Director’s Report to the National Advisory Council on Drug Abuse

February 3, 2015

Nora D. Volkow, M.D., Director

National Institute on Drug Abuse
In Memoriam

• Studied environmental, historical, and pharmacological determinants of the behavioral and cardiovascular effects of drugs

• Developed experimental procedures and identified mechanisms of drug reward and relapse

• Contributed to NIDA’s Medication development Program

Steven R. Goldberg, Ph.D.
Senior Investigator
Chief, Preclinical Pharmacology Section
NIDA Intramural Research Program
National search for DESPR Director underway
Director’s Report to the National Advisory Council on Drug Abuse

- Budget Update
- What’s New @ HHS/NIH?
- Recent NIDA Activities & Events
<table>
<thead>
<tr>
<th></th>
<th>FY 2014 Actuals</th>
<th>FY 2015 Enacted</th>
<th>FY 2016 PB</th>
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<tbody>
<tr>
<td><strong>NonAIDS</strong></td>
<td>$717,243</td>
<td>$716,843</td>
<td>$745,186</td>
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<tr>
<td><strong>AIDS</strong></td>
<td>$300,714</td>
<td>$298,862</td>
<td>$302,211</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>$1,017,957</td>
<td>$1,015,705</td>
<td>$1,047,397</td>
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</table>
30% Budget is for AIDS research
Director’s Report to the National Advisory Council on Drug Abuse

• Budget Update

• What’s New @ HHS/NIH?

• Recent NIDA Activities & Events
NIH BRAIN initiative

Brain disorders -- a leading source of disease burden and cost in the U.S.

Recent breakthroughs are transforming how we study brain structure and function.

The BRAIN initiative builds on this recent progress to create tools that will accelerate discovery and build the foundation we need to reduce the burden of brain disorders.
Funding in FY14

- $46M invested in 58 projects across 6 RFAs
- > 100 investigators in 15 states and 3 countries

<table>
<thead>
<tr>
<th>RFA</th>
<th>Topic</th>
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</thead>
<tbody>
<tr>
<td>MH-14-215</td>
<td>Cell-Type Classification</td>
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<tr>
<td>MH-14-216</td>
<td>Novel Tools - Cells and Circuits</td>
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<tr>
<td>MH-14-217</td>
<td>Next Generation Human Imaging</td>
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<td>NS-14-007</td>
<td>Large scale Recording &amp; Modulation – New Technologies</td>
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<td>NS-14-008</td>
<td>Large scale Recording &amp; Modulation – Optimization</td>
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<tr>
<td>NS-14-009</td>
<td>Integrated Approaches to Understanding Circuit Function</td>
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</table>
Brain Cell Types

Tools for Circuit Diagrams

Tech. to Monitor Neural Activity

Precise Interventional Tools

Theory and Data Analysis Tools

Advance Human Neuroscience

Integrate Approaches

Cell-Type Classification
10 awards

Novel Tools – Cells and Circuits
10 awards

Next Generation Human Imaging
9 awards

Large-scale Recording & Modulation 2 RFAs, 19 awards

Integrated Approaches to Understand Circuit Function:
10 awards
### NIH Investment in 2015

<table>
<thead>
<tr>
<th>Source</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Blueprint for Neuroscience Research (BP)</td>
<td>$9M</td>
</tr>
<tr>
<td>Mental Health (NIMH)</td>
<td>$12.38M</td>
</tr>
<tr>
<td>Neurological Disorders and Stroke (NINDS)</td>
<td>$12.3M</td>
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<tr>
<td>Base Funding Established FY14</td>
<td>$40M</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>~$74M</td>
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$25M is “new money” in FY 15 Appropriation
Funding in FY15

• $25M in new funds
• Plans for short courses and projects in human neuroscience
• Reissue:

<table>
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<tr>
<th>RFA</th>
<th>Topic</th>
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<tbody>
<tr>
<td>MH-15-200</td>
<td>Next Generation Human Imaging</td>
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<tr>
<td>NS-15-003</td>
<td>Large scale Recording &amp; Modulation – New Technologies</td>
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<td>NS-15-004</td>
<td>Large scale Recording &amp; Modulation – Optimization</td>
</tr>
<tr>
<td>NS-15-005</td>
<td>Integrated Approaches to Understanding Circuit Function</td>
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</table>
Common Fund New Programs for FY 2015

**SPARC- Stimulating Peripheral Activity to Relieve Conditions**
Investigating peripheral nervous system to catalyze development of therapies based on neuromodulation of end-organ system function.

**4D Nucleome**
Investigate principles behind nuclear organization in space and time (the fourth dimension) and the role this organization in health and disease.

**Glycoscience**
Develop accessible new tools and technologies for glycoscience biomedical research (less complex, easily available, affordable, easy to understand, adaptable).

**Pediatric Research**
Build the capability to link genotypes, exposures, and phenotypes through data sharing across IC-supported pediatric cohorts.
Planning for FY16: Enabling Exploration of the Eukaryotic Epitranscriptome (E4)

We lack tools and technologies for investigating RNA modifications (the epitranscriptome) and their role in health and disease. E4 aims to develop tools, technologies, and datasets to enable systematic study of the epitranscriptome.

- **Co-chairs:** Nora Volkow (NIDA), Dinah Singer (NCI)
- **Co-coordinators:** John Satterlee (NIDA), Randy Knowlton (NCI)
- **29 trans-NIH members**

**Mission:** develop potential new Common Fund program in Epitranscriptomics

**Epitranscriptomics:** study of covalent RNA modifications
FY16 : Mechanisms of Benefits of Physical Activity

- Deliver a human data set from people exposed to various PA regimens and deeply phenotyped
  - Multi’omic profiling
  - Physiologic measures

- Investigators interested in various health conditions would be able to mine this data to explore molecular and cellular mechanisms through which physical activity provides benefit

1. Clinical Sites
   PA study in healthy human subjects for discovery of molecular transducers of PA in blood, muscle, fat, etc.

2. ‘Omics Chemical Analysis Sites
   - Proteome
   - Transcriptome
   - Epigenome
   - Metabolome
   - miRNA

3. Data Coordination Center

4. Animal Studies
   for molecule discovery in all tissues
Director’s Report to the National Advisory Council on Drug Abuse

• Budget Update

• What’s New @ HHS/NIH?

Recent NIDA Activities & Events
Priority Areas

**Prevention Research**
(Children & Adolescents)
genetics/epigenetics
development
environment
co-morbidity

**Treatment Interventions**
(New Targets & New Strategies)

**HIV and Drugs**
Prevention
Treatment
Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol

## 2014 Monitoring the Future Study

**Key Findings - Prevalence (2013 to 2014)**

<table>
<thead>
<tr>
<th></th>
<th>8th</th>
<th>10th</th>
<th>12th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td></td>
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</tr>
<tr>
<td>Past Year</td>
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<td>-</td>
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<tr>
<td>Daily</td>
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<td>-</td>
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<tr>
<td>Synthetic MJ</td>
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<td></td>
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<tr>
<td>Past Year</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Hallucinogens o/l LSD</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lifetime</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Salvia</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Past Year</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Ecstasy (MDMA)</td>
<td></td>
<td></td>
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<tr>
<td>Lifetime</td>
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<td>-</td>
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<tr>
<td>Past Year</td>
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<td>Past Month</td>
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<tr>
<td>Crack</td>
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<tr>
<td>Lifetime</td>
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<td>-</td>
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<tr>
<td>Past Year</td>
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<td>-</td>
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<tr>
<td>Narcotics o/l heroin</td>
<td></td>
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<tr>
<td>Lifetime</td>
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<td>Past Year</td>
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<tr>
<td>Past Month</td>
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<tr>
<td>OxyContin</td>
<td></td>
<td></td>
<td>-</td>
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<tr>
<td>Past Year</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Bath Salts</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Past Year</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cough Medicine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past Year</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

SOURCE: University of Michigan, 2014 Monitoring the Future Study
## Prevalence of Past Year Drug Use Among 12th graders

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>60.2</td>
<td>Sedatives*</td>
<td>4.3</td>
</tr>
<tr>
<td>Marijuana/Hashish</td>
<td>35.1</td>
<td>Cough Medicine*</td>
<td>4.1</td>
</tr>
<tr>
<td>Hookah</td>
<td>22.9</td>
<td>Hallucinogens</td>
<td>4.0</td>
</tr>
<tr>
<td>Small cigars</td>
<td>18.9</td>
<td>MDMA (Ecstasy)</td>
<td>3.6</td>
</tr>
<tr>
<td>Amphetamines*</td>
<td>8.1</td>
<td>OxyContin*</td>
<td>3.3</td>
</tr>
<tr>
<td>Adderall*</td>
<td>6.8</td>
<td>Hall other than LSD</td>
<td>3.0</td>
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<tr>
<td>Narcotics o/t Heroin*</td>
<td>6.1</td>
<td>Cocaine (any form)</td>
<td>2.6</td>
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<tr>
<td>Synthetic Marijuana</td>
<td>5.8</td>
<td>LSD</td>
<td>2.5</td>
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<tr>
<td>Snus</td>
<td>5.8</td>
<td>Inhalants</td>
<td>1.9</td>
</tr>
<tr>
<td>Vicodin*</td>
<td>4.8</td>
<td>Salvia</td>
<td>1.8</td>
</tr>
<tr>
<td>Tranquilizers*</td>
<td>4.7</td>
<td>Ritalin*</td>
<td>1.8</td>
</tr>
</tbody>
</table>

* Nonmedical use

Categories not mutually exclusive
Past Month Use of Selected Tobacco Products, by Grade

SOURCE: University of Michigan, 2014 Monitoring the Future Study
Overdose Death Data Updates

Source: CDC

**Prescription Opioid Overdose Deaths**

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
<td>1999</td>
<td>4,030</td>
<td>4,040</td>
<td>5,528</td>
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<tr>
<td>2000</td>
<td>7,456</td>
<td>8,517</td>
<td>9,857</td>
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<tr>
<td>2001</td>
<td>9,882</td>
<td>10,928</td>
<td>14,408</td>
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<tr>
<td>2002</td>
<td>14,800</td>
<td>14,800</td>
<td>15,597</td>
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<tr>
<td>2003</td>
<td>16,651</td>
<td>16,651</td>
<td>16,917</td>
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<tr>
<td>2004</td>
<td>16,007</td>
<td>16,007</td>
<td>16,235</td>
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</table>

**Heroin Overdose Deaths**

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>1,960</td>
<td>1,960</td>
<td>1,779</td>
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<tr>
<td>2000</td>
<td>1,842</td>
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<td>1,779</td>
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<tr>
<td>2001</td>
<td>2,089</td>
<td>2,089</td>
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<tr>
<td>2002</td>
<td>2,080</td>
<td>2,080</td>
<td>2,080</td>
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<tr>
<td>2003</td>
<td>2,009</td>
<td>2,009</td>
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<td>2004</td>
<td>2,088</td>
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<td>2005</td>
<td>2,399</td>
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<td>2006</td>
<td>2,036</td>
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<td>2008</td>
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<td>2009</td>
<td>5,925</td>
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<tr>
<td>2010</td>
<td>8,257</td>
<td>8,257</td>
<td>8,257</td>
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**Source: CDC Wonder**
Priority Areas

**Prevention Research**

(Children & Adolescents)
genetics/epigenetics
development
environment
co-morbidity

**Treatment Interventions**

(New Targets & New Strategies)

**HIV and Drugs**

Prevention
Treatment
Effects of TMS on Cigarette Smoking
LPFC and insula, high- or low-frequency pulses

deep high-frequency rTMS was beneficial in treatment of resistant smokers

**New Treatment-Related FOAs**

**Translational Avant-Garde Award for Development of Medication to Treat Substance Use Disorders (UH2/UH3) RFA-DA-15-017.**

*Issued: January 16, 2015 Open date: March 15, 2015; Application Due Date: April 15, 2015.*

Supports outstanding basic and/or clinical researchers to translate research discoveries into medications for the treatment of SUD) stemming from tobacco, cannabis, cocaine, methamphetamine, heroin, or opiate use. Applicants must show ability to develop molecules to treat SUDs and advance them in drug development.

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**Reductions in Illicit Drug Use and Functional Outcomes (R21/R33) PA-15-099.**


Supports projects to determine whether reductions in illicit drug use are associated with positive changes in health-related and other functional outcomes in individuals with SUD.
Priority Areas

**Prevention Research**
(Children & Adolescents)
genetics/epigenetics
development
environment
co-morbidity

**Treatment Interventions**
(New Targets & New Strategies)

**HIV and Drugs**
Prevention
Treatment
Don C. Des Jarlais, Ph.D., Mount Sinai Beth Israel  
**Project: Combined Prevention to Reduce Initiation into IDU**  
A multi-component HIV prevention intervention study in two sites with growing heroin use — NYC and Tallinn, Estonia.

Eli Gilboa, Ph.D., University of Miami School of Medicine  
**Project: Reversing HIV T cell Dysfunction by Aptamer Targeting of Therapeutic siRNAs**  
Development of novel drugs that successfully restore the function of T cells with potential to be therapeutically transformative for AIDS.

Nichole Klatt, Ph.D., University of Washington  
**Project: Impact of Cannabis on Inflammation & Viral Persistence in Treated HIV/SIV**  
Development of HIV cure strategies with non-psychoactive cannabinoids.

Alan D. Levine, Ph.D., Case Western Reserve University  
**Project: Repairing the Intestinal Epithelium from the Dual Action of HIV & Drug Use**  
Investigation of the loss of intestinal barrier protection initiated by HIV infection and the resultant, systemic inflammation due to chronic exposure to gut-derived microbial products.

Tariq M. Rana, Ph.D., University of California San Diego  
**Project: Modeling HIV/AIDS Associated Neurological Disorders with Human Pluripotent Cells**  
Innovative approach to better understand the molecular mechanisms of brain disorders caused by HIV, and damage from methamphetamine.
New HIV/AIDS-Related FOAs

Integration of Infectious Diseases and Substance Abuse Intervention Services for Individuals Living with HIV
(R01) RFA-DA-15-013
Issued: January 7, 2015 Open date: March 14, 2015; Application Due Date: April 14, 2015.

Supports research to develop and test organizational and systems level interventions to determine how best to provide comprehensive, high quality, integrated, sustainable, cost-effective interventions to improve health outcomes of people with HIV + SUD.

Seek, Test, Treat and Retain For Youth and Young Adults Living with or at High Risk for Acquiring HIV (R01) RFA-DA-15-019.
Issued: January 8, 2015 Open date: March 15, 2015; Application Due Date: April 14, 2015.

Supports research to examine delivery of HIV services (testing, linkage, engagement and retention in care) for high risk or already HIV+ youth and young adults.
Status of Marijuana Laws in the US

Source: NORML, Drug Policy Alliance, and the Marijuana Policy Project
Ten year longitudinal study of 10,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories
Notice of Intent to Publish a Funding Opportunity Announcement for A Longitudinal Study of Adolescent Brain and Cognitive Development (ABCD) Research Sites (U01)

Notice Number: NOT-DA-15-001

Key Dates
Release Date: November 26, 2014
Estimated Publication Date of Announcement: January 2015
First Estimated Application Due Date: April 2015
Earliest Estimated Award Date: September 2015
Earliest Estimated Start Date: September 2015

Related Announcements
NOT-DA-15-002
NOT-DA-15-003

Issued by
National Institute on Drug Abuse (NIDA)
National Cancer Institute (NCI)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
NIDA Strategic Plan 2010-2015

Chalmers et al, Lancet 2014, 383, 9912, 11-17 How to increase value and reduce waste when research priorities are set
Updating NIDA Strategic Plan

• RFI released Dec 10 for feedback on draft priorities:
  – Understanding basic science of drug use, addiction, vulnerability, and recovery
  – Supporting development of new and better interventions and treatments
  – Increasing the public health impact of NIDA research
  – Enhancing the national research infrastructure

• **Comment period closed January 30th**

• Next steps:
  – Priority Area Workgroups with internal and external experts:
    • Big Data
    • Gene x Environment x Development interactions
    • Complex patients (multiple comorbidities)
    • Health disparities
  – Division strategic plans

• **Timeline**
  – RFI – Review – By March 6, 2015
  – Priority Area Workgroups – Feb-July
  – Division Strategic Plans Drafts – By February 6, 2015
  – Draft Strategic Plan to Council – May 2015
  – Final Strategic Plan – Fall 2015
2015 National Drug Facts Week (NDFW)
January 26th to February 1st

• ~ 1500 events in USA & Egypt, Kilimanjaro (Tanzania), Lithuania, Mexico and Nairobi

NIDA
• developed and distributed press and promotional materials
• cultivated radio & organizational partnerships
• pitched to select media
• coordinated Radio Media Tours for English & Spanish speaking audiences
• promoted the week via traditional & social media outreach.

2015 National Drug Facts Week (NDFW)
January 26th to February 1st

• > 8,000 questions from 70 schools
• 2,500 questions answered by > 50 scientists (including NIAAA, NIMH, and FDA CTP)

January 30, 2015

~ 1500 events in USA & Egypt, Kilimanjaro (Tanzania), Lithuania, Mexico and Nairobi

> 8,000 questions from 70 schools
2,500 questions answered by > 50 scientists (including NIAAA, NIMH, and FDA CTP)
A Glutamatergic Pathway From the Dorsal Raphe-VGluT3 Neurons to VTA Dopamine Neurons Promotes Reward


Density of labeled cells
Morales et al., Nat Neuroscience  2014
This Phased Innovation Awards Cooperative Agreement (FOA) solicits applications to support a collaborative research infrastructure involving an interdisciplinary team of basic and clinical scientists to develop the foundation for an experimental medicine approach to behavior change.

NIH Science of Behavior Change Resource and Coordinating Center (U24) RFA-RM-14-017.

Will coordinate the activities of between 5 & 9 UH2/UH3 Target Validation Projects
E⁴ Program Goal:
*Transform our understanding of the role of RNA modifications in biology & disease processes*

**RNA modification functions:** mRNA stability, fertility, dopamine circuit function, circadian rhythms, cancer, intellectual disability, etc.

- **Therapeutics**
- **Diagnostics**
- **Prevention**

**Technologies:** better assays and detection

**Data Coordination**

**Epitranscriptome Catalog**

**Discovery:** RNA modification enzymes

**Technologies:** better assays and detection

**Tools:** antibodies and small molecules

**Function**
National Institute on Drug Abuse Portfolio
FY 2013 Actual

Basic & Clinical Neuroscience & Behavioral Research -- 44%
Epidemiology, Services & Prevention Research -- 24%
Pharmacotherapies & Medical Consequences -- 12%
Clinical Trials Network – 4.5%
Intramural Research – 8.5%
RM&S -- 6%
New Prevention-Related FOAs

**Epidemiology of Drug Abuse (R01)**

Issued: October 3, 2014; Open date: January 5, 2014 (R01); January 16, 2014 (R21) & (R03).

Supports research to enhance our understanding of the nature, extent, distribution, etiology, comorbidities, & consequences of drug use, abuse, & addiction across individuals, families, communities, & diverse population groups.

**Drug Abuse Prevention Intervention Research**

Issued: January 9, 2015; Open date: May 5, 2015 (R01); May 16, 2015 (R21 and R03).

Encourages grant applications for research that will employ rigorous scientific methods to test theoretically derived hypotheses to increase understanding of the science of drug use prevention within diverse populations & settings & across the lifespan.

**Cutting-Edge Basic Research Awards (CEBRA) (R21)**
PAR-15-079.

Fosters highly innovative or conceptually creative research related to drug abuse and addiction and how to prevent and treat them.
Methods of Using Marijuana Among 12th Grade Past Year Users, 2014

SOURCE: University of Michigan, 2014 Monitoring the Future Study