

Division of Intramural Research

NAEHS Council Update

May 2009

NEW DIR LEADERSHIP

Dr. John Pritchard has agreed to serve as Acting Scientific Director of NIEHS until a permanent Scientific Director can be found. Dr. Pritchard recently retired from his former position as Principal Investigator for the NIEHS Renal Pharmacology Group. He also filled several other roles while at the Institute. He was Chief of the Laboratory of Pharmacology, Acting Chief of the Laboratory of Molecular Toxicology, and Director of the Environmental Toxicology Program. He received his Ph.D. in physiology from Harvard University in 1970. He served as Associate Professor of Physiology at the Medical University of South Carolina before joining NIEHS in 1976. He also served as Associate Editor of the American Journal of Physiology: Regulatory, Integrative and Comparative Physiology from 2001 to 2007.

DIR RECRUITMENTS

Investigators in Bioinformatics

The NIEHS is seeking an investigator in Bioinformatics/Computational Biology. Candidates will be considered for Senior Investigator or Tenure-Track Investigator, depending upon qualifications. The incumbent will develop and direct a strong research group to carry out independent and collaborative research in the general area of bioinformatics and computational biology, particularly as related to biological networks, analysis of high-dimensional data, proteomics, comparative and functional genomics, gene expression, and epigenetics. This work will provide a bioinformatic infrastructure and innovative data mining approaches to advance intramural research aimed at understanding biological responses to environmental stressors, in the context of cell biology, animal experimentation, clinical research and epidemiology. Dr. Thomas Kunkel, Laboratory of Molecular Genetics, is chair of the search committee. A candidate has been identified for the position.

Tenure-Track Reproductive Epidemiologist

The Epidemiology Branch, National Institute of Environmental Health Sciences, NIH, invites applications for a tenure-track epidemiologist to develop an independent investigator-initiated research program. Applicants must have an M.D. and/or Ph.D. in epidemiology or related field, at least two years of post-degree research experience, and a record of accomplishment, including relevant peer-reviewed publications. Expertise is welcome in areas of reproduction, infertility, pregnancy, child development, and early origins of later outcomes. Research on environmental and/or genetic contributors to outcomes is encouraged. Applicants will be evaluated on their demonstrated ability to conduct biologically-based, interdisciplinary, population-level research in reproductive or developmental epidemiology. Dr. E. Mitch Eddy, Laboratory of Reproductive and Developmental Toxicology, is chair of the search committee. A candidate has been identified for selection.

Tenure-Track X-Ray Crystallographer

The Laboratory of Structural Biology in the Division of Intramural Research of the National Institute of Environmental Health Sciences is seeking a Tenure-Track Principal Investigator in X-ray crystallography. Applicants should have a doctoral degree, a clear record of accomplishment in X-ray crystallography, and plans to develop a strong and original research program to investigate the structure and function of proteins involved in determining biological responses to environmental stress. While applicants proposing research in all areas related to the structure of biological macromolecules will be considered, we are particularly interested in candidates proposing research plans that coincide with areas of strength in the NIEHS Intramural Program, including but not limited to signal transduction, nuclear hormone receptor signaling, epigenetics, DNA replication and repair, and pulmonary biology. Dr. Michael Resnick, Laboratory of Molecular Genetics, is chair of the search committee. A candidate has been identified for the position.

Tenure-Track Embryonic Stem Cell Biologist

The Laboratory of Molecular Carcinogenesis is recruiting a Tenure-Track Investigator - Embryonic Stem Cell Biologist with intellectual and research strengths in, but not necessarily limited to, regulation of gene expression, development, chromatin and epigenetics. The successful applicant will be expected to establish a high-quality independent research program in stem cell biology, relevant to cancer, within a group with diverse research interests and backgrounds but focused upon the molecular and environmental mechanisms of carcinogenesis. Applicants should have a Ph.D, M.D. or equivalent doctoral degree with 3 years of postdoctoral research experience, and a strong publication record. Research experience with cancer models is desirable but not mandatory. Dr. Traci Hall, Laboratory of Structural Biology, is chair of the search committee. A candidate has been identified for the position.

Tenure-Track Developmental Neurobiologist

The Laboratory of Neurobiology is recruiting a Tenure-Track Investigator to lead a high-quality independent research program on any fundamental aspect of developmental neurobiology with the potential for identifying and preventing the deleterious effects of environmental exposures on human cognitive development. Applicants should have a Ph.D., M.D., or equivalent doctoral degree with at least 3 years of postdoctoral research experience in developmental neurobiology and a strong publication record. Applicants using fluorescence imaging and genetic model organisms are particularly encouraged to apply, but the emphasis will be on identifying an outstanding scientist with an innovative research program. Dr. Jan Drake, Laboratory of Molecular Genetics, is chair of the search committee. Candidates are currently being interviewed.

Tenure-Track Developmental Biologist

A position is available for a Developmental Biologist to establish an independent basic research program and form a research group in the Laboratory of Reproductive and Developmental Toxicology, Division of Intramural Research. Applications are invited from scientists with demonstrated ability for creative and productive research in cellular and molecular mechanisms of mammalian development. Of particular interest are investigators using rodent models to study cell interactions, epigenetics or other basic biomedical problems relating to the impact of the environment on development. The successful candidate will interact with investigators studying diverse problems in reproductive biology, developmental toxicology, hormone mechanisms, signal transduction, cell cycle regulation, cell growth and differentiation, apoptosis, gene regulation, mutagenesis and DNA repair, and cancer biology. Minimum qualifications are an M.D., Ph.D., D.V.M. or equivalent doctoral degree in the biomedical sciences, at least three years of postdoctoral experience, and publications in high quality journals. Dr. Darryl Zeldin, Acting Clinical Director and Laboratory of Respiratory Biology, is chair of the search committee. Candidates are currently being interviewed.

NEW APPOINTMENTS IN THE DIVISION OF INTRAMURAL RESEARCH

Dr. Raja Jothi, Biostatistics Branch

Dr. Raja Jothi recently joined the Biostatistics Branch at NIEHS as a tenure-track Investigator in computational biology. Dr. Jothi was trained in computer science (Ph.D. 2004, University of Texas at Dallas) before becoming interested in biology. His computational biology training was at the National Institutes of Health (NCBI/NLM and NHLBI). He has made significant contributions towards genome scale identification of previously unrecognized protein-protein and domain-domain interactions using comparative analysis of heterogeneous genomic data sets.

At the NIEHS, Dr. Jothi is now focusing on (1) understanding how transcription regulators and epigenetic modifications control gene expression during cellular development and differentiation, (2) the development and application of bioinformatics and genomics tools to identify tissue specific gene regulatory elements such as enhancers, silencers, and insulators by integrating heterogeneous genome-scale data, and (3) elucidating the dynamics of proteins/genes in protein-protein interaction and gene regulatory networks, and their role in systems behavior.

Selected Publications

- Jothi R, Balaji S, Wuster A, Grochow JA, Gsponer J, Przytycka TM, Aravind L, and Madan Babu M. Dissecting the dynamics of yeast transcription factors. *Mol. Syst. Biol.* (under revision)
- Barski A, Jothi R, Cuddapah C, Cui K, Roh T-Y, Schones DE, and Zhao K. Chromatin Poises miRNA and Protein-coding Genes for Expression. *Genome Res.* (under revision)
- Ho L, Jothi R, Ronan JL, Cui K, Zhao K, and Crabtree GR. An embryonic stem cell chromatin remodeling complex esBAF is an essential component of the core pluripotency transcriptional network. *Proc. Natl. Acad. Sci. USA*, 106(13):5187-5191 (2009)
- Jothi R, Cuddapah S, Barski A, Cui K, and Zhao K. Genome-wide identification of in vivo protein-DNA binding sites from ChIP-Seq data. *Nucl. Acids Res.*, 36: 5221-5231 (2008)
- Jothi R, Cherukuri PF, Tasneem A, and Przytycka TM. Co-evolutionary analysis of domains in interacting proteins reveals insights into domain-domain interactions mediating protein-protein interactions. *J. Mol. Biol.*, 362: 861-875 (2006)

DIR ACCOMPLISHMENTS

Comparative Medicine Program Receives Full Accreditation from AAALAC.

AAALAC, the Association for Assessment and Accreditation of Laboratory Animal Care International is a private, nonprofit organization that promotes the highest standards of humane care and treatment of animals in science through voluntary accreditation and assessment programs. Based on a site visit October 23-24, 2008, the AAALAC Council on Accreditation on March 17, 2009 issued a report giving the NIEHS Comparative Medicine Program under the direction of Dr. Diane Forsythe, Chief, full accreditation. The report states in part: "The Council commends you and the staff for providing and maintaining an exemplary program of laboratory animal care and use. Especially noteworthy were the personnel, at all levels of organization, who were knowledgeable about the program and their roles and responsibilities, and who were committed to maintaining the program at the highest quality." This marks the 37th year of full AAALAC accreditation for the NIEHS laboratory animal care and use program.

NIH Director's Challenge Award Program. Dr. Lutz Birnbaumer (Laboratory of Neurobiology) received one of eight grants from the NIH Director's Challenge Award Program for a project entitled, "The methylome in health and disease: survey of unmethylated CpGs." The project is a collaboration among investigators at NIEHS (Lutz Birnbaumer, Leping Li) and NIDDK (Ann Dean, Gary Felsenfeld, Karen Usdin) and is funded at a level of \$225,000 a year for FY2009 and FY2010. The project is designed to develop new technology to assess the methylome that will be applied to diabetes, fragile X syndrome, differentiation of ES cells and differentiation erythroid cell lineages. The NIH Director's Challenge Award Program aims to encourage collaboration among intramural investigators from multiple ICs, and to support innovative and high-impact research.

TRAINING AND MENTORING

2009 NIEHS/NTA Biomedical Career Fair

The Twelfth Annual NIEHS/NTA Biomedical Career Fair was held on Friday May 1, 2009 at the Environmental Protection Agency Campus, Research Triangle Park, NC. The keynote address entitled “Putting Your Science to WORK: Practical Career Strategies for Young Scientists” was given by Peter S. Fiske, MBA, Ph.D., Chief Technology Officer of PAX Mixer, Inc. and PAX Water Technology. . The keynote address was followed by panel discussions. Areas covered included Science Communications, Tenure Track Research Investigator in Academia, Science Policy, Science Outreach, Industry-Small Biotech, Technology Transfer and Entrepreneurship, Teaching Intensive Careers, Industry-Big Pharmaceuticals and Science in Action & Applied Science.

There were more than 300 registered attendees from universities and research institutions in the Triangle Area and the rest of North Carolina. This event was cosponsored by the NIEHS, Office of Scientific Director; NIEHS Trainees Assembly; United States Environmental Protection Agency; National Postdoctoral Association; Burroughs Wellcome Fund; and RTI International.

Panelists included:

- Meg Ehm, Ph.D., GlaxoSmithKline
- Elizabeth Roberts, D.V.M, Ph.D., DABT, Novartis Animal Health US, Inc.
- Eric Tien, Ph.D., Pfizer
- Robert Veneziale, Ph.D., Schering-Plough
- Suraj Dhungana, Ph.D., Enthalpy Analytical, Inc.
- Ward Peterson, Ph.D., Inspire Pharmaceuticals
- Alaina Sauve, MS, Syngenta
- Derek Schorzman, Ph.D., Liquidia Technologies, Inc.
- Courtney Cowan, North Carolina State Bureau of Investigation
- Marshall Gray, Jr., CIH, U.S. Public Health Service, EPA
- Andrew Hotchkiss, Ph.D., IRIS, NCEA, EPA
- Tom Knudsen, Ph.D., National Center for Computation Toxicology, EPA
- Marla Broadfoot, Freelance writer
- Chris Brodie, Ph.D., NC Biotech
- Katherine DeBruin, Ph.D., Kodiak Consulting Group
- David Schneider, Ph.D., IEEE Spectrum Magazine
- Juanita Forrester, Ph.D., University of Georgia
- Jeff Krause, Ph.D., Shodor Foundation
- Kelly Leovic, National Exposure Research Laboratory, EPA
- Amber Vogel, Ph.D., Morehead Planetarium and Science Center, UNC, Chapel Hill
- Jennifer Reineke Pohlhaus, Ph.D, Ripple Effect Communications
- Sheila Newton, Ph.D., NIEHS
- Jenny Noonan, MPA, EPA

- Lydia Olander, Ph.D., Nicholas Institute for Environmental Policy Solutions, Duke University
- Goldie S. Byrd, Ph.D., North Carolina A&T State University
- Jane Cavender, Ph.D., Elizabethtown College
- Kelly Hogan, Ph.D., UNC, Chapel Hill
- Kathy A. Zarilla, Ph.D., Durham Technical Community College
- Bryan Baines, Duke University Office of Licensing and Ventures
- Peter Fiske, MBA, Ph.D., CTO, PAX Mixer, Inc. and PAX Water Technologies
- Andrea Sherk, Ph.D., Alston & Bird, LLP
- Neil Shull, Ph.D., Blank Rome, LLC
- Ainsley Davis, Ph.D., Bethune-Cookman College
- Jamie DeWitt, Ph.D., East Carolina University
- Michael Lee, Ph.D., Samford University
- Sid Thakur, Ph.D., NC State University

The NIH Pathway to Independence Award (K99/R00)

The Pathway to Independence (PI) Award Program is designed to facilitate receiving an R01 award earlier in an investigator's research career. The primary, long-term goal of the PI Award Program is to increase and maintain a strong cohort of new and talented, NIH-supported independent investigators. The PI Award will provide up to five years of support consisting of two phases. The initial phase will provide 1-2 years of mentored support for highly promising, postdoctoral research scientists. This phase will be followed by up to 3 years of independent support contingent on securing an independent research position. Award recipients will be expected to compete successfully for independent R01 support from the NIH during the career transition award period. The PI Award is limited to postdoctoral trainees who propose research relevant to the mission of one or more of the participating NIH Institutes and Centers.

Minsub Shim, Ph.D., received the K99/R00 grant for his proposal entitled, "The role of COX-2 in skeletal development and osteoarthritis." Dr. Shim will train in the Laboratory of Molecular Carcinogenesis under the mentorship of Dr. Thomas Eling.

Yuan Liu, Ph.D., received the K99/R00 grant for his proposal entitled, "Mechanisms of Trinucleotide Repeat Expansion via Oxidative DNA Damage and Repair." Dr. Liu will train in the Laboratory of Structural Biology under the mentorship of Dr. Samuel H. Wilson.

The Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows (F32)

The Congress of the United States enacted the National Research Service Act (NRSA) Program in 1974 to help ensure that a diverse pool of highly trained scientists will be available in adequate numbers and in appropriate research areas to carry out the Nation's biomedical and behavioral research agenda. In 2002, the National Research Service Award Program was renamed the Ruth L. Kirschstein National Research Service Award Program as a tribute to Dr. Kirschstein's years of exceptional service to the Nation.

Scott Lujan, Ph.D., received a F32 Postdoctoral Fellowship for his proposal entitled "Probing DNA Polymerase Delta Dependent Lagging Strand Replication Fidelity." Dr. Lujan will train in the Laboratory of Molecular Genetics under the mentorship of Dr. Thomas A. Kunkel.

INTERNATIONAL ACTIVITIES IN THE DIR 2008

Dr. Joel Abramowitz (Office of the Scientific Director) collaborates with scientists at the Institute of Neuroscience and Center for Integrated Protein Science, Technical University Munich, Munich, Germany; and the Institute of Experimental and Clinical Pharmacology and Toxicology, Saarland University, Homburg (Saar), Germany to study the role of transient receptor potential channels in synaptic transmission and motor coordination.

Dr. Steven Akiyama (Deputy Scientific Director, Laboratory of Molecular Carcinogenesis) served as a reviewer for the Italian Ministry for Education University and Research grants program, Rome, Italy.

Dr. Donna Baird (Epidemiology Branch) has collaborations with scientists at the Norwegian Institute of Public Health, Oslo, Norway, to study gut flora development in early human life and with scientists at the Finnish Institute of Occupational Health, Helsinki, Finland, to study pesticide exposure and fertility.

Dr. Lutz Birnbaumer (Laboratory of Neurobiology) was an invited speaker at the Erhlich II, Second World Conference on Magic Bullets, Nuernberg, Germany, October 3-5, 2008; was a visiting professor at the Institute of Membrane and Systems Biology, Faculty of Biological Sciences, University of Leeds, Leeds, United Kingdom; London Pain Consortium, Department of Physiology, University College London, United Kingdom; the Institute of Experimental and Clinical Pharmacology and Toxicology, School of Medicine, University of the Saarland, Homburg-Saar, Germany; Laboratory of Ion Channel Research, Department of Molecular and Cell Biology, Catholic University of Leuven, Leuven, Belgium; and Institut Mondor of Biomedical Research - INSERM U841, Hôpital Henri Mondor, Paris-Créteil, France. In addition Dr. Birnbaumer collaborates with scientists in the Department of Anatomy, University of Berlin School of Medicine, Charite, Germany, to study the role of inhibitory heterotrimeric G proteins in cocaine-induced behavior; with scientists at the Institute of Neuroscience and Center for Integrated Protein Science, Technical University Munich, Munich, Germany to study the role of transient receptor potential channels in synaptic transmission and motor coordination; and with scientists in the Department of Physiology, University College London, London, United Kingdom, to study the role of inhibitory heterotrimeric G proteins in the control of heart function.

Dr. Perry Blackshear (Laboratory of Signal Transduction) has the following active collaborations with international investigators: at St. Bartholomew's Hospital, London, UK to study maternofetal microchimerism in type 1 diabetes; at the Universidad Austral de Chile, Valdivia, Chile to study Rfx34_v3 in the genesis of the subcommissural organ; at the University of Graz, Graz, Austria to study RFX4_v3 in congenital hydrocephalus; at the F. Perutz Laboratories, Department of Microbiology and Immunobiology, University of Vienna and at the Kennedy Institute of Rheumatology, Faculty of Medicine, Imperial College, London to study TTP and its regulation of mRNA turnover; in the Department of Zoology, Oxford University to study Drosophila CCCH zinc finger proteins and control of mRNA decay; at the Sir William Dunn School of Pathology,

University of Oxford to study macrophage and neutrophil immunostaining in TTP deficient mice; at the University of Calgary, Calgary, Canada to study expression of ZFP36L3 in differentiating trophoblast stem cells; at the Sir William Dunn School of Pathology, University of Oxford to study zfs1 in mRNA turnover in *S. pombe*; at the Christie Hospital, University of Manchester, Manchester, UK to study ZFP36L2 in hematopoiesis using embryonic stem cells; and at the AStar Institute, Singapore to study CCCH zinc finger proteins in *Danio* development.

Dr. Honglei Chen (Epidemiology Branch) collaborates with scientists at the Shanghai Hua-Shan Hospital and Shanghai Cancer Institute in Shanghai, China to study environmental exposures (e.g. daily second hand smoking, tea drinking, and soybean consumption) on the development of Parkinson's disease.

Dr. William Copeland (Laboratory of Molecular Genetics) is part of a multicenter North American collaboration to analyze the entire POLG DNA sequence from approximately 350 patients displaying a phenotype consistent with POLG related mitochondrial disease.

Dr. Gregg E. Dinse (Biostatistics Branch) has a collaboration with scientists at the Academy of Mathematics and Systems Science, Chinese Academy of Science, Beijing, China, and the University of Hong Kong, Pokfulam, Hong Kong, to study the estimation and regression analysis of hazard functions when some censoring indicators are missing at random.

Dr. Darlene Dixon (Cellular and Molecular Pathology Branch) has a collaboration with scientists at the School of Public Health, Nanjing Medical University, Nanjing, Jiangsu, China, to study signal transduction pathways initiated by genistein in human uterine leiomyoma cells.

Dr. John Drake (Chief, Laboratory of Molecular Genetics) has a collaborative research program with scientists at the Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland investigating the structural basis of DNA polymerase fidelity and serves as president of the International Genetics Federation.

Dr. June K. Dunnick (National Toxicology Program) has a collaboration with scientists Timrat, Israel to study environment-exposure induced disease.

Dr. E. Mitch Eddy (Laboratory of Reproductive and Developmental Toxicology) collaborates with scientists at the Instituto de Biología y Medicina Experimental, Buenos Aires, Argentina to investigate the role of Cysteine-Rich Secretory Protein 1 on the ability of sperm to fertilize eggs; with scientists in the Department of Bioenvironmental Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan and with scientists at Universidad Pablo de Olavide, Sevilla, Spain, to study the role of Type 1 Hexokinase in the control of sperm motility; with scientists at the Instituto de Investigaciones Biológicas, Universidad Nacional de Mar del Plata, Mar del Plata, Argentina, to study the role of serine proteases in fertilization; with scientists at the Gwangju Institute of Science and Technology, Gwangju, Korea to study of mouse germ

cell-specific genes from UniGene libraries; with scientists at the Monash Institute of Medical Research, Monash University, Australia and the Institute for Molecular Biosciences, The University of Queensland, Brisbane, Australia, to study the roles of SOX8 in Sertoli cell function and male fertility; and with scientist at the Chinese Center for Disease Control, Shanghai, China, to study altered patterns of gene expression in male reproductive organs after exposure to reproductive toxicants. In addition, Dr. Eddy served as a grant reviewer for the National Health and Medical Research Council, Australia.

Dr. Paul Foster (National Toxicology Program) was an invited expert participant on an international group undertaking research on behalf of the UK Food Standards Agency to investigate the toxicity of TCDD (Dioxin) on ability to produce effects on reproductive development held in York, United Kingdom and at the European Centre for the Ecotoxicology and Toxicology of Chemicals meeting held in Ispra, Italy.

Dr. Jonathan Freedman (Laboratory of Molecular Toxicology) collaborates with scientists in the Department of Veterinary Pharmacology and Toxicology, University of Bern, Bern, Switzerland, to study the effects of electromagnetic fields *in vitro* and *in vivo*.

Dr. Dori Germolec (National Toxicology Program) is a member of a WHO working group that will author an environmental health criteria document on Risk Assessment in Immunotoxicology and collaborates with scientists at the University of Milan, Milan, Italy; Utrecht University, Utrecht, The Netherlands; ECCVAM, JRC, Ispra, Italy; and RIVM (National Institute of Public Health & Environment), Bilthoven, The Netherlands to examine whether *in vitro* tests can be used to predict the potential immunotoxicity of perfluorinated compounds.

Dr. Joyce Goldstein (Laboratory of Pharmacology) collaborates with scientists at The Netherlands Cancer Institute, Amsterdam, The Netherlands, to study the role of the cytochrome P450 CYP3A enzymes in the metabolism of midazolam.

Dr. Jean Harry (Laboratory of Molecular Toxicology) collaborates with scientists in the Department of Molecular Neurobiology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi, Japan to study ability of the brain to generate new neurons as a function of age and previous chemical exposure; with scientists in the Department of Pharmacology and Centre for Neuroscience, The University of Melbourne, Victoria, Australia, to study neurodevelopment of the brain barriers and their importance in environmental exposure; and with scientists at the Laboratoire de Biochimie et de Génétique Moléculaire, Faculté des Sciences, Université de La Réunion, Réunion, France, to identify if stimulation of cytokine production from fat tissue represents a chronic threat to the nervous system and contributes to neurodegenerative disease.

Dr. Ronald Herbert (Cellular and Molecular Pathology Branch) organized and presented a toxicologic pathology on behalf of the International Institute of Biotechnology and Toxicology, in Padappai, Tamil Nadu, India, April 7-12, 2008; served on the

international Global Editorial Steering Committee (GESC) selected to oversee the review, revision, harmonization and publishing of standardized rodent toxicologic histopathological nomenclature for all organ systems; and served on the International Organ Working Group to review, revise, and update the previously published nomenclature guides for proliferative and non-proliferative lesions of the respiratory system of rodents.

Dr. Jau-Shyong Hong (Laboratory of Pharmacology) collaborates with scientists at the National Cheng-Kung University, Taianan City, Taiwan, to study the anti-inflammatory effect of dextromethorphan in atherosclerosis.

Dr. Anton Jetten (Laboratory of Respiratory Biology) has collaboration with scientists at the Division of Mucosal Immunology, Department of Microbiology and Immunology, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan; the Department of Cell Signaling, Tokyo Medical and Dental University, Tokyo, Japan; the Department of Immunology and Cell Biology, School of Medicine, Kyoto University, Kyoto, Japan; and Novartis Pharma AG, Basel, Switzerland, studying the physiological functions of retinoid-related orphan receptors in immunity and discovery of potential therapies for autoimmune diseases.

Dr. Maria Kadiiska (Laboratory of Pharmacology) as part of the Biomarkers of Oxidative Stress Study collaborates with scientists at Faculty of Medicine, Uppsala Univ., Uppsala, Sweden; Unilever Health Institute, Vlaardingen, The Netherland; University of Essex, Colchester, UK; the Heart Research Institute, Sydney, Australia; the Center for Hepatology, University College London, London, UK; the National Institute of Advanced Industrial Science and Technology, Ikeda, Osaka, Japan; the Center for Vascular Research, University of New South Wales, Sydney, Australia; and the Otto-Von-Guericke University, Magdeburg, Germany to evaluate techniques for the for non-invasive measurement of oxidative stress. Dr. Kadiiska also co-organizer and co-chaired an International symposium "Biomarkers of Oxidative Stress in Health and Disease" which was held in Osaka, Japan.

Dr. Steven Kleeberger (Acting Deputy Director, Laboratory of Respiratory Biology) collaborates with scientists at the INFANT Foundation, Buenos Aires, Argentina, to study the role of innate immunity and antioxidant enzyme genes in respiratory syncytial virus infection and disease progression, and the role of oxidant susceptibility genes in severity of neonatal diseases associated with hyperoxic injury; and with scientists at the University of Tsukuba, TARA Center, Tsukuba, Japan to study the role of *Nrf2* in susceptibility to oxidant-induced lung injury;

Dr. Kenneth Korach (Chief, Laboratory of Reproductive and Developmental Toxicology) presented the Plenary Keynote Lecture at the annual meeting of the Japanese Endocrine Society, Amori, Japan; and at the annual meeting of the Japanese Society of Toxicology, Tokyo, Japan; and was co-organizer of the 5th International Conference on the Female Reproductive Tract, Chiemsee, Germany. Dr. Korach also collaborates with scientists at the University of Wurzburg, Wurzburg, Germany; with scientists at the Prince Henry's

Institute, Monash University, Australia; and with scientists in the Department Neuroscience, Tsukuba University, Tsukuba, Japan to study the functions of the estrogen receptor alpha and beta.

Dr. Thomas Kunkel (Chief, Laboratory of Structural Biology, Laboratory of Molecular Genetics) has collaborations with scientists at the Centro de Biología Molecular Severo Ochoa, Universidad Autónoma, Madrid, Spain to study the functions of X family DNA polymerases involved in base excision repair; with scientists at the Ist Super Sanita, Rome, Italy to study translesion DNA synthesis; with scientists at the Institute of Pharmacology and Structural Biology, Centre National de la Recherche Scientifique, Toulouse, France and Department of Medical Biochemistry and Biophysics, Umeå University, Umeå, Sweden to investigate the functions and fidelity of DNA polymerase lambda and epsilon; with scientists at the Umeå University, Umeå, Sweden to study the effects of dNTP pool imbalances on mutagenesis in yeast; and with scientists at Cambridge University, Cambridge, England, to study novel DNA polymerases created by applied molecular evolution.

Dr. Larry Lazarus (Laboratory of Pharmacology) has collaborations with scientists in the Department of Pharmaceutical Sciences and Biotechnology Centre, University of Ferrara, Ferrara, Italy; in the Department of Toxicology, University of Cagliari, Cagliari, Italy; in the Department of Experimental and Clinical Medicine, Section of Pharmacology, National Institute of Neuroscience, Italy; in the Department of Physiology and Pharmacology “Vittorio Erspamer,” Sapienza, University of Rome, Rome, Italy; in the Department of Organic Chemistry, Vrije Universiteit Brussel, Brussels, Belgium; in the Department of Pharmacology, Tohoku Pharmaceutical University, Sendai, Japan; and in the Faculty of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, Japan, on the synthesis and functional bioactivity of unique opioid mimetic substances with specificity for the d- and m-opioid receptors.

Dr. Stephanie London (Epidemiology Branch and Laboratory of Respiratory Biology) collaborates with scientists at National Institute of Public Health, Cuernavaca Mexico, to study childhood asthma; with scientists at the National University of Singapore to study the risk factors for asthma and chronic bronchitis in adults with the Singapore Chinese Health Study; and with scientists at National Institute of Public Health, Oslo, Norway, to study early life factors and asthma.

Dr. Matthew Longnecker (Epidemiology Branch) has collaborations with scientists at the Erasmus University, Rotterdam, The Netherlands to study the effects of exposure to phthalates, bisphenol A, and organophosphate pesticides; with researchers at the National Institute of Public Health in Cuernavaca, Mexico to examine the relation between maternal serum levels of the androgenic DDT metabolite DDE in relation to anthropometric measures in 200 male newborns in Tapachula, Mexico; with scientists at The Norwegian Institute of Public Health, Oslo, Norway to study the relation of early-life exposure to subsequent health; and with scientists at the University of Pretoria, Pretoria, Republic of South Africa, to study the effects of DDT on reproductive function. As part of the World Health Organization-National Institutes of Health Common Core Protocol,

Dr. Longnecker also served as a reviewer for the International Core Study Protocol for a Longitudinal Survey of the Environmental and its Effects on Childhood, Wellcome Trust, London, England.

Dr. James Mason (Laboratory of Molecular Genetics) has collaborations with scientists at the Institute of Gene Biology, Russian Academy of Sciences, Moscow, Russia, to identify and clone a second mutation that increases telomere length in *Drosophila*; and with scientists in the Department of Genetics, University of Szeged, Szeged, Hungary, to study proteins that are components of telomeric chromatin.

Dr. David Miller (Laboratory of Pharmacology) collaborates with scientists at the Institut für Pharmazie und Molekulare Biotechnologie, Heidelberg University, Heidelberg, Germany, to study xenobiotic efflux transporters and their regulation in kidney and choroid plexus and with scientists at the Institute of Pharmacology, Toxicology and Pharmacy, Ludwig-Maximilians-University, Munich, Germany, to study blood-brain barrier based mechanisms that underlie drug resistance in epilepsy.

Dr. Fred Miller (Office of Clinical Research) is a member of The International Myositis Genetics Consortium (MYOGEN) to define genetic risk and protective factors for myositis; is a member of The International Myositis Assessment and Clinical Study Group to standardize the conduct and reporting of myositis clinical studies; is a member of The International Myositis Classification Criteria Project to develop new classification criteria for myositis and its subgroups; and is a member of The Pan-American League of Associations for Rheumatology (PANLAR) Myositis Consortium to study the ethnogeographic variations in risk factors and pathogenesis of myositis in the Americas.

Dr. Christopher Portier (Laboratory of Molecular Toxicology) was an invited speaker at a joint meeting of the World Health Organization (WHO) and the International Agency for Research Cancer (IARC) held in Geneva, Switzerland; chaired a session at the First International Forum Towards an Evidence-Based Toxicology Conference held in Milan, Italy; was an invited speaker at the Environmental Cancer Risk, Nutrition and Individual Susceptibility, Environmental Cancer Risk, Nutrition and Individual Susceptibility 6th European Framework Programm for Research and Development held in Mainz, Germany; was the keynote speaker at the 7th Valamo conference on Environmental and Health Approaches to Benefit Risk Analysis held in Heinavesi, Finland; was an invited speaker at the NewGeneris network held in Athens, Greece; was an invited speaker at the WHO – Environmental Issues/Climate Change meeting held in Geneva, Switzerland; was keynote speaker at the International Workshop on Risk Factors for Childhood Leukemia held in Berlin, Germany; served on the Scientific Advisory Group on for IARC Monographs in Lyon, France; and served on the National Sciences Engineering Research Council of Canada Site Visit Committee in Ottawa, Canada.

Dr. James W. Putney (Laboratory of Signal Transduction) collaborates with scientists in the Department of Physiology, University of Oxford, UK, to characterize the signal that activates store-operated channels in mammalian cells and with scientists at the University of Kyoto, Japan to study the function and activation mechanisms for transient receptor

potential (TRP) channels in B-cell receptor signaling. Dr. Putney also served as co-organizer of the Second International Congress on Cell Membranes and Oxidative Stress, held in Isparta, Turkey, June 25-28, 2008.

Dr. Manas Ray (Laboratory of Reproductive and Developmental Toxicology) collaborates with scientists at the Faculty of Agriculture, Okayama University, Okayama, Japan to study the role of limbin in bone formation; and with scientists at the Centre for Diabetes Research, Western Australian Institute for Medical Research, Perth, Australia to study BMP signaling in glucose metabolism.

Dr. Michael Resnick (Laboratory of Molecular Genetics) has collaborations with scientists in the Mutagenesis Laboratory, National Institute for Cancer Research, Genoa, Italy to study mutations in the tumor suppressor p53; and with scientists in the Institut für Pharmakologie und Toxikologie, Lehrstuhl Toxikologie, Julius-Maximilians-Universität Würzburg, Würzburg, Germany to study single nucleotide polymorphisms (SNPs) in the promoter of human FLT1. Dr. Resnick was also co-organizer of the 14th International p53 Workshop in Shanghai, China.

Dr. Lisa Rider (Office of Clinical Research) is a member of The International Myositis Genetics Consortium (MYOGEN) to define genetic risk and protective factors for myositis; is a member of The International Myositis Assessment and Clinical Study Group to standardize the conduct and reporting of myositis clinical studies. Dr. Rider also has collaborations with scientists at the IWK Health Centre, Halifax Nova Scotia, Canada and the University of Toronto, Toronto, Ontario, Canada to study cutaneous assessment of myositis and juvenile dermatomyositis.

Dr. Dale Sandler (Chief, Epidemiology Branch) collaborates with scientists at Charles University, Prague, Czech Republic and the Center for Epidemiologic Studies, Uranium Miners Health Institute, Příbram, Czech Republic to study cancer incidence and other health outcomes in a cohort of Czech uranium miners whose exposures were lower than those of most other cohorts of uranium miners; and with scientists at the Karolinska Institute, Stockholm, Sweden to study the familial risk for leukemia.

Dr. Roel M. Schaaper (Laboratory of Molecular Genetics) has collaborations with scientists at the Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland to study mechanisms of DNA replication fidelity; and with scientists in the Department of Genetics, St. Petersburg State University, St. Petersburg, Russia to study base analog detoxification by molybdenum-dependent activities.

Dr. Stephen Shears (Laboratory of Signal Transduction) has a collaboration with scientists at the Cardiff School of Biosciences, Cardiff University, Cardiff, United Kingdom to study the role of multiple inositol polyphosphate phosphatase in the control of the Rapoport–Luebering glycolytic shunt.

Dr. Robert Sills (Chief, Cellular and Molecular Pathology Branch). Cellular and Molecular Pathology Branch pathologists participate in the International Harmonization

of Nomenclature and Diagnostic Criteria Project for Lesions in Rats and Mice, a joint international initiative undertaken by the North American, European, British and Japanese Societies of Toxicologic Pathology that is aimed at global harmonization of nomenclature and diagnostic criteria used in toxicologic pathology.

Dr. William Stokes (National Toxicology Program) was an invited participant as a member of the U.S. delegation for the first meeting of the International Cooperation on Cosmetics Regulation held in Brussels, Belgium; was an invited participant on the Steering Committee for an International Evidence-Based Toxicology Forum held in, Lake of Como, Italy; was an invited participant at the Third Annual Conference of the European Partnership for Alternative Approaches to Animal Testing in Brussels, Belgium; and was an invited participant at the European Centre for the Validation of Alternative Methods Scientific Advisory Committee meetings in Ispra, Italy.

Dr. Raymond Tice (National Toxicology Program) was an invited participant at the Meeting of the Validation Study Management Team for the NICEATM-Japanese Center for the Validation of Alternative Methods-European Centre for the Validation of Alternative Methods international validation study of an *in vitro* endocrine disrupter test method; and the meeting of the Validation Study Management Team for the Japanese Center for the Validation of Alternative Methods-sponsored International Comet Assay Validation Study. All the meetings were held in Tokyo, Japan.

Dr. Kenneth Tomer (Laboratory of Structural Biology) collaborates with scientists at the Rostock University, Rostock, Germany, to determine biomarkers of immune disorders such as Sjogren's disease; and with scientists at Konstanz University, Konstanz, Germany, to study autoantibodies against Alzheimer's related proteins. Dr. Tomer also serves on the Scientific Advisory Committee of the Portuguese National Mass Spectrometry Network.

Dr. Nigel Walker (National Toxicology Program) served as a member of the Council of Canadian Academies' Expert Panel on Nanotechnology; and as a member of the International Life Sciences Institute-Health and Environmental Sciences Institute Nanomaterial Safety Subcommittee.

Dr. Clarice Weinberg (Chief, Biostatistics Branch) has a collaboration with epidemiologists at the University of Bergen, Bergen, Norway and with scientists in Odense, Denmark, studying the causes of oral clefting.

Dr. Allen Wilcox (Epidemiology Branch) has a collaboration with scientists at the University of Bergen and the Norwegian Public Health Institute to study of reproductive and perinatal problems including: the length of pregnancy on genetic characteristics passed from the father to his offspring; facial clefts in Norway; and environmental causes of pregnancy problems.

Dr. Darryl Zeldin (Acting Clinical Director, Laboratory of Respiratory Biology) had a collaboration with scientists in the Gene Therapy Center, Tongji Medical Center, Wuhan,

Peoples Republic of China to study the roles of Cytochrome P450 CYP2J2 in ischemia-reperfusion, cancer and inflammation; with scientists in the Laboratory of Pharmacology and Toxicology, University of Paris, Paris, France to design and characterize selective inhibitors of human CYP2J2; with scientists at the Institute of Cardiovascular Physiology, Johann Wolfgang Goethe University, Frankfurt, Germany to study the role of P450-derived eicosanoids in regulating hypoxic pulmonary vasoconstriction; and with scientists at the Max Delbrueck Centre for Molecular Medicine, Berlin, Germany to the role of P450-derived eicosanoids and other fatty acid products in cardiac hypertrophy.