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

September 13, 2011
In Memoriam

Charles Robert ("Bob") Schuster, Ph.D.
NIDA Director -- 1986 to 1992
Director,
Addiction Research Institute
Wayne State University

Joseph V. Brady, Ph.D.
President, Institute for Behavior Resources
and Professor Emeritus,
Johns Hopkins University
School of Medicine

Dr. Tom Brady
Program Official,
Services Research Branch, DESPR
Director’s Report to the National Advisory Council on Drug Abuse

- Budget Update

- What’s New @ NIH?

- Recent NIDA Activities & Events
<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2010</th>
<th>2011 PB</th>
<th>2011 Full Year CR</th>
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</thead>
<tbody>
<tr>
<td>NonAIDS</td>
<td>$719,556</td>
<td>$739,216</td>
<td>$763,626</td>
<td>$733,194</td>
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<td>AIDS</td>
<td>$312,901</td>
<td>$320,230</td>
<td>$330,452</td>
<td>$317,348</td>
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<tr>
<td>TOTAL</td>
<td>$1,032,457</td>
<td>$1,059,446</td>
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<tr>
<td>Increase Over Prior Year</td>
<td>+2.6%</td>
<td>+2.6%</td>
<td>+3.3%</td>
<td>-0.9%</td>
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• Budget Update

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CSR Study Sections: Preliminary Information

- **Average Score - DA Grants**
- **Average Score - Other Grants**

<table>
<thead>
<tr>
<th>Agency</th>
<th>DA Grants</th>
<th>Other Grants</th>
</tr>
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<tbody>
<tr>
<td>BRLE</td>
<td></td>
<td></td>
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<tr>
<td>BSCH</td>
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<tr>
<td>BSPH</td>
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<tr>
<td>F02A-J20</td>
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<tr>
<td>HSOD</td>
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<td>NPAS</td>
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<td>PDRP</td>
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<td>RPHB-C 10</td>
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<td>RPIA</td>
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<tr>
<td>COG</td>
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<tr>
<td>LAM</td>
<td></td>
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<td>PMDA</td>
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</table>
Data from 83,188 applications (40,069 PI) 2000–2006. Applications from Asian investigators were 16.2%, blacks 1.4%, Hispanics 3.2%, NA 0.05%, whites 69.9%, and other/unknown 9.2% of total applications.

Applications from black investigators were much less likely to be awarded an R01 than white applicants.

“the greatest differences between blacks and whites were in the effect of previous training and the probability of receiving a priority score. Although more research is needed to discern the basis for the award differences, it is possible that cumulative advantage may be involved”
(1) examine NIDA’s efforts at supporting minority investigators and at recruiting minority subjects into NIDA-funded research studies and clinical trials,

(2) explore the extent to which NIDA has implemented each of the recommendations from the 2005 report of a previous council review
SESSION IV The Economic Impact of NIH-Funded Research

- Knowledge
- Improvements in quality of life
- Economy
  - Creates Jobs “Star Metrics”
  - Creates Revenue
    » Product development
    » Savings in health care costs
From 1998 to 2003, the budget of the NIH doubled… judging by the only criterion that matters to patients and taxpayers—not how many interesting discoveries about cells or genes or synapses have been made, but how many treatments for diseases the money has bought— the return on investment to the American taxpayer has been approximately as satisfying as the AIG bailout.

Newsweek May 14, 2010
The Role of Public-Sector Research in the Discovery of Drugs and Vaccines


Background
Historically, public-sector researchers have performed the upstream, basic research that elucidated the underlying mechanisms of disease and identified promising points of intervention, whereas corporate researchers have performed the downstream, applied research resulting in the discovery of drugs for the treatment of diseases and bring them to market. However, the boundaries between the roles of the public and private sectors have shifted substantially.

Methods
We identified new drugs and vaccines approved by FDA that were discovered by public-sector research institutions (PSRIs) and classified them according to their therapeutic category and potential therapeutic effect.

Results
We found that during the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs. These drugs included 93 small-molecule drugs, 36 biologic agents, 15 vaccines, 8 in vivo diagnostic materials, and 1 over-the-counter drug. PSRI-discovered drugs are expected to have a disproportionately large therapeutic effect.

Conclusions
Public-sector research has had a more immediate effect on improving public health than was previously realized.

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>Total</td>
<td>153</td>
</tr>
<tr>
<td>Hematology or oncology</td>
<td>40</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>36</td>
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<tr>
<td>Cardiology</td>
<td>12</td>
</tr>
<tr>
<td>Metabolic disease</td>
<td>12</td>
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<tr>
<td>Central nervous system</td>
<td>12</td>
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<tr>
<td>Dermatology</td>
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<tr>
<td>Renal disease</td>
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<tr>
<td>Ophthalmology</td>
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<tr>
<td>Immunology</td>
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<tr>
<td>Gastroenterology</td>
<td>4</td>
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<tr>
<td>Women’s health</td>
<td>3</td>
</tr>
<tr>
<td>Allergy</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>2</td>
</tr>
<tr>
<td>Urology</td>
<td>2</td>
</tr>
<tr>
<td>Anesthesiology</td>
<td>1</td>
</tr>
<tr>
<td>Dental disorders</td>
<td>1</td>
</tr>
</tbody>
</table>
NIH Blueprint for Neuroscience Research Grand Challenge: Developing Novel Drugs for Disorders of the Nervous System (U01): RFA-NS-12-002

NIH-Assembled Virtual Pharma Network

Successful applicants will receive:
1) funding for biological assessment of compounds in their laboratories,
2) no-cost access (through infrastructure (in purple box)) to drug development resources that typically reside in the pharmaceutical industry
3) strategic guidance from experienced drug development consultants

Applicant must have starting compounds for chemical optimization and bioactivity assays for testing new analog compounds generated through the Blueprint Neurotherapeutics drug development network.
RFA-NS-12-002

52 Applications: Range of Diseases

- Alzheimer’s Disease
- Pain
- Stroke/TBI
- Psychiatry
- Visual
- Developmental
- Addiction/Alcohol
- Motor
- Hearing
- Multiple Sclerosis
- Brain Tumor

7 selected for funding; none in addiction

Outreach Campaign for NIDA PIs is needed
NIH Blueprint for Neuroscience Research Grand Challenge: Transition from Acute to Chronic Neuropathic Pain (R01) RFA-DE-12-008

Letter of Intent Due Date: September 4, 2011
Application Due Date: October 4, 2011
WE WANT TO HEAR FROM YOU!
Weigh in on NEW Ideas for NIH Common Fund Programs

Innovation Brainstorm Ideas

Artificial Organs as Tools for Translation
Beyond Genome-Wide Association Studies (GWAS)
Bringing Difficult Structures into Reach
Cross-Cutting Issues in Computation and Informatics
Group Effects
Microbiome: Part 2
Molecular Classification of Disease
Single-Cell Analysis
Targeting the Dynamic Complexome
NIH Award Strategies
NIH Institute/Center Ideas

Artificial Organs: From Lab Bench To The Body
Biomarkers for chronic pain using functional brain connectivity

Centers for Research and Training in Quantitative and Systems Pharmacology
Chronic Pain Conditions: A Transformative Classification for Stimulating Research, Improving Diagnosis, and Personalizing Treatment

Developmental Origins of Health and Disease: Disease Prevention Across Generations
Disruptive Proteomics Technologies: Comprehensive Protein Identification in Clinical Samples
Exploring the Extracellular Space
Gene-Based Therapeutics: Manipulating the Output of the Genome to Treat Disease
Human Microbiome, Part II - Microbial Product Characterization
Innovative Mobile and Wireless Technologies (mHealth) to Improve Health Research and Health Outcomes
Meeting the Challenge of Big Data in Biomedical and Translational Science
Molecular Phenotypes for Genome Function and Disease
NIH Global Research Administration and Training Networks (GRAT-Net)
Regulatory Science Initiative
Synergizing Omic Science with Patient Reported Outcomes
A synthetic cohort for the analysis of longitudinal effects of gene-environment interactions
Translating Findings on Human Disease Risk Variants into New Interventions: Coordinated Studies for Therapeutic Target Identification

Venture Fund for Research and Development of New Medications to Treat Chronic Pain
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Recent NIDA Activities & Events
Priority Areas

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

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

**Medical Consequences**
HIV/AIDS, HCV
Teratogenic effects
A gradient of childhood self-control predicts health, wealth, and public safety (Dunedin Study; 1000 children)

Children with low self-control had poorer health, more wealth problems, more single-parent child rearing, and more criminal convictions and drug use than those with high self-control

Moffitt et al., PNAS 2011

Since self-control can be improved by interventions early childhood intervention that enhances self-control is likely to bring a greater return on investment than harm reduction programs targeting adolescents alone.
Recent SBIRT Developments

- Working on options for adolescent drug abuse screening for medical settings:
  -- scientific workshop, May 27, 2011
  -- Met with NIAAA staff to coordinate with their efforts on adolescent alcohol screening (will be releasing a new document/approach)

- Revised NIDAMed screening to improve efficiency by starting with single screening questions for illicit drug abuse and prescription drug abuse

- Working with ONDCP and HHS on proposals for including drug abuse screening as a standard part of electronic medical records systems
New PAs and RFAs

Epidemiology of Drug Abuse (R01) PA-11-230 (R21) PA-11-231, (R03) PA-11-232

Gene-Environment Interplay in Substance Use Disorders (R01) PA-11-235 (R21) PA-11-236, (R03) PA-11-237 (with NIAAA)

Integration of Drug Abuse Prevention & Treatment in Primary Care Settings (R01) RFA-DA-12-008

Letter of Intent Receipt Date: September 30, 2011; Application Due Date: October 31, 2011
Priority Areas

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

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

**Medical Consequences**
HIV/AIDS, HCV
Teratogenic effects
Brain cannabinoid CB$_2$ receptors modulate cocaine’s actions in mice

Zhen-Xiong Xi$^1$, Xiao-Qing Peng$^{1,3}$, Xia Li$^{1,3}$, Rui Song$^{1,3}$, Hai-Ying Zhang$^1$, Qing-Rong Liu$^1$, Hong-Ju Yang$^1$, Guo-Hua Bi$^1$, Jie Li$^1$ & Eliot L Gardner$^1$

Received 25 April; accepted 13 June; published online 24 July 2011; doi:10.1038/nn.2874

**Δ^9-THC produces biphasic effects on Nac DA: low dose increase while high dose decreases**

**Δ^9-THC-induced DA increase mediated by CB$_1$Rs and DA decreases by CB$_2$Rs**

**JWH133, selective CB$_2$R agonist, inhibits Cocaine-induced DA increases in Nac and self-administration**

**Cocaine Self-Administration**

- **A (WT)**: JWH133
  - Vehicle (n=10)
  - JWH (10 mg/kg, n=5)
  - JWH (20 mg/kg, n=8)
- **B (CB$_1$-/-)**: JWH133
  - Vehicle (n=7)
  - JWH (10 mg/kg, n=6)
  - JWH (20 mg/kg, n=6)
- **Vehicle**: Vehicle
  - JWH133 (10 mg/kg)
  - JWH133 (20 mg/kg)
The aim of this study is to investigate the safety and effectiveness of buprenorphine in the presence of naltrexone for the treatment of cocaine dependence in a sample of individuals meeting diagnostic criteria for both cocaine and opioid dependence or opioid abuse.

Lead Investigator: Walter Ling, M.D.
New PAs and RFAs

2012 NIDA Translational Avant-Garde Award for Medication Development for the Treatment of Substance–Use Disorders (DP1) RFA-DA-12-010
Open Date: January 21, 2012

Remote Monitoring System for Detecting Cocaine Ingestion/Intoxication (R01) RFA-DA-12-007
Letter of Intent Receipt Date: July 18, 2011
Application Due Date: August 18, 2011
Priority Areas

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

Treatment Interventions
(New Targets & New Strategies)

HIV and Drugs
Prevention
Treatment
Dr. David Ho
Aaron Diamond AIDS Research Center
Develop a novel HIV therapy that could be administered monthly

“1996 Man of the Year”

For pioneering the early use of the antiretroviral (ARV) cocktails that have reduced the death rate from AIDS
2009
Dr. Benjamin Chen
Mt. Sinai School of Medicine
Visualizing early events of parenteral HIV transmission (cell-cell vs. free virus)

2009
Dr. Dana Gabuzda
Dana Farber Cancer Institute & Harvard Medical School
Control of T cell restoration in HIV-infected IV drug abusers

2009
Dr. Dana Gabuzda
Dana Farber Cancer Institute & Harvard Medical School
Control of T cell restoration in HIV-infected IV drug abusers

2009
Dr. Rafick-Pierre Sekaly
Vaccine & Gene Therapy Institute, FL
Novel pathways for purging the HIV reservoir

2010
Dr. Eric Verdin
Gladstone Institutes
New methods to detect and model HIV latency

2009
Dr. Jonathan Karn
Case Western Reserve University
Developing strategies for long-term HIV suppression

2008
Dr. Ileana Cristea
Princeton University
Quantifying HIV–host interactome and regulation of gene expression

2008
Dr. Jerome Groopman
Beth Israel Medical Center & Harvard Medical School
Blocking HIV transmission at the immune synapse

2008
Dr. Julio Montaner
University of British Columbia
HIV treatment as prevention in drug using populations

2011
Dr. David Ho
Aaron Diamond AIDS Research Center
Develop a novel HIV therapy that could be administered monthly
Early ART prevented linked transmission of HIV

Unlinked transmissions were noted despite intensive couples counseling

Early ART reduced the number of clinical events observed
HAART as HIV Prevention

Avant Garde 2008
Dr. Julio Montaner
UBC

Decline in Community Viral Load is Strongly Associated with Declining HIV Incidence among IDUs (ALIVE)

GD Kirk, N Galai1, J Astemborski, B Linas, D Celentano, SH Mehta, D Vlahov
Dramatic Decline in the HIV-1 RNA Level Over Calendar Time in a Large Urban HIV Practice

HIV-1 RNA level was assessed each year from 1996 through 2010 for all patients in care and followed up in the Johns Hopkins HIV Clinical Cohort.

5290 patients

Line plot of median (Med) and upper- or third-quartile (Q) human immunodeficiency virus (HIV)–1 RNA levels from 1996 through 2010 in the Johns Hopkins HIV Clinical Cohort. K, thousand; VL, viral load.

Clin Infect Dis. 2011 Sep;53(6):600-4
Proposed and organized the grantees awarded funds RFA “HIV Seek, Test, and Treat in Criminal Justice Settings: to harmonize and standardized their instruments to increase comparability across the studies.”
New PAs and RFAs

FY12 NIDA Avant-Garde Award Program for HIV/AIDS Research (DP1) RFA-DA-12-011
Open Date: February 27, 2012
Application Due Date: March 27, 2012

Mechanistic Studies of HIV-exposed Seronegative Individuals (HESN)(R21) PA-11-217; (R01) PA-11-218 (with NIAID)
Open Date: August 7, 2011

Promoting Engagement in Care and Timely Antiretroviral Initiation Following HIV Diagnosis (R01) RFA-MH-12-060 (R34) RFA-MH-12-06 (with NIMH and NIAID)
Application Due Date: September 9, 2011
2011 ISEF Addiction Science Awardees

Darby K. Schumacher
Chattanooga, TN
“Making Heartbeats go LOKO”

Sarah Susie Pak
Roslyn Heights, NY
“Would You Do It For the Kids?”

Yamini T. Naidu
Beaverton, OR
“From Models to Medications: Identification of Medication Leads for Treating Methamphetamine Addiction”
Don’t miss this free, innovative CME event!

This activity has been approved for AMA PRA Category 1 Credit™

- Dramatic reading by Debra Winger & Arliss Howard*
- Expert panel reaction
- Lively audience discussion

NIDA Frontiers in Addiction Research
Mini-Convention

Friday November 11, 2011
8:00 a.m.-5:40 p.m.

SAVE THE DATE

• Autism, Addiction, and MeCP2
• Jacob P. Waletzky Memorial Lecture
• Synapse Organization and Plasticity in Drug Addiction
• Early Career Investigators Poster Session
• Using Optogenetic Tools to Shed Light on the Neural Mechanisms of Addiction
• Neurobiology of Behavioral and Emotional Regulation/Dysregulation