

# NIAMS *IRPartners*

Summer 2005



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

## New Space for NIAMS

By Susan Bettendorf

There has been much talk about the new Mark O. Hatfield Clinical Research Center and what it has to offer patients: more light, more space and more convenience. *IRPartners* wanted to know what the new space at the clinical research center means specifically for NIAMS. Gregory Dennis, M.D., the director of clinical care and training at NIAMS, talked to *IRPartners* about the plans for NIAMS' new space.

### Good for Patients

In addition to its more spacious, light and airy feeling, says Dr. Dennis, NIAMS' new clinical space will also have some more practical benefits. When the day hospital moves to its fifth-floor home, it will offer expanded hours. Patients at the day hospital come in for evaluation and treatment. They don't spend the night, unlike patients who come to the inpatient clinic and may



Beverly Barham, R.N., B.S.N., nurse specialist (l), and Mildred Wilson, R.N., nurse specialist (r), join Dr. Dennis at one of the three spacious nurses' stations in the NIAMS new space on the fifth floor.

stay for longer treatments lasting maybe a few weeks. While currently open Monday through Friday, the day hospital will begin seeing patients on Saturdays, too. This will be more convenient for patients who might have trouble leaving their jobs or families to visit the clinic during the week.

With its added space, NIAMS will also be able to offer more flexible scheduling. Dr. Dennis expects NIAMS will be able to accommodate about 25 percent more patients than it can now. Negotiating patient visits, especially in the day hospital, with limited space has been trying for both patients and staff. Patients should have an easier time once more rooms are available. Dr. Dennis also says it should be easier to recruit patients for clinical trials. He says that while there are many considerations when recruiting subjects for clinical trials, "Recruiting patients in the future at least won't be determined by scheduling restrictions."

## From the Acting Scientific Director . . .

We are pleased to bring you the summer issue of *IRPartners*. In this issue, we'll update you on NIAMS' plans for its new clinical space in the Mark O. Hatfield Clinical Research Center. You'll also get to hear from some employees about what they are looking forward to in their new space.

You'll meet Dr. Joy Blair, a staff clinician, originally from Jamaica, who is involved in research and training in rheumatic diseases. Also, we'll tell you a little more about Pompe syndrome, a rare disease which is being researched in my laboratory, under the direction of Dr. Nina Raben.

NEW SPACE, *continued from page 1*

### Good for Employees

The new space puts NIAMS components together on the fifth floor in the clinical research center. Right now, NIAMS patient units are located on more than one floor. Once the clinic, the day hospital and the inpatient unit are all together in the same vicinity, NIAMS can focus on streamlining some efforts. Dr. Dennis estimates the new space is about 30 percent larger than NIAMS' current space.

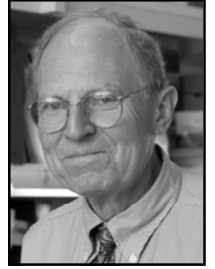
The major benefit for staff will be their ability to streamline functions in both the day hospital and the inpatient clinic. All this new space will allow NIAMS to "reorganize types of patients we see in the day hospital and the clinics," says Dr. Dennis. "We will go from having patients come in whenever we can get them in to being able to use the clinics for people who have regular appointments, and the day hospital can focus on treating people who need longer appointments or special treatments. That should increase the number of patients we can see in the clinic."

"The thing that is unique to this space as compared to our current space is that we now have three nursing stations in the inpatient unit," Dr. Dennis points out. It affords the nursing staff the opportunity to group patients according to their various diseases, so the nursing personnel can be trained to have expertise in the management of certain diseases. "Such consolidation should make patient data collection easier," he says.

One amenity Dr. Dennis points out is the specimen-processing room that will be at NIAMS' disposal. Currently, specimens are taken from the clinic to laboratories elsewhere in the building, increasing

And finally, we include a story about voluntary organizations and the roles they play in research and the lives of those with diseases under the purview of NIAMS.

We hope you enjoy this issue and that you find it informative.



*Paul H. Plotz, M.D.  
Acting Scientific Director, Intramural Research Program  
National Institute of Arthritis and Musculoskeletal  
and Skin Diseases, National Institutes of Health*

processing time and creating opportunities for delays. This new collection station will allow staff to divide, label and do some of their own initial processing before delivering specimens to the laboratories. Now staff will participate directly in that process.

And patients aren't the only ones to benefit from more light and airy rooms. Each of the rooms in the new units will be equipped to handle all the latest technology. With brighter lights, plenty of built-in equipment receptacles and closets built into the walls to store patient belongings, staff should not be hampered by cluttered or poorly lit workspaces. New space in the unit includes transitory work stations for those who need some surface space to make notes while going from patient to patient.

### What Next?

Does all of this new space mean NIAMS will drastically increase its number of protocols? Not necessarily, says Dr. Dennis. "The number of protocols we have is not determined so much by the space, but more by our budget and our ability to come up with well-designed protocols and our internal resources to implement the protocols." When developing new clinical trials, NIAMS also has to take into consideration the basic clinical center support that is available. For instance, radiological services, laboratory services, and all the other core necessities that the clinical center provides to support all the institutes are factors in determining about how much NIAMS can undertake.

When will NIAMS be able to move in? The process has already begun. NIAMS will share this space with the National Institute of Allergy and Infectious Diseases and the National Eye Institute. Clinical center nurses are already on staff treating patients. ▲

## What Do You Think of the New NIAMS Space?



Puja Chitkara, M.D., clinical fellow

**Puja Chitkara:** “I think patients love it. All the patients I’ve had have had good experiences. There is a lot of space for us to interact, to talk to patients, and to have team conferences.”

**Ms. Gelabert:** “The patients enjoy being at the new facility and hopefully, with time, everything will be in place to be more conducive to patient care in a research environment.”

**Dr. Goldbach-Mansky:** “The patients have been quite complimentary about the increased space they have and the light. We actually hope to get more flexibility to schedule clinics out of the increase in space and also to be able to consolidate our evaluations.”



Ana Gelabert (l), nurse practitioner, and Raphaela Goldbach-Mansky, M.D., staff clinician



Daly Cantave (front), Ann Hickey (back left) and Carol Levinson, clinical research nurses

**Ms. Levinson:** “Patients love the beauty of it. The rooms are much more spacious. They love having access to their own personal TVs and being able to access the internet, which is almost a necessity these days, so people can stay connected with the outside world while they’re here. And for the nurses, we have more computers.”

**Ms. Hickey:** “For the NIAMS patients who have limited mobility, everything about these rooms is better for them. The bathrooms are great. Some patients need more space because of a wheelchair, or maybe they need a special shower chair, all the things that weren’t taken into consideration 50 years ago when the first building was built.”

**Nikolay Nikolov:** “I do not have a lot of experience with the new CRC, but it is certainly impressive. It looks nice, especially for the patients.”



Nikolay Nikolov, M.D., clinical fellow

## Did You Know...What Volunteer Organizations Can Do for You?

**F**or patients and their families, volunteer organizations deliver a powerful message: You are not alone.

When someone is newly diagnosed with a disease or a disorder, the questions can seem overwhelming: How will this disease affect me? Where can I find support from others who have it? How can I keep up with new research developments? Who will represent my interests to government policy-makers?

Within the 60-member NIAMS coalition, an independent group concerned with the programs of NIAMS, more than three dozen volunteer organizations provide a voice for patients. In terms of their size, these groups run the gamut. Some provide resources and support for those with rare disorders: people who otherwise might have scant information to go on as they learn to manage their illness. Others represent the many millions of people living with more common diseases like arthritis, lupus and psoriasis.

### Help for the Many

Many organizations are well-established, raising money, funding research and providing a wealth of information and support to their large audiences.

**The Arthritis Foundation** (<http://www.arthritis.org>), as one example, has more than half a century of experience in helping millions of Americans recognize and manage their symptoms. Organized in 1948 as the Arthritis and Rheumatism Foundation, this volunteer organization has been at the forefront of many advances in arthritis care. When it began, it had four rheumatic diseases under its purview. Today, the foundation has more than 100 arthritis-related conditions of concern. Its original 13 chapters have grown to 55. As a result of its fundraising efforts, the foundation spends more than \$19 million per year for arthritis research.

### The Lupus Foundation of America

(<http://www.lupus.org>) is another example of a group that serves a large constituency. It has more than 40 chapters nationwide, all of which operate support groups. The Web site provides information on clinical trials in search of volunteers. It updates the public about new drugs that could be used to treat

lupus, and describes where the drugs stand in terms of approval by the Food and Drug Administration. It also summarizes the results of new studies on lupus and presents new treatment options.

Additionally, support groups such as the **National Psoriasis Foundation** (<http://www.psoriasis.org>) can reach out to those who are newly diagnosed and provide advice on how the disease will affect their lives. On its Web site, the Foundation has information on causes, treatments, doctors and the search for a cure. The site points out that because psoriasis mimics various diseases, it is sometimes difficult to diagnose. And those with psoriasis often face misunderstanding from others because the disease is poorly understood. "People may think it is only a cosmetic condition, when in fact it can not only have serious physical symptoms but also lead to low self-esteem and depression," the site states.

### Talking to Lawmakers

Many of these dedicated organizations bring attention to their diseases. Voluntary organizations and their members can help educate lawmakers about a disease, and the more lawmakers can hear directly from constituents and others who have the disease or have a relative with it, the more they understand the value of a strong commitment to research.

Under its advocacy section, the National Psoriasis Foundation invites those with psoriasis and their family, friends and supporters to come to Capitol Hill. Last year, for example, a 7-year-old girl with psoriasis traveled with her family to Capitol Hill to seek congressional support for psoriasis research and treatment. As her mother recounts, "It's scary to talk with people who you don't know, but people responded to her because she was the only kid." Getting others to understand that real people will benefit from research efforts is one of the things voluntary organizations do well.

### Help for the Few

Volunteer organizations also provide crucial support for those with rare diseases. When information about a disease is limited, where do you turn for practical advice?

## Joy Blair, M.D., Staff Clinician

Joy Blair, M.D., has dealt with some unique challenges before coming to the NIAMS, where she currently works as a staff clinician and researcher.

A native of Jamaica, Dr. Blair knew at a very early age that she wanted to be a doctor, and she never considered another career. She remembers that, at around the age of seven, she picked up an anatomy book that belonged to her aunt, a nursing student at the time, in order to memorize the names of bones and other parts of the anatomy. Given the influence of her aunt and her mother, who is also a nurse, Dr. Blair made an early association between science and medicine. At age 12 she wrote an essay for school about her interest in finding a cure for cancer.

In her early teens, Dr. Blair started experimenting with grafting plants. "In the tropics you grow up surrounded by trees and flowers, so observing their growth and development is something that you can do readily at home without much technology," she explains. "My dad worked for the Jamaica Agriculture Department and grafting citrus plants was one of his hobbies," she notes with nostalgia. She learned from him how to successfully graft an orange tree to a grapefruit tree. In college as one of her first biology projects, she grew and compared the stages of germination of a variety of hybrid corns.

When she was 15, Dr. Blair and her family left the warm climate of Jamaica and moved to Chicago. There, she attended a coed school for the first time. "I am very grateful to my counselor. You can imagine that, coming from another country, I needed some help understanding the new school system and environment. Mrs. Prentice, my English teacher, was especially kind and nurturing. She recognized my abilities and helped me to become confident in school. With her guidance and that of my school counselor, Mrs. McBride, I completed my high school requirements in two years." Dr. Blair graduated from Mundelein College, an all-female institution founded and run by Catholic nuns. "Going to an all-girls college put me back in a familiar environment," she says. Today, watching Dr. Blair interact with patients,



Joy Blair, M.D., staff clinician

students and her colleagues in the lab at NIAMS, one can easily see that she has again arrived in a place where she belongs.

Dr. Blair began her research training while an undergraduate at Mundelein College, and during summer work at the University of Chicago. Intent on continuing her research whenever possible, she worked during the evenings and summers in the university's labs. Gone were the days of grafting plants, however. Now, armed with the latest technology available, including light and electron microscopes, she studied the arrangement of chromosomes in plant cells. She also began to study other organisms. She says, "In the U.S. we have so many more resources in school. For my senior research project I was able to advance my studies to frogs and salamanders. I was fascinated with the potential of the cell and wanted to understand how salamanders were able to regenerate

their limbs. Doing these studies required keen commitment and taught me how to observe and document changes over time. I think this is where my love for research really started." She recalls, "Each day as I observed the salamanders for regeneration of limbs, I experienced a certain excitement and gratitude to the organisms. Each day I felt that I was sharing in their world in a special way. I learned how important it was to be attentive to details, and how important observations are for understanding how an organism functions. This excited me, and I still get excited thinking about it."

Following completion of her undergraduate studies, Dr. Blair received a medical degree from Southern Illinois University's School of Medicine, located in Springfield. She then began her residency in internal medicine at the Mayo Clinic in Rochester, Minnesota.

In pursuit of her childhood dream, she started her clinical rotation with medical oncology and radiation therapy. At the end of her internal medicine training, however, she decided that she was more interested in arthritis and musculoskeletal diseases.

## Research Updates: Pompe Syndrome

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In the laboratory of Paul Plotz, M.D., chief of the NIAMS Arthritis and Rheumatism Branch, researchers are making strides towards understanding Pompe (POM-pay) syndrome, a rare disease that causes muscles to deteriorate. Investigators there are using mice with Pompe syndrome to help them explore the many facets of this disease. Their ongoing work may eventually lead to successful therapy for this devastating disorder.

In Pompe syndrome, the heart and skeletal muscles in particular are targeted. The disease may be present in infants who appear normal at birth, but soon become limp and unable to move or eat. Their hearts become enlarged, and they rarely live past their first year. In those who live longer, the disease may not become apparent until later in childhood or adulthood, and it progresses more slowly, eventually requiring patients to become confined to a wheelchair or a bed. Patients often die in their thirties from failure of the respiratory system. (*IRPartners* wrote briefly about Pompe syndrome in "The Road to Results," in the Winter 2003/04 issue. You can find this article on the NIAMS Web site at <http://www.niams.nih.gov>.)

To understand Pompe syndrome, you need to know how the muscle processes and uses energy. The body stores energy in the muscle in molecules called glycogen. People who have Pompe syndrome are missing the gene that triggers the body to make the enzyme acid maltase, which breaks down glycogen in their lysosomes. Lysosomes are compartments in cells and are known to function as cellular clearinghouses: they ingest multiple substances, including glycogen, which is converted by the acid maltase into glucose, a sugar that fuels the muscles. In Pompe syndrome, the acid maltase activity may be dramatically reduced or nonexistent, resulting in an excessive accumulation of glycogen in the lysosome. Although there is glycogen storage in multiple tissues, heart and skeletal muscle are most severely affected, and the lysosomes in these muscles become clogged with large deposits of glycogen. As a result, the muscles are progressively weakened, especially the heart.

To learn more about Pompe syndrome and to try and develop treatments, researchers in Dr. Plotz's lab, led by staff scientist Nina Raben, M.D., Ph.D., made a mouse model of the disease that is missing the gene necessary to make acid maltase. These mice

are now used by virtually every lab involved in research and development of therapies targeted at Pompe syndrome. The researchers also generated multiple other mouse strains in which the missing gene was replaced by the normal one. These mice were created in such a way that the normal gene could be turned on and off, much like a light switch. Experiments with the mice demonstrated that the best place to insert the missing gene is into the liver, which serves as a factory for enzyme production. The enzyme is then secreted into the blood and reaches skeletal and cardiac muscle.

Although this approach can't be used in humans right now, another approach seems more realistic. By using a technique called enzyme replacement therapy, quantities of a therapeutic substance could be introduced into the body. A potential problem with this therapy is that not all substances can cross what is known as the blood brain barrier. This barrier acts as a protective shield around the brain, allowing only certain molecules in. This is important because Pompe syndrome causes glycogen accumulation not only in the muscle, but also in the brain, so any therapy would have to work in the brain as well as the muscles.

Researchers in Dr. Plotz's lab tried to inject the mice with the acid maltase enzyme, but the mouse immune system rejected it. After much trial-and-error, the researchers created another mouse model of Pompe syndrome that could tolerate multiple injections of the therapeutic drug. This was a significant accomplishment, but it also raised many new research questions.

While it was originally hoped that enzyme replacement therapy would cure Pompe syndrome, experiments in mice demonstrated only partial success. The researchers have tested a variety of different doses of the enzyme in both young and adult animals. Dr. Raben's team discovered that the therapy was very effective in clearing glycogen accumulation in heart muscle, but much less effective in skeletal muscle. Further research revealed that not all skeletal muscle responds to treatment in the same way. Muscles are made up of different fiber types, and while one type responded well to this therapy, another type did not.

Dr. Raben now focuses her research efforts on treating the resistant muscle fibers. By going back to fundamental cell biology and specifically looking at the pathway by which the therapeutic drug enters the cells and moves throughout various cellular compartments, she hopes to find a way to more efficiently deliver the drug to its final destination: the lysosome. ▲

Dr. Blair then went on to complete a fellowship in rheumatology and geriatrics at the University of Chicago. “My research career really blossomed during the course of my fellowship training, and I found my true interest in osteoarthritis research,” she states.

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“Each day as I observed the salamanders for regeneration of limbs, I experienced a certain excitement and gratitude to the organisms. Each day I felt that I was sharing in their world in a special way. I learned how important it was to be attentive to details, and how important observations are for understanding how an organism functions. This excited me, and I still get excited thinking about it.”

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Upon completion of her training at the University of Chicago, she accepted a staff position at the university that allowed her to combine her clinical and research activities. Here she established a lab to study microcrystals in the synovial fluid of patients with osteoarthritis. Her research was supported

by grants from the NIH and the Arthritis Foundation. It was the scope of this work that prompted Dr. Blair to seek additional basic science training.

A Fulbright Scholarship made it possible for her to study structural biology at the Weizmann Institute in Israel. While in Israel she also taught at the Sackler School of Medicine at Tel Aviv University. After almost four years of teaching medicine and studying in Israel, she came back to the United States with the goal of incorporating her experiences into a clinical research program. She joined NIAMS in 2003, as a member of the Intramural Research Program.

Today, Dr. Blair sees patients as one of a team of attending physicians who are responsible for overseeing the work of the rheumatology fellows in training at the NIAMS Community Health Center in Washington, D.C. The center offers rheumatologists the opportunity to train in a culturally diverse community.

Dr. Blair’s current research projects include an observational study of the pathogenesis (origin and progression) of osteoarthritis in animal models. One study compares the effects of exercise on osteoarthritis

in mice. A second focuses on the cause of spontaneous, age-related joint degeneration in Rhesus monkeys. For this research she observes the monkeys’ joints at different ages and characterizes the changes that have occurred. She uses the latest technology, including noninvasive micro-magnetic resonance imaging (micro-MRI), to study structural changes in the bones and cartilage of these animals. Lastly, she is working to develop a new clinical protocol to learn whether early diagnosis of osteoarthritis is possible. This study may help to identify treatments that could potentially modify osteoarthritis in its early stages. ▲

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**DID YOU KNOW?**, *continued from page 5*

If your child has epidermolysis bullosa (EB), a rare, genetic disease affecting two out of every 100,000 newborn babies, you may turn to the **Dystrophic Epidermolysis Bullosa Research Association of America** (<http://www.debra.org>), which provides support for those with EB and their families. This association has on its Web site the story of one couple from South Dakota whose son was born with EB, a disease characterized by extremely fragile skin and recurrent blisters. Doctors knew little of the disease and were reluctant to treat it. The parents dressed their son in fleece clothing with no zippers or buttons. They turned his socks inside out to keep the seams from rubbing against his skin. And they lived in fear of brushing the boy’s teeth because of the damage it might cause to his lips. Fortunately, the Association’s Web site has a page dedicated to giving new parents of babies born with EB the type of practical advice they need to cope with such everyday problems.

Xeroderma pigmentosum (XP) is another rare, genetic disease that threatens the lives of children. An extreme sensitivity to all ultraviolet light, and especially sunlight, makes it necessary for children to spend almost all their time in a controlled, indoor environment. **The Xeroderma Pigmentosum Society’s** (<http://www.xps.org>) logo – a globe with half moons and their acronym – represents the words of young Katie Mahar, the daughter of the Society’s founders. When she was first diagnosed, she was heard to say, “Mr. Moon is my friend.”

When faced with such an unusual disease, parents might want to get together with others who are trying to help their children live as normal a life

## NIAMS Has Free Health Information

**N**IAMS 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/](http://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.osteo.org](http://www.osteo.org). ▲

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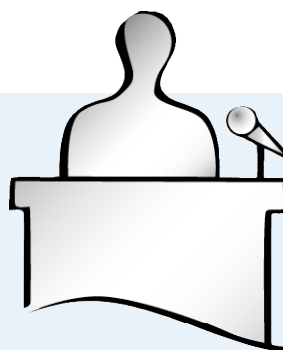
Susan Bettendorf, Associate Editor

DID YOU KNOW?, *continued from page 7*

as possible. The XP Society runs Camp Sundown, where children can come for free and enjoy indoor activities like crafts during the day and outdoor activities at night. The site also provides hope to parents and others who worry about the fate of children with XP. It points out that because the disease is diagnosed earlier and understood better today, more children with XP are living into adulthood.

NIAMS focuses its attention on doing the best research to treat and cure these difficult diseases. But organizations whose members understand what it's like to have diseases or family members with diseases are there to provide comfort, support and hope to those who need it.

*IRPartners* has mentioned some specific voluntary organizations from the **NIAMS coalition** as examples only (<http://www.niams.nih.gov/hi/coalition/resources.htm>). There are many more. **The National Library of Medicine's MedlinePlus** has a listing of health organizations (including professional, voluntary and government organizations) that deal with many topics at <http://www.nlm.nih.gov/medlineplus/otherresources.html>. ▲



### 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>