NIAID: State of the Institute and Priorities in HIV/AIDS Research

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
June 15, 2016
Brooks Steps Down as Head of Office of National AIDS Policy, Lansky Named Acting Director

Douglas M. Brooks, M.S.W.  Amy Lansky, Ph.D., M.P.H.
Goodenow Selected as Director of NIH Office of AIDS Research

Maureen M. Goodenow, Ph.D.
Willard “Ward” Cates, M.D., M.P.H.
1942-2016
Budget Update
# National Institutes of Health Budget Comparison by Institute/Center (Dollars in Thousands)

<table>
<thead>
<tr>
<th>IC</th>
<th>FY 2015 Operating Budget</th>
<th>FY 2016 Operating Budget</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCI</td>
<td>$ 4,953,028</td>
<td>$ 5,213,509</td>
<td>5.3%</td>
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<tr>
<td>NIAID¹</td>
<td>$ 4,417,558</td>
<td>$ 4,715,697</td>
<td>6.7%</td>
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<tr>
<td>NHLBI</td>
<td>2,995,865</td>
<td>3,113,533</td>
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<tr>
<td>NHGRI</td>
<td>498,677</td>
<td>513,227</td>
<td>2.9%</td>
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<td>NCATS</td>
<td>632,710</td>
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<tr>
<td>NIGMS</td>
<td>2,372,301</td>
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<td>NIA²</td>
<td>1,197,523</td>
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<td>Other ICs</td>
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<tr>
<td>Subtotal</td>
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<td>B&amp;F</td>
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<td>128,863</td>
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<tr>
<td>Total</td>
<td>$ 30,311,349</td>
<td>$ 32,311,349</td>
<td>6.6%</td>
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¹$100M increase for Antimicrobial Resistance  
²$350M increase for Alzheimer’s Disease  
³$130M increase for Precision Medicine
NIAID FY 2016 Financial Management Plan

- R01 Payline
  - Established PI: 13th percentile
  - New PI: 17th percentile

- Non-competing and competing grants: No adjustments

- Competing research initiatives: Cut up to 10%

- Estimated success rates: 21-23%
## National Institutes of Health
### Budget Comparison by Institute/Center
(Dollars in Thousands)

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<th>IC</th>
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<th>FY 2017 President’s Budget</th>
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<td>NCI¹</td>
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<td>0.0%</td>
</tr>
<tr>
<td>Subtotal</td>
<td>$30,611,286</td>
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<tr>
<td>OD²</td>
<td>1,571,200</td>
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<td>9.2%</td>
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<td>B&amp;F</td>
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<td>Total</td>
<td>$32,311,349</td>
<td>$33,136,349</td>
<td>2.6%</td>
</tr>
</tbody>
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¹Increase of $680M for National Cancer Moonshot Initiative
²Increase of $100M for Precision Medicine Initiative and $45M for BRAIN Initiative
3 Initiatives Account for All of Increase in NIH Budget, 2016 to 2017 (P.B.)

National Cancer Moonshot + $680 M

Precision Medicine + $100 M

BRAIN + $45 M
NIH Budget, FY 1998-2017 (P.B.)
Inflationary Effects on Purchasing Power

Excludes ARRA funding FY 2009-2010
NIAID Budget, FY 1998-2017 (P.B.)
Inflationary Effects on Purchasing Power

Excludes ARRA funding FY 2009-2010
NIH AIDS Budget, FY 1998 – 2017 (P.B.)
Inflationary Effects on Purchasing Power

Excludes ARRA funding FY 2009-2010
NIH Drops Special 10% Set-aside for AIDS Research

Jocelyn Kaiser
June, 2016

35 Years of AIDS Research
June 5, 1981

**Pneumocystis Pneumonia – Los Angeles**

July 4, 1981

**Kaposi’s Sarcoma and Pneumocystis Pneumonia Among Homosexual Men – New York City and California**
The Global HIV/AIDS Pandemic: Current Estimates

- 36.7 million people living with HIV (end-2015)
- 1.1 million AIDS deaths in 2015
- 2.1 million new HIV infections in 2015

Source: UNAIDS, 5/2016
NIH FY 2017 President’s Budget for HIV/AIDS, By Area of Emphasis

- **Therapeutics ($645M)**
- **Vaccines ($554M)**
- **Etiology and Pathogenesis ($599M)**
- **HIV Microbicides ($109M)**
- **Behavioral and Social Science ($421M)**
- **Training/Infrastructure/Capacity Building ($197M)**
- **Natural History and Epidemiology ($238M)**
- **Information Dissemination ($38M)**
- **Toward a Cure ($199M)**

Total = $3.0B
NIH HIV/AIDS Research: Four Focus Areas

- Prevention (including vaccines)
- Novel/innovative therapies
- Cure
- Co-morbidities (infectious and non-infectious)
NIH HIV/AIDS Research: Four Focus Areas

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Tailored Prevention Using HIV Prevention Toolkit

Provision of Tailored Prevention Services

Prevention toolbox

Combination HIV Prevention

- HIV Testing/Counseling
- Treatment as Prevention
- Medical Male Circumcision
- STI Treatment
- Microbicides
- Treatment/Prevention of Drug/Alcohol Abuse
- Clean Syringes
- Education/Behavior Modification
- Blood Supply Screening
- ARVs for PMTCT, PEP, PrEP
- Condoms
Promise of Long-Acting Antiretroviral Agents for Preventing and Treating HIV Infection

- Antiretroviral drugs

- Broadly neutralizing antibodies
Promise of Long-Acting Antiretroviral Agents for Preventing and Treating HIV Infection

- Antiretroviral drugs
- Broadly neutralizing antibodies
HPTN 076  TMC278-LA (rilpivirine) Phase II
N=136 Women
USA, Zimbabwe, South Africa
Enrollment completed/follow-up complete by ~September 2016

HPTN 077  GSK1265744  Phase Ila
N=200 Men and Women
USA, Brazil, Malawi, South Africa
Enrollment completed and follow-up done by ~late May 2017
HPTN 083  Cabotegravir v. oral Truvada  Phase IIb/3
N=~4,500 MSM, TGW
USA, Argentina, Brazil, Peru, South Africa, Thailand, Vietnam
~Q3 2016 start

HPTN 084  GSK1265744  Phase IIb/3
~mid 2017
On the Horizon: Long-Acting ARV Implants

Pharmacokinetics of Long-Acting Tenofovir Alafenamide (GS-7340) Subdermal Implant for HIV Prophylaxis

M Gunawardana, M Baum et al.

A Tunable, Biodegradable, Thin-Film Polymer Device as a Long-Acting Implant Delivering Tenofovir Alafenamide Fumarate for HIV Pre-exposure Prophylaxis

E Schlesinger, T Desai et al.
Promise of Long-Acting Antiretroviral Agents for Preventing and Treating HIV Infection

- Antiretroviral drugs

- Broadly neutralizing antibodies
Neutralizing Monoclonal Antibodies Discovered Since 2009

N332 Glycan Supersite: PGT121, PGT128 10-1074

CD4 Binding Site: VRC01, PG04, CH313BNC117, 12A12 CH103, VRC07-523

V1V2 Apex: PG6, PG16, CH01-04 PGT141-45, PGDM1400 CAP256-VRC26

Trimer (gp120/41) 8ANC195 PGT151 35022
gp41 MPER: 2F5, 4E10 10e8

Cryo-EM of viral spike by Subramaniam group. Fit with atomic level structures from Kwong and Wilson group

Courtesy John Mascola
NIH Launches Large Clinical Trials of Antibody-Based HIV Prevention

- 2 trials of antibody-mediated prevention (AMP) testing IV infusions of VRC01, an HIV NAb

- 1st trial: 2,700 men/transgender people who have sex with men in Brazil, Peru & U.S.

- 2nd trial: 1,500 sexually active women in 7 African countries
Towards an HIV Vaccine

- Improve on RV144

- Induction of Broadly Neutralizing Antibodies

- T-Cell Approach
Towards an HIV Vaccine

- Improve on RV144
- Induction of Broadly Neutralizing Antibodies
- T-Cell Approach
Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

S Rerks-Ngarm, JH Kim, NL Michael, et al. for the MOPH–TAVEG Investigators
Strategies to Amplify RV144 Response

Strength

Breadth

Durability

Potential approaches:
- Multiple boosts
- Modified vectors
- Adjuvants
Large-Scale HIV Vaccine Trial to Launch in South Africa

- HVTN 702 is Phase 2b/3 trial testing a modified RV144 regimen adapted to clade C, the predominant HIV subtype in southern Africa

- Pending regulatory approval, study will launch in November and enroll 5,400 men and women 18-35 yo at risk of HIV
Towards an HIV Vaccine

- Improve on RV144

- Induction of Broadly Neutralizing Antibodies

- T-Cell Approach
Fundamental Challenge in HIV Vaccinology: Convert Neutralizing Epitopes to Immunogens Inducing bNAbs
Towards an HIV Vaccine

- Improve on RV144

- Induction of Broadly Neutralizing Antibodies

- T-Cell Approach
T Cell Approach Towards an HIV Vaccine

- **CD4+ T Cell**
  - Provide broad help
  - Boost bNAb potency and affinity (via T follicular helper cells)

- **B Cell**
  - Provide help to CD8+ T cells

- **CD8+ T Cell**
  - Produce anti-viral cytokines
  - Kill HIV-infected CD4+ T cells

- **HIV-infected CD4+ T Cell**
  - Produce anti-viral cytokines
NIH HIV/AIDS Research: Four Focus Areas

- Prevention (including vaccines)

- Novel/innovative therapies

- Cure

- Co-morbidities (infectious and non-infectious)
Protocol in Development: ACTG 5357

- A proof-of-concept study of long-acting cabotegravir (integrase inhibitor) + VRC01LS

- Goal: maintain viral suppression in HIV-infected adults whose virus has been suppressed with conventional ART

- Collaborators: ViiV/GSK, NIAID Vaccine Research Center (VRC), NIAID Division of AIDS (DAIDS), AIDS Clinical Trials Group (ACTG)

- Protocol chairs: Babafemi O. Taiwo, M.D., M.B.B.S. (Northwestern), Pablo Tebas, M.D. (Penn)
NIH HIV/AIDS Research: Four Focus Areas

- Prevention (including vaccines)
- Novel/innovative therapies
- Cure
- Co-morbidities (infectious and non-infectious)
Addressing HIV Persistence

- Eradicate the reservoir – classic "cure"

- Control viral rebound – sustained virologic remission
Addressing HIV Persistence

- Eradicate the reservoir – classic “cure”

- Control viral rebound – sustained virologic remission
Potential Strategies to Eradicate HIV from an HIV-infected Individual

- Latency-reversing agents to deplete HIV reservoirs
- Immunotoxic therapy directed at reservoir
- Stem cell transplantation
- Gene therapy
Addressing HIV Persistence

- Eradicate the reservoir – classic “cure”

- Control viral rebound – sustained virologic remission
Post-treatment Immunological Control of HIV Infection: Sustained Virologic Remission

Early suppression of HIV viremia with ART

- Natural HIV-specific immunity
- Passive transfer of HIV-specific antibodies
- Therapeutic vaccination

Discontinuation of ART

Sustained control of HIV viremia
NIH HIV/AIDS Research: Four Focus Areas

- Prevention (including vaccines)
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- Cure
- Co-morbidities (infectious and non-infectious)
Examples of Important Co-Morbidities in HIV-Infected Individuals

- Tuberculosis
- Hepatitis B and C
- Other STIs
- Cardiovascular disease
- Metabolic abnormalities
- Bone and muscle disease
- Liver and kidney disease
- Neurological disorders
- Malignancies
- Frailty
Contacts of MDR TB patients who become infected with Mtb have a high risk of progressing to active TB (and possibly death)

Most MDR TB in children arises from household transmission

Data from RCT lacking; needed to guide the management of contacts exposed to MDR-TB patients and inform international and national guidelines
Landmark International Tuberculosis Study

- PHOENIX -- Protecting Households On Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients
- IMPAACT and ACTG collaboration
- Seminal Phase III trial to assess whether Delamanid can prevent TB disease among household contacts of MDR TB patients
- PHOENIX feasibility study complete
- Enrollment in main study, ~Q1/Q2 2017
- N= 3,452 high-risk household contacts from 1,726 households in Africa, S. America, Asia
Seventieth session
Agenda item 11
Implementation of the Declaration of Commitment on HIV/AIDS and the political declarations on HIV/AIDS

Draft resolution submitted by the President of the General Assembly

Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030

The General Assembly,
Adopts the Political Declaration on HIV and AIDS annexed to the present resolution.
Fast-Tracking the End of AIDS

- More **HIV testing** with prompt linkage to care or prevention services

- **Immediate antiretroviral therapy (ART)** for all HIV-infected people for their health and to help prevent ongoing transmission

- **Pre-exposure prophylaxis (PrEP) and other HIV prevention services** for individuals at high risk of infection
Ending the HIV–AIDS Pandemic — Follow the Science

AS Fauci & HD Marston