

NIAMS IRPartners

Fall/Winter 2010



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

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U.S. Department of Health and Human Services



National Institutes of Health



National Institute of Arthritis and Musculoskeletal and Skin Diseases

A Conversation With Dr. Juan Rivera, NIAMS Deputy Scientific Director

We asked Juan Rivera, Ph.D., the new NIAMS Deputy Scientific Director, to reflect on his career and to offer advice to up-and-coming scientists. Dr. Rivera, an outstanding mast cell biologist with an NIH career spanning 35 years, will lead NIAMS in the generation of a new strategic plan for its Intramural Research Program. In addition, he will assist with the creation of the NIH Center for Regenerative Medicine.



Dr. Juan Rivera, NIAMS Deputy Scientific Director

Was there a defining moment in your life that led you toward a career in science?

Dr. Rivera: Science was not something I ever really thought of. When I was in high school, I was leaning toward a career in music. But since chemistry was a required school subject, I didn't have a choice but to take it. And that was the defining moment in my path toward science. I had an excellent chemistry and physics teacher who engendered and fostered my curiosity in the world around me. It was at the University of Maryland where I became very interested in immunology, and in my second year of college, I started working at the NIH through the Stay-in-School program, a program for people from disadvantaged backgrounds. That was a big help to me, and, in fact, I've been at the NIH ever since.

What is your area of expertise?

Dr. Rivera: As an immunologist, I am interested in how the human body regulates inflammation and what factors are responsible for the body's inability to shut down the inflammation, which leads to autoimmune and allergic diseases, among other diseases. It is the continued inflammation in these diseases that causes damage over time. I'm particularly interested in understanding why inflammation persists in certain individuals, and what specific factors cause the persistent inflammation.

As the new NIAMS Deputy Scientific Director, what is your vision for the future of NIAMS and its Intramural Research Program?

Dr. Rivera: Recent scientific advances are propelling us into an era of unprecedented opportunities and discoveries. The unraveling of the

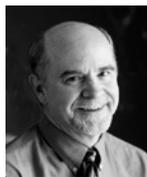
From the Scientific Director

We are pleased to bring you the fall/winter 2010 edition of *IRPartners*. In this issue's lead story, you'll hear from newly appointed NIAMS deputy scientific director, Juan Rivera, Ph.D. You'll also be introduced to a number of the Institute's most recent summer interns, a group of talented students with a wide variety of backgrounds and interests.

You'll learn about a recent trip to the Bethesda campus by students from the Schools for Educational Evolution and Development (SEED) of Washington, DC. When President Obama recently visited the school, he praised the program as a "true success story."

The issue also includes a synopsis of recent NIAMS intramural research advances and an introduction to the new NIAMS clinical fellows. Lastly, you'll learn about several new resources for health information from the Institute.

Enjoy the issue!



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

NIAMS Welcomes New Clinical Fellows

NIAMS has added three new fellows to its Rheumatology Fellowship Program. Dr. Adam Schiffenbauer, Dr. Apostolos Kontzias and Dr. David Michel are the members of the 2010–2011 Rheumatology Fellows class. The Rheumatology Fellowship Program falls under NIH's Graduate Medical Education training program, which allows students who choose to pursue an academic medical career



From left to right Apostolos Kontzias, David Michel and Adam Schiffenbauer

in rheumatology to obtain hands-on experience through clinical rotations and research activities. Applicants must have completed 2 or more years of internal medicine residency training to apply to the program.

Adam Schiffenbauer, M.D., received his medical degree from Pennsylvania State University in Hershey, Pa., in 2007. He completed an internal medicine residency at George Washington University Hospital in Washington, DC, in June 2010. Dr. Schiffenbauer has notable publications in *Arthritis & Rheumatism*, *Clinical Chemistry* and the *Journal of Virology*. From 2004 to 2007, he served as a clinical research assistant with the Department of Rheumatology at Pennsylvania State University. "It is wonderful to be starting here at NIAMS and has been a relatively smooth transition thanks to our great program coordinator," said Dr. Schiffenbauer.

Apostolos Kontzias, M.D., received his medical degree from the University of Athens Medical School in Athens, Greece, in 2004. He served as a general practitioner at the General Hospital of Korinthos, Greece, from 2004 to 2006. During this time, he also provided volunteer physician services in Tanzania with a Greek medical nongovernmental organization in 2005, and later in the Rheumatology Department at Weill Cornell Medical College in 2006. He completed an internal medicine residency at Lincoln Medical and Mental Health Center in Bronx, N.Y., in June 2010. His scholarly publications and participation in professional conferences have been impressive, including articles in *Drugs*, *Nature Clinical Practice Rheumatology* and the *Journal of Musculoskeletal Medicine*. Dr. Kontzias has served as principal and sub-investigator on rheumatology-related research projects and is an active member of the Hellenic Medical Association and the American College of Physicians. "In structure as well as function, NIH provides a cyclical path from bench to bedside where disease manifestations raise research questions, and the answers continue to improve the health of our society. As a young physician, there is not a more exciting place to be," expressed Dr. Kontzias.

David Michel, M.D., received his medical degree from Jefferson Medical College in Philadelphia, Pa., in 2007. He completed an internal medicine residency at the New York-Presbyterian Hospital/Weill Cornell Medical Center in June 2010. Throughout his medical education, he has been active in research, mentoring and teaching.

NIAMS 2010 Summer Interns Have Variety of Backgrounds and Interests

NIAMS offers a Summer Research Program that provides outstanding opportunities for high school, undergraduate, graduate and medical students contemplating a career in biomedical research or academic medicine. Our 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.



Robert Chen is a senior at the University of Rochester majoring in political science. Robert was a summer intern in the NIAMS Office of Communications and Public Liaison.

This summer he had the exciting opportunity to interview some of his peers in the Intramural Research Program (IRP) and to learn about some of their experiences. "The IRP interns are a group of talented and incredibly driven students with a wide variety of backgrounds and interests. It is my pleasure to share with you some of their stories."



Ixchel Montenegro, a junior at the University of Michigan, is majoring in brain, behavior and cognitive sciences, and minoring in gender and health.

Returning as a summer intern at NIH, Ixchel worked in the NIAMS Genetics and Genomics Branch studying auto-inflammatory diseases by screening patients for mutations in the PYPAF7 protein. The summers spent at NIH have helped Ixchel hone her interests in science and provided her with exposure to real patients and their symptoms. This has led her toward a career in health care.



Patrick Kirkland is a senior majoring in microbiology at the University of Hawaii. At NIH, he learned a variety of new lab techniques while working on display of HIV-1 epitopes on hepatitis B virus nucleocapsid

particles in NIAMS' Protein Expression Laboratory. Pat's experiences have strengthened his desire to go to medical school, and he hopes to return to NIH for another year as a post-baccalaureate student.



Amber Grace is a senior majoring in chemistry at Tuskegee University who interned in the Molecular Immunology and Inflammation Branch. Aside from learning lab techniques and expanding her knowledge in immunology, Amber

found the summer internship experience to be much more than she expected, full of networking, mentoring and learning opportunities. Her time in the lab has helped her to better understand the versatility of a medical degree and has helped to focus her career goals.



Devon Nixon is from the University of Michigan Medical School. With 2 years of previous summer experience at NIH, he worked on atypical hip fractures in the Clinical and Investigative Orthopaedics Section

under Dr. Timothy Bhattacharyya. Devon was particularly interested in being able to see the transition from research to clinical practice, while working with data collected from actual patients. These experiences have helped Devon to define a focus in orthopaedic surgery as a possible career.



Sudipa Chowdhury is a senior at the University of Kentucky majoring in biochemistry. She intends to go to medical school and is considering a career in oncology, pediatrics or neurology. Sudipa found that her

time spent as a summer intern in the Laboratory of Structural Biology Research has deepened her interest in science, as well as reinforced her decision to pursue medical school. Aside from the great opportunities and cutting-edge research at NIAMS, Sudipa also enjoyed meeting other summer interns and seeing how one question can often be solved from multiple perspectives.



Eduardo Contijoch is a junior at Princeton University majoring in physics. Returning as a summer intern in NIAMS, Eduardo worked in the NIAMS Translational Immunology Section to help develop a mouse

model for the novel auto-inflammation found in people with Wiskott-Aldrich syndrome. Eduardo particularly enjoys the work at NIH because of the flexible interplay between research and application. This has guided his career focus toward an M.D. or Ph.D. in immunology or genetics.



Originally from Nigeria, **Onyi Ochi** is a senior at Howard University majoring in biology with a minor in chemistry. She is considering a career in pediatrics or internal medicine. Unlike most interns, Onyi worked on a health outcomes project with Dr. Michael Ward. She spent a lot of time interviewing people for a survey and enjoyed the interactive aspects of the experience. Onyi found that the NIH summer intern experience offers many great learning opportunities and captivating work. It has helped to confirm her career goals in medicine.



Kevin Lee is a junior in high school from San Francisco, Calif. As a summer intern, he analyzed the effects of particle heterogeneity on the resolution analysis of electron microscopy reconstructions in the NIAMS Laboratory of Structural Biology. This experience has been very enriching for Kevin, especially seeing the variety of scientific perspectives at NIH. Kevin is still undecided about his career goals, but has found that his time spent in the lab has intensified his interests in science.



Lorangelly Rivera Torres from Puerto Rico is a senior at the Metropolitan University of Puerto Rico majoring in cell molecular biology. Her research project focused on a candidate gene approach to caspase 1 in patients with undifferentiated fever syndrome in the laboratory of NIAMS' Translational Autoinflammatory Disease Section. During her time as an intern, Lorangelly has gained greater exposure to the clinical side of research, aiding in her decision to pursue medical school and to participate in biomedical research.



Adrian Cora-Morges is a second-year medical student at the University of Puerto Rico, Medical Sciences Campus, with an interest in becoming a rheumatologist. Adrian learned many new techniques while working alongside his mentors on the discovery of novel proteins interacting with the Fas death receptor in the Immunoregulation Section of NIAMS' Autoimmunity Branch. Adrian found the summer program to be an excellent, fast-paced opportunity that has intensified his desire for a career in research.



Sheila McSweeney is a third-year medical student at the University College of Cork, Ireland. She worked on the role of TL1A and DR3 in autoimmunity in Dr. Richard Siegel's laboratory. Her time spent this summer at NIH has led her to consider rheumatology as a specific area of focus. Sheila was most surprised by the quality of the research conducted at NIH and by the level of interaction between laboratory and clinical research.



Noah Hull is a senior majoring in psychology and molecular and cellular biology at the University of Wyoming. He interned in the Office of Science and Technology where he worked on the possible implementation of laser scanning cytometry within NIAMS. He considers NIH to be the pinnacle of biomedical research, which is ideally where he wants to be. In adapting to life in the lab and meeting a variety of new people, Noah has gained a greater appreciation for a career in public health.



Torrian Brent is a recent high school graduate and will be attending the University of Maryland in the fall. She plans on majoring in general biology and hopes to pursue a career in dermatology. As a returning summer intern at NIH, Torrian worked on sequence analysis of the IL-10 pathway genes in severe early-onset Behçet's disease in Dr. Dan Kastner's laboratory. She was impressed with the variety of great resources, mentoring opportunities and activities available to NIH summer interns, and she hopes to return to NIH in the future to continue her training in the biomedical sciences.



Thomas Rigolage, from Silver Spring, Md., was a student from Montgomery College who will be transferring to Concordia University in Montreal, Quebec, Canada, as a sophomore, to major in chemistry. Thomas worked on computational analysis of assembly of SV40 in the Laboratory of Structural Biology Research, where he gained experience in both time management and problem-solving. Thomas was a participant in the newly launched NIH Community College Summer Enrichment Program. In this program, he developed a greater understanding of the technicalities and mechanisms involved in scientific research. ▲

Dr. Michel has notable publications in *Arthritis & Rheumatism* and *Expert Review of Clinical Immunology*. From 2005 to 2006, he served as a Howard Hughes Medical Institute medical fellow, investigating chronic graft versus host disease in the SLE-1 mouse model. His dedication to medicine and his interest in rheumatology are evident through his research, publications, professional memberships, honors and awards. ▲

NIAMS Launches Multimedia Web Page

The new NIAMS Multimedia page provides a centralized place on the NIAMS Web site where visitors can access videos, images and audio publications. It brings together two existing resources – the NIAMS Image Gallery, an online searchable database of NIAMS photos and illustrations, and audio publications in both English and Spanish – and adds video, which has not been included on the NIAMS Web site before. To view the Multimedia page, go to www.niams.nih.gov/News_and_Events/Multimedia/default.asp. ▲



New Website Offers Easy Access to Information on Bone Health

A new Web resource that provides people with the latest science-based information on bone health and bone disease is available through the NIH Osteoporosis and Related Bone Diseases ~ National Resource Center (NRC). The site is www.bones.nih.gov.



Strong bones are essential to overall health and quality of life. Visitors to the NRC site will learn about strategies for bone health, such as the prevention and management of osteoporosis, a common bone disease that makes bones weak and prone to fracture. One feature is the Check Up On Your Bones tool, an online interactive bone health

assessment that provides personalized information on osteoporosis risk, as well as approaches to enhance bone health.

Materials on the site fill important gaps in information, such as the lack of knowledge among men about osteoporosis. Members of various multicultural communities, including Hispanics and Latinos, African Americans, Asian Americans and Pacific Islanders, and American Indians and Alaska Natives, will find resources specific to their needs. Bone health information is available in English, Spanish and Chinese languages.

In addition to materials on bone health and osteoporosis, the NRC also provides information on the rarer Paget's disease of bone and osteogenesis imperfecta (brittle bone disease). Additional materials on other rare bone diseases are planned for the coming year.

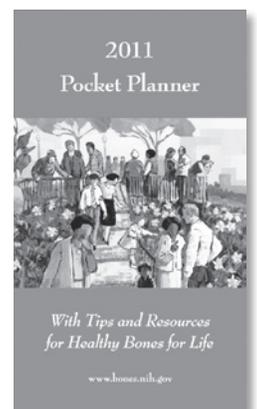
The website features quick and easy navigation tools to help identify and locate topics of interest. Landing pages provide all of the information offered on a given topic conveniently in one place. There are multiple ways to search for information, including by user type, language, reading level, key word and disease. ▲

2011 Pocket Planner Has Tips and Resources for Healthy Bones for Life

The NIH Osteoporosis and Related Bone Diseases ~ National Resource Center (NRC) has released a 12-month pocket planner that contains tips and resources for improving bone health. Each month of the planner offers a unique strategy for enhancing bone health, such as:

- getting enough calcium and vitamin D
- staying active for strong bones
- talking to your health care provider about your bone health.

The planner also includes space to schedule activities for optimizing bone health, as well as a list of selected calcium-rich foods. To order, please contact the NRC at 800-624-BONE (2663). ▲



NIAMS IRP Research in the News

NIAMS Researchers Solve Puzzle of Inflammation in TRAPS

Richard Siegel, M.D., Ph.D., and his colleagues in the NIAMS Laboratory of Clinical Investigation and the Autoimmunity Branch have discovered a new mechanism of inflammation in the tumor necrosis factor receptor 1 (TNFR1)-associated periodic fever syndrome (TRAPS). Their investigation in mice revealed that having one mutant gene and one normal gene for TNFR1 caused greater disease inflammation than having two mutant TNFR1 genes. The researchers concluded that mutant TNFR1 and normal TNFR1 must both be present to cause an increased inflammatory response in TRAPS. The study appeared in the *Proceedings of the National Academy of Sciences* (PNAS) earlier this year.

Simon A, Park H, Maddipati R, Lobito AA, Bulua AC, Jackson AJ, Chae JJ, Ettinger R, de Koning HD, Cruz AC, Kastner DL, Komarow H, Siegel RM. Concerted action of wild-type and mutant TNF receptors enhances inflammation in TNF receptor 1-associated periodic fever syndrome. Proc Natl Acad Sci U S A. 2010 May 25;107(21):9801-6. Epub 2010 May 10.

Immune Cell's Role in Lupus Nephritis Demonstrated, Paves Way for Safety Testing of Potential New Use for Asthma Drug

NIAMS Deputy Scientific Director Juan Rivera, Ph.D., and his colleagues in the NIAMS Molecular Immunology Section have discovered that the activation of immune cells called basophils causes kidney damage in a mouse model of lupus nephritis. Specifically, the team showed that self-reactive immunoglobulin Es (IgEs) (antibodies that attack the self instead of germs) attached to the surface of basophils and activated them, causing them to home to the mouse's spleen and lymph nodes, where they promoted a cascade of cellular events that enhanced the production of more self-reactive antibodies. These antibodies are already known to cause kidney damage by binding with other proteins to form immune complexes that are deposited in the kidneys. Here, they cause inflammation, damage and progressive loss of

kidney function. Furthermore, the scientists demonstrated that inducing the absence of self-reactive IgEs or depleting the population of basophils relieved many of the kidney disease features seen in the mouse model. These findings and the team's associated research in humans may lead to new treatments for lupus nephritis.

Charles N, Hardwick D, Daugas E, Illei GG, Rivera J. Basophils and the T helper 2 environment can promote the development of lupus nephritis. Nat Med. 2010 June;16(6):701-7. Epub 2010 May 30.

Study of MicroRNA Helps NIH Scientists Unlock Secrets of Immune Cells

Rafael Casellas, Ph.D., and fellow scientists in the NIAMS Genomics and Immunity Section used a new microsequencing technology to identify comprehensively all of the different microRNAs (miRNAs) existing in mouse immune cells. In addition to increasing the number of known miRNAs, the scientists discovered several cellular mechanisms that regulate miRNA abundance. The study found that some miRNA constructs exist in a dormant state within the nucleus until they receive signals from the epigenome to become active. The epigenome regulates transcription and comprises all of the nongenetic material in the nucleus. Other miRNAs, the researchers determined, are not hampered by these epigenetic mechanisms and are controlled simply through transcription. However, for some of these miRNAs, abundance depends upon the amount of target messenger RNA available in the cell. The data generated from this study represent a useful tool for immunologists and cell biologists to use for future studies on functional aspects of the immune system and basic miRNA biology.

Kuchen S, Resch W, Yamane A, Kuo N, Li Z, Chakraborty T, Wei L, Laurence A, Yasuda T, Peng S, Hu-Li J, Lu K, Dubois W, Kitamura Y, Charles N, Sun HW, Muljo S, Schwartzberg PL, Paul WE, O'Shea J, Rajewsky K, Casellas R. Regulation of microRNA expression and abundance during lymphopoiesis. Immunity. 2010 Jun 25;32(6):828-39. Epub 2010 Jun 3.

NIH Genetic Collaboration Brings New Meaning to the Silk Road

In the first large genome-wide association study (GWAS) of Behçet's disease in a Turkish population, Elaine Remmers, Ph.D., and her colleagues in the NIAMS Genetics and Genomics Branch, in collaboration with Professor Ahmet Gul's group at Istanbul University, have found susceptibility to Behçet's disease to be associated with genes involved in the body's immune response. In addition to conducting its own GWAS, the NIAMS group exchanged data with an independent group of investigators that concurrently performed a large GWAS for Behçet's disease in a Japanese population. After identifying several possible targets, NIAMS researchers performed a meta-analysis of genetic data from six independent cohorts, which included populations from Turkey, the Middle East, Europe and Asia. The researchers

identified associations on chromosome 1 with a variant of the IL-0 gene and with a variant located between the genes for the IL-23 receptor (IL23R) and a component of the IL-12 receptor (IL12RB2). The finding of these shared associations in these diverse populations suggests genetic dispersion along the ancient Silk Routes.

*Remmers EF, Cosan F, Kirino Y, Ombrello MJ, Abaci N, Satorius C, Le JM, Yang B, Korman BD, Cakiris A, Aglar O, Emrence Z, Azakli H, Ustek D, Tugal-Tutkun I, Akman-Demir G, Chen W, Amos CI, Dizon MB, Kose AA, Azizlerli G, Erer B, Brand OJ, Kaklamani VG, Kaklamani P, Ben-Chetrit E, Stanford M, Fortune F, Ghabra M, Ollier WE, Cho YH, Bang D, O'Shea J, Wallace GR, Gadina M, Kastner DL, Gül A. Genome-wide association study identifies variants in the MHC class I, IL10, and IL23R-IL12RB2 regions associated with Behçet's disease. *Nat Genet.* 2010 Aug;42(8):698-702. *Epub* 2010 Jul 11. ▲*

CONVERSATION WITH DR. JUAN RIVERA, *continued from page 1*

human genome, the development of sequencing technologies that allow us to understand how genes are expressed and regulated, and the rapid advances in reprogramming of cells to become pluripotent stem cells – these breakthroughs will change the way we prevent and treat diseases. The key is being able to translate these discoveries from the bench to the bedside.

I envision that NIAMS and the Intramural Research Program will be at the forefront in translating scientific discoveries into treatment as we seize the opportunities provided by these new advances. I also envision the Intramural Research Program as a nidus where scientists and clinicians come together to seek novel solutions towards understanding biological processes in health and disease, and where the knowledge gained is used to seek better treatments or cures for the diseases affecting our constituency and the public in general. I look forward to doing my part in leading the NIAMS Intramural Research Program in this new era of discovery and medicine. ▲

NIH Hosts Scientific Conference on Lupus



Meeting organizers included (from left) Dr. Howard Young, NCI; Dr. Silvia Bolland, NIAID; and Dr. Juan Rivera, NIAMS.

NIAMS, the National Cancer Institute, the National Institute of Allergy and Infectious Diseases and the NIH Office of Research on Women's Health recently cosponsored "Systemic Lupus Erythematosus: From Mouse Models to Human Disease and Treatment." The 2-day meeting at Lister Hill brought together basic research scientists working on models of autoimmune disease relevant to systemic lupus erythematosus (SLE), with clinicians treating lupus patients. The conference will serve as a launch pad for gathering ideas regarding future steps needed to further lupus research and the use of mouse models. ▲

SEED Students Visit NIAMS and the NIH Campus



Students from the SEED School of Washington, DC

Students from the SEED School of Washington, DC, the charter school of the Schools for Educational Evolution and Development Foundation, recently visited the NIH campus as part of a newly formed partnership with NIAMS' Intramural Research Program.

The SEED Foundation opened its first school in Washington in 1998. The school is a tuition-free, lottery selection-based boarding school that aims to provide an academically rigorous college preparatory curriculum to middle and high school students from underprivileged inner-city areas. When President Obama recently visited the SEED School of Washington, DC, he praised the program as a "true success story" with 97 percent of SEED graduates being admitted to college. In the past year, the school was featured in a segment on CBS's "60 Minutes" television show as well as on CNN.

As part of the new partnership, 15 students from the school, two of whom were Washington, DC, Science Fair winners, visited with NIAMS IRP staff for a special 1-day event featuring presentations and facility tours. SEED School of Washington, DC, staff members, Mr. Keven Cotton, external operations coordinator, and Ms. Lesli Brannon, student life logistics coordinator, accompanied the students on the visit.

During the visit, Dr. Mario Cerritelli, chief of the NIAMS Career Development and Outreach Branch, gave a presentation on career opportunities at NIH and urged the students to obtain a solid and broad

education, in addition to focusing on science and math. He talked to the students about the importance of bringing diverse perspectives to biomedical research, which promotes greater innovation in solving the complex health problems facing our nation today. The students also learned about animal care and the use of animals in research at NIAMS from Dr. Crystal Brobst-Wormell, a clinical veterinarian. This was followed by tours of the NIH Clinical Center by Dr. Cerritelli and of a laboratory in the NIAMS Genetics and Genomics Branch by Ms. Geryl Wood, a research assistant within that branch. Students were also treated to lunch in the Clinical Center cafeteria, providing them the opportunity to network with staff from the Career Development and Outreach Branch.

The students' visit offered a unique opportunity for NIAMS' outreach programs to work with populations that are underrepresented in the sciences. Along with opening new doors for networking, the NIAMS visit showed the students the variety of research taking place at NIH and, it is hoped, inspired them to consider careers in science. ▲

National Institute of Arthritis
and Musculoskeletal and
Skin Diseases/NIH
Building 31, Room 4C02
31 Center Drive, MSC 2350
Bethesda, MD 20892-2350

Produced by the National Institute of Arthritis
and Musculoskeletal and Skin Diseases/NIH

Office of Communications and Public Liaison (OCPL)

Building 31 • Room 4C02
31 Center Drive, MSC 2350
Bethesda, MD 20892
Phone: 301-496-8190
Fax: 301-480-2814
E-mail: reynoldsp2@mail.nih.gov
Web site: www.niams.nih.gov

Stephen I. Katz, M.D., Ph.D., Director

John O'Shea, M.D., Scientific Director

Richard Siegel, M.D., Ph.D., Acting Clinical Director

Janet S. Austin, Ph.D., OCPL Director

Trish Reynolds, R.N., M.S., Managing Editor

Contributors:

Robert Chen, Gerda Gallop-Goodman, M.P.H., Mimi Lising, M.P.H.,
Sharon Nouzari Louis, Sara Rosario Wilson