

NIAAA DIRECTOR'S REPORT ON INSTITUTE ACTIVITIES TO THE 162ND MEETING OF THE NATIONAL ADVISORY COUNCIL ON ALCOHOL ABUSE AND ALCOHOLISM

Thursday, February 9, 2023 Virtual Meeting

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NIAAA BUDGET

FY 2023

On December 29, 2022, the President signed H.R. 2617 - Consolidated Appropriations Act, 2023. NIH received a total of \$47.7 billion, representing a \$2.5 billion or a 5.5% increase above the Fiscal Year (FY) 2022 enacted level. This funding also includes allocations for increases for various research priorities such as cancer, Alzheimer's disease, pain and opioids, health disparities, and environmental health. The bill provides a general increase to NIH Institutes and Centers, and it continues to provide support for the Gabriella Miller Kids First Act pediatric research initiative.

The FY 2023 appropriation for NIAAA provides \$595.3 million. This represents about a \$21.7 million or a 3.8% increase over the FY 2022 budget level. NIAAA estimates it will support an estimated total of 728 research project grants in FY 2023.

FY 2024

The preparation of the FY 2024 President's Budget is underway.

HONORS AND AWARDS

Dr. Lorenzo Leggio, Chief, Laboratory on Clinical Psychoneuroendocrinology and Neuropsychopharmacology, Division of Intramural Clinical and Biological Research, received the 2023 Ward & Ryan Donovan Lectureship Award from the American College of Medical Toxicology (ACMT). He will give the Donovan lecture at the ACMT meeting in San Diego, CA, on March 31, 2023.

Dr. Pal Pacher, Chief, Laboratory of Cardiovascular Physiology and Tissue Injury, Division of Intramural Clinical and Biological Research, was included among the "Highly Cited Researchers 2022." This list was produced by the Institute for Scientific Information and reflects highly cited papers during the last decade.

Dr. Bipul Ray, Postdoctoral Visiting Fellow, Section of Molecular Pharmacology and Toxicology, Division of Intramural Clinical and Biological Research, received the KAPAL Best Oral Presentation Award at the 12th Annual Bioscience and Engineering Symposium on November 19, 2022.

Dr. Wiramon Rungratanawanich, Postdoctoral Visiting Fellow, Section of Molecular Pharmacology and Toxicology, Division of Intramural Clinical and Biological Research, received the Dr. Johng Sik Rhim Outstanding Postdoctoral Fellow Award at the 12th Annual Bioscience and Engineering Symposium on November 19, 2022.

STAFF TRANSITIONS

New Staff



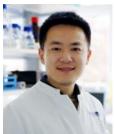
Rachel Hall joined the NIAAA Office of the Director as Executive Secretariat Liaison. In this role, Rachel provides administrative support and manages all controlled correspondence for NIAAA. Rachel joins NIAAA from the private sector where she was a manager of a large company and brings with her many administrative skills.



Yesika Valdes Villapando joined NIAAA as Program Support for the Division of Epidemiology and Prevention Research (DEPR). Yesika earned a master's degree in Clinical Epidemiology from The National Institute of Public Health (Mexico). Prior to joining NIAAA, she worked in public health administration, clinical epidemiology, and clinical nutrition settings. In her new role, Yesika is responsible for all aspects of administrative support for DEPR.



Colleen McDonough joined the Administrative Services Branch and will be assisting the Division of Intramural Clinical and Biological Research Administrative Officers and Laboratories. Colleen is joining ASB from the private sector with extensive administrative experience.



Dr. Cheng Chen joined as a Post-Doctoral Visiting Fellow working concurrently between the Laboratory of Liver Diseases (LLD) and the Laboratory of Physiologic Studies (LPS). For LLD, Dr. Chen will study alcohol metabolism in adipose tissues, its impact on organ damage, and how acetaldehyde affects the gut. For LPS, Dr. Chen will explore the role of adipocyte

Cbl) receptors in diet-induced metabolic syndrome, using global Cbl knockout mice with transgenic re-expression of Cbl on adipocytes.



Dr. Yohannes Getiye Estifanos joined the Laboratory of Cardiovascular Physiology & Tissue Injury as a Post-Doctoral Visiting Fellow. Dr. Estifanos will be involved in the development and testing of new therapeutic targets against tissue injury and inflammation, including those caused by excessive alcohol consumption. He will also study the effect of alcohol and vaping on the cardiac remodeling and cardiovascular function.



Dr. Rachel Keith joined the Section on Neural Circuits as a Post-Doctoral Fellow to identify molecular mechanisms that cause and compensate for memory and learning deficits. The findings of Dr. Keith's research may provide insights into novel therapeutic approaches to improve learning and cognition in diseased brain states arising from genetic mutations and alcohol exposure, in utero.



Dr. Luca Maccioni joined as a Post-Doctoral Visiting Fellow working concurrently between the Laboratory of Liver Diseases (LLD) and the Laboratory of Physiologic Studies (LPS). A major focus of Dr. Maccioni's research will be alcohol metabolism, including alcohol metabolism in adipose tissues, its role in organ damage, gut effects of acetaldehyde (a by-product of alcohol metabolism). Dr. Maccioni will also investigate Casitas-b-lymphoma (Cbl) receptors, including the role of adipocyte CBl receptors in diet-induced metabolic syndrome in using an animal model.



Dr. Baskar Mohana Krishnan joined the Section on Neural Circuits as a Post-Doctoral Visiting Fellow. Dr. Krishna will work to uncover the functional role of D1 and D2 receptor co-expressing neurons in motivation and reward related behaviors. This work may identify approaches for cell-specific targeting of genetically distinct neuronal subsets to treat substance use disorder.



Dr. Weizheng Yan joined the Laboratory of Neuroimaging (LNI) as a Post-Doctoral Visiting Fellow. Dr. Yan will conduct clinical research utilizing functional MR, PET and simultaneous PET/MRI in patients with substance use disorder and in healthy volunteers.

New Post-Baccalaureate Intramural Research Training Award (IRTA) Fellows:

Avery Arsenault – Office of the Clinical Director

Madelyne Etami - Laboratory of Neuroimaging

Daniel Geda – Office of the Clinical Director

Jessica Goldschlager – Section on Behavioral Science and Genetics

Ali Hamandi – Section on Clinical Genomics and Experimental Therapeutics

Jessica Laudie – Office of the Clinical Director

Aditi Madhusudan – Laboratory of Neuroimaging

Bethany Ngere – Office of the Scientific Director

Lauren Park – Section on Clinical Genomics and Experimental Therapeutics

Stephanie Ramos-Maciel – Unit on Motivation and Arousal

Samay Shivshankar – Section on Medicinal Chemistry

Megan Steck – Section of Sensory Science and Metabolism

Transitions

Dr. Yukun Guan converted from Post-Doctoral Fellow in the Laboratory of Liver Diseases to Research Fellow. Dr. Guan will work on the molecular mechanisms underlying alcohol-associated and non-alcohol-associated fatty liver diseases using a variety of mouse models. This work will include identifying novel therapeutic targets for the treatment of fatty liver diseases.

Jennifer Leese is the Staff Assistant to the Division of Metabolism and Health Effects in addition to assisting the Extramural Administrative Officers within the Administrative Services Branch. Jen previously provided program support to the Office of Resource Management, several extramural program areas, and intramural research laboratories within NIAAA.

Timothy Karacki was selected as the new NIAAA Deputy Budget Officer for the Financial Management Branch (FMB). Prior to this new role, Tim served as a Budget Analyst in the NIAAA FMB for over 6 years where he played a key role in modernization efforts that improved overall FMB management and operations.

Dr. Laura Kwako was selected as Chief of the Treatment, Health Services, and Recovery Branch within the Division of Treatment and Recovery. Dr. Kwako joined the NIAAA intramural research program in 2010, where she served as a postdoctoral fellow and later as a clinical research psychologist. In 2019, Dr. Kwako became a program officer in the NIAAA Division of Treatment and Recovery, where she oversaw the health services portfolio and led development of the Healthcare Professional's Core Resource on Alcohol. Dr. Kwako will continue to provide direct patient care on the 1SE Alcohol and Addictions unit in the NIH Clinical Center.

Donna Stringfield transitioned to the role of Grants Management Specialist within the NIAAA Grants Management Branch, Office of Extramural Activities (OEA). Donna previously served 6 years as an Administrative Technician in OEA's Extramural Project Review Branch.

Dr. Rui Zhang converted to the Research Fellow position within the NIAAA Laboratory of Neuroimaging. Dr. Zhang is currently a K99/R00 awardee working on sleep and circadian rhythm in patients with substance use disorder.

Departures

Dr. Abraham Bautista retired from the role of Director, Office of Extramural Activities, in December 2022. Dr. Bautista leaves after 20 years of federal service with the last 16 years at NIAAA. Dr. Bautista oversaw extramural grant and contract peer review, the management of chartered initial review groups and special emphasis panels, and all grants management activities. Dr. Bautista served as the Executive Secretary of NIAAA's Advisory Council and was responsible for overseeing and coordinating committee management activities, including federal advisory committees. In his retirement, Dr. Bautista looks forward to expanding his travels and finding other exciting ways to fill his days.

Dr. Etienne Lamoreaux retired from NIAAA after 44 years of federal service. He has been a leader in data management and system design since he joined the Institute in 1998. He will serve as a consultant to the Office of Resource Management/Information Technology Branch.

Dr. Jenica Patterson, a Health Science Administrator with the Medications Development Branch in the Division of Treatment and Recovery, recently departed for a position at the National Institute of Biomedical Imaging and Bioengineering, NIH.

Departing Intramural Post-Doctoral Fellows:

Dr. Natashia Giddens – Laboratory of Neuroimaging

Dr. Fatemeh Shekoohishooli - Clinical Neuroimaging Research Core

Dr. Benson Stevens – Laboratory of Human Psychopharmacology

Departing Post-Baccalaureate IRTA Fellows:

Josephine Nimely – Office of the Scientific Director Victoria Rabii – Clinical Neuroimaging Research Core Rhianna Vergeer – Laboratory of Human Psychopharmacology

RECENTLY ISSUED FUNDING OPPORTUNITIES

Funding Opportunity Announcements (FOAs) Issued by NIAAA

Limited Competition: Brain Tissue Resource Center for Alcohol Research. The purpose of this limited competition FOA is to provide general support of an already established brain tissue resource center that serves the alcohol research community. The goals of the center are to: develop a "bank" of brain tissues (fresh-frozen and formalin-fixed) from people with Alcohol Use Disorder (AUD) and control cases with confirmed clinical and pathological diagnoses, develop and promote a prospective brain donor program in Australia to enhance the "brain bank", establish an associated DNA (blood) bank from the brain donor group, and invite research groups with an interest in alcohol-related brain damage to submit applications for studies using these tissues. PAR-23-068 (R28 Clinical Trial Not Allowed).

Notices Issued by NIAAA

Notice of NIAAA Participation in PAR-22-181, "NIDA, NIMH, NINR, and NINDS Research Opportunities for New and "At-Risk" Investigators to Promote Workforce Diversity (R01 Clinical Trial Optional)".

NOT-AA-22-015. This Notice informs applicants that NIAAA participates in PAR-22-181, whose purpose is to support R01 grant applications from new investigators and at-risk investigators from diverse backgrounds, including those from groups underrepresented in the health-related sciences.

Notice of Guidance for Data Management and Sharing Plans for the National Institute on Alcohol Abuse and Alcoholism (NIAAA). NOT-AA-23-001. This notice informs the extramural research community that NIAAA expects specific information in the data management and sharing plan to be included in NIAAA grant applications for due dates on or after January 25, 2023.

Notice of NIAAA Data-Sharing Information for Human Subjects Grants Research Funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) [5th Revision]. NOT-AA-23-002. The purpose of this Notice is to revise and replace the current NIAAA language for Data Sharing requirements to align with the NIH Policy for Data Management and Sharing (NOT-OD-21-013). This Notice applies to all grant applications and awards that involve human subjects research for due dates on or after January 25, 2023 and applies to all Funding Opportunity Announcements (FOAs) in which NIAAA participates.

Notice of NIAAA's Participation in NOT-DA-22-064 "Notice of Intent to Publish a Funding Opportunity Announcement for NIH Brain Development Cohorts Biospecimen Access (X01 Clinical Trial Not Allowed)". NOT-AA-23-004. This Notice informs applicants that NIAAA is participating in NOT-DA-22-064, which announces the upcoming publication of an FOA to seek applications for the NIH Brain Development Cohorts Biospecimen Access Program, which will allow investigators to apply for access to biological samples from the Adolescent Brain Cognitive Development (ABCD) Study®.

NIH-Wide FOAs with NIAAA Participation

NIH Blueprint for Neuroscience Research: Computational Training in Neuroscience and Behavior (T90/R90 - Clinical Trial Not Allowed). RFA-DA-23-037

HEAL Initiative: Development of Therapies and Technologies Directed at Enhanced Pain Management (R41/R42 Clinical Trial Not Allowed). <u>RFA-NS-23-007</u>, (R43/R44 Clinical Trial Not Allowed). <u>RFA-NS-23-006</u>

HEAL Initiative: Prevention and Management of Chronic Pain in Rural Populations (UG3/UH3, Clinical Trials Required). RFA-NR-23-001

BRAIN Initiative: Theories, Models and Methods for Analysis of Complex Data from the Brain (R01 Clinical Trial Not Allowed). RFA-DA-23-039

HEAL Initiative: HEAL Data2Action Innovation and Acceleration Projects (R61/R33, Clinical Trial Optional). RFA-DA-23-057, (R33 Clinical Trial Not Allowed). RFA-DA-23-058

BRAIN Initiative Cell Atlas Network (BICAN): Comprehensive Center on Human and Non-human Primate Brain Cell Atlases (UM1 Clinical Trial Not Allowed). RFA-MH-22-290

BRAIN Initiative Cell Atlas Network (BICAN): Coordinating Unit for Biostatistics, Informatics, and Engagement (CUBIE) (U24 Clinical Trial Not Allowed). RFA-MH-22-291

BRAIN Initiative Cell Atlas Network (BICAN): Specialized Collaboratory on Human, Non-human Primate, and Mouse Brain Cell Atlases (R01 Clinical Trial Not Allowed). RFA-MH-22-292

BRAIN Initiative: Brain-Behavior Quantification and Synchronization Transformative and Integrative Models of Behavior at the Organismal Level (R34 Clinical Trial Not Allowed) . RFA-DA-23-030

Environmental influences on Child Health Outcomes (ECHO) Measurement Core (U24) Clinical Trial Not Allowed. RFA-OD-22-020

The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional). <u>RFA-OD-22-028</u>

HEAL Initiative Integrated Basic and Clinical Team-based Research in Pain (RM1 Clinical Trial Optional) . RFA-NS-22-069

Engineering Next-Generation Human Nervous System Microphysiological Systems (R01 Clinical Trials Not Allowed). PAR-23-046, (R21 Clinical Trials Not Allowed). PAR-23-047

HEAL Initiative: Sleep Predictors of Opioid-Use Disorder Treatment Outcomes Program (R01 Clinical Trial Optional). <u>RFA-DA-23-059</u>, Leadership and Data Co-ordinating Center (U01 Clinical Trial Optional). <u>RFA-DA-23-060</u>

Research on Community Level Interventions for Firearm and Related Violence, Injury and Mortality Prevention (CLIF-VP) (UG3/UH3 Clinical Trial Required). PAR-23-066

HEAL Initiative Advanced Postdoctoral-to-Independent Career Transition Award in PAIN and SUD Research (K99/R00 Independent Clinical Trial Not Allowed). RFA-NS-22-022, (Independent Basic Experimental Studies with Humans Required). RFA-NS-22-023, to Promote Diversity (K99/R00 Independent Basic Experimental Studies with Humans Required). RFA-NS-22-024, to Promote Diversity (K99/R00 Independent Clinical Trial Not Allowed). RFA-NS-22-025

BRAIN Initiative: Brain Behavior Quantification and Synchronization (R61/R33 Clinical Trial Optional). RFA-MH-23-335

Biomedical Knowledgebase (U24 - Clinical Trials Not Allowed). <u>PAR-23-078</u>, (U24 - Clinical Trials Not Allowed). <u>PAR-23-079</u>

Enhancing the Use of the All of Us Research Programs Data (R21 Clinical Trial Not Allowed). RFA-PM-23-001

Small Grants to Enhance the Use of the All of Us Research Programs Data (R03 Clinical Trial Not Allowed). RFA-PM-23-002

BRAIN Initiative: Transformative Brain Non-invasive Imaging Technology Development (UG3/UH3 Clinical Trial Not Allowed). RFA-EB-22-003

Ruth L. Kirschstein National Research Service Award (NRSA) Short-Term Institutional Research Training Grant (Parent T35). PA-23-080

NIH-Wide NOSIs with NIAAA Participation

Notice of Special Interest (NOSI): BRAIN Initiative: Notice of Support for Research on Interoception Circuits. NOT-AT-23-003

Notice of Special Interest (NOSI): Administrative Supplement for Research and Capacity Building Efforts Related to Bioethical Issues (Admin Supp Clinical Trial Optional). NOT-OD-23-018

Notice of Special Interest (NOSI): Administrative Supplements to Recognize Excellence in Diversity, Equity, Inclusion, and Accessibility (DEIA) Mentorship. NOT-OD-23-002

Notice of Special Interest (NOSI): Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards. NOT-OD-23-032

Notice of Special Interest: Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars. NOT-OD-23-031

Notice of Special Interest (NOSI): Firearm Injury and Mortality Prevention Research. NOT-OD-23-039

Notice of Special Interest (NOSI): BRAIN Initiative: Developing Data Archive, Informatics Tools and Data Standards for Brain Behavior Quantification and Synchronization (BBQS). NOT-MH-23-115

NIAAA DIRECTOR'S ACTIVITIES

NIAAA Director **George F. Koob**, **Ph.D.**, gave the following presentations between August 1st-December 31st:

- "State of the Art in Neurobiology" at the California Society of Addiction Medicine State of the Art Addiction Medicine Conference on August 25, 2022
- "Breaking Silos in Alcohol Research" at the Yale Conference Y Care Symposium Educational workshop (virtual) on September 10, 2022
- Substance Use Disorder Recovery Research Summit: Advancing a Recovery Ready Nation "Summit 2022" Fireside Chat (virtual) on September 12, 2022
- NIAAA Update NIAAA Liaison Meeting (Virtual) on September 13, 2022
- "Alcohol and Older Adults: An Area of Increasing Concern," Mental Health Rounds series (virtual) on September 14, 2022
- "Overview of Alcohol-Associated Liver Diseases and NIAAA's Research Priorities to close the Treatment Gap" at the American Association for the Study of Liver Diseases (virtual), Congressional Briefing on September 20, 2022
- "Alcohol Use Disorder: Our Nation's Hidden Epidemic" at the National Council for Mental Wellbeing Wellbeing Wednesdays Episode 8 on September 22, 2022, (Broadcast 9/28/2022)
- "Closing the Treatment Gap: An Alcohol Use Disorder Perspective" at International Drug Abuse Society 8th Biennial Meeting Nice, France on September 26, 2022
- "Alcohol and Drug Addiction: The Gain in the Brain is in the (Emotional) Pain" (virtual) at Addiction 2022, Villasimius Sardinia Italy on September 28, 2022
- "Hyperkatifeia, Health and Harm Reduction: An NIAAA Director's Recovery Perspective" (virtual) at Recovery Research Institute on October 13, 2022
- "Alcohol in the Workforce: What you should know" at the World Health Organization (WHO)
 Webinar on alcohol use for WHO workforce (virtual) on October 17, 2022
- "Alcohol and the Female Brain" at the 2022 National Conference on Alcohol and Other Substance Use Among Women and Girls (virtual) on October 20, 2022.

- "The Neurobiology of Alcohol Use Disorder Focus on the Negative Emotional Side of Alcohol Use Disorder: Implications for Deaths of Despair and the COVID-19 Pandemic" at Gordon Research Conference: Alcohol and the Nervous System Oxnard, California on October 23, 2022
- "NIAAA efforts in closing the AUD Treatment Gap" at the International Conference of Secular AA (virtual) on October 29, 2022.
- Opening remarks Adolescent Brain Cognitive Development Annual Meeting on November 8, 2022
- "NIAAA's Priorities" at the American College of Neuropsychopharmacology (ACNP) NIH Institute Directors Session on December 4, 2022.

NOTABLE NIAAA STAFF ACTIVITIES

Drs. Bill Dunty and Tatiana Balachova presented "Alcohol and Pregnancy Research: An NIAAA Update" at the American College of Obstetricians & Gynecologists FASD Expert Work Group Annual Meeting, Washington, DC, August 19, 2022.

Dr. Laura Kwako gave a presentation entitled, "Overview of the Healthcare Professional's Core Resource" as part of the NIAAA Liaison meeting on September 13, 2022.

Dr. Bill Dunty presented a talk entitled "Alcohol and Pregnancy Research: An NIAAA Update" and participated in the live session of the Federal Agency Roundtable at the Uniformed Services University of Health Sciences (USUHS)/FASD United workshop on September 21, 2022 in Washington D.C. **Dr. Tatiana Baclachova** was a panelist at the meeting for the "Federal Response to FASD: Agency Overview - the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders."

Drs. Deidra Roach and Raye Litten organized sessions at American Society for Addiction Medicine State of the Art Course in Addiction Medicine on September 28-October 1, 2022, in Washington DC.

Dr. Deidra Roach and Joan Romaine organized the 2022 National Conference on Alcohol and Other Substance Use in Women and Girls: Advances in Prevention, Treatment and Recovery Virtual Conference on October 20-21, 2022. In that conference, **Dr. Laura Kwako** presented "The NIAAA Alcohol Treatment Navigator and NIAAA Healthcare Professionals' Core Resource for Alcohol."

Dr. John Matochik was the Co-Chair for the two-day NIDA-NIAAA Frontiers in Addiction Research Mini-Convention held on November 1-2, 2022. He was also the Chair for the Early Career Investigators Showcase held during the convention.

Maureen Gardner, Dr. Laura Kwako, and Dr. Raye Litten attended National Committee for Quality Assurance Innovation Summit and met with senior leadership to discuss ongoing collaborations and promotion of Healthcare Professional's Core Resource on Alcohol November 1-3, 2022, in Washington, DC.

Dr. Kathy Jung presented "National Institute on Alcohol Abuse and Alcoholism: Goals and Priorities" during the NIAAA Corner at The Liver Meeting on Nov 7, 2022, in Washington, DC.

Drs. Trish Powell and Tatiana Balachova organized and led the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD) Fall 2022 Executive Meeting, November 7, 2022

Dr. Mariela Shirley presented "National Institutes of Health: Mission, Priorities and the Road Ahead" at the annual hybrid meeting of the International Society for Traumatic Stress Studies on November 10, 2022, in Atlanta, Georgia.

Dr. Tatiana Balachova was a panel speaker at the K01 Panel organized by New York University's Center for Drug Use and HIV Research on November 21, 2022.

Dr. Falk Lohoff presented "Epigenetics of Alcohol Use Disorder: novel strategies for therapeutic target discovery" at Indiana University, Indianapolis, IN, on December 1, 2022.

Dr. Mariela Shirley presented "Early-Stage Investigator Research and Training Opportunities" to the Northeast NIAAA T32 Programs (Brown University, Brandeis University, University of Buffalo, and University of Connecticut) on December 2, 2022 in Bethesda, Maryland.

Dr. Sethu Balakathiresan presented "Overview of National Institute on Alcohol Abuse and Alcoholism (NIAAA) Research", to the Joint Defense Health Program/Veterans Affairs/Department of Health and Human Services Psychological Health Review & Analysis Meeting on December 6, 2022.

Dr. Brett Hagman presented "A Brief Introduction to the new NIAAA Research Definition of Recovery from DSM-5 AUD" as part of the NIAAA recovery webinar titled "Using New Definitions and Tools to Support Alcohol Recovery" hosted on December 6, 2022. As part of the same webinar, **Dr. Laura Kwako** presented "The Healthcare Professional's Core Resource on Alcohol."

Dr. Laura Kwako attended the Annual Conference on the Science of Dissemination and Implementation in Health and chaired a panel presentation entitled: "Digging Deep into Implementation Strategies" on December 14, 2022, in Washington, DC.

WHAT'S AHEAD?

The ICCFASD 2023 Public Meeting will be held on April 17, 2023 (hybrid meeting and NIH Videocast).

The 5th International Congress on Alcoholism and Stress will be held in Volterra, Italy, May 16-19, 2023.

The <u>46th Annual Research Society on Alcoholism Scientific Meeting</u> will be held June 24-28, 2023, in Bellevue, Washington.

NIAAA RESEARCH HIGHLIGHTS

SPIRONOLACTONE AS A POTENTIAL NEW PHARMACOTHERAPY FOR ALCOHOL USE DISORDER: COVERGENT EVIDENCE FROM RODENT AND HUMAN STUDIES

<u>Significance:</u> Spironolactone is a mineralocorticoid receptor antagonist is used to treat a variety of medical conditions ranging from essential hypertension, heart failure, edema, primary hyperaldosteronism, and

hypokalemia. This study tested the effectiveness of spironolactone in animal models alcohol binge drinking and drinking in the context of alcohol dependence, and investigated the association of spironolactone medication use and self-reported alcohol consumption in a human pharmacoepidemiology analysis (using electronic medical records from the US Department of Veterans Affairs). The findings provide convergent evidence supporting the overall hypothesis that the non-selective mineralocorticoid antagonist spironolactone may represent a potential novel medication for AUD.

Abstract:

Evidence suggests that spironolactone, a nonselective mineralocorticoid receptor (MR) antagonist, modulates alcohol seeking and consumption. Therefore, spironolactone may represent a novel pharmacotherapy for alcohol use disorder (AUD). In this study, we tested the effects of spironolactone in a mouse model of alcohol drinking (drinking-in-the-dark) and in a rat model of alcohol dependence (vapor exposure). We also investigated the association between spironolactone receipt for at least 60 continuous days and change in self-reported alcohol consumption, using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), in a pharmacoepidemiologic cohort study in the largest integrated healthcare system in the US. Spironolactone dose-dependently reduced the intake of sweetened or unsweetened alcohol solutions in male and female mice. No effects of spironolactone were observed on drinking of a sweet solution without alcohol, food or water intake, motor coordination, alcohol-induced ataxia, or blood alcohol levels. Spironolactone dose-dependently reduced operant alcohol self-administration in dependent and nondependent male and female rats. In humans, a greater reduction in alcohol consumption was observed among those who received spironolactone, compared to propensity score-matched individuals who did not receive spironolactone. The largest effects were among those who reported hazardous/heavy episodic alcohol consumption at baseline (AUDIT-C≥8) and those exposed to ≥ 50 mg/day of spironolactone. These convergent findings across rodent and human studies demonstrate that spironolactone reduces alcohol use and support the hypothesis that this medication may be further studied as a novel pharmacotherapy for AUD.

Farokhnia, M., Rentsch, C.T., Chuong, V. *et al.* Spironolactone as a potential new pharmacotherapy for alcohol use disorder: convergent evidence from rodent and human studies. *Mol Psychiatry* **27**, 4642–4652 (2022). https://doi.org/10.1038/s41380-022-01736-y.

ACETATE REPROGRANS GUT MICROBIOTA DURING ALCOHOL CONSUMPTION

<u>Significance</u>: Alcohol consumption leads to changes in the gut microbiota's composition and growth, often described as dysbiosis. The cause of dysbiosis, produced by alcohol and/or its metabolites, is a fundamental biological question. In the current study, mouse models were used to investigate the metabolic impacts of alcohol consumption on the gut microbiota. They found that acetate, a by-product of alcohol metabolism, is diffused from circulation into the intestine where it provides a source of energy for bacterial growth.

Abstract:

Liver damage due to chronic alcohol use is among the most prevalent liver diseases. Alcohol consumption frequency is a strong factor of microbiota variance. Here we use isotope labeled [1-¹³C] ethanol, metagenomics, and metatranscriptomics in ethanol-feeding and intragastric mouse models to investigate the metabolic impacts of alcohol consumption on the gut microbiota. First, we show that although stable isotope labeled [1-¹³C] ethanol contributes to fatty acid pools in the liver, plasma, and cecum contents of

mice, there is no evidence of ethanol metabolism by gut microbiota ex vivo under anaerobic conditions. Next, we observe through metatranscriptomics that the gut microbiota responds to ethanol-feeding by activating acetate dissimilation, not by metabolizing ethanol directly. We demonstrate that blood acetate concentrations are elevated during ethanol consumption. Finally, by increasing systemic acetate levels with glyceryl triacetate supplementation, we do not observe any impact on liver disease, but do induce similar gut microbiota alterations as chronic ethanol-feeding in mice. Our results show that ethanol is not directly metabolized by the gut microbiota, and changes in the gut microbiota linked to ethanol are a side effect of elevated acetate levels. De-trending for these acetate effects may be critical for understanding gut microbiota changes that cause alcohol-related liver disease.

Martino C, Zaramela LS, Gao B, Embree M, Tarasova J, Parker SJ, Wang Y, Chu H, Chen P, Lee KC, Galzerani DD, Gengatharan JM, Lekbua A, Neal M, Knight R, Tsukamoto H, Metallo CM, Schnabl B, Zengler K. Acetate reprograms gut microbiota during alcohol consumption. Nat Commun. 2022 Aug 8;13(1):4630. doi: 10.1038/s41467-022-31973-2. PMID: 35941112; PMCID: PMC9359997.

GENOME-WIDE ASSOCIATION STUDY FOR CIRCULATING FGF21 IN PATIENTS WITH ALCOHOL USE DISORDER: MOLECULAR LINKS BETWEEN THE SNHG16 LOCUS AND CATECHOLAMINE METABOLISM

<u>Significance</u>: Alcohol consumption can increase circulating levels of fibroblast growth factor 21 (FGF21) and FGF 21 can decrease drinking in rodent models. The goal of this study was to identify genetic variants associated with FGF21 levels and evaluate their functional role in AUD. Results showed that plasma FGF21 levels were positively correlated with recent alcohol consumption. One variant, rs9914222, located 5' of SNHG16 chromosome 17, was associated with plasma FGF21 levels and with AUD risk. Knockdown of SNHG16 in HepG2 cells resulted in increased FGF21 levels and decreased expression and enzyme activity for COMT, an enzyme that is involved in catecholamine metabolism. Finally, alcohol significantly induced FGF21, and catechol O- methyl transferase mRNA expression in iPSC-derived brain organoids which were reversed by medications used for the treatment of alcohol use disorder. Improving the understanding of these molecular pathways will aid the development of better biomarkers and therapies for alcohol use disorder.

Abstract

derived brain organoids.

Objective: Alcohol consumption can increase circulating levels of fibroblast growth factor 21 (FGF21). The effects of FGF21 in the central nervous system are associated with the regulation of catecholamines, neurotransmitters that play a crucial role in reward pathways. This study aims to identify genetic variants associated with FGF21 levels and evaluate their functional role in alcohol use disorder (AUD). **Methods:** We performed a genome-wide association study (GWAS) using DNA samples from 442 AUD subjects recruited from the Mayo Clinic Center for the Individualized Treatment of Alcoholism Study. Plasma FGF21 levels were measured using Olink proximity extension immunoassays. Alcohol consumption at time of entry into the study was measured using the self-reported timeline followback method. Functional genomic studies were performed using HepG2 cells and induced pluripotent stem cell (iPSC)-

Results: Plasma FGF21 levels were positively correlated with recent alcohol consumption and gamma-glutamyl transferase levels, a commonly used marker for heavy alcohol use. One variant, rs9914222, located 5' of SNHG16 on chromosome 17 was associated with plasma FGF21 levels (p = 4.60E-09). This variant was also associated with AUD risk (β : -3.23; p:0.0004). The rs9914222 SNP is an eQTL for SNHG16 in several brain regions, i.e., the variant genotype was associated with decreased expression of SNHG16. The variant genotype for the rs9914222 SNP was also associated with higher plasma FGF21 levels.

Knockdown of SNHG16 in HepG2 cells resulted in increased FGF21 concentrations and decreased expression and enzyme activity for COMT, an enzyme that plays a key role in catecholamine metabolism. Finally, we demonstrated that ethanol significantly induced FGF21, dopamine, norepinephrine, and epinephrine concentrations in iPSC-derived brain organoids.

Conclusions: GWAS for FGF21 revealed a SNHG16 genetic variant associated with FGF21 levels which are associated with recent alcohol consumption. Our data suggest that SNHG16 can regulate FGF21 concentrations and decrease COMT expression and enzyme activity which, in turn, have implications for the regulation of catecholamines. (The ClinicalTrials.gov Identifier: NCT00662571).

Ho MF, Zhang C, Moon I, Wei L, Coombes B, Biernacka J, Skime M, Choi DS, Frye M, Schmidt K, Gliske K, Braughton J, Ngo Q, Skillon C, Seppala M, Oesterle T, Karpyak V, Li H, Weinshilboum R. Genome-wide association study for circulating FGF21 in patients with alcohol use disorder: Molecular links between the SNHG16 locus and catecholamine metabolism. Mol Metab. 2022 Sep;63:101534. doi: 10.1016/j.molmet.2022.101534. Epub 2022 Jun 22. PMID: 35752286; PMCID: PMC9270258.

COVID-19 PANDEMIC-RELATED CHANGES IN UTILIZATION OF TELEHEALTH AND TREATMENT OVERALL FOR ALCOHOL USE PROBLEMS

<u>Significance</u>: During the COVID-19 pandemic, specialty alcohol treatment transitioned rapidly to telehealth, a transition that may have created barriers for some patients, but increased access for others. The purpose of this study is to determine the impact of the COVID-19 pandemic on alcohol treatment utilization and potential disparities. Results showed that the transition to telehealth attracted subgroups of individuals who have historically underutilized care for alcohol use problems, particularly younger and healthier adults, without exacerbating pre-pandemic racial and ethnic disparities in treatment utilization.

Abstract:

Background: During the COVID-19 pandemic, specialty alcohol treatment transitioned rapidly to telehealth, which may have created barriers for some patients but increased access for others. This study evaluated the impact of the COVID-19 pandemic on alcohol treatment utilization and potential disparities. **Methods:** We analyzed electronic health record and claims data from Kaiser Permanente Northern California for adults with alcohol use problems (alcohol use disorder or unhealthy alcohol use diagnoses) during pre-COVID-19 (March to December 2019, n = 32,806) and COVID-19 onset (March to December 2020, n = 26,763). Generalized estimating equation models were fit to examine pre-COVID-19 to COVID-19 onset changes in alcohol treatment initiation, engagement, and retention (days in treatment). Heterogeneity in pre-COVID-19 to COVID-19 onset changes in treatment utilization by age, race, and ethnicity; neighborhood deprivation index (NDI); and comorbid medical and psychiatric disorders were also examined.

Results: Treatment initiation increased during the COVID-19 onset period (adjusted odds ratio [aOR] = 1.46; 95% CI = 1.41-1.52). The increases in odds of treatment initiation during the COVID-19 onset period compared with the pre-COVID period were largest among patients aged 18-34 years (aOR = 1.59; 95% CI = 1.48-1.71), those without medical conditions (aOR = 1.56; 95% CI = 1.49-1.65), and those without psychiatric disorders (aOR = 1.60; 95% CI = 1.51-1.69). Patients aged 18-34 years (aOR = 5.21; 95% CI = 4.67-5.81), those with the second highest NDIs (aOR = 4.63; 95% CI = 4.12-5.19), and those without medical (aOR = 4.34; 95% CI = 4.06-4.65) or psychiatric comorbidities (aOR = 4.48; 95% CI = 4.11-4.89) had the greatest increases in telehealth treatment initiation from pre-COVID-19 to COVID-19 onset. Treatment engagement and retention also increased during COVID-19 onset, with the greatest increase

among patients aged 35-49 years who initiated treatment via telehealth (engagement: aOR = 2.33; 95% CI = 1.91-2.83; retention: adjusted mean difference [aMD] = 3.3 days; 95% CI = 2.6-4.1). We found no significant variation of changes in treatment utilization by race and ethnicity.

Conclusions: The transition to telehealth in this healthcare system may have attracted subgroups of individuals who have historically underutilized care for alcohol use problems, particularly younger and healthier adults, without exacerbating pre-pandemic racial and ethnic disparities in treatment utilization.

Palzes VA, Chi FW, Metz VE, Campbell C, Corriveau C, Sterling S. COVID-19 pandemic-related changes in utilization of telehealth and treatment overall for alcohol use problems. Alcohol Clin Exp Res. 2022 Dec;46(12):2280-2291. doi: 10.1111/acer.14961. Epub 2022 Dec 17. PMID: 36527427.

COLLEGE STUDENTS VIRTUAL AND IN-PERSON DRINKING CONTEXTS DURING THE COVID-19 PANDEMIC

Significance: Although college drinking decreased at the onset of the pandemic, this study sought to identify a more nuanced understanding of changes in drinking contexts and the risks conferred by each context. Secondary data analyses were conducted on screening data from a large parent clinical trial assessing a college student drinking intervention (N = 1669). Participants across six cohorts reported on the frequency of drinking. The proportion and frequency of drinking at home virtually with others decreased, while drinking outside the home increased. The frequency of drinking outside the home was most consistently associated with more alcohol-related consequences. However, drinking at home was not without risks. Drinking home alone was associated with abuse/dependence, personal, social, hangover, and social media consequences. Drinking home with others virtually was associated with abuse/dependence and social consequences. Drinking home with others in-person was associated with drunk texting/dialing. Future prevention and intervention efforts may benefit from considering approaches specific to different drinking contexts

Abstract:

Background: The COVID-19 pandemic has resulted in pronounced changes for college students, including shifts in living situations and engagement in virtual environments. Although college drinking decreased at the onset of the pandemic, a nuanced understanding of pandemic-related changes in drinking contexts and the risks conferred by each context on alcohol use and related consequences have yet to be assessed. **Methods:** Secondary data analyses were conducted on screening data from a large parent clinical trial assessing a college student drinking intervention (N = 1669). Participants across six cohorts (from Spring 2020 to Summer 2021) reported on the frequency of drinking in each context (i.e., outside the home, home alone, home with others in-person, and home with others virtually), typical amount of drinking, and seven alcohol-related consequence subscales.

Results: Descriptive statistics and negative binomial regressions indicated that the proportion and frequency of drinking at home virtually with others decreased, while drinking outside the home increased from Spring 2020 to Summer 2021. Limited differences were observed in the proportion or frequency of individuals drinking at home alone or at home with others in-person. Negative binomial and logistic regressions indicated that the frequency of drinking outside the home was most consistently associated with more alcohol-related consequences (i.e., six of the seven subscales). However, drinking at home was not without risks; drinking home alone was associated with abuse/dependence, personal, social, hangover, and social media consequences; drinking home with others virtually was associated with abuse/dependence and social consequences; drinking home with others in-person was associated with drunk texting/dialing.

Conclusion: The proportion and frequency of drinking in certain contexts changed during the COVID-19 pandemic, although drinking outside the home represented the highest risk drinking context across the pandemic. Future prevention and intervention efforts may benefit from considering approaches specific to different drinking contexts.

Hultgren BA, Smith-LeCavalier KN, Canning JR, Jaffe AE, Kim IS, Cegielski VI, Garcia TA, Larimer ME. College students' virtual and in-person drinking contexts during the COVID-19 pandemic. Alcohol Clin Exp Res. 2022 Nov;46(11):2089-2102. doi: 10.1111/acer.14947. Epub 2022 Dec 1. PMID: 36454103; PMCID: PMC9720698.

NIAAA COMMUNICATIONS AND PUBLIC LIAISON ACTIVITIES

News Media

Dr. Koob, Dr. Aaron White, and other NIAAA scientists completed 61 media interviews from August through December 2022. Noteworthy stories include those from the New York Times, Newsweek, USA Today, CNN, and the Washington Post.

Highlights included:

- <u>NBC Nightly News</u> Dr. Lorenzo Leggio and Dr. Koob discussed recent research at the NIAAA Bar lab.
- NIAAA news for Spanish audiences NIAAA Deputy Clinical Director Dr. Nancy Diazgranados provided information about alcohol and health.
- 'Dry January' Satellite Media tour In January, Dr.
 Koob discussed behaviors during the holidays that may be signs of a problem with alcohol, and "Dry January," with an audience of approximately 1.8 million people through interviews with 17 local and national radio and television media outlets.

News releases, announcements, and blogs:

- September 2022 Press release: <u>Heart medication shows potential as treatment for alcohol use</u> disorder
- October 2022 NIAAA Director's Blog: A Growing concern: Increased drinking among older adults
- December 2022 Press release: <u>NIH-funded study finds hepatitis C treatment gap for individuals with alcohol use disorder</u>
- December 2022 NIAAA Director's Blog: <u>Holiday party? Here are tips for hosting a party including</u> guests who may not be drinking
- January 2023 NIAAA Director's Blog: Participating in Dry January? Here are tips for success
- PR Newswire Distribution to press about research, college drinking, FASD, and holiday drinking

Major Activities and Events

- December Webinar on "<u>Using New Definitions and Tools to Support Alcohol Recovery</u>" –
 Presenters included Dr. Brett Hagman (NIAAA), Dr. Laura Kwako (NIAAA), Dr. John Kelly (Harvard Medical School), and Dr. Helen Jack (University of Washington). The audience for the webinar, now available on <u>NIH Videocast</u>, included over 300 viewers, including Kaiser Permanente, the Mayo Clinic, Ohio State, and ASAM.
- **New** <u>short-takes</u> videos A new set of concise, sharable videos are available on the topics of fetal alcohol spectrum disorders, women and alcohol, hangovers, treatments for alcohol use disorder.
- International FASD Awareness Day In recognition of International Fetal Alcohol Spectrum Disorders Awareness Day on September 9, NIAAA <u>published a news story</u>, shared messages on social media, and distributed information to PR Newswire.
- National Recovery Month National Council presentation Dr. Koob presented on a National Council Wellbeing Wednesdays event on "Alcohol Use Disorder: Our Nation's Hidden Epidemic" along with Chuck Ingoglia, the National Council's President and CEO.
- NIAAA Liaison Group Virtual Roundtable In September, Dr. Koob discussed the state of NIAAA, and NIAAA's Dr. Laura Kwako and Dr. Kathy Bradley of Kaiser Permanente Washington Health Research Institute discussed the NIAAA Healthcare Professional's Core Resource on Alcohol.

Publications and Web Activities

Highlights

- Top NIAAA webpages <u>Alcohol's Effects on the Body</u>, <u>Drinking Levels Defined</u>, <u>Alcohol Facts and Statistics</u>
- Top NIAAA publications: (electronic) <u>Alcohol-Induced Blackouts</u>, <u>Alcohol Use Disorder</u>, <u>Alcohol Overdose</u>; (print) <u>Rethinking Drinking</u>, <u>Mixing Alcohol with Medications</u>, <u>Talk Your Child About Alcohol</u>.

New factsheets

- Alcohol and the Adolescent Brain (<u>English</u> and <u>Spanish</u>)
- Alcohol and the Brain: An Overview

Advances in Translations

- Launch of a webpage, Recursos en Espanol, which lists all available Spanish language fact sheets
- New Spanish translations: Wernicke-Korsakoff Syndrome and The Truth About Holiday Spirits

Social Media Highlights

NIAAA's Twitter account (@NIAAAnews) currently has more than 28,700 followers (a 0.35 percent increase since August), NIAAA's Instagram account (@NIAAAnews) has almost 3,000 followers (a 20 percent increase), and NIAAA's Facebook (@NIAAAgov) has almost 1,800 followers (a 25 percent increase).

On October 19, NIAAA and NIDAMED joined the American Society of Addiction Medicine (ASAM) in the *End Stigma Day* all-day Twitter conversation as part of National Addiction Treatment Week.

Notable shares:

- NIH
- Newsletter additions on "How many is too many" and "Rethink your holiday drinking"
- Tweeted on topics such as the cycle of addiction, Dry January, and NIAAA clinical trials





American Psychiatric Association @APApsychiatric · 16h

APA is collaborating with @NIAAAnews to help increase public awareness

around youth alcohol consumption. As #Hallon

- NIH homepage rotator slides featured
 NIAAA messages on seasonal and holiday drinking and alcohol and older adults
- Tweets from Dr. Drew (2.6 million followers) and the American Psychiatric Society



- VeryWell Health posted several links to NIAAA resources in an article about alcohol detox and treatment.
- AAAP Newsletter covered NIAAA research on alcohol related deaths during the pandemic.



een is around the corner,