

NIAMS IRPartners

Spring 2007



A newsletter for patients of the Intramural Research Program (IRP), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIAMS' Light Imaging Section – A Conversation With Evelyn Ralston, Ph.D. and Kristien Zaal, Ph.D.

The NIAMS Light Imaging Section (LIS) plays an integral role in the Institute's research by offering scientists access to state-of-the-art light imaging equipment and expertise in light imaging techniques. The facility provides training and assistance in a variety of techniques of light microscopy and digital image analysis.



A scientist examines images of mouse muscle fibers on the confocal microscope's projection screen.

According to Dr. Evelyn Ralston, the section chief of the NIAMS LIS, "Just about everyone in the course of any project in science nowadays will be helped by imaging as part of the lab work." They'll probably need some technical training too. Medical school doesn't usually expose a budding scientist to the depth of what he/she will learn in training with Drs. Ralston and Zaal in the NIAMS Light Imaging Section.

- Q.** What are the main steps for working with the resources of the Light Imaging Section?
- A.** Before starting a project that involves microscopy, a scientist schedules a meeting with Dr. Zaal or Dr. Ralston at 301-402-6479. In that meeting, the light imaging expert provides consultation and advice. She will discuss and review the project with the researcher to determine the best approach and provide training in imaging techniques. Throughout the project, scientists return to the facility with samples. They get additional advice/help in imaging as well as help with interpretation, analysis and presentation for posters and publications.

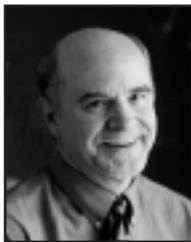
From the Scientific and Clinical Directors . . .

It has been a busy several months for the NIAMS Intramural Research Program since our last issue of *IRPartners*.

This issue contains a story about NIH researchers who recently reported strategies for enhancing communication and trust at urban clinical centers. The authors consulted with core members of the Health Partnership Program (HPP), a NIAMS diversity outreach initiative for the Metropolitan Washington, D.C. area.

Then, as we prepare to welcome new summer interns to the Institute, we feature images and insights from last year's group of aspiring scientists

*John O'Shea, M.D.
Scientific Director
Intramural Research Program
National Institute of Arthritis and
Musculoskeletal and Skin Diseases,
National Institutes of Health*



and administrators. You'll also learn about three new educational products developed by the Institute: a curriculum supplement for middle school students, a CD-ROM containing health information on lupus, and a fotonovela on bone health.

Additionally, we feature information on the NIAMS Light Imaging Section, and on exciting research by IRP's Vittorio Sartorelli, M.D., in which a drug was shown to counteract the effects of muscular dystrophy in mice.

We hope you enjoy this issue, and we look forward to sharing future highlights and advances with you.



*Daniel Kastner, M.D., Ph.D.
Clinical Director
Intramural Research Program
National Institute of Arthritis and
Musculoskeletal and Skin Diseases,
National Institutes of Health*

LIGHT IMAGING SECTION, *continued from page 1*

- Q.** What's a "real life" example of how a NIAMS scientist might work with the resources of the Light Imaging Section?
- A.** Often a scientist wants to track and observe how something is behaving (like what a protein is doing – where it is acting, perhaps in normal tissue). Or perhaps what's needed is to see how a mutated protein acts. For instance, Dr. Plotz's lab is working on Pompe disease. The scientists know of a mutation in an enzyme (acid maltase) that's involved in the metabolism of glycogen. They are investigating enzyme replacement therapy in a mouse model. Microscopy is the tool they use to see if the enzyme goes to the right place in the cell, and if its presence makes a difference in this part of the muscle. They use an antibody (fluorescently stained) to highlight the enzyme to see where the enzyme goes.

Q. What types of microscopes does the NIAMS Light Imaging Section have?

A. LIS has two main types of microscopes: wide-field conventional and confocal.

The capabilities of the microscopes are complementary to each other. They differ

particularly in their sources of light: the conventional microscope uses white light and the confocal uses laser light. For the confocal microscope, a computer is needed to create what the user sees, since the laser scans the specimen, then constructs the image and then displays it on the computer screen. A conventional microscope lets the user view a specimen through eyepieces. Confocal microscopes have a number of lasers. One way this is challenging to a new user is in getting to know the microscope and its particular laser setup. This is important when staining or dyeing a specimen, because the dye can be optimized relative to the exact laser setup of the particular confocal microscope. A confocal microscope is often used for a thicker specimen. It is possible to even look at a small live animal (anesthetized) using a confocal microscope. For instance, the user may want to see blood flowing through the blood vessels.

For more description of the principles of light and confocal microscopes, visit this page of the NIAMS Web site:

http://www.niams.nih.gov/rtbc/labs_branches/ost/core_facility/lightimaging/microscopy.htm.

Engaging Diverse Audiences in Clinical Research

NIH researchers recently reported a community discussion about strategies for ensuring ethical research practices in urban clinical centers. Their report, published in the *American Journal of Public Health*, was a collaborative effort with the NIH Department of Clinical Bioethics and the NIH Department of Nursing. According to study author Christine Grady, Ph.D., “We learned that disclosing comprehensive information, involving advocates, and monitoring care needs during and at the end of a trial are strategies that enhance trust, a vital component of good research.”

The Community Engagement Process

Researchers consulted with core members of the Health Partnership Program (HPP), a NIAMS diversity outreach initiative for the Metropolitan Washington, D.C. area. Using focus-group methodology, Grady and her colleagues carried out a community engagement process. The research team solicited input from ten HPP “partners” who represented various local community organizations. The partners were presented with three research case examples designed to stimulate discussion regarding the ethics of conducting research among individuals with limited health care access.

Important Lessons Learned

Several valuable lessons emerged from the community engagement process. For example, the HPP partners emphasized that a key strategy to elicit trust from the community is to establish and maintain open communication. Full and honest communication is not only essential prior to a study’s enrollment, but during and after a study as well. Community members felt strongly that a clear plan needed to be in place for follow-up care or referral, so that participants would not feel used or exploited once a study had ended.

Community partners also believed that research teams should include individuals who have similar backgrounds and speak their language. Familiarity with the community’s customs and values was also important. In addition, the partners stressed that communication and trust could be further enhanced by the use of advocates who helped explain study-

related information and provided support to study participants. It was felt that individuals who were part of the medical team (as opposed to the investigator’s team) would be better positioned to advocate for patients.

Overall, the HPP partners believed that clinical research was valuable, and they did not suggest excluding individuals with limited health care access from research studies.

“We learned that disclosing comprehensive information, involving advocates, and monitoring care needs during and at the end of a trial are strategies that enhance trust, a vital component of good research.”

Says Grady, “Our community partners articulated support for clinical research and appreciated the opportunity to express their views. They underscored the importance of being familiar with and respectful of the values, circumstances, needs and welfare of research participants.”

About the Health Partnership Program

NIAMS established the Health Partnership Program in 2000 as part of its ongoing mission to facilitate research on health disparities. The HPP embraces approximately 68 community partners representing members of the African American and Hispanic/Latino communities of Washington, D.C. A key component of the HPP is the NIAMS Community Health Center (CHC), located in D.C.’s Shaw/Cardozo community. The CHC serves as a venue for clinical research on rheumatic diseases in urban communities, provides a community base for health education and offers training opportunities for health professionals. ▲

Questions To Consider Before Joining a Study

- What is the purpose of the study?
- What is required of me?
- Will the study benefit me or others?
- Are there risks? If so, what are they and what are the chances that they will occur?
- What discomforts are involved?
- How long will the study last?
- What will happen if I decide to leave the study?

NIAMS Interns Reflect on a Summer of Experience

The NIAMS Summer Research Program provides outstanding opportunities for high school, undergraduate, graduate and medical students contemplating a career in biomedical research or academic medicine. Interns learn new skills, receive career mentoring from NIAMS

researchers, attend lectures and symposia, engage in basic and clinical research and gain credentials that help them pursue their career goals. As the Institute prepares to welcome a new group of summer interns, here's what some of last year's group had to say about their experiences:



Stephen Butler

Office of Clinical Director
University of Maryland College Park
Junior

"It has been a great experience working at NIAMS. I learn something new every day. I have been learning so much about the different types of diseases studied at NIAMS and all the people affected by them."



Jennifer Jacobi

Cartilage Biology and
Orthopaedics Branch
University of Missouri Rolla Senior

"Working at NIH has allowed me to witness various ways of approaching science and carrying out experiments. I am learning so much, but I feel more like a colleague than a student."



Ben Solomon

Lymphocyte Cell Biology Section
Cornell University Sophomore

"I have found that my time in the labs has been an immense experience. The staff and scientists at NIAMS have really helped me accomplish things that I didn't think would be possible at this point in time as a college sophomore."



Brittany Manvilla

Laboratory of Structural Biology
Graduated from University of Maryland
College Park

"Without my experience in a NIAMS lab, I wouldn't have found my field of study for graduate school."



Katie Marrow

Office of Communications and
Public Liaison
Towson University Junior

"As a returning summer student at NIAMS, I have continued to gain knowledge that I know I will use for the rest of my life. I am very thankful to be a part of an organization that has such a huge impact on the world."



Rocio Nieto

Genetics and Genomics Branch
Montgomery College second year

"It has been more than just a learning experience working at NIAMS; it has allowed me to interact with the Latino population and their health needs."



Bode Ogunwole

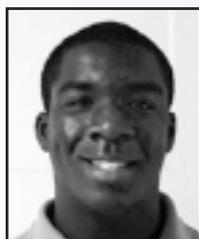
Laboratory of Structural Biology
Harvard University Senior

"NIAMS has so many opportunities and resources. It has been such a great experience; it far exceeds any previous research experiences that I have had in the past."



Natalie Leong
Cartilage Biology and
Orthopaedics Branch
Columbia University Senior

"It has been a privilege to work with so many talented scientists in the field."



Chukwuma Ogunwole
Genetics and Genomics Branch
Georgetown Prep Junior

"I am glad to have this opportunity to work at one of the best institutes in the world."



Yemmy Oladiran
Office of Clinical Director
McDaniel College Sophomore

"I love working at NIH; I feel very comfortable with the people I work with and feel as if I can come back and seek help if ever I need it in the future."



Ben Sobel
X-Ray Crystallography Facility
Walt Whitman High School Junior

"I really enjoy working in the labs; the people are very nice and I have learned a lot about science, diseases and crystallography."



Laura Ciaccia
Molecular Immunology and
Inflammation Branch
Boston University Senior

"My internship this summer has really been a watershed for me; it has altered the path of my career."

NIAMS Releases Curriculum Supplement

Looking Good, Feeling Good: From the Inside Out, a new curriculum supplement for middle school students, was released by NIAMS this past year.

Consisting of seven lessons, the supplement focuses on bone, muscle and skin, helping students explore how these systems function and interact and what happens when they do not work properly. The material is designed for use by middle school teachers as a part of the science curriculum. Teachers can use the lessons over a period of 7 to 9 days or as individual lessons that support or enhance the treatment of specific concepts in middle school science.



This curriculum supplement was designed to complement existing life science curricula at both the state and local levels, and to be consistent with *National Science Education Standards*. It was developed and tested by a team composed of teachers from across the country, scientists, medical experts, other professionals with relevant subject-area expertise from institutes and medical schools across the country, representatives from the NIAMS, and curriculum-design experts from the Biological Sciences Curriculum Study (BSCS) and the AiGroup. The authors incorporated real scientific data and actual case studies into classroom activities. A 2-year development process included geographically dispersed field tests by teachers and students.

Looking Good, Feeling Good: From the Inside Out was produced by the NIH Office of Science Education (OSE) as a part of the NIH Curriculum Supplement Series along with input from NIAMS. The NIH Curriculum Supplement Series is composed of interactive teaching units that combine cutting-edge science research discoveries from NIH, one of the world's foremost medical research centers, with state-of-the-art instructional materials. Teachers can download these materials free of charge from the OSE Web site, or may order printed copies. ▲

NIAMS Launches Lupus CD-ROM

NIAMS is now offering *Lupus Information for You and Your Patients* on a CD-ROM. It is an informative and cost-effective educational tool for doctors and other health professionals who treat patients with lupus.



Lupus is one of many disorders of the immune system known as autoimmune diseases. In autoimmune diseases, the immune system turns against

parts of the body it is designed to protect. This leads to inflammation and damage to various body tissues. Lupus can affect many parts of the body, including the joints, skin, kidneys, heart, lungs, blood vessels and brain. Although people with the disease may have many different symptoms, some of the most common ones include extreme fatigue, painful or swollen joints (arthritis), unexplained fever, skin rashes and kidney problems. More women than men have lupus, and it is more prevalent in African American, Asian, Hispanic and Native American women than in Caucasian women.

“Lupus is a complex disease and presents many challenges,” according to NIAMS Director Stephen I. Katz, M.D., Ph.D. “The CD-ROM will provide information and valuable resources to doctors and their patients, as well as nurses and other health professionals to help them better understand this disease.”

This CD-ROM includes:

- A collection of print-friendly PDF files of selected patient education brochures
- Professional educational resources, including information from the updated *Lupus Nurses Guide (3rd edition)*
- Web links to numerous useful resources from the NIH, other federal agencies and nonprofit organizations.

Free copies are available to anyone upon request. Health professionals, patients and family members, faculty at health professions schools and nonprofit

organizations serving individuals with lupus and their families will find this CD particularly useful.

To order a free copy of the CD-ROM, contact the NIAMS Clearinghouse at 1-877-22-NIAMS (1-877-226-4267), or niamsinfo@mail.nih.gov or visit <http://www.niams.nih.gov>. ▲

NIAMS's Kastner Receives Engleman Award



Clinical Director of the NIAMS IRP Daniel Kastner, M.D., Ph.D.

Daniel Kastner, M.D., Ph.D., clinical director of the NIAMS IRP, was honored at University of California San Francisco Medical School as the 10th annual Jean S. and Ephraim P. Engleman visiting professor of rheumatology. The award's namesake, Dr. Ephraim Engleman, played an important role in NIAMS' history. Engleman chaired the 1975-1976 National

Commission on Arthritis whose National Arthritis Research Plan resulted in the creation of what is now NIAMS. During his visit to the university, Drs. Kastner and Engleman discussed emerging areas in arthritis research and celebrated in style at the gala dinner. Congratulations, Dr. Kastner! ▲

NIAMS Community Health Center

The NIAMS has set up the NIAMS Community Health Center to help doctors and scientists understand the causes of rheumatic diseases and why many of these diseases occur more often and more severely in certain minority communities.

With this information, we can find better ways to treat and prevent these diseases. There are no experimental treatments or medications being used at the Community Health Center.

Call 202-673-0000 for information.

Experimental Cancer Drug Shows Promise as Treatment for Muscular Dystrophy

NIAMS scientists have demonstrated for the first time that a single drug can restore muscle function in mice with diseases similar to two forms of muscular dystrophy in humans. The advance, which was reported online in *Nature Medicine*, was a collaborative effort lead by Vittorio Sartorelli, M.D. of the NIAMS Muscle Biology Laboratory, and Pier Lorenzo Puri, M.D., Ph.D., now at Dulbecco Telethon Institute (DTI) in Rome, Italy and The Burnham Institute in La Jolla, California.

Muscular dystrophy (MD) is an inherited condition in which muscle fibers are easily damaged, resulting in progressive muscle weakness and dysfunction. There are several forms of muscular dystrophy. Dr. Sartorelli's work was based on two animal models that mimic two human dystrophy types: Duchenne and limb-girdle. Duchenne MD is the most common and most severe form of muscular dystrophy. Affecting mostly boys, it is caused by the absence of dystrophin, a protein that helps maintain muscle integrity. The onset of the disease is typically between 3 and 5 years of age, and the disorder progresses rapidly. (Most boys are unable to walk by age 12, and eventually need a respirator to breathe.) Limb-girdle MD usually begins in the teenage years and progresses more slowly than Duchenne. There is no cure for these or any other forms of muscular dystrophy.

Sartorelli's research featured trichostatin A (TSA), a compound from a family of drugs known as histone deacetylase (HDAC) inhibitors that are currently being studied as possible cancer treatments. The scientists tested TSA in two mouse models of muscular dystrophy (MD): one that naturally develops a disease similar to Duchenne muscular dystrophy in humans, the other genetically altered to develop a form of dystrophy similar to the human limb-girdle muscular dystrophy. At 45 to 90 days of age, the muscles of the MD mice showed much fibrous tissue and infiltration of inflammatory cells. Unlike healthy



Vittorio Sartorelli, M.D.

mice, the mice with MD were unable to either run on a treadmill or swim. MD mice given TSA daily for 2 to 3 months, however, were virtually indistinguishable from healthy mice, and biophysical studies showed virtually no difference between the muscle strength of the mice with MD given the deacetylase inhibitor and healthy mice.

"This is the first example of using a drug to counteract muscular dystrophy in mouse models," says Dr. Sartorelli. Yet he points out that the drug is only promoting muscle regeneration – it is not curing the defect that causes muscle deterioration. Further studies are needed to determine how long the drug works and if it works in larger animals with

bigger muscles, such as dogs, before such drugs can be tested in people. ▲

LIGHT IMAGING SECTION, *continued from page 2*

Q. Where are the NIAMS LIS microscopes?

A. Most of the equipment of the Light Imaging Section is on the first floor of Building 50. The microscopes there are the Zeiss 510 confocal microscope, the Leica SP5 confocal microscope, and the Leica DMRI (inverted wide-field microscope with microinjection setup). In Building 10 there is also a conventional fluorescence microscope, the Leica DMLB2, in room 9D40.

Q. What information resources are available?

A. Because microscopy is complex and time consuming, it's good for a user to know exactly what he or she wants to see, and it's important to plan ahead. The Web site has some additional useful information. It even has step-by-step procedures for types of staining and image capture at:

http://www.niams.nih.gov/rtbc/labs_branches/ost/core_facility/lightimaging/protocols.htm. ▲

NIAMS Has Free Health Information

NIAMS has free health information (some in Spanish) available to the public, health professionals and organizations. Information is available on arthritis, lupus and other rheumatic diseases, skin disorders, joint problems and musculoskeletal diseases.

Contact the NIAMS at 1-877-22-NIAMS (free call), TTY: 301-565-2966. Check our Web site at www.niams.nih.gov/hi/. Many of our publications can be printed directly from our site.

Free information on osteoporosis, Paget's disease of bone, osteogenesis imperfecta, primary hyperparathyroidism and other metabolic bone diseases and disorders is also available from the NIH Osteoporosis and Related Bone Diseases~ National Resource Center (NIH ORBD ~ NRC). Contact the NIH ORBD ~ NRC at 1-800-624-BONE, TTY: 202-466-4315, or at www.niams.nih.gov/bone. ▲

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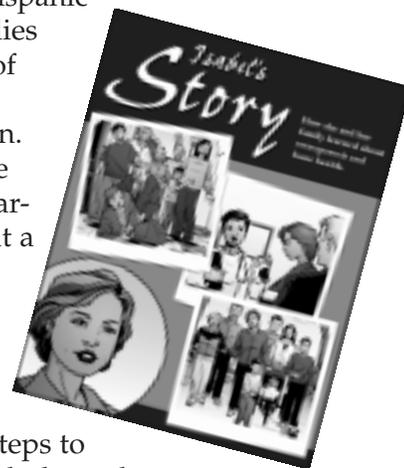
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NIAMS Develops Fotonovela on Bone Health

NIAMS has developed a bilingual fotonovela (illustrated storybook) entitled *Isabel's Story: How She and Her Family Learned About Osteoporosis and Bone Health*. The publication is designed to educate Hispanic women and their families about the importance of bone health and osteoporosis prevention. The fotonovela tells the story of Isabel, a 50-year-old woman who falls at a family gathering and breaks her wrist. A bone density test reveals that Isabel has osteoporosis, which motivates her to take steps to improve her bone health through nutrition and exercise. Isabel's family members also take steps to protect their bones, as they and the reader learn that bone health is indeed a family matter.



Isabel's Story: How She and Her Family Learned About Osteoporosis and Bone Health is available in an English/Spanish back-to-back flip format. To order a copy, contact the NIH Osteoporosis and Related Bone Diseases ~ National Resource Center at 1-800-624-2663. ▲



Need an NIH Speaker?

The NIH Speakers Bureau is a service that lists NIH researchers, clinicians and other professionals who are available to speak to

school groups and other local and national organizations. Speakers have expertise in such areas as arthritis, osteoporosis, autoimmunity and several dozen other topics covered by the NIH. To find out more about this service, sponsored by NIH's Office of Science Education, visit its Web site at:

<http://science-education.nih.gov/spkbureau.nsf>