NIAAA Director's Report on Institute Activities to the 157th Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

May 11, 2021
Virtual Meeting

George F. Koob, Ph.D.
Director
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health

https://www.niaaa.nih.gov/about-niaaa/advisory-council

In Memoriam
Mary Jeanne Kreek, M.D.

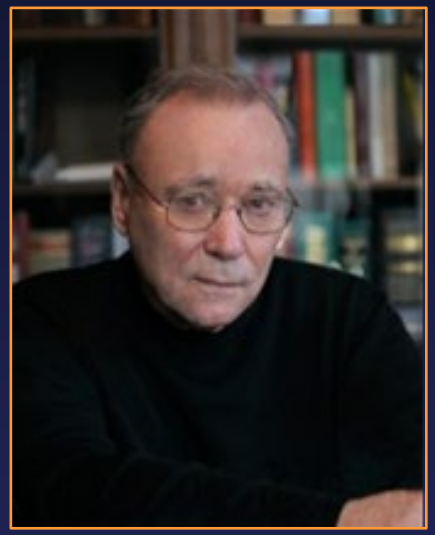
Dr. Kreek contributed enormously to the study of addiction, and her work has been crucial in eroding the stigma that still surrounds addiction and its treatment. Her seminal contributions include her work with Drs. Vincent Dole and Marie Nyswander helping to develop the first medication for opioid use disorder, methadone, and contributing to the development of another medication for opioid use disorder, buprenorphine.

She also identified injection drug use as the second major risk behavior for HIV transmission, and she contributed significantly to our basic research understanding of the neurobiology of addiction.

Dr. Kreek received many awards and honors during her illustrious career, including the Association for Multidisciplinary Education and Research in Substance Use and Addiction Betty Ford Award, the National Institute on Drug Abuse Lifetime Science Award, the American Academy of Addiction Psychiatry Founders' Award, and the Nathan B. Eddy Memorial Award for Lifetime Excellence in Drug Abuse Research from the College on Problems of Drug Dependence.

In Memoriam
Emanuel (Manny) Rubin, M.D.

Dr. Rubin was an internationally recognized academic pathologist with an all-encompassing knowledge of molecular pathology and investigator of the alcohol-induced pathogenesis of heart and liver disease.



His seminal contributions to the study of alcohol's effects on the body include providing definitive evidence that alcohol toxicity, rather than poor nutrition, was responsible for organ damage related to alcohol misuse (a collaboration with Dr. Charles Lieber) and identifying mitochondrial dysfunction in the heart and liver as the target of alcohol toxicity.

Dr. Rubin's achievements have been recognized through numerous honors, including the 2015 Lifetime Achievement Award from the Research Society on Alcoholism and the Gold-Headed Cane Award from the American Society of Investigative Pathology.

Welcome to New NIAAA Staff

Shera Smith joined NIAAA as an Extramural Support Assistant in the Review Branch, Office of Extramural Activities. Prior to joining NIAAA, Mrs. Smith was the lead technician at Moncrief Army Health Clinic, Department of the Army, Columbia, South Carolina, and worked as a Human Resource Specialist.

Dr. Khushbu Agarwal joined the Section of Sensory Science and Metabolism, Division of Intramural Clinical and Biological Research (DICBR), as a Postdoctoral Visiting Fellow. Dr. Agarwal will apply her expertise and skills in neuroimaging techniques and data analysis to the study of the relationship between hedonic pathways, sensory systems, and disease.

Dr. Abhishek Basu joined the Section on Fibrotic Disorders, DICBR, as a Postdoctoral Visiting Fellow. Dr. Basu will explore the molecular mechanisms involved in pulmonary fibrosis, including alcohol-induced lung injury, and test novel therapeutic agents.

Welcome to New NIAAA Staff

Dr. Yukun Guan joined the Laboratory of Liver Diseases, DICBR, as a Postdoctoral Visiting Fellow. In the Laboratory of Liver Diseases, Dr. Guan will study the roles of innate immune cells and cytokines in liver injury, regeneration, and cancer.

Dr. Markos Woldeyohannes joined the Section of Sensory Science and Metabolism, DIBCR, as a Postdoctoral Visiting Fellow. In this role, Dr. Woldeyohannes will design experiments and conduct epigenomic data analysis in support of research on the intersection of nutrition and psychiatry.

Staff Transitions

Internal Transitions

Dr. Resat Cinar transitioned to Tenure Track Investigator and Acting Chief for the Section on Fibrotic Disorders, Division of Intramural Clinical and Biological Research (DICBR).

Dr. Malliga Iyer transitioned to Tenure Track Investigator and Acting Chief for the Section on Medicinal Chemistry, DICBR.

Dr. Janos Paloczi transitioned to Research Fellow in the Laboratory on Cardiovascular Physiology Tissue Injury, DICBR.

Departing Staff

Emily Buzgierski, former Administrative Officer, departed the Administrative Services Branch, Office of Resource Management, for a new position with the Division of Management Services, Center for Scientific Review, where she will serve as an Administrative Officer.

Carlos Gomez, former Administrative Officer, departed NIAAA to begin a new opportunity serving as an Administrative Officer for Office of the Director, Office of Extramural Research, Strategic Management and Contracts Office.

FY 2021 Budget

- NIH received a total of $42.9 billion for FY 2021, including:
  - General increases to NIH Institutes and Centers
  - Coronavirus supplemental appropriations
  - Allocations for the HEAL Initiative, the 21st Century Cures Act, the BRAIN Initiative, and research on influenza
  - Continued support for the Gabriella Miller Kids First Act pediatric research initiative
- NIAAA received a total of $554.9 million for 2021.

Preparation of the FY 2022 President's Budget is underway.

Selected Funding Opportunities

(See Director's Report for Complete Listing)

Issued by NIAAA

- SARS-CoV-2, COVID-19, and Consequences of Alcohol Use (R01/R03/R21) RFA-AA-21-002; RFA-AA-21-003; RFA-AA-21-004
- Specialized Alcohol Research Centers (P50) RFA-AA-21-005
- Comprehensive Alcohol Research Centers (P60) RFA-AA-21-006

NIH-wide with NIAAA participation

- BRAIN Initiative: Development and Validation of Novel Tools to Probe Cell-Specific and Circuit-Specific Processes in the Brain (R01) RFA-MH-21-175
- Emergency Award: RADx-UP - Social, Ethical, and Behavioral Implications (SEBI) Research on Disparities in COVID-19 Testing among Underserved and Vulnerable Populations (U01) RFA-OD-21-009
- NIH Blueprint and BRAIN Initiative Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00) RFA-NS-21-012

Special Notices for Early Career Investigators

- Notice of Special Interest: Availability of Administrative Supplements for Childcare Costs for Ruth L. Kirschstein National Research Service Award (NRSA) Individual Fellows NOT-OD-21-070, NOT-OD-21-074, NOT-OD-21-075
- Reminder – Requesting Extensions for Early Career Scientists Whose Career Trajectories Have Been Significantly Impacted by COVID-19 NOT-OD-21-052
- Notice of Continuation of Temporary Extension of Eligibility for the NIH K99/R00 Pathway to Independence Award During the COVID-19 Pandemic NOT-OD-21-106

Priority: Addressing Diversity and Health Disparities in the Alcohol Field

- NIAAA fully supports and is committed to the NIH UNITE initiative, a coordinated effort to address structural racism and promote racial equity and inclusion at NIH and within the larger biomedical research enterprise
  - see *www.nih.gov/ending-structural-racism*

- To advance equity, diversity, and inclusion in the alcohol research enterprise, NIAAA is also focusing on 3 primary areas:
  - improving the NIAAA intramural and extramural *workplace and culture*
  - increasing diversity and equity in the scientific and administrative alcohol research *workforce*
  - enhancing the NIAAA intramural and extramural scientific *research portfolio*

Priority: Addressing Health Disparities
Examples of Current Funding Opportunities

- *Improving Health Disparities in Alcohol Health Services*; RFA-AA-21-001
  - Health disparate and vulnerable populations face unique and intersecting barriers to treatment including but not limited to stigma, mistrust, bias, and structural racism
  - This new funding opportunity seeks to expand alcohol health services research on health disparities as well as encourage new studies on the accessibility, appeal, costs, dissemination, and implementation on alcohol use disorder treatment
- *Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities*; RFA-MD-21-004
  - Despite increased awareness of the contribution of racism and discrimination to poorer health outcomes, these issues are not routinely included as determinants of health in biomedical research
  - The goal of this initiative is to support observational or intervention research to understand and address the impact of structural racism and discrimination on minority health and health disparities

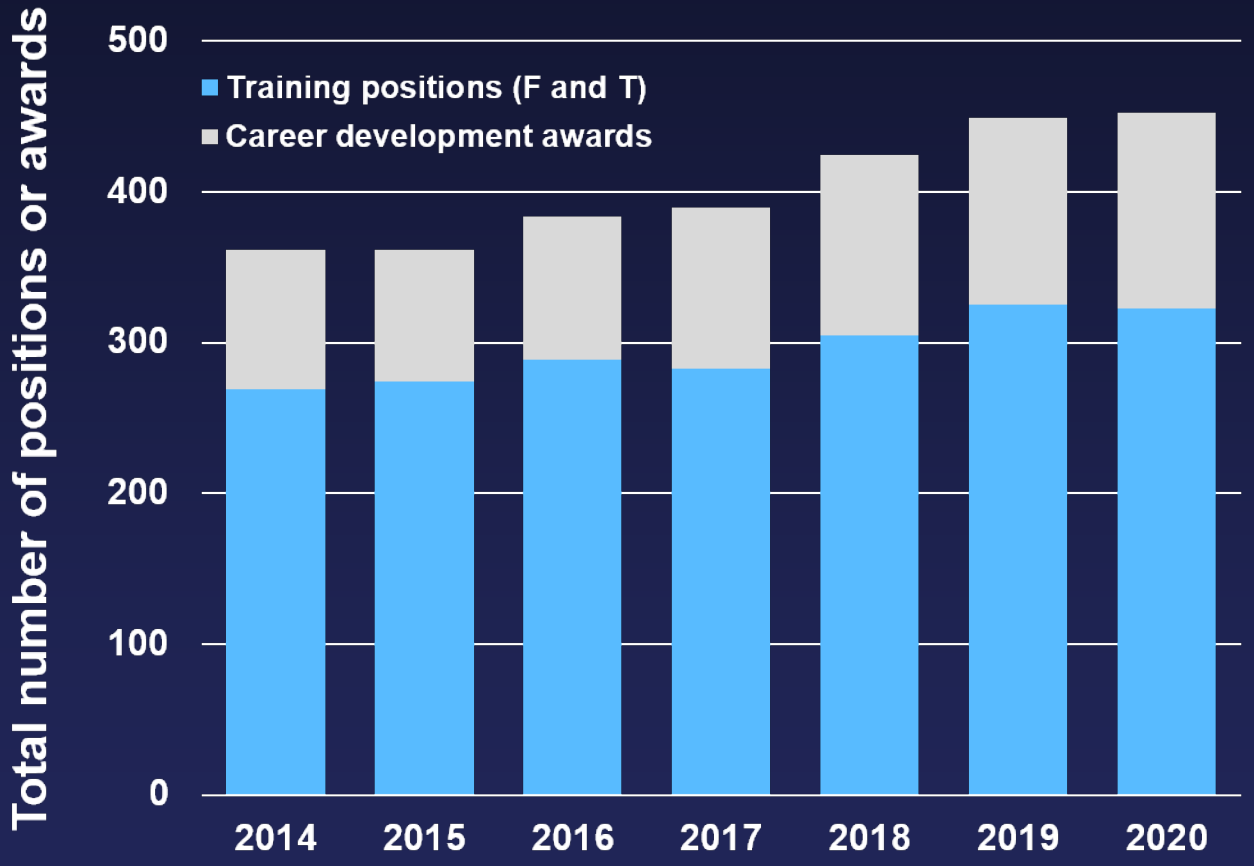
Priority: Training Opportunities to Support a Diverse Workforce

- NIH Ruth L. Kirschstein NRSA for Individual Predoctoral Fellowships to Promote Diversity in Health-Related Research (F31); PA-20-251
- NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00); RFA-NS-21-012
- BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity (K99/R00); RFA-NS-19-043; RFA-NS-19-044
- Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to Promote Diversity (K99/R00); PAR-19-343
- Diversity supplements (PA-21-071) provide supplements to existing NIH-funded active grants to increase the diversity of the research workforce by supporting and recruiting students, and postdoctoral and other new investigators from groups that are underrepresented
  - More details on our website: https://go.usa.gov/xHf2j

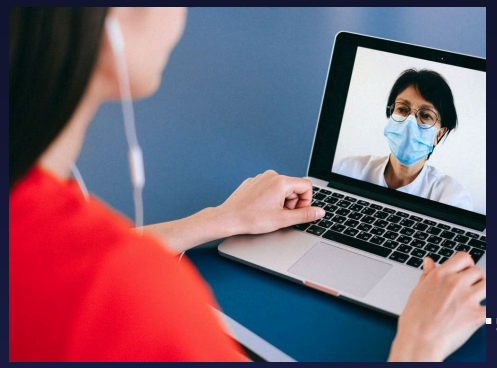
The NIAAA Research Training website has more information:
https://www.niaaa.nih.gov/research-training-and-career-development

Priority: Supporting the Next Generation of Alcohol Researchers

Increases in NIAAA Training and Career Development Awards



Priority: How Do We Envision the Role of Telehealth in Addressing Alcohol Use Disorder in the Post-Pandemic Era?



- The COVID-19 pandemic caused a rapid expansion in the use of telehealth
- Evidence suggests telehealth can be effective for addressing alcohol misuse and can reach people who might not otherwise get support (Kiluk et al., 2018; Oesterle et al., 2020)
- **NIAAA supports a variety of telehealth projects** (pre-pandemic and pandemic-related):
  - SBIRT with clinicians by phone or video chat
  - CBT with a clinician or self-guided (CBT4CBT)
  - Telehealth to address PTSD and alcohol use following sexual assault
  - Video-conferencing based MI for alcohol misuse and medication adherence in patients living with HIV
- The NIAAA Treatment Navigator links to effective options
  - *see* *https://alcoholtreatment.niaaa.nih.gov/*
- We anticipate a larger role for telehealth for alcohol prevention, treatment, and recovery going forward

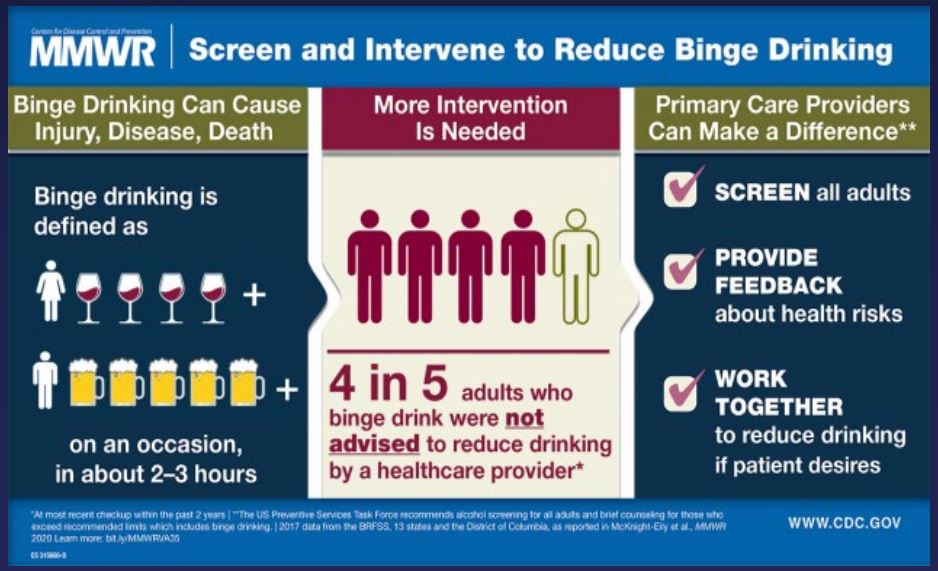
Priority: Expanding Uptake of SBI/SBIRT

(Screening, Brief Intervention/and Referral to Treatment)

- The U.S. Preventive Services Task Force recommends alcohol screening and brief intervention (alcohol SBI) or counseling in primary care settings for adults age 18 and older
- However, evidence highlights missed opportunities for healthcare providers to intervene with patients who report binge drinking

Among patients 18+ who saw a healthcare provider in the past 2 years:

- 81% were asked at least one question about their alcohol use, but only 38% were asked whether they binged in the past month
- Among those who reported binge drinking, about 1 in 5 were given advice to cut down
- Women were less likely than men to be advised about the risks of binge drinking (33% vs 47%)
- Women who reported binge drinking were less likely to be advised to cut down than men who reported binge drinking (14% vs 25%)
- Older drinkers (65+) less likely to be screened or advised to cut down!



McKnight-Eily LR, Okoro CA, Turay K, Acero C, Hungerford D. MMWR Morb Mortal Wkly Rep. 2020 Mar 13;69(10):265-270.

Priority: SBI/SBIRT Offers An Opportunity to Narrow the Treatment Gap

According to 2018-2019 NSDUH data:

- Very few people who report drinking to a healthcare provider are asked if they have any problems related to their drinking (~7%) and even fewer (<5%) are offered additional information about alcohol or advised to cut down

This is concerning for multiple reasons:

- Many patients are prescribed medications that could interact negatively with alcohol
- Alcohol misuse is increasing among women and older drinkers, two groups that are less likely to be given advice or offered more information about alcohol

Alcohol screening has other implications for health:

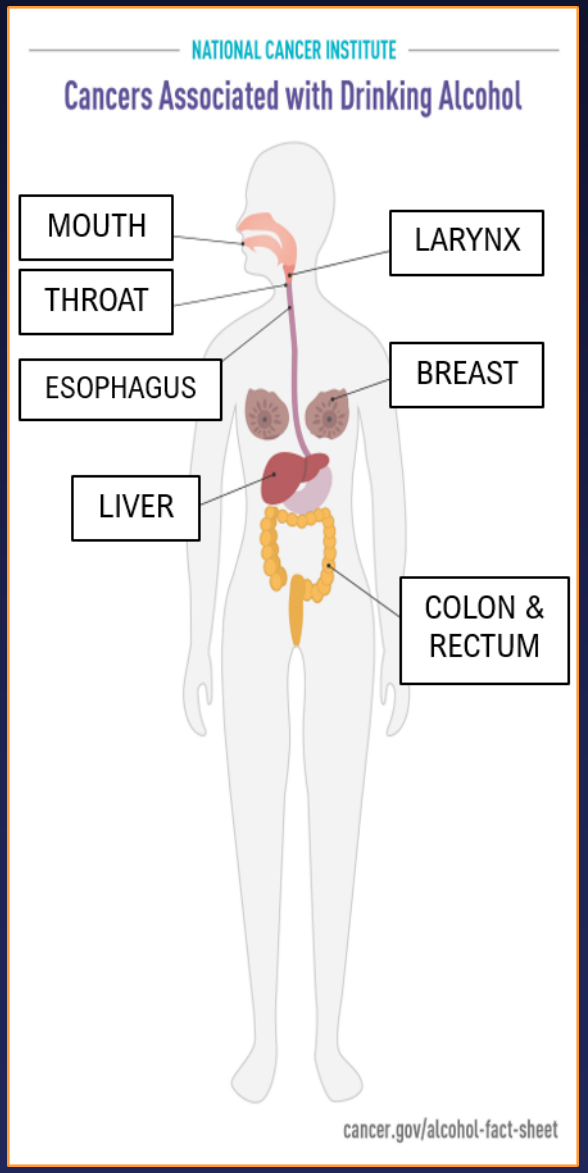
- Questions about alcohol misuse can provide clues about other important aspects of health (e.g., binge drinkers are more likely to have serious thoughts of suicide and to misuse Rx opioids or sedatives)

NIAAA's core resource for healthcare providers aims to provide physicians the information they need to become more comfortable discussing alcohol misuse with patients *(Coming later this year!)*

Healthy People 2030 is an HHS initiative that has outlined a goal of increasing the percentage of people with SUDs receiving specialty treatment from 11% to 14%. SBIRT offers a route for achieving this goal!

Priority: Alcohol and Cancer

- American Cancer Society estimates that about 41% of men and 39% of women will eventually develop cancer, and about 5.6% of newly diagnosed cases are alcohol-attributable.
- A recent study estimated that 75,000 new cancer cases—and 19,000 cancer deaths—per year are attributed to alcohol consumption in America. (Goding Sauer et al., 2021)
- Surveys reveal a common lack of awareness:
  - A 2017 survey from the American Society for Clinical Oncology found that of 4,016 respondents, fewer than one-third recognized that alcohol can cause cancer
  - Similarly, a 2019 survey from the American Institute for Cancer Research found that fewer than 50% of respondents recognized the cancer risks posed by alcohol
- *Reminder* Notice of Special Interest: Alcohol and Cancer Control NOT-CA-20-034 (NIAAA and NCI)

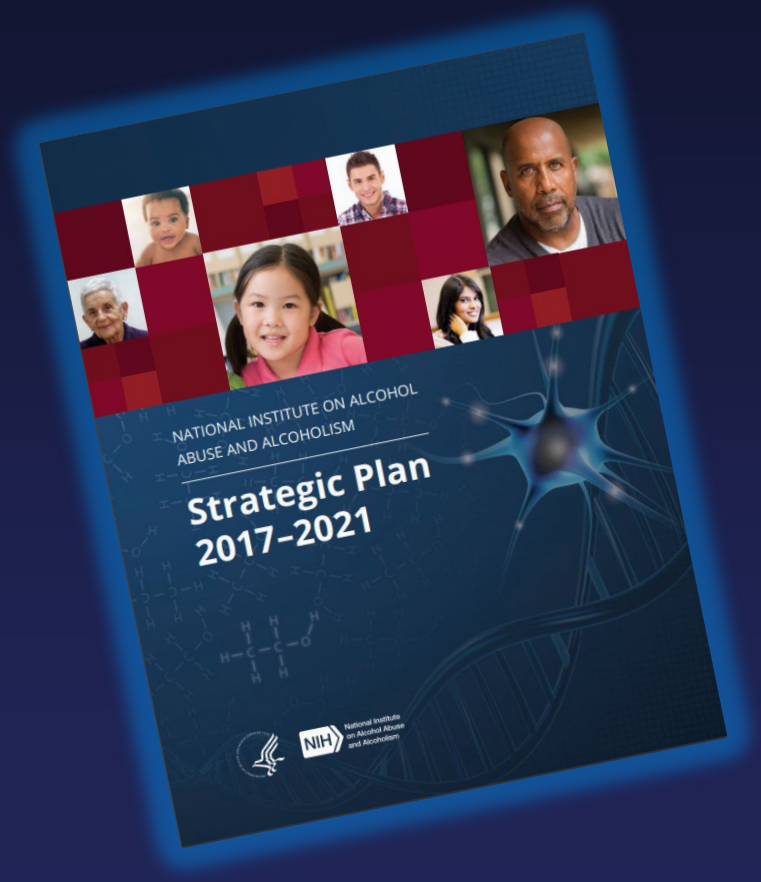


NESARC-III Genetic Data Now Available to Researchers

- The NESARC-III is a large, nationally representative epidemiologic survey of substance use and mental health in adults in the United States. More than 36,000 people aged 18 and older were interviewed in 2012-2013. Among them, roughly 23,000 also provided samples of their DNA. Genetic data are now available to the research community.
- **The combination of genotypic data and phenotypic data about substance use and mental health makes NESARC-III unique:** Exploration of the new genetic dataset with its rich phenotypic and family background variables could yield important insight into the relationships between genes and observable behaviors, including AUD and other substance use disorders, depression, post-traumatic stress disorder and other conditions, all diagnosed using criteria from the DSM-5.
- The NESARC-III genetic dataset will be a critical resource for helping scientists to better understand these disorders and develop novel diagnostic methods and treatments.

For more information, view the news release on the NIAAA website:
https://go.usa.gov/xHfTt

On the Horizon:
A New Strategic Plan for NIAAA



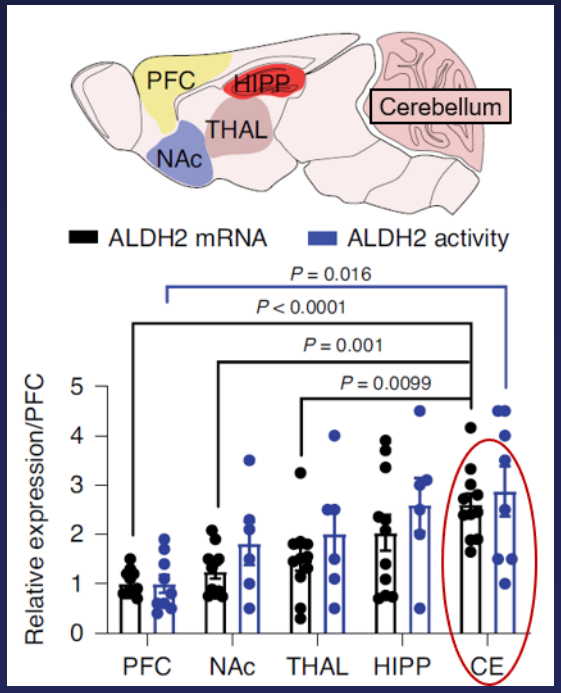
- We are currently developing the 2022-2026 Strategic Plan
- Stay tuned for a public "Request for Information" – your opportunity to weigh in on our priorities and objectives

Research Highlights

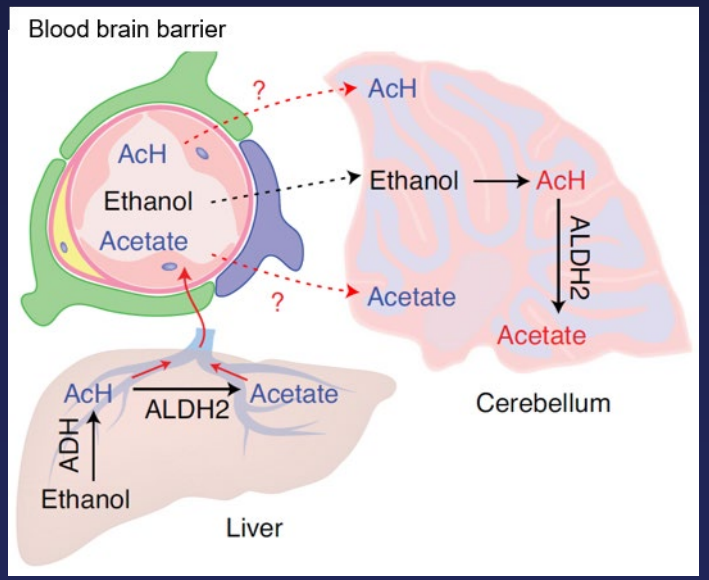
Brain Ethanol Metabolism by Astrocytic ALDH2 Drives the Behavioral Effects of Ethanol Intoxication (Slide 1 of 2)

Ethanol metabolites such as acetate, thought to be primarily the result of ethanol breakdown by hepatic aldehyde dehydrogenase 2 (ALDH2), contribute to behavioral effects of alcohol. The possibility that ethanol is metabolized inside the brain has been a long-standing topic of controversy in alcohol research. Researchers first examined ALDH2 expression in multiple brain regions. Because ALDH2 was most abundant in the cerebellum, they next explored the cell-type-specific distribution of ALDH2 in this brain region.

ALDH2 mRNA expression and activity in 5 brain regions



Schematic of metabolic pathways from ethanol to acetate in the liver and brain



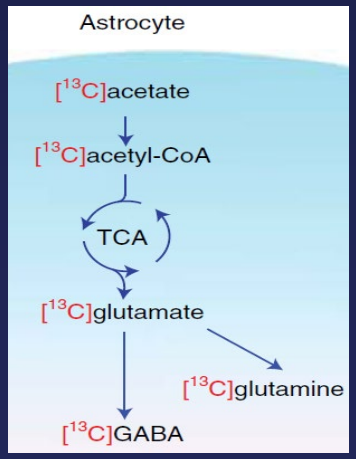
Jin S, Cao Q, Yang F, Zhu H, Xu S, Chen Q, Wang Z, Lin Y, Cinar R, Pawlosky RJ, Zhang Y, Xiong W, Gao B, Koob GF, Lovinger DM, Zhang L. *Nat Metab.* 2021 Mar;3(3):337-351.

Brain Ethanol Metabolism by Astrocytic ALDH2 Drives the Behavioral Effects of Ethanol Intoxication (Slide 2 of 2)

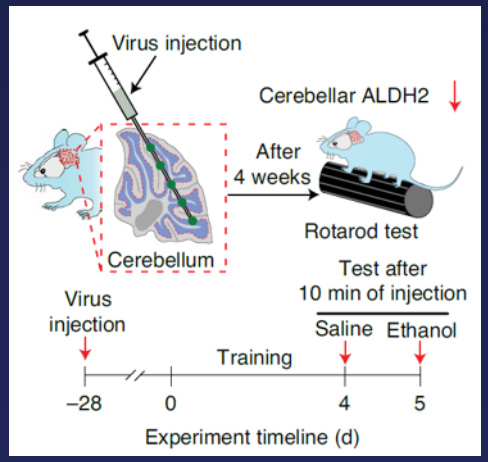
Ethanol metabolites such as acetate, thought to be primarily the result of ethanol breakdown by hepatic aldehyde dehydrogenase 2 (ALDH2), contribute to behavioral effects of alcohol. The possibility that ethanol is metabolized inside the brain has been a long-standing topic of controversy in alcohol research.

Investigators identified the presence of ALDH2 in the brains of both humans and mice in cerebellar astrocytes. Astrocytic ALDH2 was found to mediate both ethanol- and acetate-induced cellular and behavioral effects, including impairment of balance and coordination skills, via GABAergic signaling. The findings indicate astrocytic ALDH2 as a potential target for the pathophysiology of alcohol use disorder.

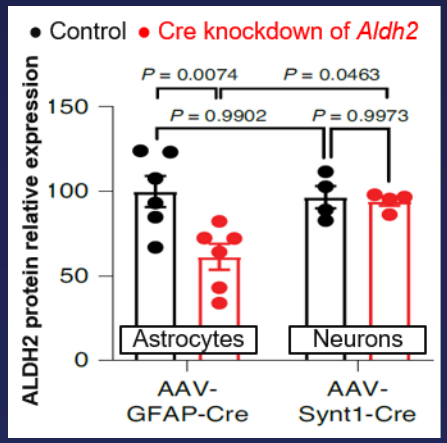
Hypothetical diagram of ethanol, acetate, and GABA synthesis in astrocytes



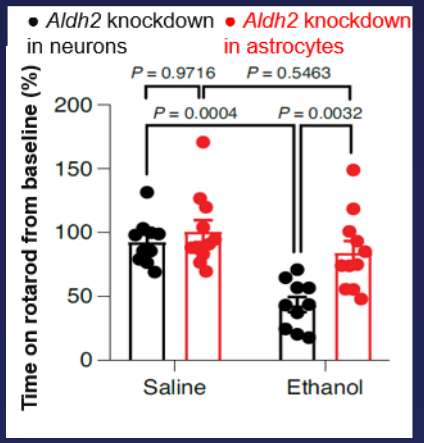
Experimental overview: Viral knockdown of Aldh2 followed by behavioral testing



Knockdown of cerebellar Aldh2 in astrocytes but not neurons resulted in reduced expression of ALDH2 protein



Cerebellar knockdown of Aldh2 in astrocytes reduces ethanol-induced motor impairment in the rotarod test



Jin S, Cao Q, Yang F, Zhu H, Xu S, Chen Q, Wang Z, Lin Y, Cinar R, Pawlosky RJ, Zhang Y, Xiong W, Gao B, Koob GF, Lovinger DM, Zhang L. *Nat Metab.* 2021 Mar;3(3):337-351.

TRAIL Mediates Neuronal Death in AUD: A Link between Neuroinflammation and Neurodegeneration

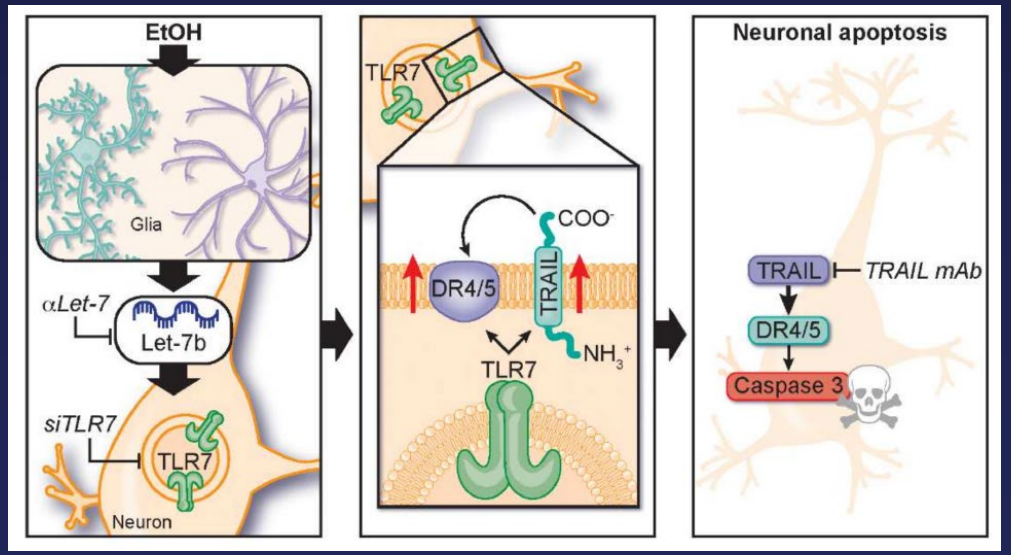
Analysis of postmortem human cortex of individuals diagnosed with alcohol use disorder (AUD) implicated the induction of tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) apoptotic death receptors as a mediator of neuronal death. TRAIL acts via the Toll-like receptor 7 (TLR7) neuroimmune signaling pathway and its endogenous ligand, microRNA let-7b.

Chronic binge levels of ethanol exposure in mice increased let-7b/TLR7 signaling and enhanced TLR7-mediated cell death responses through TRAIL, mimicking the increased TLR-7 induction and neurodegeneration observed in human cortex in AUD. Additionally, inhibition of TLR7 and let-7b blocked ethanol-induced neuronal death. Together, these findings suggest that TRAIL is a mediator of neuronal death involving TLR7 activation in AUD.

Ethanol causes induction of both let-7b and TLR7

TLR7 induces expression of death receptor ligand TRAIL and its receptors

TRAIL induces neuronal death through induction of caspase cascades

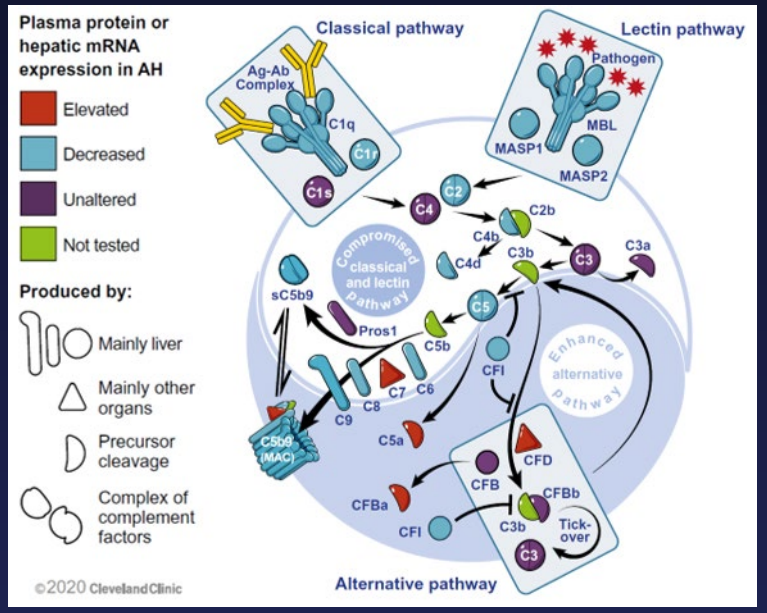


Qin L, Zou J, Barnett A, Vetreno RP, Crews FT, Coleman Jr LG. *Int J Mol Sci*. 2021 Mar 4;22(5):2547.

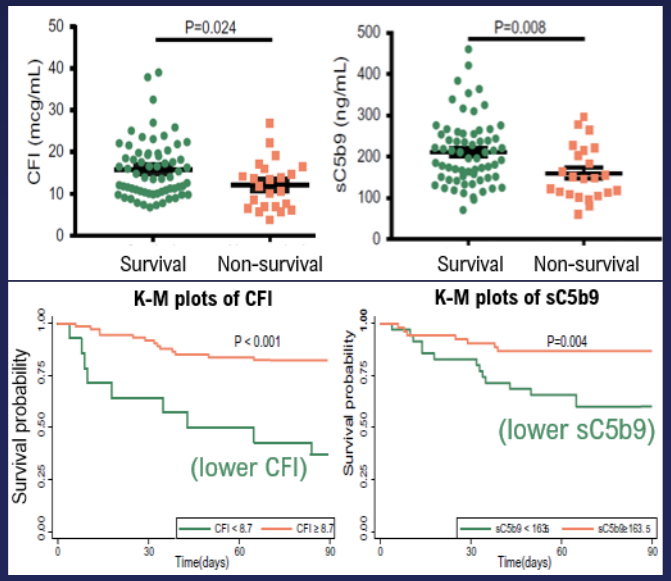
Diagnostic and Prognostic Significance of Complement in Patients with Alcohol-Associated Hepatitis (AH)

Researchers compared plasma samples of participants with moderate or severe AH to healthy controls to assess whether complement proteins, which have a critical role in the innate immune system, correlated with AH disease status and progression. Complement factor I (CFI) and soluble complement 5b-9 (sC5b9) were decreased in non-survivor AH participants and predicted 90-day mortality.

Schematic summary of dysregulation of expression and activation of complement in AH



CFI and sC5b9 were decreased in non-survivor AH patients and predict 90-day mortality



Integration of CFI and sC5b9 with current models for predicting 90-day mortality, including MELD (Model for End-Stage Liver Disease) and mDF (Maddrey's discriminant function), improved predictions compared to current models alone. Results suggest that complement factors are valuable diagnostic and prognostic biomarkers in patients with AH.

Fan X, McCullough RL, Huang E, Bellar A, Kim A, Poulsen KL, McClain CJ, Mitchell M, McCullough AJ, Radaeva S, Barton B, Szabo G, Dasarathy S, Rotroff DM, Nagy LE. *Hepatology*. 2021 Mar;73(3):983-997.

Evaluation of the Addictions Neuroclinical Assessment (ANA) Framework through Deep Phenotyping of Problem Drinkers

ANA is a neuroscience-informed framework for addictive disorders that captures three functional domains: incentive salience, negative emotionality, and executive function.

Investigators conducted an independent test of the ANA framework using a large clinical sample of participants across a range of alcohol misuse phenotypes. Participants completed a battery of scales and behavioral tasks of alcohol use and misuse, mood, attention, and impulsivity, which were analyzed to derive a factor solution that explained biobehavioral variation in the sample.

Results implicated four functional domains that complemented and extended the ANA domains: negative alcohol-related consequences, incentive salience, negative emotionality, and executive function. Of note, ANA domains were distinct from latent factors that reflect AUD phenomenology (i.e., alcohol-related consequences). This study largely supports and extends the ANA framework for understanding the heterogeneity in AUD.

Pattern matrix for the exploratory factor analysis using measures from several domains

Incentive salience | Negative emotionality | Executive function

	Latent Factors (Eigenvalues / % Variance Explained)				
	Factor 1 35.66 / 66.65 %	Factor 2 6.65 / 12.44 %	Factor 3 4.56 / 8.53 %	Factor 4 3.64 / 6.81 %	Factor 5 2.98 / 5.57 %
ADS Loss of Control	**0.440**	0.385	0.196	0.245	0.115
ADS Obsessive	0.381	**0.685**	0.240	−0.147	0.055
ADS Withdrawal	**0.427**	0.337	0.357	−0.112	0.079
AUDIT Consumption	0.273	**0.544**	0.049	0.066	0.022
AUDIT Dependence	**0.508**	**0.630**	0.156	−0.177	0.031
AUDIT Problems	**0.578**	**0.419**	0.201	−0.022	0.054
BAI Total	0.303	0.286	**0.599**	−0.020	0.200
BDI Total	0.226	0.185	**0.738**	−0.180	0.025
STAI Trait	0.249	0.201	**0.882**	−0.033	0.050
OCDS Obsessive	0.390	**0.686**	0.247	−0.158	0.043
OCDS Compulsive	0.355	**0.753**	0.212	0.036	0.095
PACS Total	0.218	**0.812**	0.207	−0.036	0.048
Digit Span Forward	0.012	0.058	−0.125	**0.725**	0.042
Digit Span Backward	−0.048	0.037	−0.106	**0.770**	0.048
BIS Motor	0.125	0.145	0.181	0.025	**0.635**
BIS Nonplanning	−0.096	−0.095	−0.165	0.087	0.356
BIS Attentional	0.090	0.125	0.179	−0.007	**0.847**
Delay Discounting (k)	0.096	0.214	−0.044	**−0.407**	−0.018
DrInC Physical	**0.705**	**0.404**	0.269	0.008	0.045
DrInC Interpersonal	**0.865**	0.286	0.145	−0.150	0.005
DrInC Intrapersonal	**0.777**	0.224	0.267	−0.068	0.006
DrInC Impulse Control	**0.740**	0.326	0.123	−0.049	0.045
DrInC Social Responsibility	**0.829**	0.272	0.170	−0.035	0.017

Nieto SJ, Grodin EN, Green R, Ray LA. *Drug Alcohol Depend*. 2021 Apr 1;221:108603.

Changes in Young Adults' Alcohol and Marijuana Use, Norms, and Motives From Before to During the COVID-19 Pandemic

Individual changes in alcohol and marijuana use, norms, and motives during the COVID-19 pandemic were estimated in a community sample of young adults (median age 25) from Washington state. Using a repeated measures design, data were collected prior to the pandemic (January 2020) and again following the implementation of major physical/social distancing restrictions (April/May 2020).

The results indicated an increase in the frequency of alcohol consumption with no significant change in the total amount of alcohol consumed on average. No variation in marijuana use was identified. Young adults overestimated peer alcohol/marijuana use compared to actual rates, but correctly perceived an increase in alcohol use frequency. Motives for alcohol and marijuana use also changed during the pandemic.

Social-related motivation for alcohol use decreased while depression/coping motives increased. Celebration-related motives for marijuana use decreased while boredom motives increased.

Alcohol and marijuana use motives before and during pandemic with regression models estimating change over time

Variable	Pre-COVID Mean (*SD*)	During-COVID Mean (*SD*)	Effect of time (*b*)	*p*	BH adjusted *p*	95% confidence interval	% That decreased	% That was unchanged	% That increased
Alcohol Use Motives ($n = 505$)									
Anxiety Coping Motives	2.08 (.85)	1.99 (.79)	−.06	.163	.163	[−.15, .02]	44.62%	17.41%	37.97%
Depression Coping Motives	1.38 (.68)	1.48 (.76)	**.11**	**.001**	**.002**	**[.04, .18]**	24.45%	37.30%	38.24%
Social Motives	2.76 (.95)	1.77 (.82)	**−.97**	**<.001**	**<.001**	**[−1.07, −.87]**	86.60%	4.42%	9.78%
Enhancement Motives	2.66 (.99)	2.42 (1.08)	**−.21**	**<.001**	**<.001**	**[−.30, −.11]**	56.47%	11.04%	32.49%
Conformity Motives	1.22 (.49)	1.15 (.46)	**−.08**	**.003**	**.004**	**[−.13, −.03]**	22.88%	68.65%	8.46%
Marijuana Use Motives ($n = 265$)									
Enjoyment Motives	3.60 (1.23)	3.62 (1.18)	.05	.578	.795	[−.13, .23]	42.44%	25.18%	32.37%
Conformity Motives	1.10 (.31)	1.08 (.32)	−.03	.325	.715	[−.08, .02]	10.79%	79.14%	10.07%
Coping Motives	1.57 (.92)	1.56 (.82)	.02	.801	.801	[−.11, .14]	22.96%	51.11%	25.93%
Experimentation Motives	1.20 (.55)	1.17 (.52)	−.05	.238	.655	[−.14, .03]	13.87%	76.64%	9.49%
Boredom Motives	2.07 (1.10)	2.42 (1.18)	**.36**	**<.001**	**<.001**	**[.19, .54]**	27.14%	26.43%	46.43%
Alcohol-Related Motives	1.28 (.68)	1.18 (.41)	−.10	.033	.121	[−.20, −.01]	15.01%	74.82%	10.07%
Celebration Motives	1.81 (1.00)	1.46 (.73)	**−.38**	**<.001**	**<.001**	**[−.54, −.21]**	44.20%	31.88%	23.91%
Altered Perceptions Motives	2.24 (1.35)	2.24 (1.26)	.02	.790	.801	[−.16, .20]	29.50%	34.53%	35.97%
Perceived Low Risk Motives	2.07 (1.27)	2.02 (1.19)	−.03	.710	.801	[−.18, .12]	27.14%	45.00%	27.86%
Sleep Motives	1.87 (1.13)	1.84 (.99)	−.05	.437	.740	[−.27, .08]	30.22%	42.44%	27.34%
Availability Motives	2.08 (1.08)	2.03 (.99)	−.05	.471	.740	[−.20, .09]	32.37%	37.41%	30.22%

Graupensperger S*, Fleming CB, Jaffe AE, Rhew IC, Patrick ME, Lee CM.
J Adolesc Health. 2021 Apr;68(4):658-665. **NIAAA-supported trainee*

Network Meta-Analysis on the Mechanisms Underlying Alcohol Augmentation of COVID-19 Pathologies

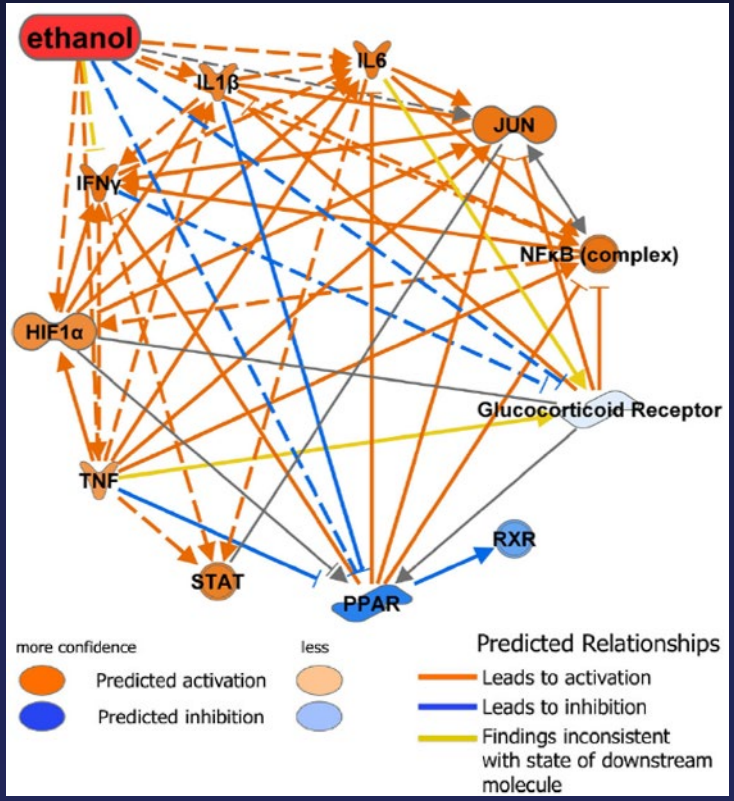
Investigators examined the possible relationships between alcohol exposure and COVID-19 pathologies by performing a network meta-analysis of gene expression changes reported in patients with COVID-19 derived from three sources:

- Literature searches
- Gene Expression Omnibus database (RNA-sequencing data from autopsied lungs of COVID-19 patients)
- Qiagen Coronavirus Network Explorer (QCNE)

Analysis indicated that alcohol **augmented** effects of SARS-CoV-2 on the **hepatic fibrosis signaling pathway, cellular metabolism and homeostasis, inflammation, and neuroinflammation** and **inhibited** effects of SARS-CoV-2 on anti-inflammatory mediators such as the **glucocorticoid receptor.**

These findings suggest that alcohol consumption may augment SARS-CoV-2-induced inflammation by altering the activity of key inflammatory mediators, potentially leading to poorer clinical outcomes.

Connectivity map and action of alcohol on the key molecules consistently identified in the top 10 canonical pathways, upstream regulators, or networks regulated by predicted top upstream regulators in the pathway analysis for core analysis of molecules affected by both alcohol and COVID-19



Huang W, Zhou H, Hodgkinson C, Montero A, Goldman D, Chang SL. *Alcohol Clin Exp Res.* 2021 Feb 13;10.1111/acer.14573.

THANK YOU!

Special thanks to:

Rachel Anderson

Abe Bautista

Cara Breeden

Judit O'Connor

Patricia Powell

Pamela Wernett

Aaron White

Bridget Williams-Simmons