDRI at 1-800-222-6374.

HOT TOPICS

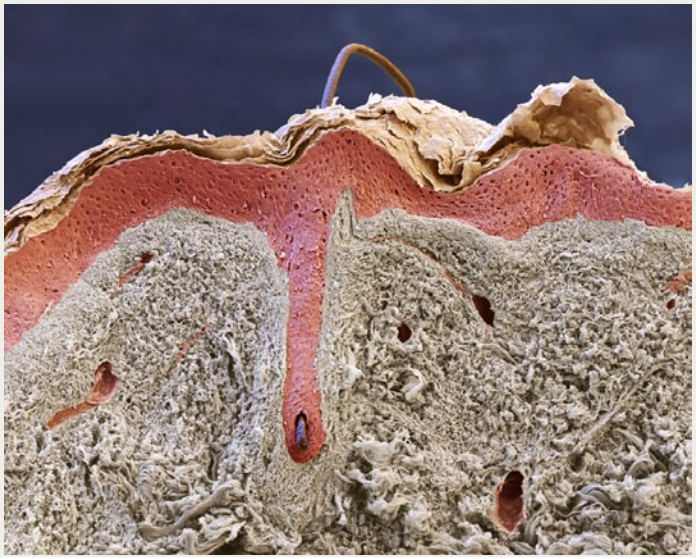
Research Need for Skin Grows

While answers to some medical mysteries are hidden in the far reaches of the body, many others are literally skin deep.

The demand for skin for biomedical research is growing rapidly. Today, more than 20 NDRI-affiliated researchers are seeking donated skin for important scientific investigations. Research is wide-ranging and includes recovery of stem cells from hair follicles, assessment of the safety of transdermal patches for drug delivery, evaluation of the toxicity of certain pollutants and finding cures for skin diseases.

Skin that may be used for research is often rejected for transplant because of the presence of moles, wrinkles or other blemishes. Skin in some regions, such as the chest or abdomen, is also bypassed for transplant because it is not possible to remove the larger grafts traditionally required for transplant.

Using donated skin, researchers are searching for stem cells on hair follicles.



Some examples of research include:

- Researchers at the Medical College of Wisconsin in Milwaukee and the University of California in San Francisco are investigating the potential of retrieving stem cells

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► *Research Need for Skin continued*

in human hair follicles in hopes of developing a wide range of tissues including bone, muscle, cartilage and tooth enamel.

- With the growing popularity of transdermal patches for drug delivery, researchers at the Food and Drug Administration are using donated skin to develop new methods to assess penetration of various drugs and to improve the safety of the patches.
- Researchers supported by the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), and the National Institute of Occupational Safety and Health (NIOSH) are investigating how much various workplace chemicals and pollutants penetrate the skin.
- Certain skin conditions stem from genetic flaws, including the inherited blistering disorder epidermolysis bullosa (EB) and some kinds of skin cancer. In hopes of developing cures or treatments, researchers are using innovative techniques to deliver normal versions of the flawed genes into skin cells.

You can help these projects and other skin research move forward by contacting NDRI with referrals of potential dermatome skin donors. Remember, amounts typically needed and recovered for research are significantly smaller than those recovered for transplant -- often no more than 1 x 1 cm to 10 x 10 cm. NDRI's experienced staff will coordinate the retrieval and transport of the skin to researchers. For more information, contact 1-800-222-NDRI.

Mystery MICROSCOPY

Win a $25 Amazon.com Gift Certificate

© Dennis Kunkel Microscopy, Inc.

Be the first to identify this image and win a $25 gift certificate to Amazon.com. Simply send an email to Jeff Thomas at jthomas@ndriresource.org with your answer. The first person to email Jeff with the correct answer will be the winner. Good luck!

RULES: You may only win this contest one time. Winner must be a primary recipient of this newsletter or employed by an organization affiliated with NDRI as a donor agency, tissue or eye bank or other scientific or medical organization. Please no family members or friends. By participating, you agree to allow NDRI to publish your name in a future edition of NDRI Research Brief if you win.

DID YOU KNOW?

NDRI Supports Research to Find HIV's Hiding Places

Did you know that the introduction of highly aggressive combination therapy against the Human Immunodeficiency Virus (HIV) has substantially extended the lives of many people with HIV, and essentially turned an imminently deadly disease into a long-term chronic condition? In the mid-1990s, a new class of Anti-HIV drugs, known as protease inhibitors, was added to the standard treatment mix. At that time, the number of people that died from AIDS each year in this country dramatically dropped to below half of what it was before such treatment began, data from the Centers from Disease Control and Prevention reveal.

The success of such combination therapy hinges on the principle that although HIV can quickly become resistant to one class of anti-HIV drug, it seems to rarely change into a virus that can resist the multi-pronged attack of two or more drug classes. If people infected with HIV adhere to such treatment regimes, they may live a normal lifespan and die of causes other than AIDS. But the side effects of such treatment can be onerous,

Tissues donated by people with HIV but with no symptoms of an active infection are critical to research.

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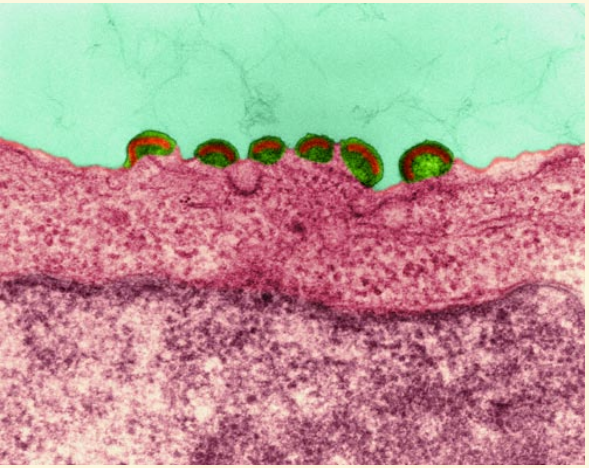
▶ *NDRI Supports HIV Research continued*

and the treatment does not fully eradicate HIV from the body. Once treatment stops, the latent virus quickly emerges from the numerous hiding places it has in the body and actively starts killing cells of the immune system, several studies show.

These findings have led to a concerted effort to understand more about latent HIV and ways to eradicate it from the body. Critical to this research and other research on latent HIV are tissues donated from people infected with HIV but with no symptoms of an active HIV infection. Those tissues may hold the answers to such questions as how the virus stops the immune system from attacking it, and how extensive its hiding places are in the body. HIV is known to hide out in certain cells and tissues of the immune system, but the full range of human tissues has yet to be tested for the latent virus. Answers to those basic questions may lead to treatments that cure people of HIV infection, rather than just keep the virus in check.

A transmission electron microscopic image of HIV in human lymph tissue.



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Since 2000, NDRI's HIV Research Program has provided researchers with donated tissues from people with HIV, including HIV-positive biopsy tissue discarded after surgery. NDRI is actively seeking tissues from people with symptomatic as well as asymptomatic HIV infections and does not rule out donors if they have other infections or substance abuse.

Funded by the NIH's National Institute of Allergy and Infectious Diseases, NDRI's HIV Research Program has experienced coordinators available to respond to confidential inquiries from HIV-positive patients or their families who wish to donate for research. Coordinators will speak directly with care providers about options for organ and tissue donation and coordinate the logistics of tissue recovery and delivery to appropriate researchers.

Please call NDRI with information about excluded HIV positive patients. For more information about the HIV Research Program, go to http://www.ndriresource.org/html/spec_hiv.htm or call 1-800-222-6374, extension 222.

▶ *NDRI Turns 25 continued from page 1*

scientists in a continuous way, and that changed research forever," noted Ms. Ducat. "We set up a customized service that would allow a scientist to base a whole research project on the steady flow of human tissue to his laboratory." The end result is that more than 500 severely diabetic individuals have received islet cell transplants.

Soon scientists researching other diseases also began requesting human tissues for their investigations. This led NDRI to expand its focus beyond the diabetes arena to embrace more than 100 diseases and become the National Disease Research Interchange a few years after its inception. Recognizing NDRI's important role in furthering their efforts, the National Institutes of Health began funding NDRI in 1981.

"We were the first organization to make human tissue available to scientists in a continuous way, and that changed research forever."

Lee Ducat,
NDRI President and Founder

During the past 25 years NDRI has added several specialized initiatives to its original organ and tissue retrieval program including:

- The Human Biological Data Interchange (HBDI), a centralized collection of family data, cell lines and DNA for the genetic study of diseases, particularly diabetes, and including an extensive collection to aid autism research.
- The Rare Disease Initiative, which matches researchers of rare diseases with human tissue from affected donors. Many of these donors are excluded from transplant programs.

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MOST WANTED

Top Research Needs

Below are some of the most frequently requested* normal and diseased organs and tissues from NDRI-affiliated researchers.

TISSUE/ORGAN	RESEARCH EXAMPLES*
Liver	Gene therapy for hemophilia; liver regeneration studies; diet-related metabolic and genetic studies
Pancreas	Autoimmunity in type 1 diabetes; islet cell transplant
Lung	Lung cancer; causes of asthma; causes of fibrosis in the lung
Heart	Stem cell isolation to heal MI; gene expression studies in normal vs. diseased heart tissue; prevention of amyloid deposits in cardiac tissue
Skin	Culturing of stem cells from hair follicles; transdermal drug delivery; effects of mustard gas agents; wound healing in ischemic limbs
Cartilage	Osteoarthritis; tissue engineering for cartilage regeneration
Muscle	Age-related muscle loss studies; genetics of diabetic risk factors; stem cell biology for treatment of muscular dystrophy and other disorders
Vertebral Bodies	Recovery of marrow stem cells
Ocular Tissue	Macular Degeneration, Glaucoma, Diabetic Retinopathy

* Partial list only

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- Pancreas for Islet Cells program which supplies pancreatic islet cells for diabetes research.
- The HIV Research Program, which provides donated tissues and organs from people with HIV.
- The Retrieval of Human Cancer program, which provides about 2,000 cancer tumors each year to researchers.
- The Stem Cell Initiative to provide stem cell preparations tailored to the individual needs of investigators.

NDRI maintains the nation's largest database of scientists who use human biomaterials for their research. Its network of human tissue providers includes 54 organ procurement organizations, 45 eye banks, 25 tissue banks, and 14 hospitals. To date, NDRI has helped provide more than 200,000 human tissues or organs to more than 2,000 researchers at top universities, hospitals, and medical research centers in the United States.

NDRI-supported research has led to more than 2,500 publications in scientific journals across all disciplines of biomedical research. Major research advances that have stemmed from NDRI-supported research include:

- Methods to better preserve and maintain viable pancreas islet cells that have helped more than 500 severely diabetic individuals receive islet cell transplants.
- The growth of cartilage cells in culture, which may eventually enable cartilage repair and regeneration therapies for people with arthritis, sports injuries and other joint disorders.
- Discovery of a gene that appears to inhibit breast cancer growth and might lead to a new anti-breast cancer drug.
- Discovery of genes key to retina function that will help researchers uncover the causes of several eye disorders.

NDRI has helped provide
200,000 human tissues and organs to researchers
in the United States.

"Today NDRI provides a unique service to investigators all over the world and has become indispensable to many research projects," commented Arthur H. Rubenstein, M.B.B.Ch., of the University of Pennsylvania, School of Medicine.

NDRI will continue to look for new ways to facilitate the recovery and preservation of human organs and tissues for research in order to fulfill its mission as an "indispensable" partner in the search for new treatments and cures for disease.

The need for human tissue for research continues to grow. More than 80 percent of NDRI-affiliated researchers report an ongoing need for more tissues for their investigations. Please help support the progress of biomedical research by referring potential donors of research tissues and organs.

Human Tissues and Organs for Tomorrow's Scientific Breakthroughs

NDRI is committed to providing the nation's top scientific laboratories with donated human cells, tissues and organs in order to better understand diseases and help develop new drugs and therapies for treatments and cures.

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