

# Mystery MICROSCOPY

**CONGRATULATIONS to Rob Teaster**, Clinical Educator at Carolina Donor Services, the winner of our first Mystery Microscopy contest, who correctly identified last issue's image as a **kidney nephron**.

## Win a \$25 Amazon.com Gift Certificate

Be the first to identify this image and you will win a \$25 gift certificate to Amazon.com. Simply send an email to Jeff Thomas at NDRI at [jthomas@ndriresource.org](mailto: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.



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## DID YOU KNOW?

### NDRI Supports Rare Disease Research

**D**id you know one in ten Americans has a rare disease, according to the National Organization for Rare Disorders?

Technically a rare disease is defined as one that does not afflict more than 200,000 people in the United States. But since there are close to 7,000 rare diseases, they have a collective impact that is hard to ignore. In other words, rare diseases are not so rare.

Rare diseases include well-known disorders such as sickle-cell anemia, cystic fibrosis, and muscular dystrophy and a host of others of which most people have never heard. Research aimed at finding the causes, and ultimately treatments, for these disorders could benefit many thousands of people. And because many of these rare diseases share symptoms or pathologies with more common diseases, research on rare disorders often provides useful insight into more prevalent afflictions.

For example, some children have a rare disorder called familial hypercholesterolemia (FH), which causes exceptionally high blood cholesterol levels and makes these children likely to have heart attacks during their teenage years. Research on FH led Drs. Michael Brown and Joseph Goldstein to the findings that won

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► *Informed consent continued*

tion to exclude certain tissues or organs from the donation. Families also must be informed how the anatomical gifts will be used. Research guidelines require that families be informed that their loved ones' anatomical gifts will be processed and preserved prior to use in research.

A concern for some families is whether their loved one's tissues or organs will be donated to a for-profit organization or used for commercial purposes. Myer said that LifeNet lets families know that although it is a non-profit organization, it is affiliated with for-profit organizations that may be involved in the recovery, distribution, and use of the anatomical gifts. But LifeNet also stresses to the family that these for-profit organizations have to meet strict ethical and medical standards and be consistent with the mission and values of LifeNet.

NDRI also explains to families that it sometimes will supply tissues to for-profit companies, but emphasizes that these companies conduct basic medical research into the development of new medical therapies. If the next of kin objects to the involvement of a for-profit organization, the NDRI coordinator will note on the consent form that the gift is a "non-profit only donation."

According to Myer, many families that donate for research want follow up on the research projects for which their loved one's gifts were used. This information is provided by LifeNet's aftercare specialists who keep in touch with families for 18 months after the donation takes place. For this they use NDRI's reports on what happens to donated tissue and organs.

"This gives families some closure as to

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Kevin Myer, Executive Director, LifeNet OPO

*We treat every family with compassion and support while advocating for the opportunity in front of them, which is to donate and help others.*

Kevin Myer, Executive Director, LifeNet OPO

what happened with a loved one's gifts and it means a lot to them," said Myer.

Families also take comfort in knowing their gift has helped further medical progress, Stiltner noted. "Some people are not aware that they can donate their loved one's tissues or organs for research, but once they learn of that option, they usually are excited about it because that way their loved one is going to continue to do beneficial things," he said. Myer concurred that because so many families are receptive to donating tissues and organs

for research, "we've elevated organ and tissue recovery for research to a level that is parallel to that of transplantation here at LifeNet."

LifeNet provides families written background information on the research projects for which their loved one's anatomical gifts could be used, and makes sure their coordinators that talk with families are aware of the research opportunities available and can explain the various research projects to them. "Donating for research is more than just an option. It's an opportunity," said Myer.

Stiltner stressed that asking a family to authorize an anatomical donation is a process and not just a matter of getting a signature on a form.

"If families know you genuinely care about them and their loved ones, they will be more receptive to listening to you and ultimately will make more informed decisions," he said.

► *NDRI Supports Rare Disease Research continued*

them the Nobel Prize for Physiology or Medicine in 1985. These researchers uncovered fundamental cholesterol-regulating processes that not only go awry in children with FH, but in people who have high-cholesterol diets. This discovery ultimately led to the development of cholesterol-reducing statin drugs.

"Once researchers start looking at these rare disorders, they may find clues that will lead them to understand the causes of not only rare diseases, but more common diseases," noted Dr. Stephen Groft, Director of the Office of Rare Diseases at the National Institutes of Health.

For that reason, many researchers are eager to conduct studies on rare diseases, according to Dr. Groft. But many rare disease investigators find their explorations stymied by a lack of resources, he added. There is a lack of animal models for rare diseases that truly reflect these disorders. Consequently, tissues and organs donated by people who had a rare disease are extremely valuable for research.

"Ready access to these resources stimulates research on rare diseases," Dr. Groft said. But such access is difficult to find, given the rareness of the conditions. "Many times we don't have patients grouped together in one location, so as a result, we don't have easy access to tissue samples," Dr. Groft pointed out.

Close to 90 percent of rare diseases have a genetic cause, so donated tissues are critical for the genetic studies that are likely to reveal their molecular triggers.



Eye of Science / Photo Researchers, Inc

Sickle cell anemia is one of the rare diseases for which researchers are actively seeking donor tissues and organs. The crescent-shape red blood cells shown here result from a change in the amino acid sequence of the cells' hemoglobin.

"Because of mapping of the human genome and more sophisticated research techniques that weren't available 15 to 20 years ago, we have even greater need for tissue and DNA samples from patients with rare diseases," Dr. Groft said. "This will let us get down to the genetic and molecular levels of inquiry that should lead to a better understanding of the disease and eventually treatments."

To help researchers detect the genetic causes of rare diseases, NDRI recently established a DNA and cell line bank for rare diseases.

Several researchers are using new genetic techniques to investigate tissues provided by NDRI for underlying genetic defects. For example, researchers are exploring

*Research on rare disorders often provides insight into more prevalent afflictions.*

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## Rare Diseases Research Requests

Here's a list of the top ten rare diseases for which NDRI gets the most requests for tissues from researchers:

RARE DISEASE	DESCRIPTION
<b>Cystic fibrosis</b>	A defective gene causes the body to produce a faulty protein that leads to abnormally thick mucus that clogs the lungs and can result in fatal lung infections. The mucus also obstructs the pancreas, causing difficulty for a person to absorb nutrients in food and can block the bile duct in the liver.
<b>Duchenne muscular dystrophy</b>	Progressive form of muscular dystrophy primarily affecting boys that causes the wasting of muscles in the limbs and pelvic area, eventually affecting all muscles including the heart.
<b>Friedreich's ataxia</b>	This disease, which begins in childhood, causes muscle weakness, curvature of the spine, and eventual paralysis and death.
<b>Goodpasture syndrome</b>	Autoimmune disease that affects the kidneys and lungs, causing coughing, difficulty breathing, kidney malfunctioning, and bleeding in the lungs.
<b>Kawasaki disease</b>	Affects young children, particularly of Asian or Pacific Island descent. Kawasaki syndrome has replaced rheumatic fever as the leading cause of acquired heart disease in children in the United States and Japan.
<b>Limb-girdle muscular dystrophy</b>	A form of muscular dystrophy that appears anywhere from late childhood to middle age and is characterized by progressive muscular weakness beginning either in the shoulder or pelvic area.
<b>Myotonic muscular dystrophy</b>	A severe but slowly progressing form of muscular dystrophy marked by muscle weakness and wasting that first affects the face, feet, hands and neck and then spreads to the arms and shoulders and legs and hip
<b>Pulmonary fibrosis</b>	Progressive scarring of the lungs that impairs breathing and ultimately is fatal.
<b>Sarcoidosis</b>	An inflammatory disorder characterized by small growths in the lungs, lymph nodes and other organs, which causes breathing problems and chest pain.
<b>Sickle-cell anemia</b>	A chronic and often fatal anemia that is particularly prevalent in African-Americans and causes joint pains, fever, and jaundice.
<b>Sjogren's syndrome</b>	Autoimmune disorder that causes destruction of the glands that produce tears and saliva, resulting in dry mouth and eyes.

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a genetic explanation for what makes certain Asian populations susceptible to Kawasaki disease, which causes heart abnormalities in children.

NDRI currently supplies tissue to more than 100 investigators of rare diseases. Other NDRI-supported researchers are using human tissue donated by cystic fibrosis patients to develop cell culture models of the disease that investigators can use to explore the cause of cystic fibrosis and better ways to treat it. Many NDRI-supported researchers use tissues from rare disease patients to explore if there are any abnormal amounts of certain compounds being produced, overactive genes, or other molecular abnormalities that might play a role in causing these diseases.

Many people with rare diseases will not meet criteria for donation of organs or tissues for transplantation. But the family of a loved one with a rare disease is often more than willing to donate for research on the disease, according to Rick Hasz, Vice President of Clinical Services at Gift of Life Donor Program in Philadelphia.

"It makes the family feel better knowing their donation might be able to prevent another family from going through what they went through," said Hasz.

But with so many rare diseases around, it can be a challenge to educate hospital staff and procurement staff to be on the lookout for potential rare disease donors.

"Trying to name all 6,000 or so rare diseases is an exercise in futility," noted

Hasz. "We partner with NDRI to find out the most needed rare disease tissues, which we highlight when we do our internal staff training and hospital education."

When Gift of Life's call center staff discovers a potential donor has died from a rare disease, he added, they alert a NDRI Rare Disease Coordinator or Private Donor Manager who contacts the family. In addition, while gathering the medical history of donors, if the staff at Gift of Life discovers the donor had a rare disease, it will refer those donors to NDRI.

"While rare diseases are not our main focus, giving rare disease families the opportunity to donate is certainly in line with our core mission and core values," noted Hasz.

LifeNet, located in Virginia, also has "a heightened sense of awareness about the need for tissues for research on rare diseases," said Kevin Myer, LifeNet Executive Director. "When our staff conducts a medical history and finds out the donor had a rare disease, that's a red flag to let the family know about the need for the donor's tissue for research," he said. But both Myer and Hasz noted that more could be done to boost the biospecimen donations from people with rare diseases.

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*Donated tissues are critical for studies that are likely to reveal their molecular triggers of rare diseases.*

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"It's still an untapped resource," said Hasz.

To help NDRI advance research into rare diseases, become familiar with some of the diseases for which researchers request tissue the most. (See box insert.) It may also be helpful to have a list of rare diseases readily available for those staff who screen potential donors. (For a complete list of rare diseases, go to <http://www.rarediseases.org/search/rdblist.html>). In addition, if you discover a potential donor had a rare disease, please suggest to the donor's family the possibility of donating the loved one's tissues and organs to research, or have NDRI contact the donor's family.

*Each pancreas donated for research can potentially yield enough islet cells to benefit up to 20 researchers.*

## A Pancreas is a Terrible Thing to Waste

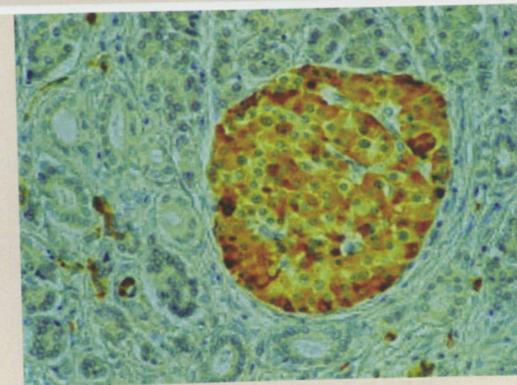
*Reducing Cold Time Critical for Research*

**D** diabetes is increasing at a rapid pace in the United States leading some experts to claim we are in the midst of a diabetes epidemic. More than 20 million Americans are currently afflicted with diabetes, including an estimated 5 to 10 percent diagnosed with type 1 diabetes. Today, diabetes is one of the most common chronic diseases in children and adolescents below the age of 20, according to Centers for Disease Control and Prevention.

Although insulin treatments and other drugs can prevent some of the life-threatening effects of this disorder, these medicines do not cure diabetes, and often are not enough to stave off its disabling or life-threatening complications.

Research on diabetes has expanded greatly during the past two decades aided by NDRI which was first organized in 1980 to help provide donated pancreata for research.

Today, researchers hope that by fine-tuning our understanding of what causes this disease, down to the nitty-gritty of molecular operators, they will be able to develop more effective treatments, if not a cure for type 1 diabetes. In addition, physicians and researchers are working to improve the success rate of islet cell transplants, which are currently performed on a limited number of people with diabetes.



This image shows tissue from a normal human pancreas and a section of an Islet of Langerhans, the insulin producing cell of the pancreas.

With the growing need for pancreata for research, NDRI cannot meet the demands of all investigators. NDRI coordinates with organ procurement organizations around the nation to procure pancreata not suitable for whole organ transplant, and in 2005 NDRI was offered 436 pancreata for research. Of the 436 only 51 were able to be used for research. Unfortunately, many of the pancreata offered cannot be used for diabetes or islet cell transplantation research because of extended cold ischemic time.

The islet cells in the pancreas are extremely sensitive to cold ischemic time. The more cold time, the more the organ and its cells begin to degrade. This can make them unsuitable for the culturing and expansion that is needed to conduct research on them.

Unlike most other organs donated for research, diabetes researchers need pancreata that have experienced cold ischemic time of no longer than eight

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