



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)

IC	FY 2015 Operating Budget	FY 2016 Operating Budget	Percent Change
NCI	\$ 4,953,028	\$ 5,213,509	5.3%
NIAID¹	4,417,558	4,715,697	6.7%
NHLBI	2,995,865	3,113,533	3.9%
NHGRI	498,677	513,227	2.9%
NCATS	632,710	685,417	8.3%
NIGMS	2,372,301	2,512,437	5.9%
NIA ²	1,197,523	1,598,246	33.5%
Other ICs	\$ 11,701,090	\$ 12,259,220	4.8%
Subtotal	\$ 28,768,752	\$ 30,611,286	6.4%
OD ³	1,413,734	1,571,200	11.1%
B&F	128,863	128,863	0.0%
Total	\$ 30,311,349	\$ 32,311,349	6.6%

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%

FY 2017 President's Budget Released February 9, 2016

The President's BUDGET

For Fiscal Year 2017



National Institutes of Health Budget Comparison by Institute/Center (Dollars in Thousands)

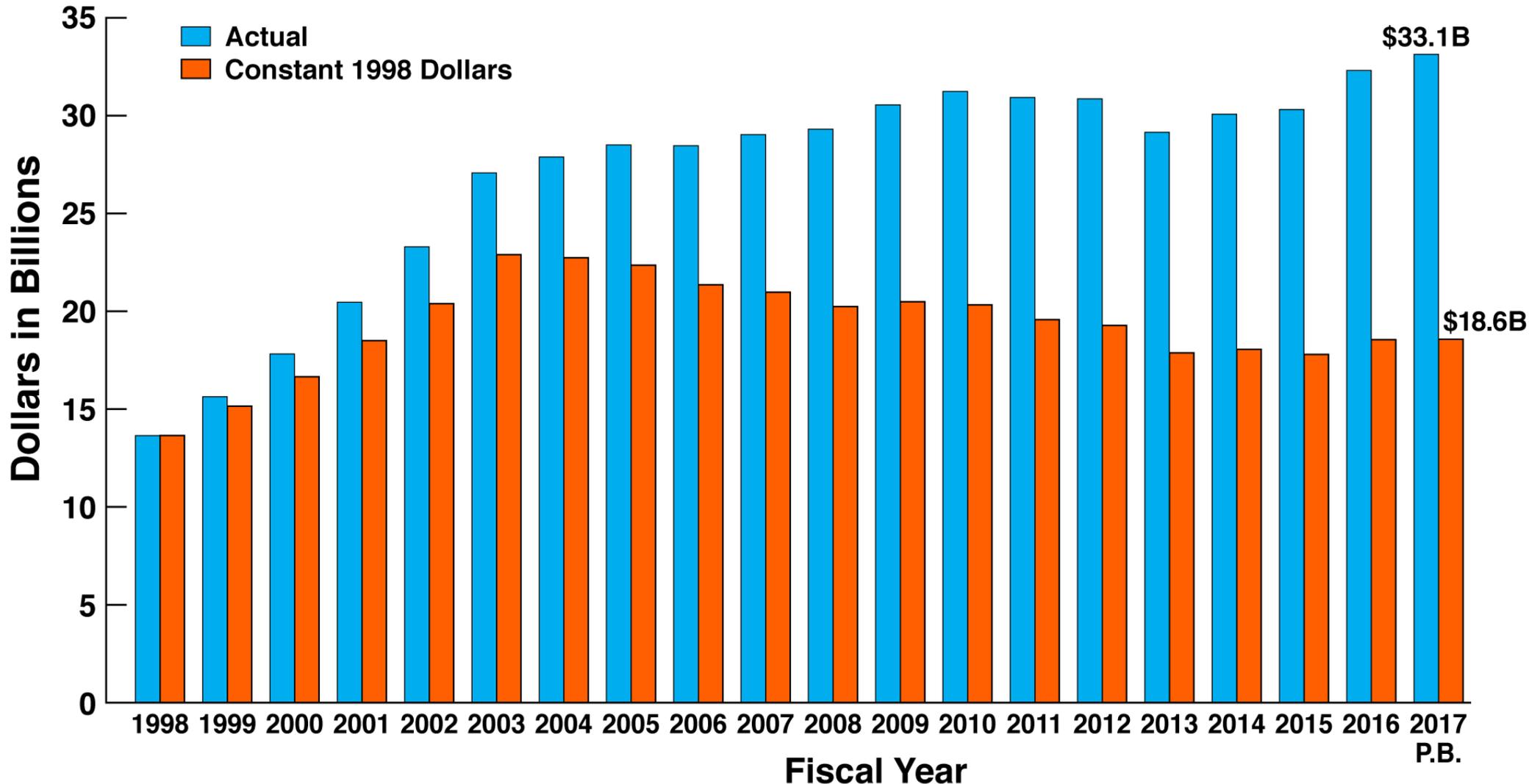
IC	FY 2016 Enacted	FY 2017 President's Budget	Percent Change
NCI ¹	\$ 5,213,509	\$ 5,893,509	13.0%
NIAID	4,715,697	4,715,697	0.0%
NHLBI	3,113,533	3,113,533	0.0%
NHGRI	513,227	513,227	0.0%
NCATS	685,417	685,417	0.0%
NIGMS	2,512,437	2,512,437	0.0%
NIA	1,598,246	1,598,246	0.0%
Other ICs	\$ 12,259,220	\$ 12,259,220	0.0%
Subtotal	\$ 30,611,286	\$ 31,291,286	2.2%
OD ²	1,571,200	1,716,200	9.2%
B&F	128,863	128,863	0.0%
Total	\$ 32,311,349	\$ 33,136,349	2.6%

¹Increase of \$680M for National Cancer Moonshot Initiative

²Increase of \$100M for Precision Medicine Initiative and \$45M for BRAIN Initiative

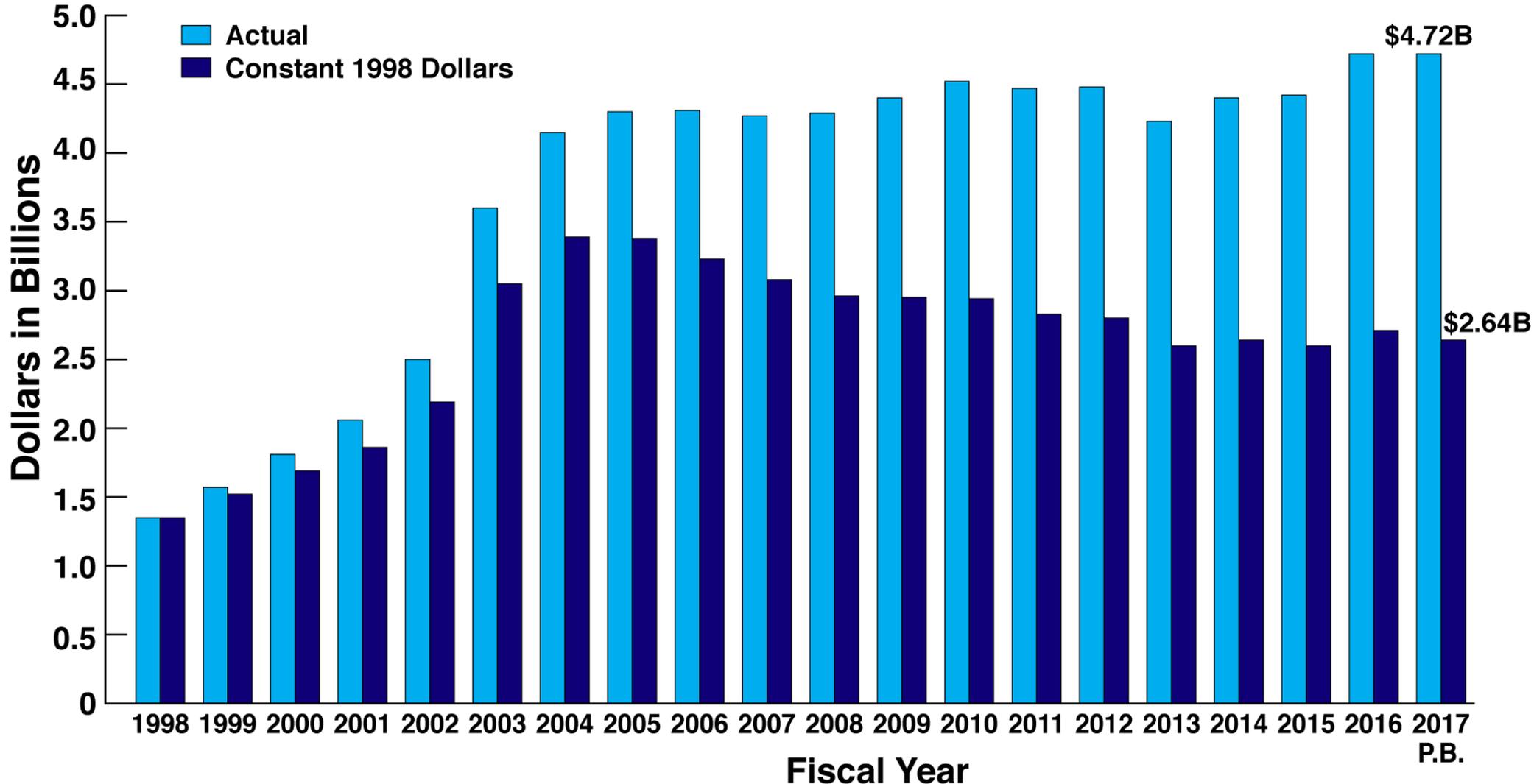
NIH Budget, FY 1998-2017 (P.B.)

Inflationary Effects on Purchasing Power



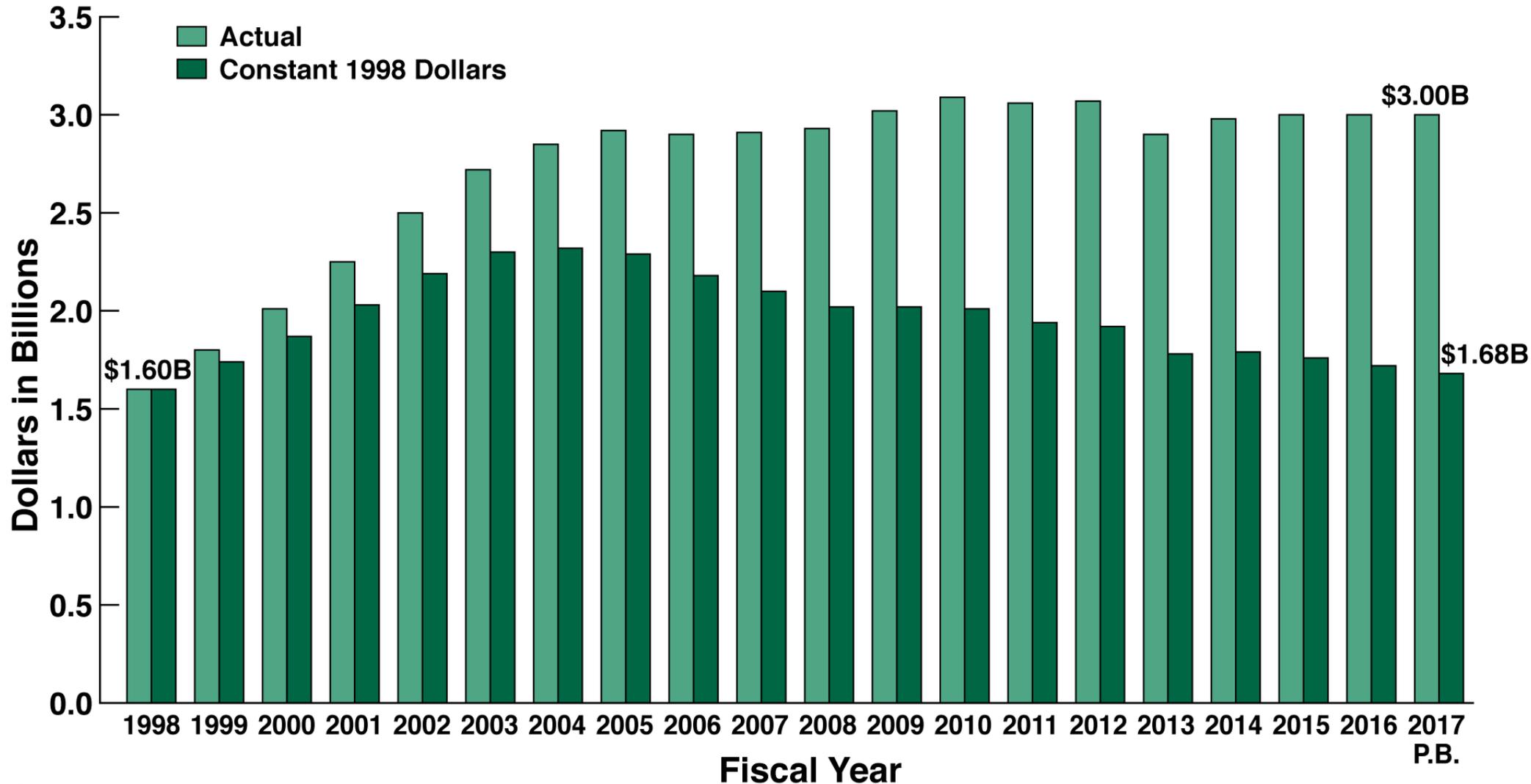
Excludes ARRA funding FY 2009-2010

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

December 11, 2015

Science

NIH Drops Special 10% Set-aside for AIDS Research

Jocelyn Kaiser

June, 2016

**35 Years of AIDS
Research**

CENTERS FOR DISEASE CONTROL

MNWRTM

MORBIDITY AND MORTALITY WEEKLY REPORT

June 5, 1981

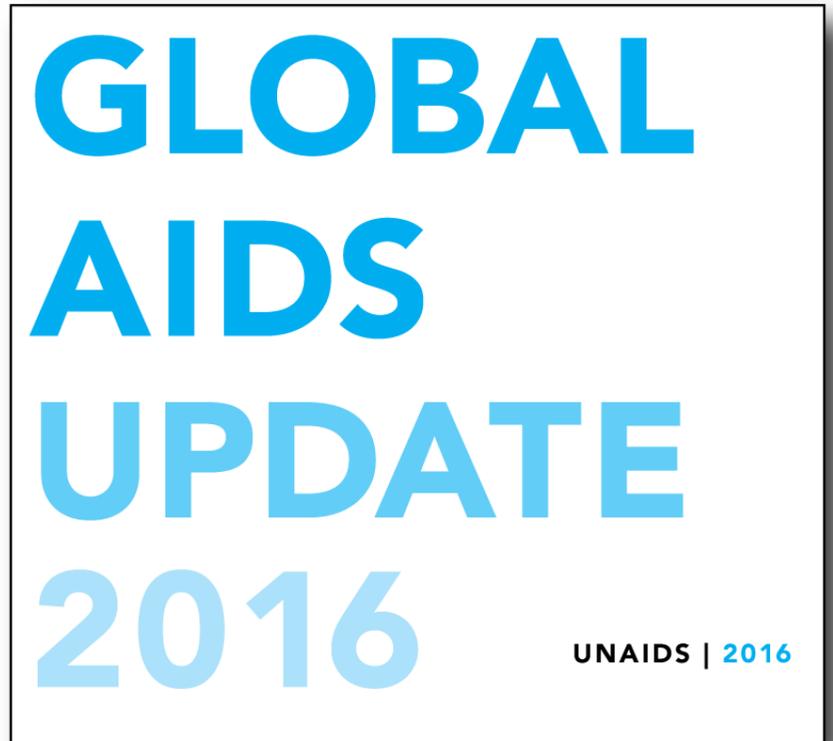
***Pneumocystis Pneumonia –
Los Angeles***

July 4, 1981

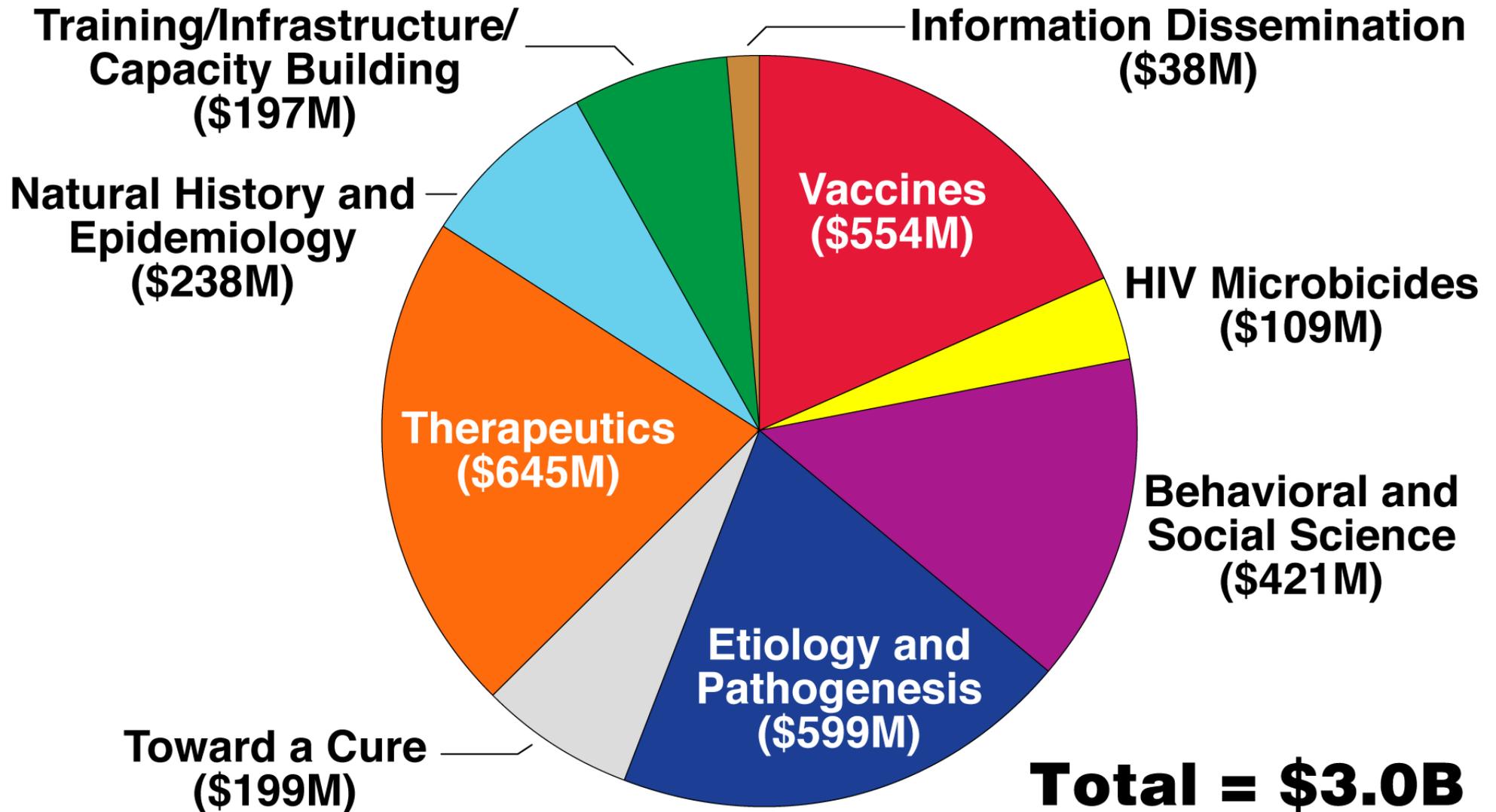
***Kaposi's Sarcoma and
Pneumocystis Pneumonia Among
Homosexual Men –
New York City and California***

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**



NIH FY 2017 President's Budget for HIV/AIDS, By Area of Emphasis





FY 2017

Trans-NIH Plan for HIV-Related Research



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

■ Prevention (including vaccines)

■ Novel/innovative therapies

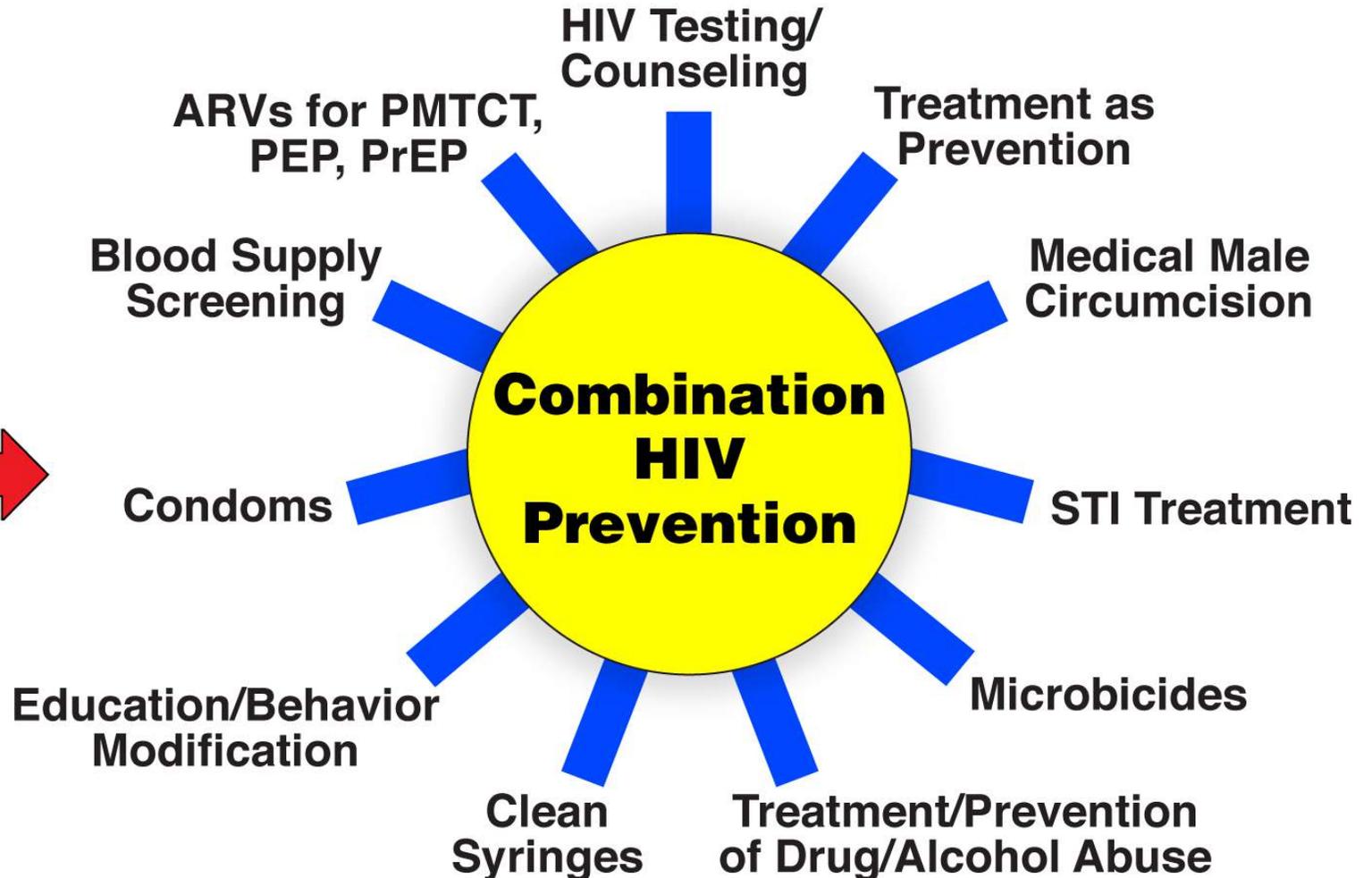
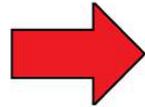
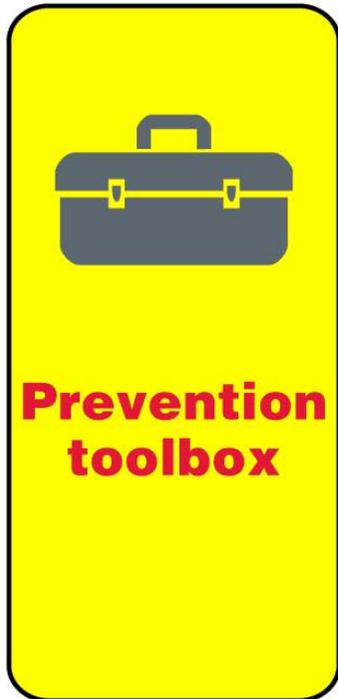
■ Cure

■ Co-morbidities (infectious and non-infectious)



Tailored Prevention Using HIV Prevention Toolkit

Provision of Tailored Prevention Services



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

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Selected NIAID Progress with Long-Acting Injectables for PrEP

■ 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 IIa

N=200 Men and Women

USA, Brazil, Malawi, South Africa

Enrollment completed and follow-up done by ~late May 2017

Selected NIAID Progress with Long-Acting Injectables for PrEP (cont.)

■ 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

July 2015 Vol 59 No 7

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY

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

M Gunawardana, M Baum et al.

PHARMACEUTICAL RESEARCH

July 2016

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

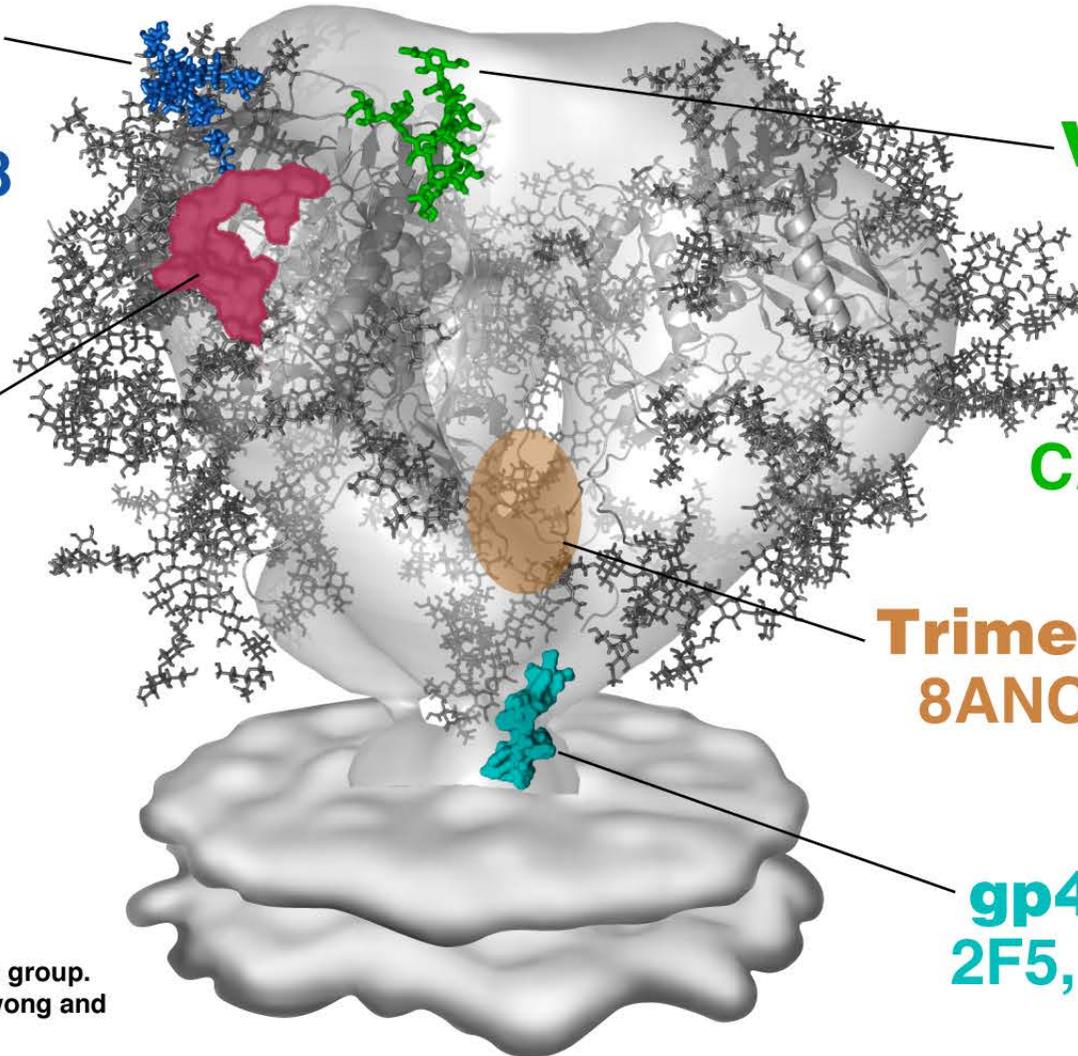
V1V2 Apex:
PG6, PG16,
CH01-04
PGT141-45,
PGDM1400
CAP256-VRC26

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





National Institute of Allergy and Infectious Diseases

Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

FOR IMMEDIATE RELEASE

Thursday, April 7, 2016

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



Model of HIV NAb
VRC01

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**

First Signal of Efficacy (31%) in an HIV Vaccine Clinical Trial – RV144



The
New England
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Volume 361

December 3, 2009

Number 23

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**



FOR IMMEDIATE RELEASE

Wednesday, May 18, 2016

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**

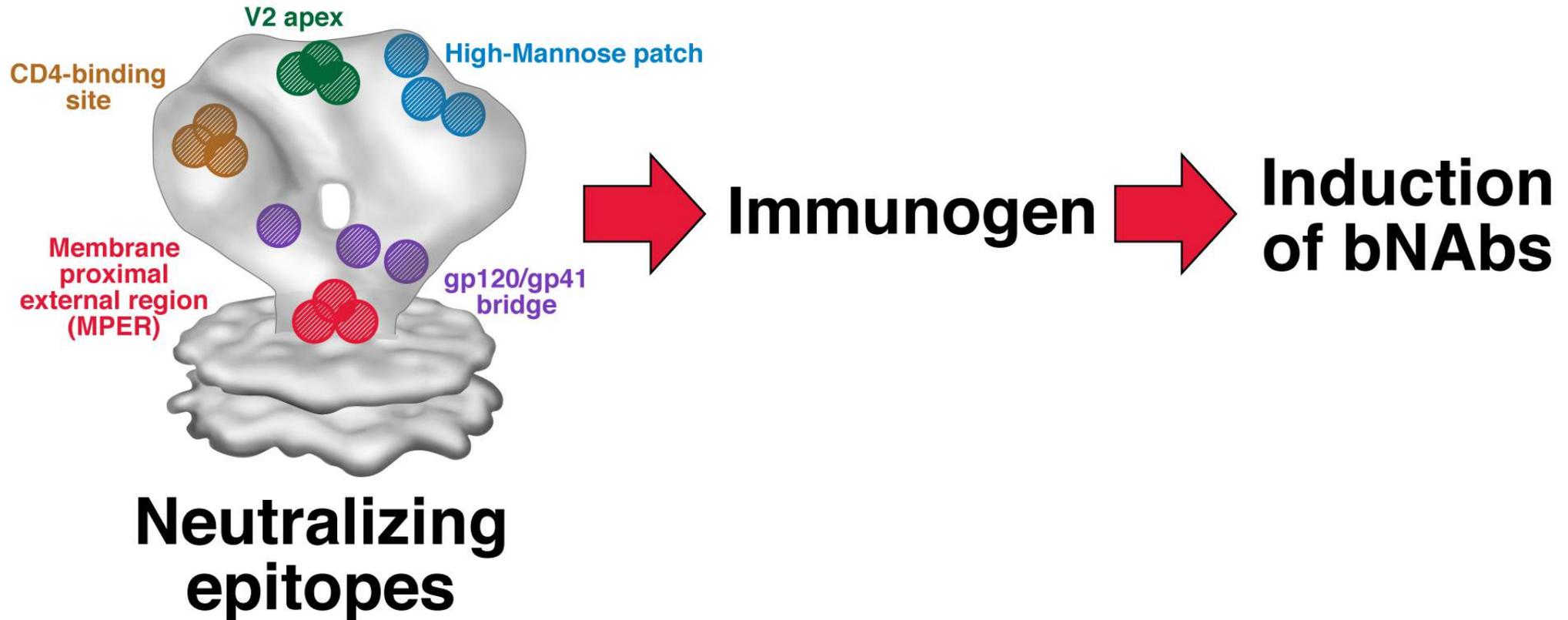
Towards an HIV Vaccine

■ **Improve on RV144**

■ **Induction of Broadly Neutralizing Antibodies**

■ **T-Cell Approach**

Fundamental Challenge in HIV Vaccinology: Convert Neutralizing Epitopes to Immunogens Inducing bNAbs



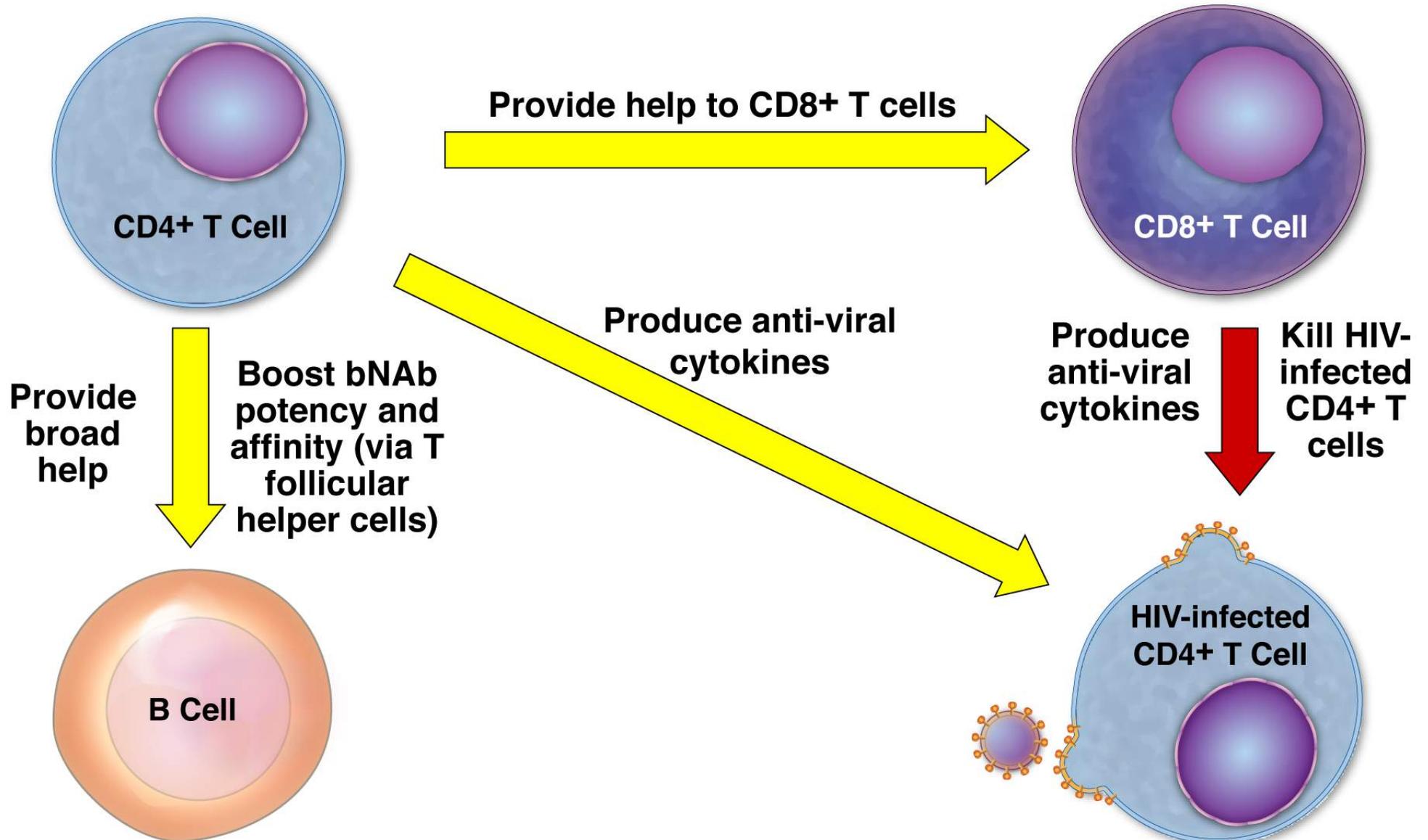
Towards an HIV Vaccine

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T Cell Approach Towards an HIV Vaccine



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)**

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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**

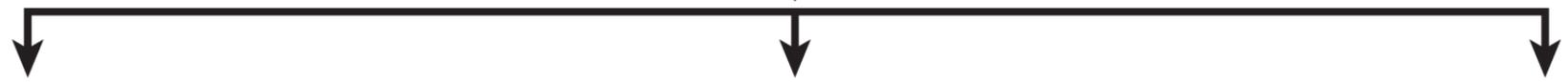
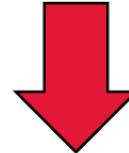
Addressing HIV Persistence

■ 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)**

■ **Novel/innovative therapies**

■ **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**

MDR TB and Household Contacts

- **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**

2016 Political Declaration to End AIDS Adopted by UN General Assembly

United Nations

A/70/L.52



General Assembly

Distr.: Limited
7 June 2016

Original: English

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



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Ending the HIV-AIDS Pandemic – Follow the Science

AS Fauci & HD Marston