Division of Intramural Research

NAEHS Council Update

February 2023

DIR RECRUITMENTS

Chief of the Epigenetics and Stem Cell Biology Laboratory
NIEHS is searching for a highly qualified, established investigator for the position of Chief of the Epigenetics and Stem Cell Biology Laboratory (ESCBL) within the Division of Intramural Research (DIR). The position was vacated by Dr. Trevor Archer when he assumed his new leadership role as the Deputy Director of NIEHS. The ideal candidate will have an outstanding academic record of achievement, leadership capabilities, and broad interests in transcriptional regulation, epigenetics, chromatin architecture, RNA biology, and stem cell biology. In addition to directing his/her own independent research program, the Chief will be responsible for leading ESCBL and providing vision and directions as research in transcriptional regulation and environmental health science continue to evolve. Applicants should have a Ph.D., M.D., or equivalent doctoral degree and a strong interest and publication record in mammalian cell biology and signal transduction. Dr. Anton Jetten, Senior Investigator and Deputy Chief of the Immunity, Inflammation and Disease Laboratory serves as chair of the search committee launched June 2022. Four outstanding candidates were interviewed in December 2022 and January 2023 and an offer will be extended to the top candidate based on committee recommendations.

Medical Director of the Clinical Research Unit
NIEHS is inviting applications for a Senior Clinician in the Clinical Research Branch (CRB), Division of Intramural Research (DIR) at the NIEHS campus in Research Triangle Park, NC to serve as Medical Director of the Clinical Research Unit (CRU) and Director of Clinical Operations for the NIEHS Personalized Environment and Genes Study (PEGS), a large cohort of over 19,000 participants, initiated in 2002 to study interaction between genes, the environment and health. PEGS offers outstanding research opportunities to intramural scientists and extramural collaborators interested in personalized environmental medicine. While it is expected that the successful candidate will be able to collaborate broadly on projects utilizing the CRU and/or PEGS cohort, resources will also be made available for conducting self-initiated research projects. The successful candidate will require evidence of strong leadership skills and significant experience in patient-oriented research, defined as research that requires direct interaction with human subjects. The individual will have a track record of national presentations and publications in respected journals in their field. Research areas may include understanding the mechanisms of human disease, genotype-phenotype studies, therapeutic interventions, and/or clinical trials. Applicants should have an M.D. or equivalent doctoral degree and must possess a current, active, full and unrestricted license to practice medicine in the United States and be eligible to be credentialed for patient care by the NIH Clinical Center. Dr. Michael Fessler, Chief of the Immunity, Inflammation and Disease Laboratory serves as chair of the search committee which was launched on May 25, 2021. A pending offer was made to an outstanding candidate with expertise in maternal fetal health.

Chief of the Administrative and Research Services Branch
The search process has been initiated for an outstanding administrative leader to serve as Lead Administrative Officer and Chief of the Administrative and Research Services Branch (ARSB). ARSB performs program planning and resource management activities to support the intramural research programs and scientists at NIEHS. The position was vacated by J'Ingrid Mathis on July

17, 2022, when she assumed her new leadership role as the Associate Director for Management and Executive Officer at NIEHS. An advisory committee chaired by Dr. Jerrel Yakel, Chief of the Neurobiology Laboratory, DIR was formed to facilitate identification of a small pool of outstanding candidates to advance to interviews. Three outstanding candidates have been interviewed and an offer will be made to a top candidate in early 2023.

Tenure-Track Investigator in the Genome Integrity and Structural Biology Laboratory
NIEHS is recruiting a Tenure-Track Investigator in the area of genomic maintenance, DNA replication, DNA repair, and/or DNA recombination. The successful candidate is expected to lead an innovative, independent research program exploring the mechanisms of genome integrity, and how these processes are impacted in human disease in the context of environmental stressors. Applicants should have a Ph.D., M.D. and/or equivalent doctoral degree with at least 3 years of postdoctoral research experience and an outstanding publication record. The emphasis will be on identifying an exceptional scientist with an innovative and productive research program. Dr. Robin Stanley, Senior Investigator in the Signal Transduction Laboratory serves as chair of the search committee which launched December 2022.

Tenure-Track Investigator in the Immunity, Inflammation and Disease Laboratory
NIEHS is recruiting a Tenure-Track Investigator to study fundamental mechanisms by which immune and inflammatory responses are triggered and regulated in the lung and other organs and contribute to disease, with a particular focus on asthma, host defense/innate immunity, lung fibrosis, and cardiovascular disease. In addition to building upon current strengths, areas of special interest for future growth of IIDL include: (i) immunometabolism (programming of the immune response by changes in cellular metabolic pathways); (ii) mucosal immunity (lung, gut, other) including the heterogeneity, ontogeny, and/or function of immune, epithelial, and stromal tissue-resident cells; and (iii) systems biology of the immune response. However, we enthusiastically welcome applications from outstanding scientists in all fields of immunology. The successful candidate is expected to lead an innovative, independent research program exploring the mechanism of immune responses that enhances our understanding of 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. Anant Parekh, Senior Investigator and Chief of the Signal Transduction Laboratory will serve as chair of the search committee which will launch February 2023.

Recruitment of NIH Earl Stadtman Investigator Finalists
In addition to targeted recruitment, DIR is actively seeking outstanding scientists through the central NIH Stadtman recruitment mechanism. DIR Principal Investigators will serve on most of the 26 Stadtman subcommittees in 2022-23 representing a range of disciplines central to the NIEHS mission. Three outstanding Stadtman finalists have been selected for interviews February thru April 2023.

DIR STAFF UPDATES

Senior Investigator
Dr. Shyamal Peddada, Chief of the Biostatistics and Bioinformatics Branch of NICHD, has accepted an offer to join the Biostatistics and Computational Biology Branch (BCBB) as a Senior Investigator. His continuing research program aims to develop broadly applicable statistical methods motivated by applications in biomedical sciences aligned with the NIEHS mission, such as microbiome, genomics, toxicology and health effects of climate change. Dr. Peddada started at NIEHS in the December 7, 2022.

Deputy Chief of the Comparative Medicine Branch
Dr. Andrew Gorman has accepted an offer to join NIEHS as the Deputy Chief of the Comparative Medicine Branch (CMB). In this role, Dr. Gorman will be responsible for assisting with the management of an AAALAC International accredited animal care and use program and to support NIEHS animal research programs with a strong emphasis on rodent animal models. He will have supervisory responsibility of section heads within CMB and will serve on the NIEHS Animal Care and Use Committee (ACUC) as well as other committees. Dr. Gorman started at NIEHS on October 24, 2022.

Tenure-Track Investigator
Dr. Stavros Garantziotis, Medical Director of the NIEHS Clinical Research Unit and head of the Matrix Biology Group has accepted an offer to join the Immunity, Inflammation and Disease Laboratory as a Tenure-Track Investigator. Dr. Garantziotis will continue and expand his independent research program focused on extracellular matrix biology, innate immunity, lung inflammatory diseases, and airway remodeling triggered by the environment. He is expected to start as a Tenure-Track Investigator in early 2023.

BSC REVIEW OF THE SIGNAL TRANSDUCTION LABORATORY

The NIEHS DIR Board of Scientific Counselors reviewed the Signal Transduction Laboratory, Dr. Roel Schaaper and Dr. Guohong Cui, December 4-6, 2022

Members of the Board of Scientific Counselors:

- Anita H. Corbett, Ph.D., Samuel C. Dobbs Professor of Genetics, Cell and Developmental Biology, Emory University, Atlanta, GA
- Walter J. Chazin, Ph.D., Professor of Biochemistry and Chancellor's Chair in Medicine Department of Biochemistry and Chemistry, Vanderbilt University, Nashville, TN
- Sarah K. England, Ph. D., Professor, Department of Obstetrics and Gynecology at the Washington University School of Medicine, St. Louis, MO
- Katherine B. Ensor, Ph.D., Noah G. Harding Professor of Statistics and Director, Center for Computational and Economic Systems at the George R. Brown School of Engineering, Rice University, Houston, TX
- Serpil C. Erzurum, M.D., Chief Research and Academic Officer and Chair, Cleveland Clinic/Lerner Research Institute, Cleveland, OH
- Ji-Yong Julie Kim, Ph.D., Susy Y. Hung Professor of Obstetrics and Gynecology and Co-Director, Center for Reproductive Science, Northwestern University, Chicago, IL
- Frances M. Leslie, Ph.D., Professor Emerita, Department of Pharmaceutical Sciences, School of Pharmacy, University of California, Irvine, CA
- Jose A. Luchsinger, M.D., Professor of Medicine and Epidemiology and Vice-Chair for Clinical & Epidemiologic Research, Columbia University, New York, NY
- Heather B. Patisaul, Ph.D., BSC Chair, Associate Dean for Research and Professor, Department of Biological Sciences and Center for Human Health and the Environment, North Carolina State University, Raleigh, NC
- Roland A. Owens, Ph.D., Ex-Officio BSC Member, Office of Intramural Research, NIH, Bethesda, MD
- Jerry L. Workman, Ph.D., Investigator and Director Postdoctoral Affairs, Stowers Institute of Medical Research, Kansas City, MO

Ad Hoc Reviewers:

- Susan K. Buchanan, Ph.D., Deputy Scientific Director and Chief, Laboratory of Molecular Biology, National Institute of Diabetes and Digestive and Kidney Diseases, NIH, Bethesda, MD
- Eduardo N. Chini, M.D., Ph.D., Anesthesiology and Perioperative Medicine, Mayo Clinic, Jacksonville, FL
- Christopher P. Ford, Ph.D., Professor of Pharmacology and Physiology, University of Colorado, Denver, Aurora, CO
- Ryan C. Duggan, Ph.D., Oncology Discovery/Cytometry, AbbVie, North Chicago, IL

- Elise P. Gomez-Sanchez, D.V.M., Ph.D., Professor, Nonclinical Endocrinology, Neurobiology and Anatomical Sciences, The University of Mississippi Medical Center, Jackson, MS
- Stephen R. Hammes, M.D., Ph.D., Louis S. Wolk Distinguished Professor, Department of Medicine, University of Rochester Medical Center, Rochester, NY
- Patrick Hogan, Ph.D., Professor, Center for Autoimmunity and Inflammation, Center for Cancer Immunotherapy, La Jolla Institute of Immunology, La Jolla, CA
- Ph.D., Director of Neuroscience Microscopy Core, University of North Carolina, Chapel Hill, NC 27599
- Andrei Kuzminov, Ph.D., Professor of Microbiology, School of Molecular and Cellular Biology, University of Chicago at Urbana-Champaign, Urbana, IL
- Jiandie Lin, Ph.D., Bradley M. Patten Collegiate Professor in the Life Sciences and Professor of Cell and Developmental Biology, University of Michigan Life Sciences Institute, Ann Arbor MI
- Shmuel Muallem, Ph.D., Senior Investigator, National Institute of Dental and Craniofacial Research, NIH, Bethesda, MD
- Joaquin Ortega, Ph.D., Professor of Anatomy and Cell Biology, McGill University, Montreal, QC Canada
- Adam D. Pfefferle, Ph.D., Director, Translational Genomics Laboratory, University of North Carolina School of Medicine, Chapel Hill, NC
- Margaret E. Rice, Ph.D., Professor, Departments of Neurosurgery, Neuroscience, and Physiology, New York University Langone Health, New York, NY
- Mark Sutton, Ph.D., Professor, Department of Biochemistry, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY
- Judith R. Walters, Ph.D., Senior Investigator, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD

Agenda

Sunday, December 4 – Zoom meeting
Closed Evening Session

7:00 - 8:00 p.m.	Welcome and Discussion of Past Board Reviews, Drs. Rick Woychik, Darryl Zeldin, Anant Parekh, Jerry Yakel, Bill Copeland and Heather Patisaul
8:00 – end	BSC Discussion of Review, Dr. Heather Patisaul and panel

Monday, December 5 - NIEHS Rodbell Conference Rooms 101 ABC and Zoom Hybrid
Morning Session

9:00 - 9:15 a.m.	Welcome, Drs. Heather Patisaul and Richard Woychik
9:15 - 9:45	Overview, Signal Transduction Laboratory, Anant Parekh, D. Phil.
9:45 - 10:35	Calcium Signaling in Health and Disease Group, Anant Parekh, D. Phil.
10:35 - 10:50	Break
10:50 – 11:15	Inositol Signaling Group, Stephen Shears, Ph.D.
11:15 – 12:05	Molecular Endocrinology Group, John Cidlowski, Ph.D.

Afternoon Session

12:05 – 1:05 p.m.	Nucleolar Integrity Group, Robin Stanley, Ph.D.
1:55 – 2:45	Metabolism, Genes, and Environment Group, Xiaoling Li, Ph.D.
2:45 – 3:00	Break
3:00 – 4:00	Closed Sessions with Investigators, Drs. Anant Parekh John Cidlowski, Robin Stanley and Xiaoling Li
4:00 – 4:50	In Vivo Neurobiology Group, Neurobiology Laboratory, Guohong Cui, M.D., Ph.D.
4:50 – 5:05	Closed Session with Investigator, Dr. Guohong Cui

Tuesday December6 - NIEHS Rodbell Conference Rooms 101 ABC and Zoom Hybrid
Morning Session

8:45 – 9:35 a.m.	Mechanism of Mutation Group, Genome Integrity & Structural Biology Laboratory, Roel Schaaper, Ph.D.
9:35 – 9:50	Break
9:50 – 10:05	Closed Session with Investigator, Dr. Roel Schaaper
10:05 – 12:20	Poster Session - Fellows and Staff Scientists -Zoom Meeting
12:20 – 1:10	Closed Session with Fellows and Staff Scientists – Zoom Meeting
1:10 – 2:10	Closed Working Lunch
2:10 – 3:25	Closed Session with Core Directors – Carl Bortner, Kevin Gerrish and Charles Tucker
3:25 – 3:40	Break
3:40 – 4:50	Closed BSC Discussion and completion of individual review assignments
4:50 – 5:45	Closed Session and Debriefing to NIEHS/DIR Leadership
5:45 pm	Adjourn

MENTOR AND TRAINEE OF THE YEAR AWARDS

A special award ceremony was held on December 16, 2022 to announce the NIEHS Mentor and Fellow of the Year for 2022. These prestigious awards are conferred each year on recipients nominated and chosen by committees of NIEHS scientists, staff and trainees for outstanding achievement and dedication to mentoring

Mentor of the Year: Paul Wade, Ph.D., Senior Investigator and Acting Chief,
Epigenetics and Stem Cell Biology Laboratory, DIR

Fellow of the Year: Ciro Amato, Ph.D., IRTA Postdoctoral Fellow
Reproductive Developmental Biology Group
Reproductive and Developmental Biology Laboratory, DIR

DIR COMMITMENT TO DIVERSITY, EQUITY, INCLUSION AND ACCESSIBILITY

NIH Distinguished Scholars Program
Dondrae Coble, D.V.M., DACLAM, Senior Scientist and Chief of the Comparative Medicine Branch (CMB) was selected to participate in the NIH Distinguished Scholars Program (DSP). This program was recently expanded to include Senior Investigators/Scientists/Clinicians with a strong commitment to enhancing diversity. Dr. Coble joins four DIR Tenure-Track Investigators previously selected to the DSP: Drs. Joe Rodriguez (ESCBL), Benedict Anchang (BCBB), Jason Watts (ESCBL) and Carlos Guardia (RDBL).

DIR Diversity, Equity, Inclusion and Accessibility (DEIA) Working Group
A voluntary working group of more than 50 members including administrative, scientific and scientific support employees, trainees, and contractors representing all DIR Laboratories and Branches has been organized and is co-chaired by Dr. Raja Jothi, Senior Investigator in ESCBL and Dr. Steven Tuyishime, Assistant Scientific Director. This working group has been charged with proposing recommendations to the Scientific Director to improve and enhance diversity, equity, inclusion, and accessibility throughout the DIR workforce. Initial recommendations were provided to the Scientific Director and DIR Council in late 2022 and an action plan is currently being developed to prioritize and implement new policies and programs in 2023.

The working group is divided into four thematic subgroups each with two co-leaders:

Subgroup 1: Recruitment and Retention (Joe Rodriguez and Yesenia Rodriguez)
Subgroup 2: Career Development (Jackson Hoffman and Vince Guerrero)
Subgroup 3: Performance, Evaluation, and Recognition (Justin Kosak and Francesco DeMayo)
Subgroup 4: Outreach and Engagement (Anne Marie Jukic and Steve Tuyishime)

DIR PAPERS OF THE YEAR FOR 2022

Zhou ZX, Lujan SA, Burkholder AB, St Charles J, Dahl J, Farrell CE, Williams JS, Kunkel TA. How asymmetric DNA replication achieves symmetrical fidelity. *Nat Struct Mol Biol*. 2021 Dec;28(12):1020-1028. doi: 10.1038/s41594-021-00691-6. Epub 2021 Dec 9. PMID: 34887558; PMCID: PMC8815454.

> Accurate DNA replication of an undamaged template depends on polymerase selectivity for matched nucleotides, exonucleolytic proofreading of mismatches, and removal of remaining mismatches via DNA mismatch repair (MMR). DNA polymerases (Pols) δ and ε have 3'-5' exonucleases into which mismatches are partitioned for excision in cis (intrinsic proofreading). Here we provide strong evidence that Pol δ can extrinsically proofread mismatches made by itself and those made by Pol ε, independently of both Pol δ's polymerization activity and MMR. Extrinsic proofreading across the genome is remarkably efficient. We report, with unprecedented accuracy, in vivo contributions of nucleotide selectivity, proofreading, and MMR to the fidelity of DNA replication in Saccharomyces cerevisiae. We show that extrinsic proofreading by Pol δ improves and balances the fidelity of the two DNA strands. Together, we depict a comprehensive picture of how nucleotide selectivity, proofreading, and MMR cooperate to achieve high and symmetrical fidelity on the two strands.

Hoffman JA, Trotter KW, Day CR, Ward JM, Inoue K, Rodriguez J, Archer TK. Multimodal regulatory elements within a hormone-specific super enhancer control a heterogeneous transcriptional response. *Mol Cell*. 2022 Feb 17;82(4):803-815.e5. doi: 10.1016/j.molcel.2021.12.035. Epub 2022 Jan 24. PMID: 35077705; PMCID: PMC8897972.

> The hormone-stimulated glucocorticoid receptor (GR) modulates transcription by interacting with thousands of enhancers and GR binding sites (GBSs) throughout the genome. Here, we examined the effects of GR binding on enhancer dynamics and investigated the contributions of individual GBSs to the hormone response. Hormone treatment resulted in genome-wide reorganization of the enhancer landscape in breast cancer cells. Upstream of the DDIT4 oncogene, GR bound to four sites constituting a hormone-dependent super enhancer. Three GBSs were required as hormone-dependent enhancers that differentially promoted histone acetylation, transcription frequency, and burst size. Conversely, the fourth site suppressed transcription and hormone treatment alleviated this suppression. GR binding within the super enhancer promoted a loop-switching mechanism that allowed interaction of the DDIT4 TSS with the active GBSs. The unique functions of each GR binding site contribute to hormone-induced transcriptional heterogeneity and demonstrate the potential for targeted modulation of oncogene expression.

Diaz-Santana MV, O'Brien KM, Park YM, Sandler DP, Weinberg CR. Persistence of Risk for Type 2 Diabetes After Gestational Diabetes Mellitus. *Diabetes Care*. 2022 Apr 1;45(4):864-870. doi: 10.2337/dc21-1430. PMID: 35104325; PMCID: PMC9016728.

OBJECTIVE: Gestational diabetes mellitus complicates ~6% of pregnancies and strongly predicts subsequent type 2 diabetes. It has not been fully elucidated how risk depends on the number of affected pregnancies or how long the excess risk persists.
RESEARCH DESIGN AND METHODS: We assessed reproductive histories in relation to risk of type 2 diabetes using a nationwide cohort of 50,884 women. Among participants who initially did not have diabetes, 3,370 were diagnosed with diabetes during 10 years of follow-up. We used Cox proportional hazards models that allowed risk to depend on age, cumulative number of pregnancies with gestational diabetes mellitus, and time since the most recent affected pregnancy, adjusting for BMI, educational level, and race/ethnicity.
RESULTS: History of one or more pregnancies with gestational diabetes mellitus predicted elevated age-specific risk of type 2 diabetes, with a hazard ratio of 3.87 (95% CI 2.60-5.75) 6-15 years after an affected pregnancy. Risk increased steeply with multiple affected pregnancies. The age-specific associations attenuated over time after an affected pregnancy, with an estimated 24% reduction of the hazard ratio per decade. Risk remained elevated, however, for >35 years.
CONCLUSIONS: Gestational diabetes mellitus predicted markedly increased rates of type 2 diabetes. Relative risk increased substantially with each additional affected pregnancy. The estimated hazard ratio declined with time after a pregnancy with gestational diabetes mellitus but remained elevated for >35 years. Women recalling a history of gestational diabetes mellitus should be screened regularly for type 2 diabetes, even late in life.

Anchang B, Mendez-Giraldez R, Xu X, Archer TK, Chen Q, Hu G, Plevritis SK, Motsinger-Reif AA, Li JL. Visualization, benchmarking and characterization of nested single-cell heterogeneity as dynamic forest mixtures. *Brief Bioinform*. 2022 Mar 10;23(2):bbac017. doi: 10.1093/bib/bbac017. PMID: 35192692; PMCID: PMC8921621.

A major topic of debate in developmental biology centers on whether development is continuous, discontinuous, or a mixture of both. Pseudo-time trajectory models, optimal for visualizing cellular progression, model cell transitions as continuous state manifolds and do not explicitly model real-time, complex, heterogeneous systems and are challenging for benchmarking with temporal models. We present a data-driven framework that addresses these limitations with temporal single-cell data collected at discrete time points as inputs and a mixture of dependent minimum spanning trees (MSTs) as outputs, denoted as dynamic spanning forest mixtures (DSFMix). DSFMix uses decision-tree models to select genes that account for variations in multimodality, skewness and time. The genes are subsequently used to build the forest using tree agglomerative hierarchical clustering and dynamic branch cutting. We first motivate the use of forest-based algorithms compared to single-tree approaches for visualizing and characterizing developmental processes. We next benchmark DSFMix to pseudo-time and temporal approaches in terms of feature selection, time correlation, and network similarity. Finally, we demonstrate how DSFMix can be used to visualize, compare and characterize complex relationships during biological processes such as epithelial-mesenchymal transition, spermatogenesis, stem cell pluripotency, early transcriptional response from hormones and immune response to coronavirus disease. Our results indicate that the expression of genes during normal development exhibits a high proportion of non-uniformly distributed profiles that are mostly right-skewed and multimodal; the latter being a

characteristic of major steady states during development. Our study also identifies and validates gene signatures driving complex dynamic processes during somatic or germline differentiation.

Lee M, Huan T, McCartney DL, Chittoor G, de Vries M, Lahousse L, Nguyen JN, Brody JA, Castillo-Fernandez J, Terzikhan N, Qi C, Joehanes R, Min JL, Smilnak GJ, Shaw JR, Yang CX, Colicino E, Hoang TT, Bermingham ML, Xu H, Justice AE, Xu CJ, Rich SS, Cox SR, Vonk JM, Prokić I, Sotoodehnia N, Tsai PC, Schwartz JD, Leung JM, Sikdar S, Walker RM, Harris SE, van der Plaat DA, Van Den Berg DJ, Bartz TM, Spector TD, Vokonas PS, Marioni RE, Taylor AM, Liu Y, Barr RG, Lange LA, Baccarelli AA, Obeidat M, Fornage M, Wang T, Ward JM, Motsinger-Reif AA, Hemani G, Koppelman GH, Bell JT, Gharib SA, Brusselle G, Boezen HM, North KE, Levy D, Evans KL, Dupuis J, Breeze CE, Manichaikul A, London SJ. Pulmonary Function and Blood DNA Methylation: A Multiancestry Epigenome-Wide Association Meta-analysis. *Am J Respir Crit Care Med*. 2022 Aug 1;206(3):321-336. doi: 10.1164/rccm.202108-1907OC. PMID: 35536696; PMCID: PMC9890261.

RATIONALE: Methylation integrates factors present at birth and modifiable across the lifespan that can influence pulmonary function. Studies are limited in scope and replication. Objectives: To conduct large-scale epigenome-wide meta-analyses of blood DNA methylation and pulmonary function.
METHODS: Twelve cohorts analyzed associations of methylation at cytosine-phosphate-guanine probes (CpGs), using Illumina 450K or EPIC/850K arrays, with FEV1, FVC, and FEV1/FVC. We performed multiancestry epigenome-wide meta-analyses (total of 17,503 individuals; 14,761 European, 2,549 African, and 193 Hispanic/Latino ancestries) and interpreted results using integrative epigenomics.
MEASUREMENTS AND MAIN RESULTS: We identified 1,267 CpGs (1,042 genes) differentially methylated (false discovery rate, <0.025) in relation to FEV1, FVC, or FEV1/FVC, including 1,240 novel and 73 also related to chronic obstructive pulmonary disease (1,787 cases). We found 294 CpGs unique to European or African ancestry and 395 CpGs unique to never or ever smokers. The majority of significant CpGs correlated with nearby gene expression in blood. Findings were enriched in key regulatory elements for gene function, including accessible chromatin elements, in both blood and lung. Sixty-nine implicated genes are targets of investigational or approved drugs. One example novel gene highlighted by integrative epigenomic and druggable target analysis is TNFRSF4. Mendelian randomization and colocalization analyses suggest that epigenome-wide association study signals capture causal regulatory genomic loci.
CONCLUSIONS: We identified numerous novel loci differentially methylated in relation to pulmonary function; few were detected in large genome-wide association studies. Integrative analyses highlight functional relevance and potential therapeutic targets. This comprehensive discovery of potentially modifiable, novel lung function loci expands knowledge gained from genetic studies, providing insights into lung pathogenesis.

Frazier MN, Wilson IM, Krahn JM, Butay KJ, Dillard LB, Borgnia MJ, Stanley RE. Flipped over U: structural basis for dsRNA cleavage by the SARS-CoV-2 endoribonuclease. *Nucleic Acids Res*. 2022 Aug 12;50(14):8290-8301. doi: 10.1093/nar/gkac589. PMID: 35801916; PMCID: PMC9371922.

> Coronaviruses generate double-stranded (ds) RNA intermediates during viral replication that can activate host immune sensors. To evade activation of the host pattern recognition receptor MDA5, coronaviruses employ Nsp15, which is a uridine-specific endoribonuclease. Nsp15 is proposed to associate with the coronavirus replication-transcription complex within double-membrane vesicles to cleave these dsRNA intermediates. How Nsp15 recognizes and processes dsRNA is poorly understood because previous structural studies of Nsp15 have been limited to small single-stranded (ss) RNA substrates. Here we present cryo-EM structures of SARS-CoV-2 Nsp15 bound to a 52nt dsRNA. We observed that the Nsp15 hexamer forms a platform for engaging dsRNA across multiple protomers. The structures, along with site-directed mutagenesis and RNA cleavage assays revealed critical insight into dsRNA recognition and processing. To process dsRNA Nsp15 utilizes a base-flipping mechanism to properly orient the uridine within the active site for cleavage. Our findings show that Nsp15 is a distinctive endoribonuclease that can cleave both ss- and dsRNA effectively.

Welch BM, Keil AP, Buckley JP, Calafat AM, Christenbury KE, Engel SM, O'Brien KM, Rosen EM, James-Todd T, Zota AR, Ferguson KK; Pooled Phthalate Exposure and Preterm Birth Study Group; Alshawabkeh AN, Cordero JF, Meeker JD, Barrett ES, Bush NR, Nguyen RHN, Sathyanarayana S, Swan SH, Cantonwine DE, McElrath TF, Aalborg J, Dabelea D, Starling AP, Hauser R, Messerlian C, Zhang Y, Bradman A, Eskenazi B, Harley KG, Holland N, Bloom MS, Newman RB, Wenzel AG, Braun JM, Lanphear BP, Yolton K, Factor-Litvak P, Herbstman JB, Rauh VA, Drobnis EZ, Sparks AE, Redmon JB, Wang C, Binder AM, Michels KB, Baird DD, Jukic AMZ, Weinberg CR, Wilcox AJ, Rich DQ, Weinberger B, Padmanabhan V, Watkins DJ, Hertz-Picciotto I, Schmidt RJ. Associations Between Prenatal Urinary Biomarkers of Phthalate Exposure and Preterm Birth: A Pooled Study of 16 US Cohorts. *JAMA Pediatr*. 2022 Sep 1;176(9):895-905. doi: 10.1001/jamapediatrics.2022.2252. PMID: 35816333; PMCID: PMC9274448.

> IMPORTANCE: Phthalate exposure is widespread among pregnant women and may be a risk factor for preterm birth.
> OBJECTIVE: To investigate the prospective association between urinary biomarkers of phthalates in pregnancy and preterm birth among individuals living in the US.
> DESIGN, SETTING, AND PARTICIPANTS: Individual-level data were pooled from 16 preconception and pregnancy studies conducted in the US. Pregnant individuals who delivered between 1983 and 2018 and provided 1 or more urine samples during pregnancy were included.
> EXPOSURES: Urinary phthalate metabolites were quantified as biomarkers of phthalate exposure. Concentrations of 11 phthalate metabolites were standardized for urine dilution and mean repeated measurements across pregnancy were calculated.
> MAIN OUTCOMES AND MEASURES: Logistic regression models were used to examine the association between each phthalate metabolite with the odds of preterm birth, defined as less than 37 weeks of gestation at delivery (n = 539). Models pooled data using fixed effects and adjusted for maternal age, race and ethnicity, education, and prepregnancy body mass

index. The association between the overall mixture of phthalate metabolites and preterm birth was also examined with logistic regression. G-computation, which requires certain assumptions to be considered causal, was used to estimate the association with hypothetical interventions to reduce the mixture concentrations on preterm birth.
RESULTS: The final analytic sample included 6045 participants (mean [SD] age, 29.1 [6.1] years). Overall, 802 individuals (13.3%) were Black, 2323 (38.4%) were Hispanic/Latina, 2576 (42.6%) were White, and 328 (5.4%) had other race and ethnicity (including American Indian/Alaskan Native, Native Hawaiian, >1 racial identity, or reported as other). Most phthalate metabolites were detected in more than 96% of participants. Higher odds of preterm birth, ranging from 12% to 16%, were observed in association with an interquartile range increase in urinary concentrations of mono-n-butyl phthalate (odds ratio [OR], 1.12 [95% CI, 0.98-1.27]), mono-isobutyl phthalate (OR, 1.16 [95% CI, 1.00-1.34]), mono(2-ethyl-5-carboxypentyl) phthalate (OR, 1.16 [95% CI, 1.00-1.34]), and mono(3-carboxypropyl) phthalate (OR, 1.14 [95% CI, 1.01-1.29]). Among approximately 90 preterm births per 1000 live births in this study population, hypothetical interventions to reduce the mixture of phthalate metabolite levels by 10%, 30%, and 50% were estimated to prevent 1.8 (95% CI, 0.5-3.1), 5.9 (95% CI, 1.7-9.9), and 11.1 (95% CI, 3.6-18.3) preterm births, respectively.
CONCLUSIONS AND RELEVANCE: Results from this large US study population suggest that phthalate exposure during pregnancy may be a preventable risk factor for preterm delivery.

Rodriguez KF, Brown PR, Amato CM, Nicol B, Liu CF, Xu X, Yao HH. Somatic cell fate maintenance in mouse fetal testes via autocrine/paracrine action of AMH and activin B. *Nat Commun*. 2022 Jul 15;13(1):4130. doi: 10.1038/s41467-022-31486-y. PMID: 35840551; PMCID: PMC9287316.

Fate determination and maintenance of fetal testes in most mammals occur cell autonomously as a result of the action of key transcription factors in Sertoli cells. However, the cases of freemartin, where an XX twin develops testis structures under the influence of an XY twin, imply that hormonal factor(s) from the XY embryo contribute to sex reversal of the XX twin. Here we show that in mouse XY embryos, Sertoli cell-derived anti-Mullerian hormone (AMH) and activin B together maintain Sertoli cell identity. Sertoli cells in the gonadal poles of XY embryos lacking both AMH and activin B transdifferentiate into their female counterpart granulosa cells, leading to ovotestis formation. The ovotestes remain to adulthood and produce both sperm and oocytes, although there are few of the former and the latter fail to mature. Finally, the ability of XY mice to masculinize ovaries is lost in the absence of these two factors. These results provide insight into fate maintenance of fetal testes through the action of putative freemartin factors.

Sciolino NR, Hsiang M, Mazzone CM, Wilson LR, Plummer NW, Amin J, Smith KG, McGee CA, Fry SA, Yang CX, Powell JM, Bruchas MR, Kravitz AV, Cushman JD, Krashes MJ, Cui G, Jensen P. Natural locus coeruleus dynamics during feeding. *Sci Adv*. 2022 Aug 19;8(33):eabn9134. doi: 10.1126/sciadv.abn9134. Epub 2022 Aug 19. PMID: 35984878; PMCID: PMC9390985.

Recent data demonstrate that noradrenergic neurons of the locus coeruleus (LC-NE) are required for fear-induced suppression of feeding, but the role of endogenous LC-NE activity in natural, homeostatic feeding remains unclear. Here, we found that LC-NE activity was suppressed during food consumption, and the magnitude of this neural response was attenuated as mice consumed more pellets throughout the session, suggesting that LC responses to food are modulated by satiety state. Visual-evoked LC-NE activity was also attenuated in sated mice, suggesting that satiety state modulates LC-NE encoding of multiple behavioral states. We also found that food intake could be attenuated by brief or longer durations of LC-NE activation. Last, we found that activation of the LC to the lateral hypothalamus pathway suppresses feeding and enhances avoidance and anxiety-like responding. Our findings suggest that LC-NE neurons modulate feeding by integrating both external cues (e.g., anxiogenic environmental cues) and internal drives (e.g., satiety).

Riccio AA, Bouvette J, Perera L, Longley MJ, Krahn JM, Williams JG, Dutcher R, Borgnia MJ, Copeland WC. Structural insight and characterization of human Twinkle helicase in mitochondrial disease. *Proc Natl Acad Sci U S A*. 2022 Aug 9;119(32):e2207459119. doi: 10.1073/pnas.2207459119. Epub 2022 Aug 1. PMID: 35914129; PMCID: PMC9371709.

Twinkle is the mammalian helicase vital for replication and integrity of mitochondrial DNA. Over 90 Twinkle helicase disease variants have been linked to progressive external ophthalmoplegia and ataxia neuropathies among other mitochondrial diseases. Despite the biological and clinical importance, Twinkle represents the only remaining component of the human minimal mitochondrial replisome that has yet to be structurally characterized. Here, we present 3-dimensional structures of human Twinkle W315L. Employing cryo-electron microscopy (cryo-EM), we characterize the oligomeric assemblies of human full-length Twinkle W315L, define its multimeric interface, and map clinical variants associated with Twinkle in inherited mitochondrial disease. Cryo-EM, crosslinking-mass spectrometry, and molecular dynamics simulations provide insight into the dynamic movement and molecular consequences of the W315L clinical variant. Collectively, this ensemble of structures outlines a framework for studying Twinkle function in mitochondrial DNA replication and associated disease states.

Chang CJ, O'Brien KM, Keil AP, Gaston SA, Jackson CL, Sandler DP, White AJ. Use of Straighteners and Other Hair Products and Incident Uterine Cancer. *J Natl Cancer Inst*. 2022 Dec 8;114(12):1636-1645. doi: 10.1093/jnci/djac165. PMID: 36245087.

BACKGROUND: Hair products may contain hazardous chemicals with endocrine-disrupting and carcinogenic properties. Previous studies have found hair product use to be associated with a higher risk of hormone-sensitive cancers including breast and ovarian cancer; however, to our knowledge, no previous study has investigated the relationship with uterine cancer.
METHODS: We examined associations between hair product use and incident uterine cancer among 33 947 Sister Study participants aged 35-74 years who had a uterus at enrollment (2003-2009). In baseline questionnaires, participants in this large, racially and ethnically diverse prospective cohort self-reported their use of hair products in the prior 12 months, including

hair dyes; straighteners, relaxers, or pressing products; and permanents or body waves. We estimated adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) to quantify associations between hair product use and uterine cancer using Cox proportional hazard models. All statistical tests were 2-sided.
RESULTS: Over an average of 10.9 years of follow-up, 378 uterine cancer cases were identified. Ever vs never use of straightening products in the previous 12 months was associated with higher incident uterine cancer rates (HR = 1.80, 95% CI = 1.12 to 2.88). The association was stronger when comparing frequent use (>4 times in the past 12 months) vs never use (HR = 2.55, 95% CI = 1.46 to 4.45; Ptrend = .002). Use of other hair products, including dyes and permanents or body waves, was not associated with incident uterine cancer.
CONCLUSION: These findings are the first epidemiologic evidence of association between use of straightening products and uterine cancer. More research is warranted to replicate our findings in other settings and to identify specific chemicals driving this observed association.

Akhtari FS, Lloyd D, Burkholder A, Tong X, House JS, Lee EY, Buse J, Schurman SH, Fargo DC, Schmitt CP, Hall J, Motsinger-Reif AA. Questionnaire-Based Polyexposure Assessment Outperforms Polygenic Scores for Classification of Type 2 Diabetes in a Multiancestry Cohort. *Diabetes Care*. 2022 Nov 16:dc220295. doi: 10.2337/dc22-0295. Epub ahead of print. PMID: 36383734.

OBJECTIVE: Environmental exposures may have greater predictive power for type 2 diabetes than polygenic scores (PGS). Studies examining environmental risk factors, however, have included only individuals with European ancestry, limiting the applicability of results. We conducted an exposome-wide association study in the multiancestry Personalized Environment and Genes Study to assess the effects of environmental factors on type 2 diabetes.
RESEARCH DESIGN AND METHODS: Using logistic regression for single-exposure analysis, we identified exposures associated with type 2 diabetes, adjusting for age, BMI, household income, and self-reported sex and race. To compare cumulative genetic and environmental effects, we computed an overall clinical score (OCS) as a weighted sum of BMI and prediabetes, hypertension, and high cholesterol status and a polyexposure score (PXS) as a weighted sum of 13 environmental variables. Using UK Biobank data, we developed a multiancestry PGS and calculated it for participants.
RESULTS: We found 76 significant associations with type 2 diabetes, including novel associations of asbestos and coal dust exposure. OCS, PXS, and PGS were significantly associated with type 2 diabetes. PXS had moderate power to determine associations, with larger effect size and greater power and reclassification improvement than PGS. For all scores, the results differed by race.
CONCLUSIONS: Our findings in a multiancestry cohort elucidate how type 2 diabetes odds can be attributed to clinical, genetic, and environmental factors and emphasize the need for exposome data in disease-risk association studies. Race-based differences in predictive scores highlight the need for genetic and exposome-wide studies in diverse populations.

FY2022 AWARDS AND HONORS

Scientific Awards

Dr. Dondrae Coble (Chief, Comparative Medicine Branch) and Dr. Jesse Cushman (Neurobiology Laboratory) received the NIH Director's Challenge Innovation Award for "Machine vision-enabled behavioral tracking for cross-species extrapolation".

Dr. Francesco DeMayo (Chief, Reproductive and Developmental Biology Laboratory) was selected to receive the Distinguished Scientist Award for 2022 from the Society for Reproductive Investigation (SRI).

Dr. Janet Hall (Clinical Director and Chief of the Clinical Research Branch) was elected to Elected to the American Clinical and Climatological Association.

Dr. Traci Hall (Epigenetics and Stem Cell Biology Laboratory) received the RNA Society of North Carolina Stewardship Award, which recognizes "outstanding service, mentorship, participation, and scientific contributions to the field of RNA Science.

Dr. Chandra Jackson (Epidemiology Branch) received the Diversity, Equity & Inclusion Leadership Award from the Associated Professional Sleep Societies.

Dr. Frederick Miller (Clinical Research Branch) received the inaugural Scientific Hero Award from The Myositis Association

Dr. Geoffrey Mueller (Genome Integrity and Structural Biology Laboratory) received the John W. Yunginger, M.D., Memorial Lectureship Award from the American Academy of Allergy Asthma and Immunology.

Dr. Anant Parekh (Chief, Signal Transduction Laboratory) received the Annual Review Prize from The Physiological Society in recognition of his transformative research that has wide interest and impact.

Dr. Lisa Rider (Clinical Research Branch) received an Award of Distinction for Excellence in Investigative Mentoring from the American College of Rheumatology

Dr. Darryl Zeldin (Scientific Director and Immunity, Inflammation and Disease Laboratory) received two NIH Director's Awards for extraordinary initiative in the implementation and administration of the NIH COVID Vaccine Clinics at Multiple Geographical Locations and for the dynamic and visionary oversight of a multi-million dollar shared scientific/administrative resource across the NIH Intramural Research Program that directly supports the NIH mission.

Named Professorships/Lectures

Dr. Chandra Jackson (Epidemiology Branch) was invited as the Keynote Speaker at the 2023 at the World Sleep Society Meeting in Brazil.

Dr. Janet Hall (Clinical Director and Chief of the Clinical Research Branch) presented the Keynote address at the International Menopause Society meeting in Lisbon, Portugal.

Dr. Thomas Kunkel (Genome Integrity and Structural Biology Laboratory) gave the Keynote address at the 6th Annual International DNA Polymerase Meeting in Stockholm, Sweden

Dr. Geoffrey Mueller (Genome Integrity and Structural Biology Laboratory) was selected to present the 2022 John W. Yunginger Memorial Lectureship at the American Academy of Allergy, Asthma and Immunology (AAAAI) Annual Meeting.

Dr. Skand Shekhar (Clinical Research Branch) presented the Dr. Uma Shankdhar Memorial Lecture of the Uttar Pradesh Diabetes Association, India.
Dr. Stephen Shears (Signal Transduction Laboratory) presented the Keynote Address at the 2022 International Inositol Phosphate Meeting.
Dr. Allen Wilcox (Epidemiology Branch) presented the Keynote address at the Annual meeting of the Danish Epidemiology Society.
Dr. Carmen Williams (Reproductive and Developmental Biology Laboratory) was invited to present the inaugural Stuart Moss Memorial Lecture at the University of Pennsylvania.

Advisory/Editorial Boards

Dr. Trevor Archer (NIH Distinguished Investigator and Chief, Epigenetics and Stem Cell Biology Laboratory) served on the Board of Reviewing Editors of *Science*.
Dr. Dondrae Coble (Chief, Comparative Medicine Branch) was elected to the Board of Directors for the *American*, the *College of Laboratory Animal Medicine* (ACLAM), thee *North Carolina Academy of Laboratory Animal Medicine* (NCALAM) and the *North Carolina Association of Biomedical Research* (NCABR). He also served on the NCBR Executive Council.
Dr. Donald Cook (Immunity, Inflammation and Disease Laboratory) served the editorial boards of the *American Journal of Respiratory Cell and Molecular Biology* and *Frontiers in Chemoattractants.*
Dr. William Copeland (Chief, Genome Integrity and Structural Biology Laboratory) served on the Mitochondrial Disease Gene Curation Expert Panel for the Children's Hospital of Philadelphia. He also served as Chair of the Genetics subgroup for the NINDS Mitochondrial Common Disease Elements Group.
Dr. Francesco DeMayo (Chief, Reproductive and Developmental Biology Laboratory) served as Past President and Board Member of Society for the Study of Reproduction.
Dr. Paul Doetsch (Deputy Scientific Director and Genome Integrity and Structural Biology Laboratory) served on the Department of Defense Programmatic Panel (Grants Council) for Cancer Research Program. He also served as an Academic Editor for *BioMed Research International, Biochemistry Research International* and on the editorial boards *Nucleic Acids Research* and *DNA Repair*.
Dr. Serena Dudek (Neurobiology Laboratory) was appointed to the Editorial Board of the *Journal of Neuroscience.* She was also elected to the Molecular and Cellular Cognition Society Council
Dr. Matthew Edin (Immunity, Inflammation and Disease Laboratory) served as Associate Editor of *Prostaglandins and Other Lipid Mediators*
Dr. Kelly Ferguson (Epidemiology Branch) served on the Editorial Board of *Environmental Research* and was invited to serve as Associate Editor starting in July 2023.
Dr. Michael Fessler (Chief, Immunity, Inflammation and Disease Laboratory) served as an Associate Editor for the *American Journal of Respiratory Cell and Molecular Biology.* He also served on the Scientific Grant Review Committee for the American Thoracic Society
Dr. Stavros Garantziotis (Immunity, Inflammation and Disease Laboratory) served on the Editorial Board of *Matrix Biology*, *American Journal of Respiratory Cell and Molecular*

Biology and the *American Journal of Physiology – Lung Cellular and Molecular Physiology*. He served as an Associate Editor for *Lung.*

Dr. Dmitry Gordenin (Genome Integrity and Structural Biology Laboratory) served as Associate Editor for *PLoS Genetics* and on the Editorial Board of *Mutation Research, Fundamental and Molecular Mechanisms of Mutagenesis*.

Dr. Chandra Jackson (Epidemiology Branch) was elected to the Board of Directors of the Sleep Research Society. She also served on the Editorial Board of *Sleep Health: Journal of the National Sleep Foundation*

Dr. Patricia Jensen (Neurobiology Laboratory) served as a member of the External Advisory Committee for the Metabolic Basis of Disease Center for the Pennington Biomedical Research Center. She is also served on the Editorial Board of *Brain Research.*

Dr. Anton Jetten (Immunity, Inflammation and Disease Laboratory) was appointed to the Editorial Board of *Frontiers in Endocrinology*. He also served on the Editorial Boards for *Nuclear Receptor Research*, *Stem Cell Investigation* and *Cells*

Dr. Anne Marie Jukic (Epidemiology Branch) served on the Editorial Board of *Environmental Health Perspectives.*

Dr. Alison Motsinger-Reif (Chief, Biostatistics and Computational Biology Branch) served as a Statistical Associate Editor for *Exposome* and on the Statistical Board of Reviewing Editors (sBORE) for *Science*.

Dr. Geoffrey Mueller (Genome Integrity and Structural Biology Laboratory) served as a review editor for *Frontiers in Allergy*. He also served on the World Health Organization / International Union of Immunological Societies Allergen Nomenclature Subcommittee.

Dr. Anant Parekh (Chief, Signal Transduction Laboratory) served as Executive Editor of *Function* and served on the Editorial Board of *Cells*.

Dr. Lalith Perera (Genome Integrity and Structural Biology Laboratory) served on the Editorial Board of *International Journal of Molecular Sciences* and as an Associate Editor of *Frontiers in Chemistry*.

Dr. Lisa Rider (Clinical Research Branch) served as Associate Editor for *Arthritis & Rheumatology*, and *Frontiers in Immunology* (Autoimmune and Autoinflammatory Disorders Section and the Autoimmune Disorders Section). She also served on the Editorial Boards of *Clinical Experimental Rheumatology* and the *Journal of Neuromuscular Diseases*. Dr. Rider also served as Chair of the Cure JM Foundation Medical Advisory Committee and on the Stanley Manne Children's Research Institute/ Ann & Robert H. Lurie Children's Hospital of Chicago Cure Juvenile Myositis Center of Excellence Biorepository and Registry Review Committee, the American College of Rheumatology Annual Meeting Abstract Selection Committee and the Foundation of NIH Biomarkers Consortium Inflammation and Immunity Steering Committee

Dr. Dale Sandler (Chief, Epidemiology Branch) served on the Scientific Advisory Board of the U.K. Biobank and was elected to the Steering Committee for the Cancer Cohort Consortium

Dr. Natalie Shaw (Clinical Research Branch) served on the Editorial Board for *Pediatric Endocrinology*, a section within *Frontiers in Endocrinology* and *Frontiers in Pediatrics*.

Dr. Skand Shekhar (Clinical Research Branch) served as a Member of the Endocrine Society Special Programs Committee

Dr. Keith Shockley (Biostatistics and Computational Biology Branch) served on the editorial boards of *Toxicologic Pathology*, *Frontiers in Toxicogenomics*, *Frontiers in*

Computational Toxicology and Informatics. He also appointed as Associate Editor for *Toxigenomics*.

Dr. Carmen Williams (Reproductive and Developmental Biology Laboratory) was appointed as Associate Editor of *Biology of Reproduction* served as Academic Editor for *PLoS Biology*.

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

Dr. Humphrey Yao (Reproductive and Developmental Biology Laboratory) served as the Director for the Society for the Study of Reproduction (SSR) on the Editorial Board for *Sexual Development* and on the Board of Reviewing Editors for *Biology of Reproduction.* Dr. Yao was also selected as a regular member of the Cellular, Molecular and Integrative Reproduction Study Session for the NIH. He also served on the Reviewing board for the Angence Nationale de la Recherche, France and as Co-Chair for the 9th International Symposium on Vertebrate Sex Determination

Dr. Darryl Zeldin (Scientific Director and Immunity, Inflammation and Disease Laboratory) served as an Associate Editor for *Pharmacology and Therapeutics* and on the Editorial, Reviewer Board or Guest Editor of *Journal of Allergy and Clinical Immunology, Journal of Biological Chemistry*, the *American Journal of Physiology: Lung Cellular and Molecular Biology*, *Prostaglandins and Other Lipid Mediators*, *Open Environmental Research Journal, Molecular and Cellular Pharmacology, Pharmacology and Therapeutics, Cancer and Metastasis Reviews, Advances in Pharmacology* and the *Journal of Lipid Research.* He also served on the National Asthma Education and Prevention Program Federal Advisory Committee.

Dr. Shanshan Zhao (Biostatistics and Computational Biology Branch) served as an Associate Editor of *Biometrics* and as an academic advisor for *PLoS One*.

TRAINING AND MENTORING

NIEHS Trainee Alumni

From January 1, 2022 through December 31, 2022, 4 pre-doctoral trainees left NIEHS to continue their doctoral studies in their respective universities. 26 post-baccalaureate trainees left NIEHS. The majority of them went to either medical school or graduate school. 25 postdoctoral trainees left NIEHS. Below is a summary of the analysis of where the postdoctoral trainees have gone upon completing their training, what they are doing and the level of the positions they took.

What are they doing?

Additional postdoctoral training	2
Internship	0
Additional advanced degree	0
Primarily teaching	0
Primarily basic research	6
Primarily clinical research	0
Primarily clinical practice	0
Primarily applied research	8
Primarily patient care	0
Regulatory affairs	1
Science administration/project management	1
Intellectual property/ licensing and patenting	1
Consulting	0
Public policy	0
Science writing or communications	1
Grants management	0
Business development or Operations	0
Computation/informatics	3
Sales/marketing	0
Technical/customer support	0
Unknown or Undecided	2
Other	0
Unemployed	0
TOTAL	25

Where did they go?

Academic institution	7
Government agency	4
For-profit company	12
Non-profit organization	0
Private medical practice	0
Independent/self-employed	0
Unknown or Undecided	2
Unemployed	0
TOTAL	25

What is the level of their position?

Tenure track faculty	6
Non-tenure track faculty	0
Professional staff	15
Support staff	0
Management	0
Trainee	2
Unknown or Undecided	2
Unemployed	0
TOTAL	25