NIAAA Director’s Report on Institute Activities to the 138th Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

February 5, 2015
Rockville, MD

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

National Institute on Alcohol Abuse and Alcoholism

(Dollars in Thousands)

<table>
<thead>
<tr>
<th></th>
<th>FY 2013 Actual</th>
<th>FY 2014 Enacted</th>
<th>FY 2015 President's Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-AIDS</td>
<td>406,000</td>
<td>417,947</td>
<td>418,604</td>
</tr>
<tr>
<td>AIDS</td>
<td>26,732</td>
<td>27,464</td>
<td>27,413</td>
</tr>
<tr>
<td>Total</td>
<td>432,732</td>
<td>445,411</td>
<td>446,017</td>
</tr>
</tbody>
</table>
NIAAA Budget - FY 2014

• Fiscal Year (FY) 2014 closed on September 30th.

• FY 2014 appropriation for NIAAA: $446 million.

• Within this appropriation, NIAAA:
  – Awarded 657 research project grants (RPGs), including 180 competing awards (success rate of 19%).
  – Funded 17 research centers for $26.4 million.
  – Funded 137 other research grants for $36.1 million, including Career awards, one Cooperative Clinical Agreement, and several resource and conference grant awards.
  – Supported 269 full-time training positions for $11.6 million.
  – Funding for our Research and Development (R&D) contract portfolio was $36.5 million.
  – Support for intramural research totaled $49.0 million.
NIAAA Budget - FY 2015

- The Consolidated and Further Continuing Appropriations Act for FY 2015 was signed by the President on December 16, 2014.

- NIH received a total of $30.3 billion, $150 million above the FY 2014 level.

- NIAAA received $447.4 million, $1.4 million or 0.3% above the FY 2014 level.

- NIAAA estimates it will support a total of 668 RPGs in FY 2015, including 167 competing awards.
NIAAA Budget - FY 2016

• Preliminary work on the budget for FY 2016 is beginning. After intermediate stages of review, the President’s budget request will be presented to Congress in February 2015, at which time it will become available to the public.
**Staff Transitions**

**New Staff**

- **Dr. Jennifer A. Hobin** joined the Office of Science Policy and Communications, Science Policy Branch in October 2014 as a *Senior Health Science Policy Analyst*. Dr. Hobin comes to NIAAA from the American Association for Cancer Research where she served as Director of Science Policy. Prior to AACR, Jennifer spent seven years at the Federation of American Societies for Experimental Biology where she worked on a broad range of research policy issues and played an instrumental role in the development of a “myIDP,” a career planning tool for scientists.

- **Dr. Falk Lohoff** recently joined the Laboratory of Clinical & Translational Studies, Division of Intramural Clinical and Biological Research, as *Chief of the Section on Clinical Genomics and Experimental Therapeutics*. Dr. Lohoff was Assistant Professor of Psychiatry at the University of Pennsylvania from 2007-2014, after which he joined the NIH intramural program as a Lasker Clinical Research Scholar. His research is focused on translational medicine and spans areas of molecular genetics, epigenetics, imaging-genetics, pharmacogenetics, and clinical experimental trials.
Staff Transitions

New Staff

- **Joan Romaine, M.P.H.**, joined the Office of the Director as a Health Specialist in the HIV/AIDS Research Program. Joan’s background is in public health, with a focus on international health policy and programs. Joan comes to NIAAA from the NIH Office of AIDS Research (OAR) where she spent three years working on OAR-supported HIV/AIDS bilaterals with Russia and South Africa, as well as overseeing the Program Planning and Analysis group, which is responsible for the coordination of the development of the Trans-NIH Plan for HIV-Related Research and OAR’s Advisory Council.

New Positions

- **Erin Manor** was selected to fill the position of Chief, Administrative Services Branch. Previously, Erin served as the Intramural Research Program Section Chief at NIAAA. Prior to NIAAA, Erin was a Supervisory Administrative Officer with NIMH, and also worked with the Intramural Research Program of NIDA in Baltimore.
Honors & Awards

- **Dr. George Koob** received the 2014 Innovator Award from the Treatment Research Institute in recognition of his scientific contributions and outstanding leadership in advancing understanding of how the brain and body respond to alcohol consumption.

- **Dr. Kari Johnson**, postdoctoral fellow in the Section on Synaptic Pharmacology, Laboratory for Integrative Neuroscience, was awarded a Postdoctoral Research Associate (PRAT) fellowship. The award was effective October 1, 2014. This is a prestigious fellowship given to outstanding trainees for training in pharmacological sciences.
New RFAs and PAs (NIAAA Issued)

• Alcohol Biosensors (STTR/SBIR) (R41-44)

• Consortium on the Neurobiology of Adolescent Drinking in Adulthood (NADIA) (U01/U24)

• Investigational New Drug (IND)-enabling Development of Medications to Treat Alcohol Use Disorder and Alcohol-related Disorders (UT2/U44)

• Alcohol Education Project Grants (R25)

• Mechanistic Studies of Pain and Alcohol Dependence (R01)

• Secondary Analyses of Existing Alcohol Epidemiology Data (R01/R03/R21)

• Unconventional Roles of Ethanol Metabolizing Enzymes, Metabolites, and Cofactors in Health and Disease (R01/R21)
New RFAs and PAs (NIAAA Participating)

- NIAAA is participating in new FOAs on the following topics:
  - NIH BRAIN Initiative
  - NIH Big Data to Knowledge (BD2K) Initiative
  - Systems science and health in behavioral and social sciences
  - Tobacco regulatory research
  - Pediatric HIV/AIDS
  - Behavioral targets to improve adolescent substance abuse interventions
  - Research on sex and gender

- Collaborating ICs include: NIDA, NINDS, NIMH, NICHD, NCI, NLM.
**Significance:** Higher levels of maternal alcohol consumption during pregnancy were associated with lower levels of axial diffusivity (a measure of axonal structural integrity) in white matter fiber tracts in the brain of two-week-old human newborns; levels of radial diffusivity (a measure of myelination) were not. (Taylor PA, Jacobson SW, van der Kouwe A, Molteno CD, Chen G, Wintermark P, Alhamud A, Jacobson JL, and Meintjes EM. *Human Brain Mapping* 2014 Sept 3 [Epub].)

Examples of parameter maps and whole brain tractography for one healthy control (left) and one prenatal alcohol exposed infant (right).
MICRORNA-30A-5P IN THE PREFRONTAL CORTEX CONTROLS THE TRANSITION FROM MODERATE TO EXCESSIVE ALCOHOL CONSUMPTION

**Significance:** A causal link between alcohol-induced miRNA expression and regulation of BDNF on binge alcohol consumption was demonstrated by genetically manipulating the expression of miRNA in the prefrontal cortex. These effects were specific to mice that transitioned from moderate to binge consumption. (Darcq E, Warnault V, Phamluong K, Besserer GM, Liu F, and Ron D. *Mol Psychiatry.* 2014 Nov 11 [Epub].)

Excessive alcohol consumption decreases BDNF expression and increases miRNA expression in the medial prefrontal cortex.
Significance: Adolescent voluntary binge drinking reduces the density of myelinated axons in the medial prefrontal cortex and has long-lasting effects on prefrontal white matter. (Vargas WM, Bengston L, Gilpin NW, Whitcomb BW, and Richardson HN. J. Neuroscience. 34(44):14777-14782; 2014.)

Adolescent alcohol decreases myelinated fiber density in the medial prefrontal cortex and predicts poor T-maze performance in adulthood.
DURABLE FEAR MEMORIES REQUIRE PSD-95

**Significance:** Genetically interfering with a key synaptic plasticity molecule, PSD-95, in the prefrontal cortex led to a significant weakening of fear memories in mice. Targeting PSD-95-related mechanisms represents a novel approach to alleviating trauma-related anxiety associated with AUD. (Fitzgerald PJ, Pinard CR, Camp MC, Feyder M, Sah A, Bergstrom H, Graybeal C, Liu Y, Schlüter O, Grant SGN, Singewald N, Xu W, and Holmes A. *Molecular Psychiatry*. 2014, 1-12.)

**PSD-95 deletion disrupts activation of the infralimbic cortex during remote fear memory retrieval.**
OSTEOPONTIN DEFICIENCY DOES NOT PREVENT BUT PROMOTES ALCOHOLIC NEUTROPHILIC HEPATITIS IN MICE

**Significance:** A high saturated fat/high cholesterol diet (HCFD) and continual intra-gastric alcohol infusion (ALC), plus weekly “binge” administration of alcohol generates a high level of liver injury in mice with histopathological and clinical features remarkably similar to those observed in humans. Osteopontin exerts a protective role. This animal model is a promising tool for better understanding human alcoholic hepatitis. (Lazaro R, Wu R, Lee S, Zhu NL, Chen CL, French SW, Xu J, Machida K and Tsukamoto H. *Hepatology*. 2014 Nov 25 [Epub].)

**Liver qPCR analysis shows up-regulation of myeloperoxidase, Gro-α and osteopontin in HCFD+ALC+binge mice.**

**In HCFD+ALC+binge mice, hepatic mRNA expression of interleukin (IL)-17a was markedly increased; IL-22 was reduced.**
Where we want to be

1. FDA approval for medications for treatment of alcoholism
2. Implementation of effective behavioral treatments for alcoholism
3. Implementation of effective prevention strategies for adolescent drinking
4. Implementation of effective prevention strategies for drinking during pregnancy
5. Elimination of alcohol-related HIV pathology
6. Establishment of effective treatments for fetal alcohol spectrum disorder (FASD)
7. Development of effective treatments for alcoholic liver disease
8. Appropriate treatment of co-morbidities associated with alcoholism
9. Successful recruitment of young investigators to the alcohol field; elimination of disparities in the alcohol field; equal pay for women and minorities in the alcohol field.
Key NIAAA Initiatives and Programs

1. Fetal Alcohol Syndrome/ Fetal Alcohol Spectrum Disorders – Early Diagnosis
2. Underage and College Drinking – N-CANDA, ABCD, CollegeAIM
3. Treatment – Medications Development
4. Co-Morbidity – PTSD
5. Alcoholic Liver Disease
6. Alcohol and HIV/AIDS
7. Biosensors
ABCD Funding Opportunity Announcements (FOAs)

- Participating Organization(s)
  - National Institute on Drug Abuse (NIDA)
  - National Institute on Alcohol Abuse and Alcoholism (NIAAA)
  - National Cancer Institute (NCI)
  - Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
  - National Institute of Mental Health (NIMH)
  - National Institute on Minority Health and Health Disparities (NIMHD)
  - Office of Behavioral and Social Sciences Research (OBSSR)

- Funding Opportunity Titles
  - Adolescent Brain Cognitive Development (ABCD) Study - Coordinating Center (U24)
  - Adolescent Brain Cognitive Development (ABCD) Study - Research Project Sites (U01)
  - Adolescent Brain Cognitive Development (ABCD) Study - Data Analysis and Informatics Center (U24)
New: Request For Proposals (RFP)

Title: Human Laboratory Paradigms (HLAB)  
NIH-NIAAA-DTRR-2015-04

• Issued on February 3, 2015
• Seeking contractors to form a network of highly experienced, quality laboratory sites capable of conducting multiple human laboratory paradigms
• HLAB will serve as screening model for candidate compounds to treat alcohol use disorder
• Pre-Proposal Teleconference: March 3, 2015, 10:00 AM
• Due date: April 9, 2015
• Information: Jacquelin Jones, Contracting Officer phone: 301-435-6965 or email: jacquelin.jones@nih.gov
Thank You!

Special Thanks
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health

Vivian Faden
Joanne Fertig
Bob Huebner
Keith Lamirande
Raye Litten
Peggy Murray
Antonio Noronha
Patricia Powell
Kenneth Warren