Division of Intramural Research

NAEHS Council Update

February 2018

DIR RECRUITMENTS

Chief of the Administrative Research and Services Branch
The National Institute of Environmental Health Sciences (NIEHS) is seeking an accomplished individual to serve as the Chief of the Administrative Research and Services Branch (ARSB). This individual will serve as principal advisor to senior management on all phases of the administrative management of the Division of Intramural Research (DIR), the Division of the National Toxicology Program (DNTP), and Clinical Research Branch for NIEHS; and oversee the implementation of a variety of management services essential to the direction and operation of the Institute. The successful candidate will: Provide guidance and oversight for procurement, contracts, property management and operational management functions; Oversee and monitor the operating budget process to ensure the timely, appropriate, and efficient expenditure of funds against annual allotment; anticipate changes in funding levels; prepare proposals and justify current and increased expenditures; Serve as a principal advisor on all human resource management activities and ensures compliance with all applicable regulatory requirements; Oversee all administrative management matters associated with programs and operations; with responsibility for the analysis of organizational priorities and the development and implementation of administrative policies and procedures; Participate in and oversee the planning sessions related to the following space, telecommunications, travel, and/or timekeeping and leave; and Supervise the activities for administrative, technical and support staff. Dr. Jerry Yakel, Chief of the Neurobiology Laboratory, is chair of the Search Committee.

Chief of the Biostatistics and Computational Biology Branch
The National Institute of Environmental Health Sciences (NIEHS) is seeking an accomplished individual to serve as the Chief of the Biostatistics and Computational Biology Branch (BCBB). The ideal candidate will be tenure-eligible based on an outstanding academic record of achievement, leadership capabilities, and broad interests in biostatistics and computational biology. In addition to directing their own independent research program, they will have responsibility for leading BCBB in new directions as biostatistics and environmental science data continually evolve. The successful candidate should have a keen interest in collaborating both with members of BCBB and with other investigators within NIEHS. Principal investigators in the NIH intramural program have no formal teaching duties, are funded internally, and work with a great deal of protected time. They engage directly in research and methods development with postdoctoral fellows, students, and support staff, and collaborate with colleagues in solving important scientific problems. Dr. Jack Taylor, Epidemiology Branch, is chair of the search committee.

Staff Scientist Biostatisticians
The National Institute of Environmental Health Sciences (NIEHS) is seeking two experienced biostatisticians at the rank of Staff Scientist in the Biostatistics and Computational Biology Branch (BCBB) of the Division of Intramural Research (DIR). The incumbents will collaborate extensively with researchers in the DIR and the Division of the National Toxicology Program (DNTP). The successful candidates will also play a major role in analyses for the National Toxicology Program (NTP), they will provide statistical leadership and ensure the statistical integrity of its research program. In addition, the positions involve management and oversight of statistical support service contracts. Development of new statistical methods is encouraged, but

will not be a major component of the jobs. Drs. Kathy Laber, Comparative Medicine Branch and Rick Paules, DNTP, are co-chairs of the search committee.

Tenure-Track Investigator in Transcription, Epigenetics or Chromatin Biology
The National Institute of Environmental Health Sciences (NIEHS) is seeking an exceptional individual as a Tenure-Track Investigator in the Epigenetics and Stem Cell Biology Laboratory within the Division of Intramural Research. The successful candidate is expected to lead an innovative, independent research program exploring epigenetics, chromatin architecture or transcription that enhances our understanding the effects of the environment on human health. Applicants should have a Ph.D., M.D. and/or equivalent doctoral degree with at least 3 years of postdoctoral research experience in their field and an outstanding publication record. The emphasis will be on identifying an exceptional scientist with an innovative and productive research program. Dr. Thomas Kunkel, Genome Integrity and Structural Biology Laboratory, chairs the search committee.

Tenure-Track Investigator in Reproductive Endocrinology
The National Institute of Environmental Health Sciences (NIEHS) is seeking an exceptional individual as a Tenure-Track Investigator in the Reproductive and Developmental Biology Laboratory within the Division of Intramural Research. The successful candidate is expected to have a strong record of accomplishments in the field of Reproductive Endocrinology, with a research emphasis on conducting mechanistic investigations of the estrogen hormone signaling pathways and functions in biological systems. This person will be expected to develop an outstanding independent research program that complements and benefits from the other research programs within the Reproductive and Developmental Biology Laboratory and the Division of Intramural Research at NIEHS, and is consistent with the mission of the NIEHS and NIH. Applicants should have a Ph.D., M.D., D.V.M., or an equivalent doctoral degree, with three or more years of postdoctoral training in mammalian reproductive biology and molecular endocrinology, demonstrated ability to design and carry out original and innovative research as evidenced by an outstanding publication record. Dr. Anton Jetten, Immunity, Inflammation, and Disease Laboratory, is chair of the search committee.

NEW APPOINTMENTS IN DIR

Deputy Scientific Director

Dr. Paul Doetsch is the new Deputy Scientific Director in DIR. He comes to NIEHS from Emory University where he was Associate Chair and Director, Division of Cancer Biology, Department of Radiation Oncology; Professor, Departments of Biochemistry and Radiation Oncology, and of Hematology and Medical Oncology; Department of Radiation Oncology Distinguished Chair of Cancer Research; and Associate Director for Basic Research Winship Cancer Institute of Emory University. At NIEHS Dr. Doetsch will also be Senior Investigator in the Genome Integrity and Structural Biology Laboratory (GISBL) where he will be investigating the regulation of base excision repair and transcriptional mutagenesis and retromutagenesis.

BSC REVIEW OF THE EPIDEMIOLOGY BRANCH

The NIEHS DIR Board of Scientific Counselors reviewed the Epidemiology Branch, May 7-9, 2017

Members of the Board of Scientific Counselors that Attended:

- Kenneth B. Adler, Ph.D. [BSC Chair], Professor, Dept. of Molecular Biomedical Sciences, North Carolina State University, College of Veterinary Medicine, Raleigh, NC
- Christopher I. Amos, Ph.D., Professor, Dept. of Community and Family Medicine, Geisel School of Medicine at Dartmouth, Hanover, NH
- Juan C. Celedón, M.D., Dr.P.H., Niels K. Jerne Professor of Pediatrics, Dept. of Pediatrics, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Pittsburgh, PA
- Monica J. Justice, Ph.D., Head and Senior Scientist, Genetics & Genome Biology Program, SickKids Research Institute, The Peter Gilgan Centre for Research and Learning, Toronto, ON, Canada
- Donald P. McDonnell, Ph.D., Glaxo-Wellcome Professor and Chairman of Pharmacology and Cancer Biology, Duke University School of Medicine, Durham, NC
- Ivan Rusyn, M.D., Ph.D., Professor, Department of Veterinary Integrative Biosciences, Texas A&M University College of Veterinary Medicine & Biomedical Sciences, College Station, TX
- Daniel O. Stram, Ph.D., Professor, Division of Biostatistics and Genetic Epidemiology, Department of Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, CA
- Karen M. Vasquez, Ph.D., Professor, Division of Pharmacology and Toxicology, Dell Pediatric Research Institute, The University of Texas at Austin, Austin, TX
- Roland A. Owens, Ph.D., Ex-Officio BSC Member, Assistant Director, Office of Intramural Research, NIH, Bethesda, MD

Ad Hoc Reviewers that Attended:

- Leslie Bernstein, Ph.D., Professor, Division of Biomarkers of Early Detection and Prevention, Department of Population Sciences, Beckman Research Institute of the City of Hope, City of Hope Comprehensive Cancer Center, Duarte, CA
- Jane A. Cauley, Dr. P.H., Distinguished Professor of Epidemiology, Epidemiology Associate Dean for Research, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA
- Crystal W. Cené, M.D., M.P.H., Associate Professor, Division of General Medicine and Clinical Epidemiology, Associate, Center for Health Equity Research, University of North Carolina School of Medicine, Chapel Hill, NC
- Susan M. Gapstur, Ph.D., M.P.H., Vice President, Epidemiology, American Cancer Society, Inc., Atlanta, GA
- Tamara Harris, M.D., M.S., Chief, Interdisciplinary Studies of Aging Section, Laboratory of Epidemiology and Population Science, National Institute on Aging, Baltimore, MD

- Lifang Hou, M.D., M.S., Ph.D., Chief, Division of Cancer Epidemiology & Prevention, Department of Preventive Medicine, Director, Global Health Initiative, Robert H. Lurie Comprehensive Cancer Center, Director, Center for Population Epigenetics, Feinberg School of Medicine, Northwestern University, Chicago, IL
- Anita Kozyrskyj, Ph.D., Professor, Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada
- Andrew F. Olshan, Ph.D., Barbara S. Hulka Distinguished Professor and Chair, Department of Epidemiology, University of North Carolina, Gilling's School of Global Public Health, Chapel Hill, NC
- Melissa J. Perry, ScD, M.H.S., FACE, Professor of Environmental and Occupational Health, Interim Associate Dean for Research, Milken Institute School of Public Health, The George Washington University, Washington, DC
- Regina M. Santella, Ph.D., Professor, Environmental Health Sciences, Vice Dean, Faculty Affairs, and Research, Columbia University, Mailman School of Public Health, New York, NY
- Kathryn L. Terry, ScD, Associate Professor of Obstetrics Gynecology and Reproductive Biology, Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
- Katherine L. Tucker, Ph.D., Professor of Nutritional Epidemiology, Department of Clinical Laboratory & Nutritional Sciences, Director, University of Massachusetts Lowell Center for Population Health, University of Massachusetts Lowell, Lowell, MA
- Martha M. Werler, ScD, Professor and Chair, Department of Epidemiology, Boston University School of Public Health, Director, Boston University Reproductive Health, Perinatal & Pediatric Epidemiology Training Program, Boston, MA

Agenda:

Sunday, May 7 – Doubletree by Hilton
Closed Evening Session

7:00 – 8:00 p.m.	Welcome and Discussion of Past Board Reviews, Drs. Linda Birnbaum, Darryl Zeldin, Dale Sandler, Kevin Gardner
8:00 – end	BSC Discussion of Review, Dr. Ken Adler and panel

Monday, May 8 - NIEHS Rodbell Conference Rooms 101 ABC
Morning Session

8:30 - 8:45 a.m.	Welcome, Dr. Kenneth Adler
8:45 - 9:05	Overview, Epidemiology Branch, Dale Sandler, Ph.D.
9:05 - 9:55	Chronic Disease Epidemiology Group, Dale Sandler, Ph.D.
9:55 - 10:10	COFFEE BREAK
10:10 - 11:00	Perinatal and Early Life Epidemiology Group, Kelly Ferguson, Ph.D.
11:00 - 11:30	Closed 1:1 Sessions with Investigators, Drs. Sandler and Ferguson
11:30 - 1:00	Closed Working Lunch

Afternoon Session

1:00 - 2:00 p.m.	Poster Session—Epidemiology Branch Trainees and Staff Scientists, Rodbell Lobby

2:00 - 3:00	Closed Sessions with Trainees and Staff Scientists, 101ABC
3:00 - 3:15	BREAK
3:15 - 4:05	Molecular and Genetic Epidemiology, Jack Taylor, M.D., Ph.D.
4:05 - 4:55	Genetics, Environment, and Respiratory Disease Group, Stephanie London, M.D.
4:55 - 5:25	Closed 1:1 Sessions with Investigators, Drs. London and Taylor
5:45	Return to Doubletree Hotel

Closed Evening Session

6:00 – end	BSC Discussion and completion of individual review assignments by each member, All BSC reviewers at hotel

Tuesday, May 9 - NIEHS Rodbell Conference Rooms 101 ABC

Morning Session

8:30 - 9:00 a.m.	Social and Environmental Determinants of Health Equity Group, Chandra Jackson, Ph.D.
9:00 - 9:50	Women's Health Group, Donna Baird, Ph.D.
9:50 - 10:20	Closed 1:1 Session with Investigators, Drs. Jackson and Baird
10:20 - 11:30	Closed BSC Discussion, completion of individual review assignments
11:30 - 12:30	Closed Debriefing to NIEHS/NIMHD/DIR Leadership
12:30	Adjourn

BSC REVIEW OF THE GENOME INTEGRITY AND STRUCTURAL BIOLOGY LABORATORY

The NIEHS DIR Board of Scientific Counselors reviewed Genome Integrity and Structural Biology Laboratory, November 12-14, 2017.

Members of the Board of Scientific Counselors that Attended:

- Kenneth B. Adler, Ph.D. [BSC Chair], Professor, Dept. of Molecular Biomedical Sciences, North Carolina State University, College of Veterinary Medicine, Raleigh, NC
- Christopher I. Amos, Ph.D., Professor, Dept. of Community and Family Medicine, Geisel School of Medicine at Dartmouth, Hanover, NH
- Juan C. Celedón, M.D., Dr.P.H., Niels K. Jerne Professor of Pediatrics, Dept. of Pediatrics, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Pittsburgh, PA
- Carol A. Lange, Ph.D., Professor, Departments of Medicine and Pharmacology, University of Minnesota, Minneapolis, MN
- Donald P. McDonnell, Ph.D., Glaxo-Wellcome Professor and Chairman of Pharmacology and Cancer Biology, Duke University School of Medicine, Durham, NC
- Ivan Rusyn, M.D., Ph.D., Professor, Department of Veterinary Integrative Biosciences, Texas A&M University College of Veterinary Medicine & Biomedical Sciences, College Station, TX
- Daniel O. Stram, Ph.D., Professor, Division of Biostatistics and Genetic Epidemiology, Department of Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, CA
- Karen M. Vasquez, Ph.D., Professor, Division of Pharmacology and Toxicology, Dell Pediatric Research Institute, The University of Texas at Austin, Austin, TX
- Roland A. Owens, Ph.D., Ex-Officio BSC Member, Assistant Director, Office of Intramural Research, NIH, Bethesda, MD

Ad Hoc Reviewers that Attended:

- Jason Bielas, Ph.D., Associate Member, Public Health Sciences Division, Associate Member, Human Biology Division, Fred Hutchinson Cancer Research Center, Seattle, WA
- Prescott Deininger, Ph.D., Director, Tulane Cancer Center, The Joe W. and Dorothy Dorsett Brown Foundation Chair in Oncology, Professor of Epidemiology, Tulane Cancer Center, New Orleans, LA
- Sylvie Doublie, Ph.D., Professor of Microbiology and Molecular Genetics, University of Vermont, Burlington, VT
- AIba Guarne, Ph.D., Professor, McGill Biochemistry, Montreal, QC, Canada
- Dorit Hanein, Ph.D., Professor, Bioinformatics and Structural Program, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA

- Jeffrey J. Hayes, Ph.D., Chair, Department of Biochemistry and Biophysics, Shohei Koide Professor in Biochemistry and Biophysics, University of Rochester Medical Center, School of Medicine and Dentistry, Rochester, NY
- Wolf-Dietrich Heyer, Ph.D., Professor and Chair, Department of Microbiology and Molecular Genetics, Section of Microbiology, University of California, Davis, Davis, CA
- Deanna Kroetz, Ph.D., Professor, Department of Bioengineering and Therapeutic Sciences, School of Pharmacy, UCSF, San Francisco, CA
- Michael Lichten, Ph.D., Senior Investigator and Deputy Chief, Laboratory of Biochemistry and Molecular Biology, National Cancer Institute, NIH, Bethesda, MD
- Lawrence A. Loeb, M.D., Ph.D., Professor, Department of Pathology, Professor, Department of Biochemistry, University of Washington School of Medicine, Seattle, WA
- Susan Lovett, Ph.D., Abraham S. and Gertrude Burg Professor of Microbiology, Department of Biology, Rosenstiel Basic Medical Sciences, Brandeis University, Waltham, MA
- Georges Mer, Ph.D., Professor of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN
- Michael J. Miley, Ph.D., Co-director, UNC Center for Structural Biology, Director, UNC Macromolecular Crystallography, Protein Expression, and Antibody Core Facilities, Associate Professor, UNC Department of Pharmacology, Center for Structural Biology, University of North Carolina School of Medicine, Chapel Hill, NC
- Carlos T. Moraes, Ph.D., Lichtenstein Professor of Neurology, Professor of Cell Biology and Anatomy, University of Miami Miller School of Medicine, Miami, FL
- Nathan Nicely, Ph.D., Director, X-ray Crystallography Shared Resource, Duke Human Vaccine Institute, Duke University, Durham, NC
- Pengyu Ren, Ph.D., Associate Professor and William J. Murray Fellow in Engineering, Department of Biomedical Engineering, The University of Texas at Austin, Austin, TX
- Ralph D. Sanderson, Ph.D., Endowed Professor in Cancer Pathobiology, Department of Pathology, University of Alabama Birmingham, Birmingham, AL
- Keshav K. Singh, Ph.D., Director, Cancer Genetics Program, Joy and Bill Harbert Endowed Chair in Cancer Genetics, Professor, Departments of Genetics, Pathology, and Environmental Health, Department of Genetics, School of Medicine, University of Alabama Birmingham, Birmingham, AL
- Craig Vander Kooi, Ph.D., Associate Professor, Department of Molecular and Cellular Biochemistry, University of Kentucky College of Medicine, Lexington, KY
- Graham C. Walker, Ph.D., Howard Hughes Medical Institute (HHMI) Professor, American Cancer Society Professor, Department of Biology, Massachusetts Institute of Technology, Cambridge, MA
- David J. Weber, Ph.D., Director, The Center for Biomolecular Therapeutics, Professor, Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, MD
- Wei Yang, Ph.D., NIH Distinguished Investigator, Laboratory of Molecular Biology, National Institute of Diabetes, Digestive and Kidney Diseases, NIH, Bethesda, MD

Agenda

Sunday, November 12 – Doubletree Hotel
Closed Evening Session

7:00 - 8:00 p.m.	Welcome and Discussion of Past Board Reviews, Drs. Darryl Zeldin and Bill Copeland
8:00 – end	BSC Discussion of Review, Dr. Ken Adler and panel

Monday, November 13 - NIEHS Rodbell Conference Rooms 101 ABC
Morning Session

8:30 - 8:45 a.m.	Welcome, Dr. Linda Birnbaum
8:45 - 9:05	Overview, Genome Integrity and Structural Biology Laboratory, William Copeland, Ph.D.
9:05 - 10:00	Mitochondrial DNA Replication Group, William Copeland, Ph.D.
10:00 - 10:15	COFFEE BREAK
10:15 - 11:05	Structure Function Group, Lars Pedersen, Ph.D.
11:05 - 11:55	Mammalian Genome Group, Richard Woychik, Ph.D.
11:55 - 12:40	Closed 1:1 Sessions with Investigators, Drs. Bill Copeland, Lars Pedersen, and Richard Woychik
12:40 - 1:45	Closed Working Lunch, 101 ABC

Afternoon Session

1:45 - 2:40 p.m.	Nuclear Magnetic Resonance Group, Robert London, Ph.D.
2:40 - 3:30	DNA Replication Fidelity Group, Thomas Kunkel, Ph.D.
3:30 - 3:45	COFFEE BREAK
3:45 - 4:35	Mechanisms of Genome Dynamics Group, Dmitry Gordenin, Ph.D.
4:35 - 5:25	Closed 1:1 Sessions with Investigators, Drs. Robert London, Thomas Kunkel and Dmitry Gordenin
5:35	Return to Doubletree Hotel
6:15 – end	Closed BSC Discussion of Review, All BSC reviewers at hotel

Tuesday November 14 - NIEHS Rodbell Conference Rooms 101 ABC
Morning Session

8:30 - 9:20 a.m.	Structural Biology Group, Scott Williams, Ph.D.
9:20 - 10:10	Mechanisms of Mutation Group, Roel Schaaper, Ph.D.
10:10 - 10:25	COFFEE BREAK
10:25 - 11:15	DNA Repair and Nucleic Acid Enzymology Group, Samuel Wilson, M.D.
11:15 - 12:00	Closed 1:1 Sessions with Investigators, Drs. Scott Williams, Roel Schaaper, and Samuel Wilson
12:00 - 1:00	Closed Working Lunch, 101 ABC

Afternoon Session

1:00 - 2:15 p.m.	Poster Session – GISBL Fellows and Staff Scientists, Rodbell Lobby
2:15 - 3:00	Closed Session with Fellows and Staff Scientists, 101 ABC

2:15 - 3:30	Closed Review of Protein Expression Core Facility, Molecular Modeling Core Facility, X-Ray Crystallography Core Facility, and Molecular Microscopy Consortium, Drs. Robert Petrovich, Lalith Perera, Lars Pedersen, and Mario Borgnia
3:30 – 5:00	Closed 1:1 Sessions with Core Facility Leadership, BSC Discussion of Reviews, Drs. Robert Petrovich, Lalith Perera, Lars Pedersen and Mario Borgnia
5:00 - 6:30	Closed Debriefing to NIEHS/DIR Leadership, 101 ABC
6:30	Adjourn

NIEHS SCIENCE DAYS

The Fifteenth Annual NIEHS Science Days were held on November 2-3, 2017, at the Rall Building on the NIEHS Campus to celebrate the achievements of NIEHS scientists. The event was open to the public and more than 250 attendees from universities and research institutions in the Triangle Area attended. NIEHS Science Days consisted of a mini-symposium on the Developmental Origins of Health and Disease in which presentations were given by scientists in DIR and DNTP and a DERT grantee, a presentation by a former NIEHS trainee, presentations were also given by the winners of the new DIR Innovation Research Award, 8 oral presentations given by fellows, students, and technicians, 91 poster presentations and an Awards Ceremony. Judging for the awards was done by extramural scientists from universities and research organizations in the Triangle Area, Intramural Scientists and the NIEHS Trainees Assembly.

Mentor of the Year: Paul Foster, Ph.D., Toxicology Branch
Fellow of the Year: Natalie Saini, Ph.D., Genome Integrity and Structural Biology Laboratory
Best Poster Presentation by a Fellow or Technician:

1. Yufeng Qin, Ph.D., Epigenetics and Stem Cell Biology Laboratory, "An obesity-associated gut microbiome reprograms the intestinal epigenome and leads to altered colonic gene expression."
2. Jessica Wojtaszek, Ph.D., Genome Integrity and Structural Biology Laboratory, "Structural analysis of the 3′→5′ exonuclease Apn2 of *Saccharomyces cerevisiae*."
3. Daisy Lo, Ph.D., Signal Transduction Laboratory, "Structural Analysis Reveals the Features of Ribosome Assembly Factor WDR74 Important for Localization and Interaction with the AAA-ATPase NVL2."
4. Barbara Nicol, Ph.D., Reproductive and Developmental Biology Laboratory, "RUNX1 and FOXL2 play synergistic roles in maintaining the identity of fetal granulosa cells in mice."
5. Rajneesh Pathania, Ph.D., Epigenetics and Stem Cell Biology Laboratory, "Identification and Characterization of Metastatis-Initiating Cells in Triple Negative Breast Cancer."
6. Kathryn McClelland, Ph.D., Reproductive and Developmental Biology Laboratory, "Loss of COUP-TFII (NR2F2) Affects Fetal Testicular Development."
7. Xiaoqiu Wang, Ph.D., Reproductive and Developmental Biology Laboratory, Cistromic Analysis and Genome Editing Identify an Uterine Specific Enhancer Critical for Indian Hedgehog Expression."
8. Jian Liu, Ph.D., Reproductive and Developmental Biology Laboratory, "Lkb1 inactivation drives lung squamous cell carcinoma development governed by JNK1/2 pathway."
9. Douglas Ganini Da Silva, Ph.D., Immunity, Inflammation, and Disease Laboratory, "Switch of mitochondrial superoxide dismutase into a prooxidant peroxidase in manganese-deficient cells and mice."
10. Monica Pillon, Ph.D., Signal Transduction Laboratory, "Grc3 Programs the Essential Endoribonuclease Las1 for Specific RNA Cleavage."

Best Poster Presentation by a Post-Baccalaureate Student: Jeffrey Ramsey, Reproductive and Developmental Biology Laboratory, "Steroid receptor hormonal actions of Lavender and Tea Tree oil components."

Best Oral Presentation: Sreenivasa Ramaiahgari, Ph.D., Biomolecular Screening Branch, "High Throughput Transcriptomics (S1500+ gene set) on Differentiated and Undifferentiated Hepatocytes Identifies Deficiencies in Tissue Modeling and Molecular Mechanisms Potentially Associated with Compound-induced Liver Injury."

DIR PAPERS OF THE YEAR FOR 2017

Shaw ND, Brand H, Kupchinsky ZA, Bengani H, Plummer L, Jones TI, Erdin S, Williamson KA, Rainger J, Stortchevoi A, Samocha K, Currall BB, Dunican DS, Collins RL, Willer JR, Lek A, Lek M, Nassan M, Pereira S, Kammin T, Lucente D, Silva A, Seabra CM, Chiang C, An Y, Ansari M, Rainger JK, Joss S, Smith JC, Lippincott MF, Singh SS, Patel N, Jing JW, Law JR, Ferraro N, Verloes A, Rauch A, Steindl K, Zweier M, Scheer I, Sato D, Okamoto N, Jacobsen C, Tryggestad J, Chernausek S, Schimmenti LA, Brasseur B, Cesaretti C, García-Ortiz JE, Buitrago TP, Silva OP, Hoffman JD, Mühlbauer W, Ruprecht KW, Loeys BL, Shino M, Kaindl AM, Cho CH, Morton CC, Meehan RR, van Heyningen V, Liao EC, Balasubramanian R, Hall JE, Seminara SB, Macarthur D, Moore SA, Yoshiura KI, Gusella JF, Marsh JA, Graham JM Jr, Lin AE, Katsanis N, Jones PL, Crowley WF Jr, Davis EE, FitzPatrick DR, Talkowski ME. SMCHD1 mutations associated with a rare muscular dystrophy can also cause isolated arhinia and Bosma arhinia microphthalmia syndrome. *Nat. Genet.*, 49: 238-248, 2017.

Arhinia, or absence of the nose, is a rare malformation of unknown etiology that is often accompanied by ocular and reproductive defects. Sequencing of 40 people with arhinia revealed that 84% of probands harbor a missense mutation localized to a constrained region of SMCHD1 encompassing the ATPase domain. SMCHD1 mutations cause facioscapulohumeral muscular dystrophy type 2 (FSHD2) via a trans-acting loss-of-function epigenetic mechanism. We discovered shared mutations and comparable DNA hypomethylation patterning between these distinct disorders. CRISPR/Cas9-mediated alteration of smchd1 in zebrafish yielded arhinia-relevant phenotypes. Transcriptome and protein analyses in arhinia probands and controls showed no differences in SMCHD1 mRNA or protein abundance but revealed regulatory changes in genes and pathways associated with craniofacial patterning. Mutations in SMCHD1 thus contribute to distinct phenotypic spectra, from craniofacial malformation and reproductive disorders to muscular dystrophy, which we speculate to be consistent with oligogenic mechanisms resulting in pleiotropic outcomes.

O'Brien KM, Sandler DP, Taylor JA, Weinberg CR. Serum Vitamin D and Risk of Breast Cancer within Five Years. *Environ. Health Perspect.*, 125: 077004, 2017.

BACKGROUND: Vitamin D is an environmental and dietary agent with known anticarcinogenic effects, but protection against breast cancer has not been established.
OBJECTIVE: We evaluated the association between baseline serum 25-hydroxyvitamin D [25(OH)D] levels, supplemental vitamin D use, and breast cancer incidence over the subsequent 5 y of follow-up.
METHODS: From 2003-2009, the Sister Study enrolled 50,884 U.S. women 35-74 y old who had a sister with breast cancer but had never had breast cancer themselves. Using liquid chromatography-mass spectrometry, we measured 25(OH)D in serum samples from 1,611 women who later developed breast cancer and from 1,843 randomly selected cohort participants. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of developing breast cancer using Cox proportional hazards models.
RESULTS: We found that 25(OH)D levels were associated with a 21% lower breast cancer hazard (highest versus lowest quartile: adjusted; CI: 0.63, 0.98). Analysis of the first 5 y of follow-up for all 50,884 Sister Study participants showed that self-reported vitamin D

supplementation was associated with an 11% lower hazard [(CI: 0.81, 0.99)]. These associations were particularly strong among postmenopausal women [(CI: 0.57, 0.93) and (CI: 0.74, 0.93), respectively].
CONCLUSIONS: In this cohort of women with elevated risk, high serum 25(OH)D levels and regular vitamin D supplement use were associated with lower rates of incident, postmenopausal breast cancer over 5 y of follow-up. These results may help to establish clinical benchmarks for 25(OH)D levels; in addition, they support the hypothesis that vitamin D supplementation is useful in breast cancer prevention.

Pillon MC, Sobhany M, Borgnia MJ, Williams JG, Stanley RE. Grc3 programs the essential endoribonuclease Las1 for specific RNA cleavage. *Proc. Natl. Acad. Sci. U.S.A.*, 114: E5530-E5538, 2017.

Las1 is a recently discovered endoribonuclease that collaborates with Grc3-Rat1-Rai1 to process precursor ribosomal RNA (rRNA), yet its mechanism of action remains unknown. Disruption of the mammalian Las1 gene has been linked to congenital lethal motor neuron disease and X-linked intellectual disability disorders, thus highlighting the necessity to understand Las1 regulation and function. Here, we report that the essential Las1 endoribonuclease requires its binding partner, the polynucleotide kinase Grc3, for specific C2 cleavage. Our results establish that Grc3 drives Las1 endoribonuclease cleavage to its targeted C2 site both in vitro and in Saccharomyces cerevisiae. Moreover, we observed Las1-dependent activation of the Grc3 kinase activity exclusively toward single-stranded RNA. Together, Las1 and Grc3 assemble into a tetrameric complex that is required for competent rRNA processing. The tetrameric Grc3/Las1 cross talk draws unexpected parallels to endoribonucleases RNaseL and Ire1, and establishes Grc3/Las1 as a unique member of the RNaseL/Ire1 RNA splicing family. Together, our work provides mechanistic insight for the regulation of the Las1 endoribonuclease and identifies the tetrameric Grc3/Las1 complex as a unique example of a protein-guided programmable endoribonuclease.

Jamsen JA, Beard WA, Pedersen LC, Shock DD, Moon AF, Krahn JM, Bebenek K, Kunkel TA, Wilson SH. Time-lapse crystallography snapshots of a double-strand break repair polymerase in action. *Nat. Commun.*, 8: 253, 2017.

DNA polymerase (pol) μ is a DNA-dependent polymerase that incorporates nucleotides during gap-filling synthesis in the non-homologous end-joining pathway of double-strand break repair. Here we report time-lapse X-ray crystallography snapshots of catalytic events during gap-filling DNA synthesis by pol μ. Unique catalytic intermediates and active site conformational changes that underlie catalysis are uncovered, and a transient third (product) metal ion is observed in the product state. The product manganese coordinates phosphate oxygens of the inserted nucleotide and PPi. The product metal is not observed during DNA synthesis in the presence of magnesium. Kinetic analyses indicate that manganese increases the rate constant for deoxynucleoside 5'-triphosphate insertion compared to magnesium. The likely product stabilization role of the manganese product metal in pol μ is discussed. These observations provide insight on structural attributes of this X-family double-strand break repair polymerase that impact its biological function in genome maintenance. DNA polymerase (pol) μ functions in DNA double-strand break repair. Here the authors use time-

lapse X-ray crystallography to capture the states of pol μ during the conversion from pre-catalytic to product complex and observe a third transiently bound metal ion in the product state.

Zhao F, Franco HL, Rodriguez KF, Brown PR, Tsai MJ, Tsai SY, Yao HH. Elimination of the male reproductive tract in the female embryo is promoted by COUP-TFII in mice. *Science*, 357: 717-720, 2017.

The sexual differentiation paradigm contends that the female pattern of the reproductive system is established by default because the male reproductive tracts (Wolffian ducts) in the female degenerate owing to a lack of androgen. Here, we discovered that female mouse embryos lacking Coup-tfII (chicken ovalbumin upstream promoter transcription factor II) in the Wolffian duct mesenchyme became intersex-possessing both female and male reproductive tracts. Retention of Wolffian ducts was not caused by ectopic androgen production or action. Instead, enhanced phosphorylated extracellular signal-regulated kinase signaling in Wolffian duct epithelium was responsible for the retention of male structures in an androgen-independent manner. We thus suggest that elimination of Wolffian ducts in female embryos is actively promoted by COUP-TFII, which suppresses a mesenchyme-epithelium cross-talk responsible for Wolffian duct maintenance.

Wellman AS, Metukuri MR, Kazgan N, Xu X, Xu Q, Ren NSX, Czopik A, Shanahan MT, Kang A, Chen W, Azcarate-Peril MA, Gulati AS, Fargo DC, Guarente L, Li X. Intestinal Epithelial Sirtuin 1 Regulates Intestinal Inflammation During Aging in Mice by Altering the Intestinal Microbiota. *Gastroenterology*, 153: 772-786, 2017.

BACKGROUND & AIMS: Intestinal epithelial homeostasis is maintained by complex interactions among epithelial cells, commensal gut microorganisms, and immune cells. Disruption of this homeostasis is associated with disorders such as inflammatory bowel disease, but the mechanisms of this process are not clear. We investigated how Sirtuin 1 (SIRT1), a conserved mammalian NAD+-dependent protein deacetylase, senses environmental stress to alter intestinal integrity.
METHODS: We performed studies of mice with disruption of Sirt1 specifically in the intestinal epithelium (SIRT1 iKO, villin-Cre+, Sirt1flox/flox mice) and control mice (villin-Cre-, Sirt1flox/flox) on a C57BL/6 background. Acute colitis was induced in some mice by addition of 2.5% dextran sodium sulfate to drinking water for 5-9 consecutive days. Some mice were given antibiotics via their drinking water for 4 weeks to deplete their microbiota. Some mice were fed with a cholestyramine containing diet for 7 days to sequester their bile acids. Feces were collected and proportions of microbiota were analyzed by 16S rRNA amplicon sequencing and quantitative PCR. Intestines were collected from mice and gene expression profiles were compared by microarray and quantitative PCR analyses. We compared levels of specific mRNAs between colon tissues from age-matched patients with ulcerative colitis (n=10) vs without inflammatory bowel disease (n=8, controls).
RESULTS: Mice with intestinal deletion of SIRT1 (SIRT1 iKO) had abnormal activation of Paneth cells starting at the age of 5-8 months, with increased activation of NF-κB, stress pathways, and spontaneous inflammation at 22-24 months of age, compared with control mice. SIRT1 iKO mice also had altered fecal microbiota starting at 4-6 months of age

compared with control mice, in part due to altered bile acid metabolism. Moreover, SIRT1 iKO mice with defective gut microbiota developed more severe colitis than control mice. Intestinal tissues from patients with ulcerative colitis expressed significantly higher levels of SIRT1 mRNA than controls. Intestinal tissues from SIRT1 iKO mice given antibiotics, however, did not have signs of inflammation at 22-24 months of age, and did not develop more severe colitis than control mice at 4-6 months.
CONCLUSIONS: In analyses of intestinal tissues, colitis induction, and gut microbiota in mice with intestinal disruption of SIRT1, we found this protein to prevent intestinal inflammation by regulating the gut microbiota. SIRT1 might therefore be an important mediator of host-microbiome interactions. Agents designed to activate SIRT1 might be developed as treatments for inflammatory bowel diseases.

Whitehead GS, Thomas SY, Shalaby KH, Nakano K, Moran TP, Ward JM, Flake GP, Nakano H, Cook DN. TNF is required for TLR ligand-mediated but not protease-mediated allergic airway inflammation. *J. Clin. Invest.*, 127: 3313-3326, 2017.

Asthma is associated with exposure to a wide variety of allergens and adjuvants. The extent to which overlap exists between the cellular and molecular mechanisms triggered by these various agents is poorly understood, but it might explain the differential responsiveness of patients to specific therapies. In particular, it is unclear why some, but not all, patients benefit from blockade of TNF. Here, we characterized signaling pathways triggered by distinct types of adjuvants during allergic sensitization. Mice sensitized to an innocuous protein using TLR ligands or house dust extracts as adjuvants developed mixed eosinophilic and neutrophilic airway inflammation and airway hyperresponsiveness (AHR) following allergen challenge, whereas mice sensitized using proteases as adjuvants developed predominantly eosinophilic inflammation and AHR. TLR ligands, but not proteases, induced TNF during allergic sensitization. TNF signaled through airway epithelial cells to reprogram them and promote Th2, but not Th17, development in lymph nodes. TNF was also required during the allergen challenge phase for neutrophilic and eosinophilic inflammation. In contrast, TNF was dispensable for allergic airway disease in a protease-mediated model of asthma. These findings might help to explain why TNF blockade improves lung function in only some patients with asthma.

Schellenberg MJ, Lieberman JA, Herrero-Ruiz A, Butler LR, Williams JG, Muñoz-Cabello AM, Mueller GA, London RE, Cortés-Ledesma F, Williams RS. ZATT (ZNF451)-mediated resolution of topoisomerase 2 DNA-protein cross-links. *Science*, 357: 1412-1416, 2017.

Topoisomerase 2 (TOP2) DNA transactions are essential for life, and proceed via formation of the TOP2 cleavage complex (TOP2cc), a covalent enzyme-DNA reaction intermediate that is vulnerable to trapping by potent anticancer TOP2 drugs. How genotoxic TOP2 DNA-protein cross-links are resolved is unclear. We found that the SUMO ligase ZATT (ZNF451) is a multifunctional DNA repair factor that controls cellular responses to TOP2 damage. ZATT binding to TOP2cc facilitates a proteasome-independent tyrosyl-DNA phosphodiesterase 2 (TDP2) hydrolase activity on stalled TOP2cc. The ZATT SUMO ligase activity further promotes TDP2 interactions with SUMOylated TOP2, regulating efficient TDP2 recruitment through a "split-SIM" SUMO2 engagement platform. These findings

uncover a ZATT-TDP2-catalyzed and SUMO2-modulated pathway for direct resolution of TOP2cc.

Cinghu S, Yang P, Kosak JP, Conway AE, Kumar D, Oldfield AJ, Adelman K, Jothi R. Intragenic Enhancers Attenuate Host Gene Expression. *Mol. Cell*, 68: 104-117.e6, 2017.

Eukaryotic gene transcription is regulated at many steps, including RNA polymerase II (Pol II) recruitment, transcription initiation, promoter-proximal Pol II pause release, and transcription termination; however, mechanisms regulating transcription during productive elongation remain poorly understood. Enhancers, which activate gene transcription, themselves undergo Pol II-mediated transcription, but our understanding of enhancer transcription and enhancer RNAs (eRNAs) remains incomplete. Here we show that transcription at intragenic enhancers interferes with and attenuates host gene transcription during productive elongation. While the extent of attenuation correlates positively with nascent eRNA expression, the act of intragenic enhancer transcription alone, but not eRNAs, explains the attenuation. Through CRISPR/Cas9-mediated deletions, we demonstrate a physiological role for intragenic enhancer-mediated transcription attenuation in cell fate determination. We propose that intragenic enhancers not only enhance transcription of one or more genes from a distance but also fine-tune transcription of their host gene through transcription interference, facilitating differential utilization of the same regulatory element for disparate functions.

Steiner AZ, Pritchard D, Stanczyk FZ, Kesner JS, Meadows JW, Herring AH, Baird DD. Association Between Biomarkers of Ovarian Reserve and Infertility Among Older Women of Reproductive Age. *JAMA*, 318: 1367-1376, 2017.

Importance: Despite lack of evidence of their utility, biomarkers of ovarian reserve are being promoted as potential markers of reproductive potential.
Objective: To determine the associations between biomarkers of ovarian reserve and reproductive potential among women of late reproductive age.
Design, Setting, and Participants: Prospective time-to-pregnancy cohort study (2008 to date of last follow-up in March 2016) of women (N = 981) aged 30 to 44 years without a history of infertility who had been trying to conceive for 3 months or less, recruited from the community in the Raleigh-Durham, North Carolina, area.
Exposures: Early-follicular-phase serum level of antimüllerian hormone (AMH), follicle-stimulating hormone (FSH), and inhibin B and urinary level of FSH.
Main Outcomes and Measures: The primary outcomes were the cumulative probability of conception by 6 and 12 cycles of attempt and relative fecundability (probability of conception in a given menstrual cycle). Conception was defined as a positive pregnancy test result.
Results: A total of 750 women (mean age, 33.3 [SD, 3.2] years; 77% white; 36% overweight or obese) provided a blood and urine sample and were included in the analysis. After adjusting for age, body mass index, race, current smoking status, and recent hormonal contraceptive use, women with low AMH values (<0.7 ng/mL [n = 84]) did not have a significantly different predicted probability of conceiving by 6 cycles of attempt (65%; 95% CI, 50%-75%) compared with women (n = 579) with normal values (62%; 95% CI, 57%-

66%) or by 12 cycles of attempt (84% [95% CI, 70%-91%] vs 75% [95% CI, 70%-79%], respectively). Women with high serum FSH values (>10 mIU/mL [n = 83]) did not have a significantly different predicted probability of conceiving after 6 cycles of attempt (63%; 95% CI, 50%-73%) compared with women (n = 654) with normal values (62%; 95% CI, 57%-66%) or after 12 cycles of attempt (82% [95% CI, 70%-89%] vs 75% [95% CI, 70%-78%], respectively). Women with high urinary FSH values (>11.5 mIU/mg creatinine [n = 69]) did not have a significantly different predicted probability of conceiving after 6 cycles of attempt (61%; 95% CI, 46%-74%) compared with women (n = 660) with normal values (62%; 95% CI, 58%-66%) or after 12 cycles of attempt (70% [95% CI, 54%-80%] vs 76% [95% CI, 72%-80%], respectively). Inhibin B levels (n = 737) were not associated with the probability of conceiving in a given cycle (hazard ratio per 1-pg/mL increase, 0.999; 95% CI, 0.997-1.001).
Conclusions and Relevance: Among women aged 30 to 44 years without a history of infertility who had been trying to conceive for 3 months or less, biomarkers indicating diminished ovarian reserve compared with normal ovarian reserve were not associated with reduced fertility. These findings do not support the use of urinary or blood follicle-stimulating hormone tests or antimüllerian hormone levels to assess natural fertility for women with these characteristics.

Li P, Wang L, Bennett BD, Wang J, Li J, Qin Y, Takaku M, Wade PA, Wong J, Hu G. Rif1 promotes a repressive chromatin state to safeguard against endogenous retrovirus activation. *Nucleic Acids Res.*, 45: 12723-12738, 2017.

Transposable elements, including endogenous retroviruses (ERVs), constitute a large fraction of the mammalian genome. They are transcriptionally silenced during early development to protect genome integrity and aberrant transcription. However, the mechanisms that control their repression are not fully understood. To systematically study ERV repression, we carried out an RNAi screen in mouse embryonic stem cells (ESCs) and identified a list of novel regulators. Among them, Rif1 displays the strongest effect. Rif1 depletion by RNAi or gene deletion led to increased transcription and increased chromatin accessibility at ERV regions and their neighboring genes. This transcriptional de-repression becomes more severe when DNA methylation is lost. On the mechanistic level, Rif1 directly occupies ERVs and is required for repressive histone mark H3K9me3 and H3K27me3 assembly and DNA methylation. It interacts with histone methyltransferases and facilitates their recruitment to ERV regions. Importantly, Rif1 represses ERVs in human ESCs as well, and the evolutionally-conserved HEAT-like domain is essential for its function. Finally, Rif1 acts as a barrier during somatic cell reprogramming, and its depletion significantly enhances reprogramming efficiency. Together, our study uncovered many previously uncharacterized repressors of ERVs, and defined an essential role of Rif1 in the epigenetic defense against ERV activation.

Kang HS, Kumar D, Liao G, Lichti-Kaiser K, Gerrish K, Liao XH, Refetoff S, Jothi R, Jetten AM. GLIS3 is indispensable for TSH/TSHR-dependent thyroid hormone biosynthesis and follicular cell proliferation. *J. Clin. Invest.*, doi: 10.1172/JCI94417. [Epub ahead of print]

Deficiency in Krüppel-like zinc finger transcription factor GLI-similar 3 (GLIS3) in humans is associated with the development of congenital hypothyroidism. However, the functions of GLIS3 in the thyroid gland and the mechanism by which GLIS3 dysfunction causes hypothyroidism are unknown. In the current study, we demonstrate that GLIS3 acts downstream of thyroid-stimulating hormone (TSH) and TSH receptor (TSHR) and is indispensable for TSH/TSHR-mediated proliferation of thyroid follicular cells and biosynthesis of thyroid hormone. Using ChIP-Seq and promoter analysis, we demonstrate that GLIS3 is critical for the transcriptional activation of several genes required for thyroid hormone biosynthesis, including the iodide transporters Nis and Pds, both of which showed enhanced GLIS3 binding at their promoters. The repression of cell proliferation of GLIS3-deficient thyroid follicular cells was due to the inhibition of TSH-mediated activation of the mTOR complex 1/ribosomal protein S6 (mTORC1/RPS6) pathway as well as the reduced expression of several cell division-related genes regulated directly by GLIS3. Consequently, GLIS3 deficiency in a murine model prevented the development of goiter as well as the induction of inflammatory and fibrotic genes during chronic elevation of circulating TSH. Our study identifies GLIS3 as a key regulator of TSH/TSHR-mediated thyroid hormone biosynthesis and proliferation of thyroid follicular cells and uncovers a mechanism by which GLIS3 deficiency causes neonatal hypothyroidism and prevents goiter development.

AWARDS AND HONORS

Scientific Awards

Dr. Trevor Archer (Chief, Epigenetics and Stem Cell Biology Laboratory) received the 2017 NIH Equity, Diversity, and Inclusion Award of the Year.
Dr. John Cidlowski (Chief, Signal Transduction Laboratory) received an Honorary Ph.D. in Biotechnology from the University of Perugia School of Medicine in Italy.
Dr. Kelly Ferguson (Epidemiology Branch) was named one of the Collaborative on Health and the Environment's 20 Pioneers Under 40 in Environmental Public Health for 2017.
Dr. Kenneth Korach (Reproductive and Developmental Biology Laboratory) received the 2017 Senior Scientist Award from the Campion Foundation, Washington, DC.
Dr. Fredrick Miller (Clinical Research Branch) received the Achievement Award for Leadership in the Field at the Global Conference on Myositis, Potomac, MD, May 2017.
Dr. Lisa Rider (Clinical Research Branch) received the 2017 Lifetime Achievement in Research from the Cure Juvenile Myositis Foundation.
Dr. Natalie Saini (Genome Integrity and Structural Biology Laboratory) received the 2017 Environmental Mutagenesis and Genomics Society (EMGS) Young Scientist Award, June 24, 2017.
Dr. Darryl Zeldin (Scientific Director, (Immunity, Inflammation and Disease Laboratory) received the Eicosanoid Research Foundation's Outstanding Achievement Award in October 2017.

Named Professorships/Lectures

Dr. Francesco DeMayo (Chief, Reproductive and Developmental Biology Laboratory) was the Keynote Speaker at the Center for Reproductive Medicine's Annual Meeting at Baylor College of Medicine, Houston, TX.
Dr. Dmitry Gordenin (Genome Integrity and Structural Biology Laboratory) presented the Plenary Lecture at the 2017 Environmental Mutagenesis and Genomics Society (EMGS) annual meeting, Raleigh, NC, September 9-13, 2017,
Dr. Steven Kleeberger (Immunity, Inflammation and Disease Laboratory) presented the Plenary Lectures at RSV16. 10th International Respiratory Syncytial Virus Symposium. Patagonia, Argentina, September 2016 "Genetic determinants of RSV pathogenesis"; The 2017 Japan-NIH Joint Symposium on Advances in Biomedical Research and Disease. Tohoku University, Japan, February 2017 "Genetic susceptibility to acute lung injury: interaction between nuclear and mitochondrial genomes; and the First Annual Symposium on Experimental and Translational Research in Child Health. Porto Alegre, Brazil, November 2017 "Determinants of susceptibility to severe RSV disease; Genetic susceptibility to neonatal acute lung injury."
Dr. Thomas Kunkel (Genome Integrity and Structural Biology Laboratory) was the Keynote Speaker at the 3rd Oslo-London Cancer Network Meeting: Genome Stability and Instability in Cancer, Queen's College, Oxford, UK, 2017.
Dr. Stephanie London (Epidemiology Branch) was invited to give the plenary talk at the Airway Vista 2018 international conference in Seoul, Korea in March 2018.

Dr. Fredrick Miller (Clinical Research Branch) was the Keynote Speaker at the Annual Meeting of the Japanese Society for Hygiene, Miyazaki, Japan, Environmental Factors in Autoimmune Diseases - What We Know in 2017, March 2017.

Dr. Lisa Rider (Clinical Research Branch) presented the Suzanne Bowyer Memorial Lectureship, Riley Hospital for Children at Indiana University Health, September 13, 2017.

Dr. Samuel H. Wilson (Genome Integrity and Structural Biology Laboratory) presented the Keynote Lecturer at the 48th Annual Meeting of the Environmental Mutagenesis & Genomics Society, Raleigh, NC, September 2017.

Dr. Darryl Zeldin (Scientific Director, (Immunity, Inflammation and Disease Laboratory) gave the Keynote Lecture at the Inaugural Session, 15th International Conference on Bioactive Lipids in Cancer, Inflammation, and Related Diseases, Puereto Vallarta, Mexico: "Thromboxane Attenuates Th9 Cell Differentiation and Function During Allergic Lung Inflammation," October 2017. He also gave the Keynote Lecture, 13th Research Symposium on Human Natural Defense System, Seoul, South Korea: "Thromboxane Attenuates Th9 Cell Differentiation and Function in Allergic Lung Inflammation," October 2017.

Advisory/Editorial Boards

Dr. Trevor Archer (Chief, Epigenetics and Stem Cell Biology Laboratory) Co-Organized the 2017 ASCB-EMBO annual meeting.

Dr. Hye-Youn Cho (Immunity, Inflammation and Disease Laboratory) was appointed to the Editorial Board of the *Journal of Respiratory Medicine and Lung Disease*.

Dr. Stavros Garantziotis (Immunity, Inflammation and Disease Laboratory) was a guest Editor for a special issue on Hyaluronan, in the *Journal Matrix Biology*.

Dr. Zhenglin Gu (Neurobiology Laboratory) served on the Editorial Board *of Health Care: Current Reviews*.

Dr. Traci Hall (Epigenetics and Stem Cell Biology Laboratory) was named a contributing member of the *Structure: RNA Section of F1000*.

Dr. Fredrick Miller (Clinical Research Branch) served on the Editorial Board of *Annals of the Rheumatic Diseases*.

Dr. James Putney (Signal Transduction Laboratory) served on the Editorial Boards of the *Journal of Cell Science* and *Cell Calcium.* He also served on the Governing Board of the European Calcium Society.

Dr. Lisa Rider (Clinical Research Branch) was an Associate Editor for *Annals of Pediatric Rheumatology*, and served on the Editorial Boards of *Journal of Neuromuscular Diseases* and *International Journal of Rheumatology*.

Dr. Keith Shockley (Biostatistics and Computational Biology Branch) has been asked to serve on the Editorial Board of *Toxicologic Pathology*.

Dr. R. Scott Williams (Genome Integrity and Structural Biology Laboratory) was appointed to the Editorial Board of the *Journal of Biological Chemistry*.

Dr. Shanshan Zhao (Biostatistics and Computational Biology Branch) served as a scientific editor for the journal *PLOS One*.

TRAINING AND MENTORING

NIEHS Trainee Alumni

DIR has recently analyzed where recent postdoctoral trainees have gone upon completing their training, what they are doing and the level of the positions they took. Below is a summary of the analysis of 29 postdoctoral trainees that left NIEHS from January 1, 2017 through December 31, 2017.

What are they doing?

Additional postdoctoral training	**4**
Internship	**0**
Additional advanced degree	**0**
Primarily teaching	**2**
Primarily basic research	**6**
Primarily clinical research	**0**
Primarily clinical practice	**0**
Primarily applied research	**9**
Primarily patient care	**0**
Regulatory affairs	**1**
Science administration/project management	**1**
Intellectual property/ licensing and patenting	**0**
Consulting	**0**
Public policy	**0**
Science writing or communications	**0**
Grants management	**1**
Business development or Operations	**0**
Computation/informatics	**0**
Sales/marketing	**0**
Technical/customer support	**2**
Unknown or Undecided	**2**
Other	**0**
Unemployed	**1**
TOTAL	**29**

Where did they go?

Academic institution	14
Government agency	3
For-profit company	8
Non-profit organization	1
Private medical practice	0
Independent/self-employed	0
Unknown or Undecided	2
Unemployed	1
TOTAL	29

What is the level of their position?

Tenure track faculty	4
Non-tenure track faculty	3
Professional staff	13
Support staff	2
Management	0
Trainee	4
Unknown or Undecided	2
Unemployed	1
TOTAL	29