THE DIVISION OF INTRAMURAL RESEARCH

NAEHS COUNCIL REPORT

MAY 2001

DIR Recruitments
February 2001

Scientific Director
A national search has been reopened to fill the position of Director, Division of Intramural Research, NIEHS. This individual serves as Scientific Director and directs laboratory and clinical research through 18 Laboratories and Branches with approximately 1100 government employees and contract personnel and an annual budget of approximately 140 million dollars. The Scientific Director is the principal advisor to the Institute Director on scientific affairs involving multidisciplinary biomedical research programs. The search committee, chaired by Dr. Samuel Wilson, has forwarded a short list of candidates to Dr. Olden.

Chief, Laboratory of Pulmonary Pathobiology
A national search for a new Chief of the Laboratory of Pulmonary Pathobiology (LPP) is taking place. The LPP is engaged in research on the biology of the respiratory tract system at the cellular, biochemical and molecular level to develop a better understanding of pathogenetic mechanisms involved in development of airway diseases. The search committee, Chaired by Dr. Perry Blackshear (Clinical Director), has recommended a candidate and negotiations are in the final stages.

Staff Scientist-Veterinary Pathologist
The Laboratory of Environmental Pathology is seeking a highly motivated Toxicologic Pathologist experienced in rodent toxicology and carcinogenicity studies to work within the National Toxicology Program (NTP). The successful candidate will be involved primarily in the management and oversight of the pathology peer review (evaluation) and interpretation and reporting of the data. Also the candidate will be expected to identify and pursue special projects that will advance the understanding of various biological endpoints. The search committee, chaired by Dr. Gary Boorman (National Toxicology Program), is reviewing applications.

Tenure-Track Neuroscientist
The Division of Intramural Research is recruiting for a tenure-track neuroscientist to conduct independent research that will complement or expand ongoing activities in neuropharmacology, neuroimmunology, signal transduction, synaptic plasticity, reproductive and developmental toxicology and neurotoxicology. The search committee, chaired by Dr. Jean Harry, Acting Chief, Laboratory of Toxicology, has recommended a candidate to the Scientific Director.

Staff Scientist-Knockout Core Facility Manager
The Laboratory of Reproductive and Developmental Toxicology is recruiting a Staff Scientist with expertise in mouse molecular genetics or a related discipline to serve as the Head of the Transgenic Knockout Core Facility. The successful applicant will generate mutant mice using embryonic stem cell technologies, plan and provide scientific oversight in the conduct of targeting vector design, and serve as a resource expert on mouse genetics and embryology. The Scientific Director has selected a candidate and the official offer is pending approval of Dr. Olden.

Staff Scientist-NMR Chemist
The Laboratory of Structural Biology is seeking a chemist to serve as the technical expert for the preparation and structural analysis of isotopically labeled proteins using Nuclear Magnetic

Resonance (NMR) techniques. Experience in multidimensional NMR techniques as well as the design, preparation, isolation, purification and concentration of biological macromolecules is essential. After a national search, Dr. Geoffrey Mueller has been selected. Dr. Mueller received his Ph.D. from the University of Virginia in 1998 and is currently a post-doctoral fellow with Dr. Lewis Kay at the University of Toronto.

Tenure-Track Epidemiologist

A national search is being conducted for a tenure-track investigator who will develop an independent research program in noncancer chronic disease epidemiology, with emphasis on the potential environmental causes of neurological diseases and dysfunctions in humans such as Parkinson's disease, Alzheimer's disease and multiple sclerosis. Individuals with the ability to integrate basic and molecular biology, genetics, toxicology, exposure assessment and epidemiology are sought. The Search Committee, chaired by Dr. Clarice Weinberg (Chief, Biostatistics Branch), has interviewed candidates and has forwarded a recommendation to the Scientific Director.

Tenure-track Molecular Toxicologist

The Laboratory of Computational Biology and Risk Analysis is conducting a national search for a tenure-track researcher to develop an independent research program in molecular toxicology focusing on mechanisms of carcinogenicity and toxicity initiated through ligand-receptor interactions. A search committee, chaired by Dr. Douglas Bell, Laboratory of Computational Biology and Risk Analysis, has been formed and the position should be advertised in the very near future.

Chief, Laboratory of Toxicology

The Environmental Toxicology Program plans to conduct an international search to recruit a senior research toxicologist to serve as Chief of the Laboratory of Toxicology with tenure. Priority will be given to applicants with demonstrated ability to foster effective utilization of molecular technology in the research of the Laboratory, is internationally recognized as an expert in the field of toxicology, and possess a level of managerial and executive ability to create an atmosphere for maximum creativity and scientific productivity. Priority will be given to researchers whose primary interests are in developmental and/or reproductive toxicology with a focus on the molecular basis for environmental causes of disfunction in these areas. A search committee chaired by Dr. John Pritchard, Chief, Laboratory of Pharmacology and Chemistry has been formed.

New Appointments in the Division of Intramural Research

Dr. Frederick Miller

Dr. Frederick Miller was recently recruited to initiate a new NIEHS clinical program at the Warren Grant Magnuson Clinical Center on the Bethesda campus to study genetic and environmental contributions to the pathogenesis of autoimmune diseases. He will serve as the Chief, Environmental Autoimmunity Group in the Office of Clinical Research. The Environmental Autoimmunity Group will conduct a broad program of clinical investigation in the area of adult and pediatric autoimmune diseases. These studies include epidemiologic surveys and clinical investigations in disease pathogenesis, as well as the development of clinical tools for assessment of innovative therapies. Volunteer patients are referred by physicians worldwide and participate in the studies by signed informed consent. This group will also serve as a liaison to others in NIEHS who wish to conduct clinical studies or obtain clinical specimens for research purposes.

Dr. Miller received his M.D. and Ph.D. degrees from the Case Western Reserve University School of Medicine and did post-doctoral clinical training at Emory University, Stanford University and the National Institute of Arthritis, Musculoskeletal and Skin Diseases, NIH. He is board certified in Internal Medicine and Rheumatology. Dr. Miller's research background is in the pathogenesis of human autoimmune diseases, focusing on multidisciplinary studies of the myositis syndromes.

Selected Recent Publications

Rider, L.G., Shamim, E., Okada, S., Pandey, J.P., Targoff, I.N., O'Hanlon, T.P., Han, H., Kim, H., Lim, Y., Song, Y. and Miller, F.W. (1999). Genetic Risk and Protective Factors for Idiopathic Inflammatory Myopathy in Koreans and Caucasians: A Tale of Two Loci. Arthritis Rheum. 42:1285-1290.

O'Hanlon, T.P., Lawless O.J., Katzin, W.E., Feng, L.J., Miller, F.W. (2000). Restricted and shared patterns of TCR beta-chain gene expression in silicone breast implant capsules and remote sites of tissue inflammation. J Autoimmunity 14: 283-293

Miller, F.W., Hess, E.V., Clauw, D.W., Hertzman, P.A., Pincus, T., Silver, R.M, Mayes, M.D., Varga, J., Medsger, T.A. and Love, L.A. (2000). Approaches for identifying and defining environmentally associated rheumatic disorders. Arthritis Rheum 43:243-249

Rider, L.G., Artlett, C.M., Foster, C.B., Ahmed,.A., Neeman, T. Chanock, S.J., Jimenez, S.A. and Miller, F.W. (2000). Polymorphisms in the interleukin-1receptor antagonist VNTR are possible risk factors for juvenile idiopathic inflammatory myopathies. Clin Exp Immunology 121:47-52.

Artlett, C.M., Ramos, R., Jiminez, S.A., Patterson, K. Miller, F.W. and Rider, L.G. (2000) Chimeric cells of maternal origin in juvenile idiopathic inflammatory myopathies. Lancet 356: 2155-2156.

Training and Mentoring

2001 NIEHS/NTA Science and Career Fair

The Fourth Annual NIEHS/NTA Science and Career Fair was held on May 4, 2001 in the Rodbell Conference Center, NIEHS. The keynote speaker was Mr. David Jensen, Principal Consultant, Search Masters International who gave the presentation "Develop an Industrial Strength Job Search to Find Your Career Destiny." The panel discussion this year focused on "Exploring Career Opportunities in Science." It was moderated by Dr. Thomas Kunkel, Chief, Laboratory of Structural Biology, and Scientific Program Director, Environmental Biology Program, NIEHS. Panel participants included Mr. David Jensen; Dr. Laura Bottomly, Director of Women Engineering and Outreach, North Carolina State University; Dr. Salil Patel, President and Chief Scientific Officer, GeneEd, Inc.; Dr. Catherine Hammett-Stabler, Assistant Professor of Pathology and Laboratory Medicine, University of North Carolina-Chapel Hill; Dr. Ruth Winecker, Chief Toxicologist, Office of the Chief Medical Examiner, University of North Carolina; and Dr. Rueben Warren, Associate Administrator for Urban Affairs, ATSDR. Other events at the Science and Career Fair include two poster sessions, three breakout sessions run by Dr. Chandra Louise, President, Peer Productions, Inc. and Dr. George O'Neill, Career Consultant, American Chemical Society, and a reception. The breakout sessions covered resume preparation/review, interviewing skills, and opportunity and challenges for international trainees in the American workplace. There were approximately 250 attendees from institutions in the Triangle Area as well as from other universities and NIH Institutes. More than 25 companies were represented. The NIEHS, the North Carolina Biotechnology Center, the Chemical Industry Institute of Toxicology, the Burroughs Wellcome Fund, Merck and Co., Inc, and S & M Separation Technologies, Inc. cosponsored this event.

Awards and Honors in the Division of Intramural Research
May 2001

Dr. Mike Cunningham (Environmental Toxicology Program) was named an Associate Editor for *Toxicological Sciences*.

Dr. James Huff (Office of the Scientific Director) was appointed as Co-Chair of the Committee on Cancer Policy, International Ramazzini Foundation, Carpi, Italy for 2001.

Dr. Larry Lazarus (Laboratory of Computational Biology and Risk Analysis) was invited to be a Plenary Speaker at the 4th Symposium on Frontiers in Protein Chemistry and Biotechnology at the Chengde Medical College, People's Republic of China, August 16-20, 2001.

Dr. Ron Melnick (Laboratory of Computational Biology and Risk Analysis) was appointed as Co-Chair of the Committee on Cancer Policy, International Ramazzini Foundation, Carpi, Italy for 2001.

Dr. Elizabeth Murphy (Laboratory of Signal Transduction) was selected as an Inaugural Fellow of the American Heart Association. She was also elected as a member of the International Council of the International Society for Heart Research.

Ms. Retha Newbold (Laboratory of Toxicology) was invited as one of three key scientific lectures at the DES Action International Colloquium held April 1-2, 2001 in Washington, DC.

Mr. Tomo Oshimura (Laboratory of Molecular Carcinogenesis) won an award in the Biological Sciences Category at the North Carolina State Senior Project Poster Presentation for his poster "Identification of Estrogen Responsive Genes in MCF7-C7 Breast Tumor Cell Line Using cDNA Microarrays".

Ms. Kelli Reynolds (Laboratory of Molecular Carcinogenesis) won an award in the Engineering and Technology Category at the NC State Senior Project Poster Presentation with her poster "Automation of Bioinformatics Processes for Microarray Data.

Dr. Ken Tomer (Laboratory of Structural Biology) presented a plenary lecture entitled Mass Spectrometry in the Characterization of Protein:Protein Interactions at the 34th Meeting of the German Society for Mass Spectrometry March 5, 2001 in Munich, Germany.

Dr. Allen Wilcox (Epidemiology Branch) was elected President of the American Epidemiological Society for 2002-2003. He was invited to present the keynote address at the Annual Meeting of the ISEE (International Society of Environmental Epidemiology), in Garmisch, Germany, September 2001.

Dr. Sam Wilson (Laboratory of Structural Biology) was Chair of the Mammalian DNA Repair Gordon Research Conference January 21-26, 2001. He was the Keynote Speaker at the Midwest DNA Repair Meeting held June 2 in Indianapolis, Indiana

Dr. Darryl Zeldin (Laboratory of Pulmonary Pathology) has developed an asthma website which won the Lightspan Academic Excellence Award.

HIGHLIGHTS FROM THE NATIONAL TOXICOLOGY PROGRAM (NTP)
May 2001

- The NTP has received a request from the California Congressional delegation, the California Environmental Protection Agency, and the California Health and Human Services Agency to perform definitive rodent cancer studies on hexavalent chromium in response to concerns raised over contamination of source water supplies. While the toxicity and carcinogenicity of hexavalent chromium compounds have been recognized for some time, adequate long-term oral toxicity studies are largely unavailable and there remain gaps in our collective knowledge regarding any potential health risks. The NTP has accepted this nomination and is in the process of designing studies to address this issue.

- The technologies to allow genome-wide analysis of gene expression are heavily influencing drug discovery and preclinical safety studies in the pharmaceutical companies. Genomic expression analysis also has the potential to revolutionize toxicological evaluation of environmental chemicals. The NTP in collaboration with the NIEHS National Center for Toxicogenomics is exploring ways to incorporate these new technologies into NTP evaluations.

NTP Board of Scientific Counselors

- The NTP Board of Scientific Counselors meets May 25, 2001 at the NIEHS. The meeting begins at 8:30 AM and is open to the public. The NTP Board of Scientific Counselors is composed of scientists from the public and private sectors and provides scientific oversight to the NTP. Primary agenda topics include:
  - review and discussion of draft guidelines for the NTP Center for the Evaluation of Risks to Human Reproduction's (CERHR) expert panels,
  - the NTP Interagency Committee for Chemical Evaluation and Coordination's (ICCEC) testing recommendations for substances nominated for future NTP studies, and
  - presentations about chemical disposition and toxicokinetic studies of substances by the NTP and use of this data in pharmacokinetic modeling.

  There will also be updates on activities of the Board's Report on Carcinogens and Technical Reports Review Subcommittees. The Board will review a concept proposal for the continued use of a contract mechanism to investigate the mechanisms of toxicity, absorption, tissue distribution, metabolism, and clearance of substances under study by the NTP.

NTP Board of Scientific Counselors Report on Carcinogens Subcommittee

- The 9th Edition of the Report on Carcinogens (RoC) was published in May 2000. An addendum to the 9th Report was issued in January 2001 to change the listing of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (also known as "dioxin" or "TCCD") to a *known to be a human carcinogen* from *reasonably anticipated to be a human carcinogen*. Publication of the addendum followed the ruling by the US Court of Appeals for the District of Columbia Circuit denying the request for an injunction to prevent the listing of TCDD as a *known human carcinogen* in the 9th Report pending appeal of the district court's decision upholding the listing.

NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

- NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) collaborate to develop, validate, and achieve regulatory acceptance of new and improved test methods. In 2001, ICCVAM/NICEATM expect to publish several reports from previous meetings that they sponsored.
  - the May 2000 Expert Panel Meeting evaluating the Frog Embryo Teratogenesis Assay—*Xenopus* (FETAX)
  - the July 2000 Peer Review Meeting on the Up-and-Down Procedure (UDP) for Acute Oral Toxicity
  - the October 2000 International Workshop on *In Vitro* Methods for Assessing Acute Systemic Toxicity
  - the Guidance Document on using *in vitro* data to estimate *in vivo* starting doses for acute toxicity, a report which resulted from the *In Vitro* Methods Workshop

NTP Workshops and Conferences

- The NTP is a co-sponsor for the 23rd Annual Meeting of the Bioelectromagnetics Society (BEMS) being held June 10-14, 2001 in St. Paul, Minnesota. The NTP receives input on electromagnetic field issues relative to power lines and radio-frequencies from experts in this society.

- The *ICLAS-CCAC International Symposium on Regulatory Testing and Animal Welfare* is being held June 21-23, 2001 in Quebec City, Canada. The International Council for Laboratory Animal Science (ICLAS) fosters international harmonization of animal care and use practices. The Canadian Council of Animal Care (CCAC) has responsibility for overseeing the ethical use of animals in Canadian science. The NTP is a co-sponsor for this workshop and Dr. William Stokes, Director, NTP Center for the Evaluation of Alternative Toxicological Methods, is a member of the Steering Committee.

- The NTP, along with the EPA, FDA and the Office of Rare Diseases/NIH, is sponsoring a workshop, *Assessment of the Allergenic Potential of Genetically Modified Foods*, to be held September 24-26, 2001 at the Durham Marriott at the Civic Center in Durham, NC. This meeting will bring together experts in food allergy, genetically modified crops, and the regulatory aspects of these products along with bench scientists and clinicians. Topics to be covered include the current state of knowledge in this area, identification of critical issues regarding these materials, and the development of testing strategies for examining their potential toxicities. Dr. Dori Germolec, Laboratory of Toxicology, is the primary contact for this meeting.

- Since January 1, 2001 the National Center for Toxicogenomics (NCT) has conducted two workshops*: Functional Proteomics in Environmental Health Science* at the Arizona Cancer Center in Tucson, AZ and *Bioinformatics Strategies for Application of Genomic Tools to Environmental Health Research* at NC State University in Raleigh, NC. Summaries of these workshops can be found via the NCT web site www.niehs.nih.gov/nct/workshop.htm.