

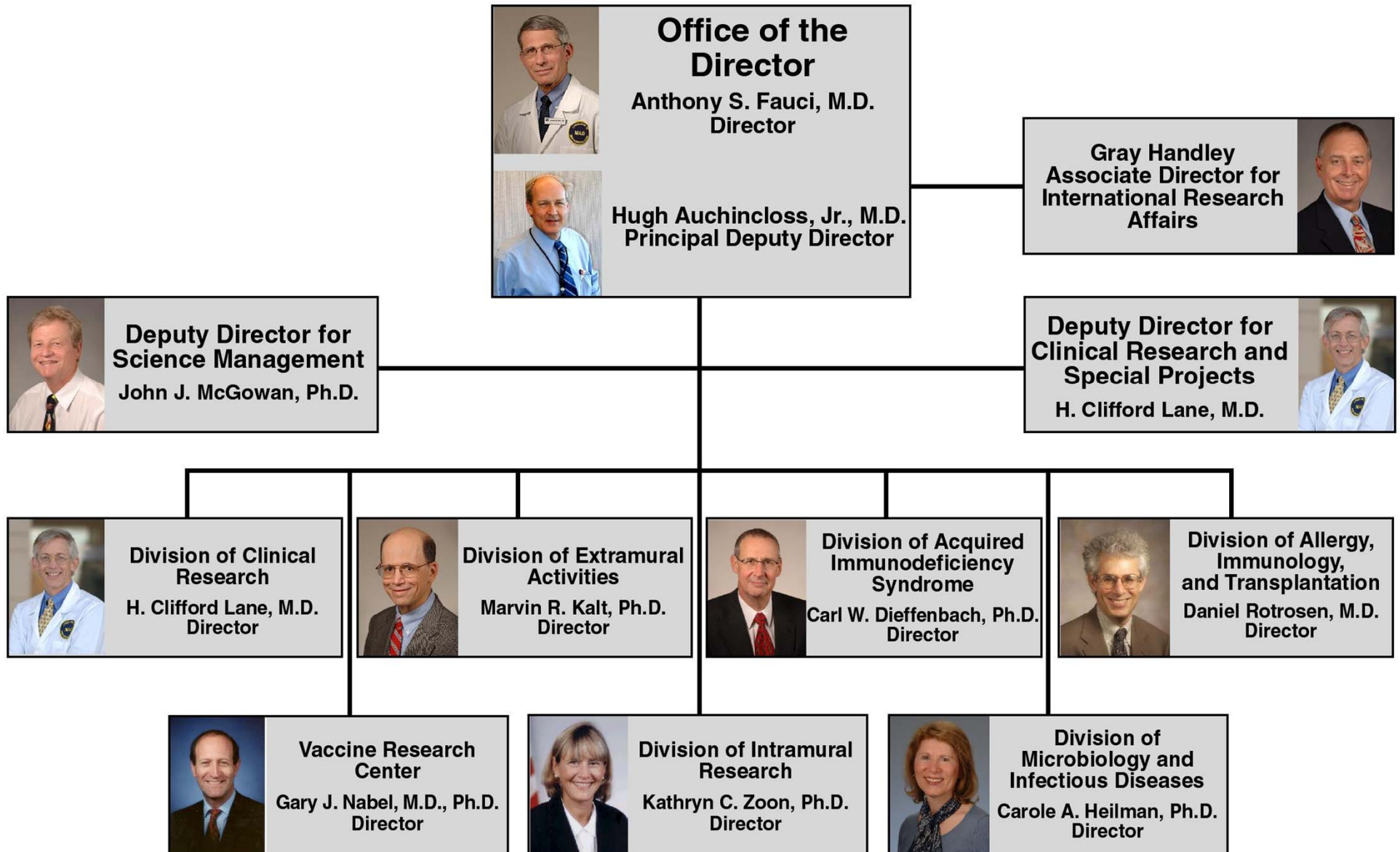
Overview of NCI- Frederick support to NIAID

H. Clifford Lane, MD

**Deputy Director for Clinical Research and Special Projects
National Institute of Allergy and Infectious Diseases
January 25, 2012**



NIAID Organizational Structure



National Institutes of Health

Budget Comparison by Institute/Center

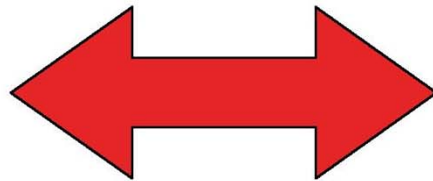
(Dollars in Thousands)

IC	FY 2011 Enacted	FY 2012 Enacted	Percent Change
NCI	\$ 5,058,577	\$ 5,072,183	0.3%
NIAID	4,478,668	4,490,711	0.3
NHLBI	3,069,723	3,079,021	0.3
NHGRI	511,497	512,873	0.3
NCRR	1,257,754	-	-100.0
NCATS	-	575,366	-
NIGMS	2,033,782	2,430,036	19.5
Other ICs	12,913,127	13,037,334	1.0
Subtotal	\$29,323,128	\$29,197,524	-0.4%
OD	1,166,963	1,459,117	25.0
B & F	49,900	125,344	151.2
Total	\$30,539,991	\$30,781,985	0.8%

FY 2011 excludes the \$297.3M passed through to the Global Fund to allow comparison with FY 2012

NIAID Research: A Dual Mandate

Maintain and “grow” a robust basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated diseases



Respond rapidly to new and emerging disease threats



New/Improved Interventions

The Frederick Post

A real friend is someone who takes a winter vacation on a sun-drenched beach and *doesn't* send a card.

—Farmers' Almanac

RALEIGH QUAKER, JR.
P. O. BOX 115
BRUNSWICK MD 21716
APR 8 78

res Frederick, Maryland 21701

Saturday, March 18, 1978

4 Sections

Press Run 18,325
Today News 13,425 Total 31,750

15¢

Detrick labs to house gene manipulation work

By ROLLIE ATKINSON
Staff Writer

Once a tiny airfield in the 1930s, and then the home of the U.S. Army Chemical Corps' massive effort into biological warfare research from 1943-1972, Frederick's Fort Detrick is now destined to become the home of the nation's major containment laboratory for genetic manipulation research.

In between, the complex of highly specialized scientific research facilities has been used for basic cancer research and continuing investigations into infectious diseases and development of new medical protection for the nation's armed forces. It remains the home of the Frederick Cancer Research Center and the U.S. Army Medical Research Institute of Infectious Diseases.

Friday, officials of the National In-

stitutes of Health (NIH) announced the launching of controversial recombinant DNA experiments at Fort Detrick in renovated germ warfare labs.

The international scientific community continues to express interest in Fort Detrick — the home of the first attempts in biocontainment procedures and the testing ground for much of today's knowledge into biosafety and work with hazardous organisms and substances.

When NASA sought expertise in developing a containment facility to receive and study its "moon rocks" — it borrowed designs and practices developed through the years of Detrick's experience with germ warfare.

The national Communicable Disease Center in Atlanta, Ga. also looked to Fort Detrick's experience and personnel in devising new laboratories to contain

studies with dangerous disease organisms.

And, when NIH sought a location for elaborate and expensive maximum containment facilities they logically turned again to Fort Detrick, with its former germ warfare labs standing idle.

Now, with \$250,000 worth of renovation and new equipment, Frederick will gain new notoriety as the home of the nation's major effort into controversial

gene-splicing experiments.

That new notoriety may not always be positive.

Friday, for the first time since Vietnam War days, protesters bearing placards reading "Who should play God?" and "Do the ends always justify the means?" stood vigil at Fort Detrick outside a large press briefing near build-

(Continued On Page A-6)

Are DNA hazards overrated?

By ROLLIE ATKINSON
Staff Writer

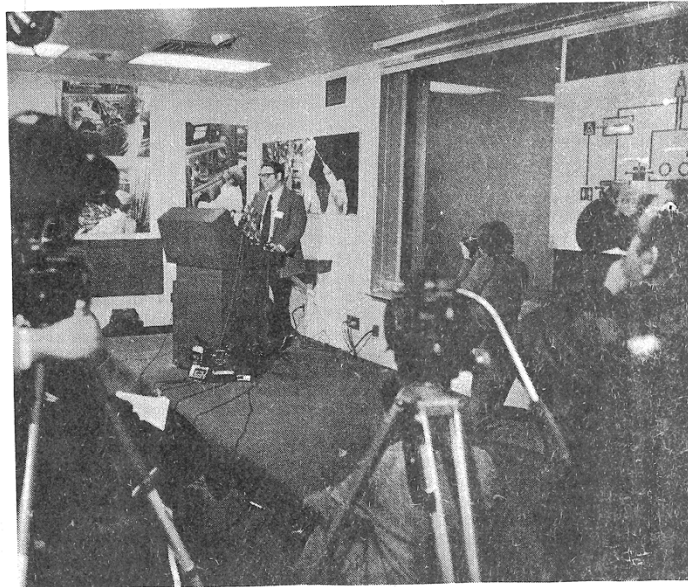
Dr. Malcolm Martin, who will direct the risk assessment experiments here into recombinant DNA techniques, believes, as many other scientists now do, that the precautionary measures, public controversy and elaborate and expensive safety facilities of gene-splicing may all be "exaggerated."

But, there was a time, a short three years ago, when many scientists like Dr. Martin issued public warnings on the potential hazards of recombinant DNA work.

A group of prominent scientists led a successful move to ban certain recombinant DNA tests with known pathogens and human cells and instigated the formation of National Institutes of Health (NIH) safety guidelines on the research.

Now, however, some of those same scientists regret sounding the alarm which also created wider spread public protests and debate, such as a small demonstration by local people Friday at Fort Detrick.

"You will never be able to answer all the possible risk scenarios involved in recombinant work," Dr. Martin admit-



Scientists and pickets

Members of the international press filled a meeting room at Fort Detrick Friday morning to hear presentations on the recombinant DNA experiments to be conducted there. Shown here speaking before still and television cameras is Dr. Bernard Talbot, special assistant for Intramural Affairs. While



the meeting progressed smoothly indoors, demonstrators from the People's Business Commission and Western Maryland Clergy and Laity Concerned remained present but peaceful outside. For more photos see page A-3. (Photos by C. Kurt Holter)

Are DNA hazards underrated?

By ROLLIE ATKINSON
Staff Writer

A member of a silent vigil opposing the opening of a local recombinant DNA lab at Fort Detrick stepped forward Friday during a press briefing to challenge "the spending of taxpayer's money for the federal government to experiment with the creation of new life forms."

Jeremy Rifkin, author of *Who Should Play God*, a critical book on the subject of recombinant DNA and genetic engineering, encountered National Institutes of Health (NIH) officials by saying: "You are right, this is an historical moment for all of us. Our government is about to embark into the Brave New World of manipulating the genes of life. We should be asking why do this type of research at all."

Outside, near the recently-renovated maximum containment gene-splicing laboratory, a group of local citizens, clergy and other members of Rifkin's Peoples Business Commission stood in silence with signs reading, "Who should play God?" and "Do the ends always justify the means?"

Asked if the protest was in any way connected to former germ warfare research at Fort Detrick, one protester

NIAID / NCI Frederick Timeline

- **1978 – Recombinant DNA experiments in Bldg. 550**
- **1985 – Immunologic monitoring of patients with AIDS in Bldg. 560; later moved to Bldg. 469**
- **1986 – Mike Baseler hired**
- **1994 – Virologic monitoring of patients with AIDS in Bldg. 550**
- **2005 – Vaccine Pilot Plant**

Support Provided by NCI-Frederick to NIAID

- **Clinical Research Infrastructure**
- **Support to “Special Projects”**

Clinical Research Infrastructure Support Provided by NCI-Frederick

- **MDs, Nurses,
Pharmacists**
- **Protocol
Development**
- **IND Management**
- **Clinical Research
Monitoring**
- **Laboratory Support**
 - **Monitoring**
 - **Biomarker analysis**
 - **Repository**
 - **Biopharmaceuticals**
 - **Vaccine Production**
 - **Education**

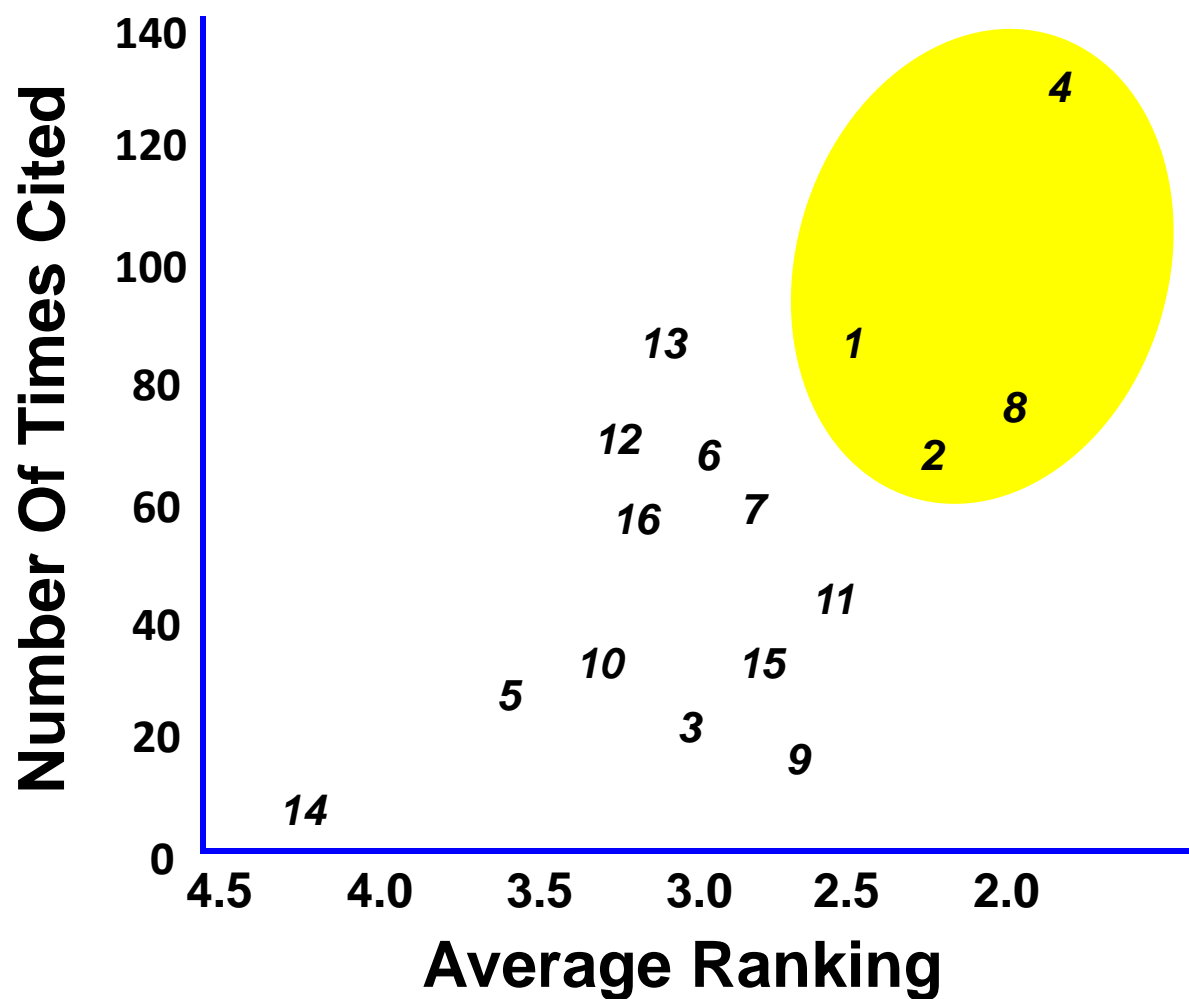
Clinical Research Infrastructure Support Provided by NCI-Frederick

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Barriers to Clinical Research Project (2007)

- **Identify key policies, practices. Regulations, and legislation governing NIH-sponsored human subject clinical research that limit the effectiveness and efficiency of clinical research**
- **Make recommendations to facilitate and improve effectiveness and efficiency of clinical research**

Initial Targeted Barriers- Based on Frequency and Ranking

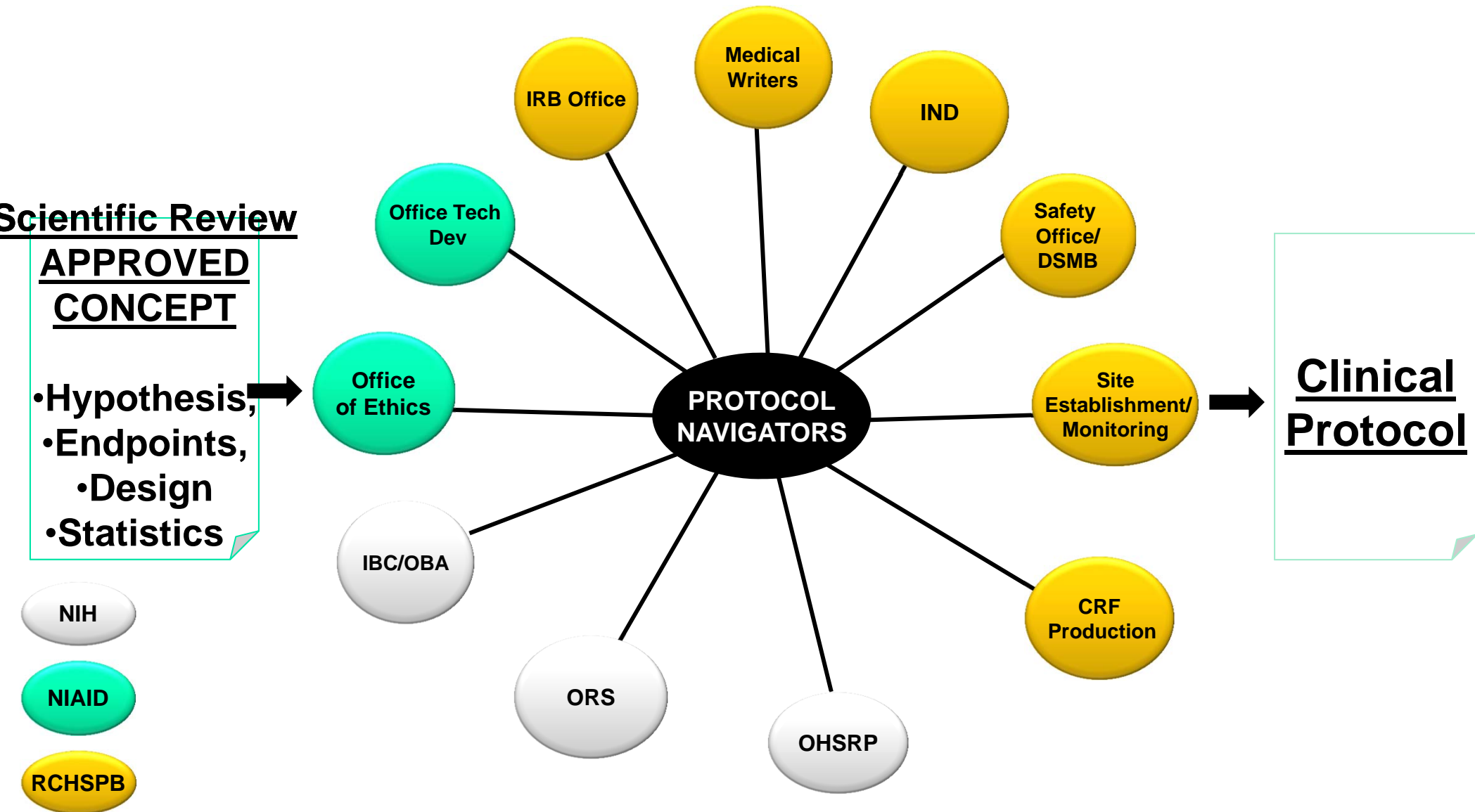


BARRIER	
1	Scientific Review / Approval Protocols
2	Interaction – Industry / Tech Transfer
3	Bio-Safety Committee Review
4	IRB & Ethical Issues
5	Site Registration / Approval
6	Informed Consent & Documentation
7	Conflict Of Interest
8	Adequacy Of Resources
9	Conflicts – U.S. / Local Requirements
10	Adverse Event reporting
11	FDA / OHRP Interactions
12	Protocol Monitoring & Compliance
13	Management Of Samples
14	Research-related Injury
15	Work In International Settings
16	Collaborations

Survey of Intramural Investigators: Results and Response

- **Identified that Clinical Research Support Services were inadequate to meet the increasingly complex demands of clinical research.**
- **In response to this need, NIAID moved forward to develop a Protocol Navigation/Protocol Development Program.**

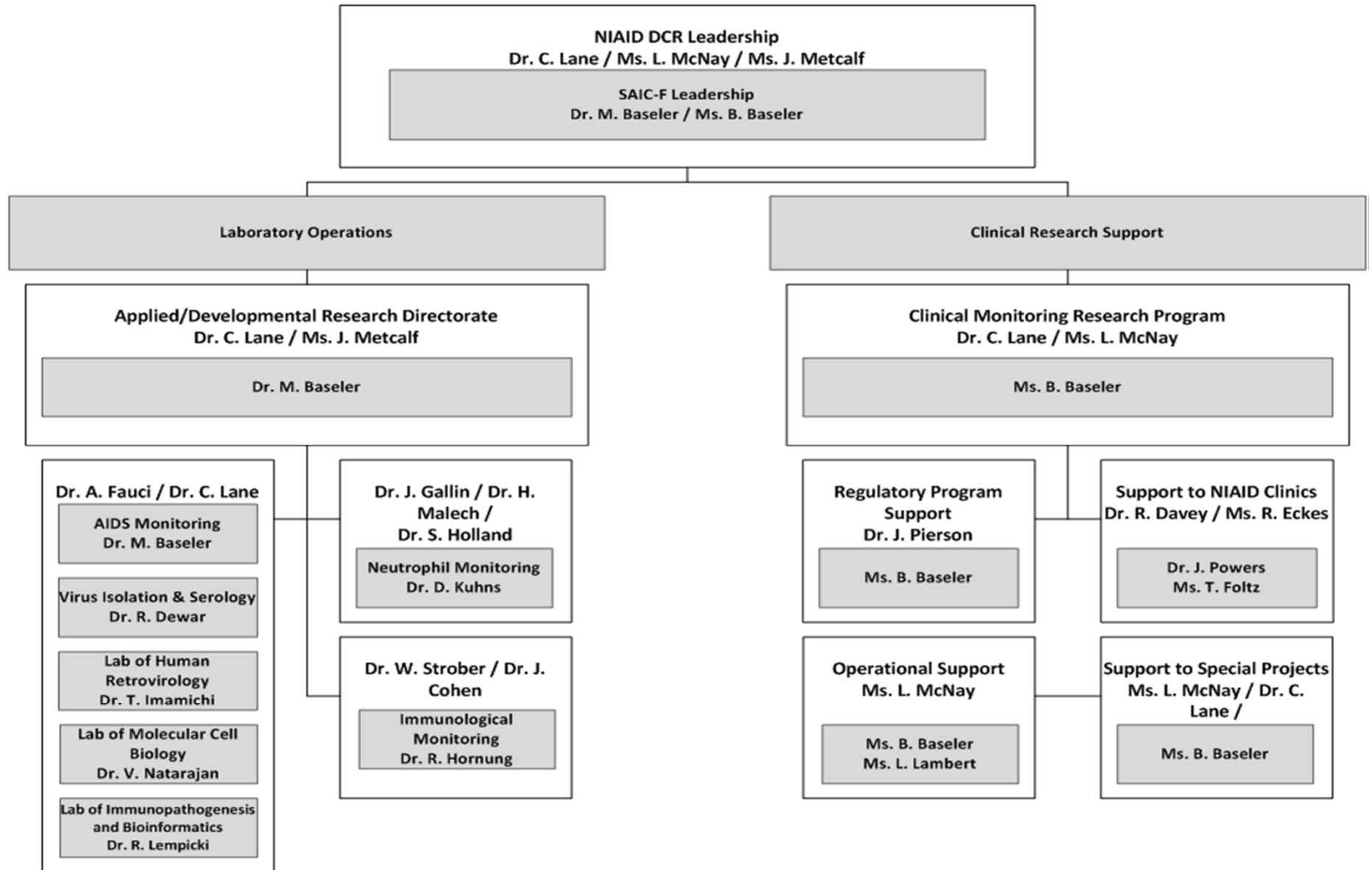
The Protocol Navigator Interface



Factors Leading to Choice of NCI-Frederick for a Given Task

- **Need for an ongoing, close working relationship**
- **Recurrent similar tasks, minimize need for training new staff**
- **Rapid response**
- **Complement other awards**

NCI-Frederick Support to NIAID Clinical Research and Special Projects



Clinical Research Infrastructure Support Provided by NCI-Frederick

- MDs, Nurses,
Pharmacists
- Protocol
Development
- IND Management
- Clinical Research
Monitoring

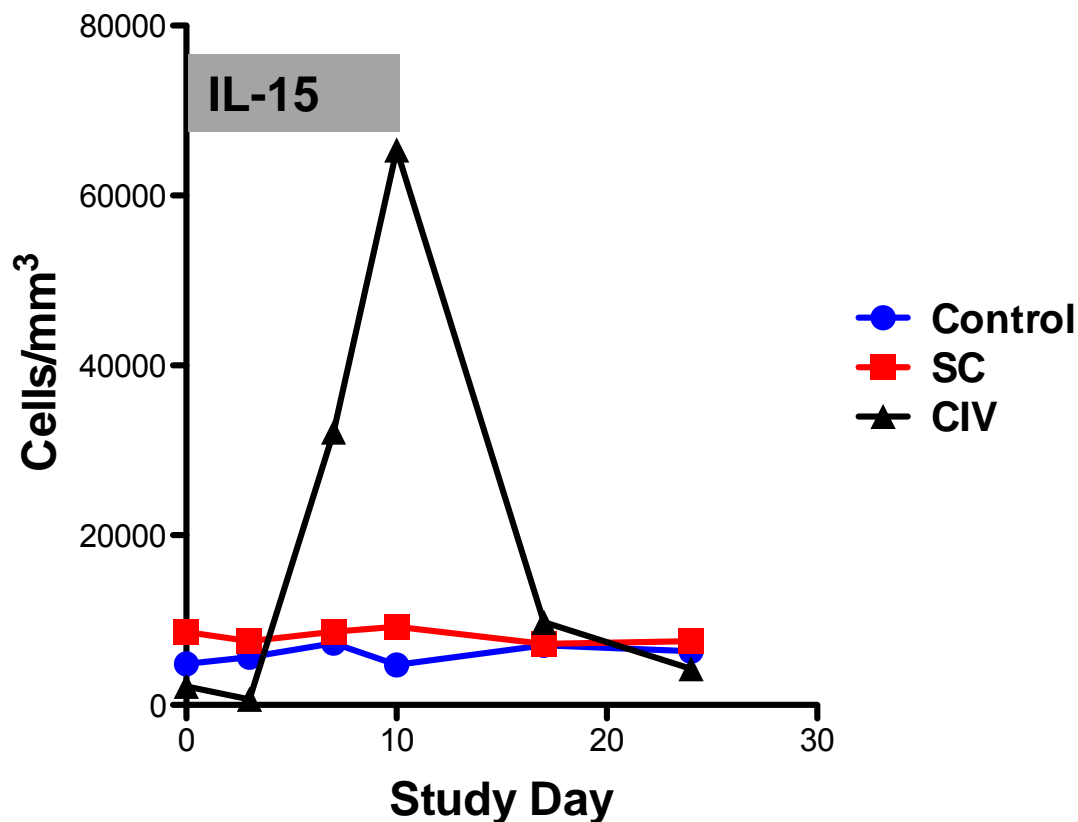
- **Laboratory Support**
 - Monitoring
 - Biomarker analysis
 - Repository
 - **Biopharmaceuticals**
 - Vaccine Production
- Education

Development of IL-15 as a Potential Treatment for HIV/AIDS

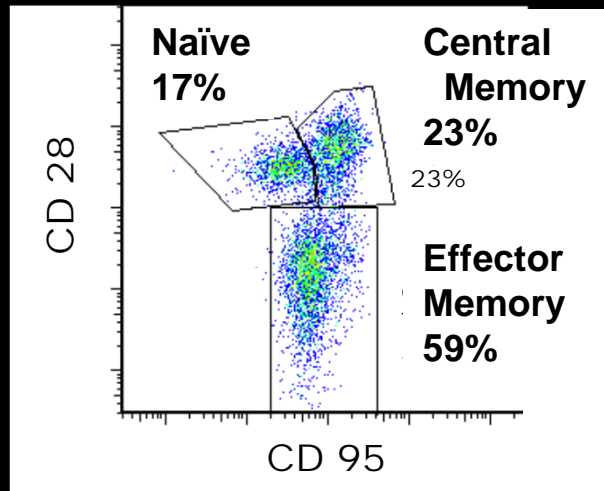
- **Common gamma-chain using cytokine with potent effects on CD8+ T cells**
- **Studied by Tom Waldmann for many years but no commercial development**
- **Working together with Tom and NCI-Frederick, clinical grade IL-15 has been produced and is in clinical trials**

100-Fold Increase in Effector CD8+ T Cells in Non-Human Primates Treated with a 10-Day Continuous IV Infusion of IL-15

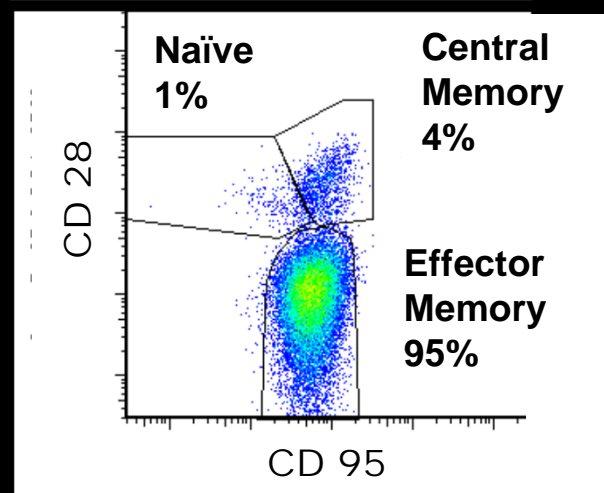
Total CD8 T Lymphocyte Counts



Day 0



Day 10



Support Provided by NCI-Frederick to NIAID

- Clinical Research Infrastructure
- **Support to “Special Projects”**

Characteristics of NIAID Special Projects

- **Identified by NIAID Director**
 - **High priority**
 - **Urgent and compelling**
 - **No other mechanism could easily meet the need**
 - **Often involve other governments**

Current Special Projects in NIAID

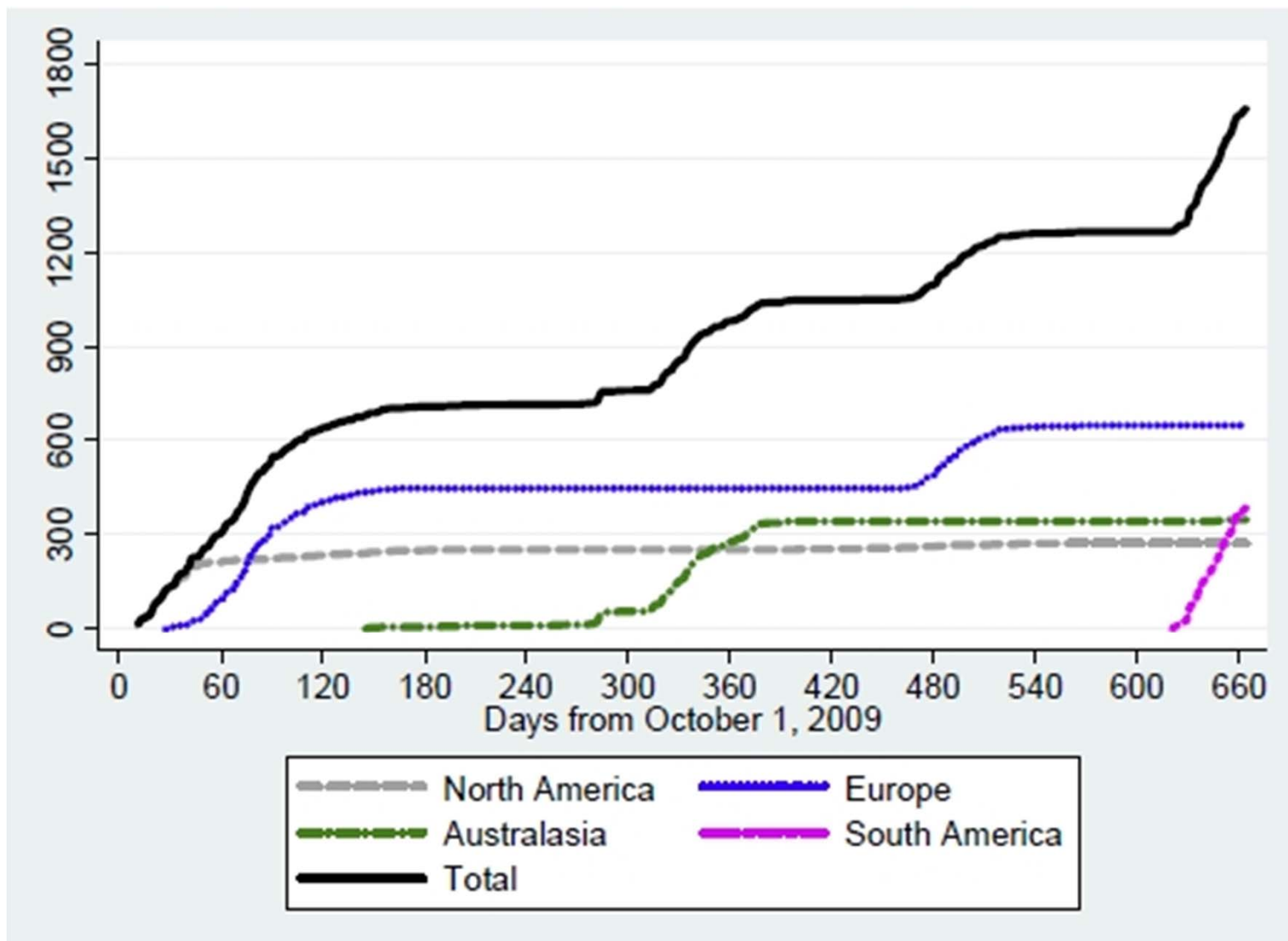
- **Influenza**
 - **Observational cohort studies**
 - **Interventional studies**
- **Project Phidisa (US-South Africa)**
- **DC Partnership for HIV/AIDS**
- **US DoD ID Clinical Research Program**

One Never Knows Where the Next Influenza Pandemic Will Arise



INSIGHT- Observational Cohort Study FLU 002

Cumulative enrollment over time by geographic region.



D-dimer and Risk of Bad Outcome in FLU 002 and FLU 003

D-dimer Tertile*	Odds Ratio (CI)		
	FLU 002	FLU 003 General Ward	FLU 003 ICU
1 (lowest)	1.0	1.0	1.0
2	1.9 (0.6-6.1)	3.3 (0.8-12.9)	4.9 (0.9-25.7)
3 (highest)	4.2 (1.3-13.8)	6.8 (1.9-24.9)	22.0 (3.1-157.3)

*Univariate model; tertiles computed separately for each cohort

Special Project: La Red- Mexico



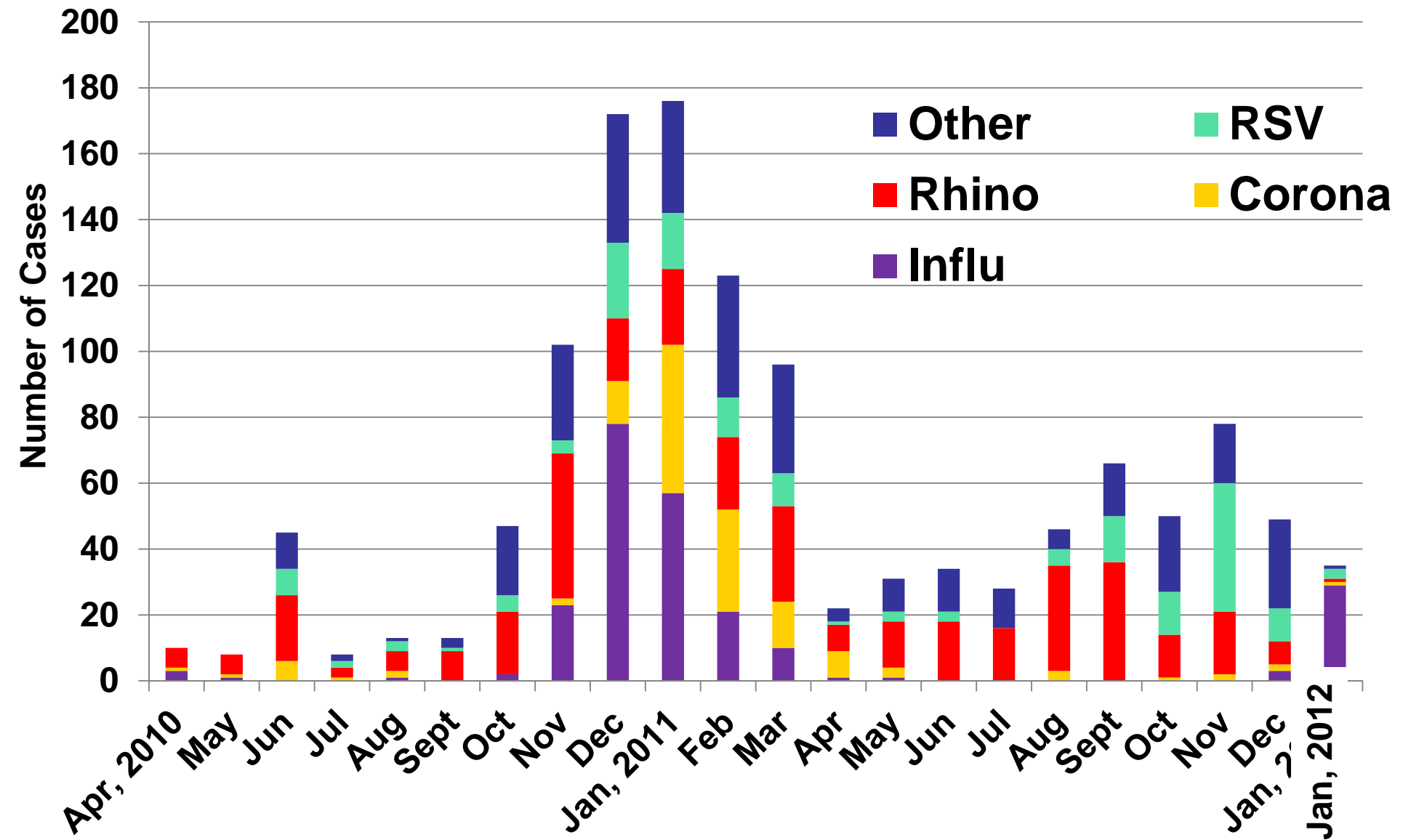
**Signing of the Letter of Intent with the Mexico Minister of Health
2009**

La Red- Mexico Emerging Infectious Diseases Clinical Research Network

- LOI between NIAID and MoH of Mexico in 2009
- 5 clinical sites in Mexico City
- Observational Study of Influenza-like illness in Mexico
- Influenza Combination Therapy Trial



ILI002 – Enrollment as of Jan 10, 2012. n=1,776



Special Project: Phidisa

■ Partnership between South African National Defense Force, NIH, US DoD, and US State Department

■ Goals

- Provide treatment to HIV-positive SANDF members and their dependents in the context of clinical research
- Answer research questions relevant to S. Africa
- Build research capacity within the South African Military Health Service (SAMHS)

■ Over 6000 volunteers enrolled as of December, 2011



Signing of Formal Agreements between US and RSA by US Embassy and South African Officials



Amb. Frasier and Minister Lakota
April 26, 2005

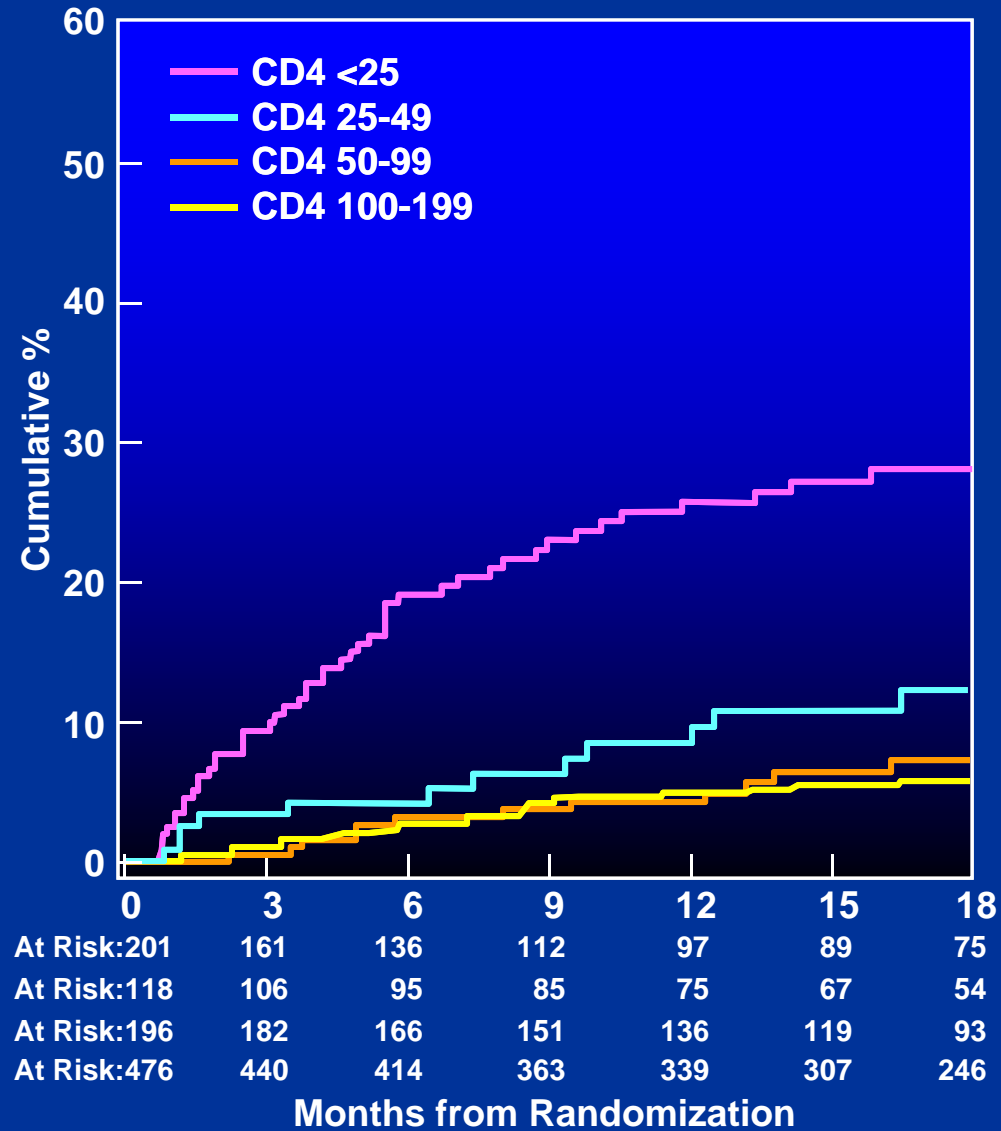
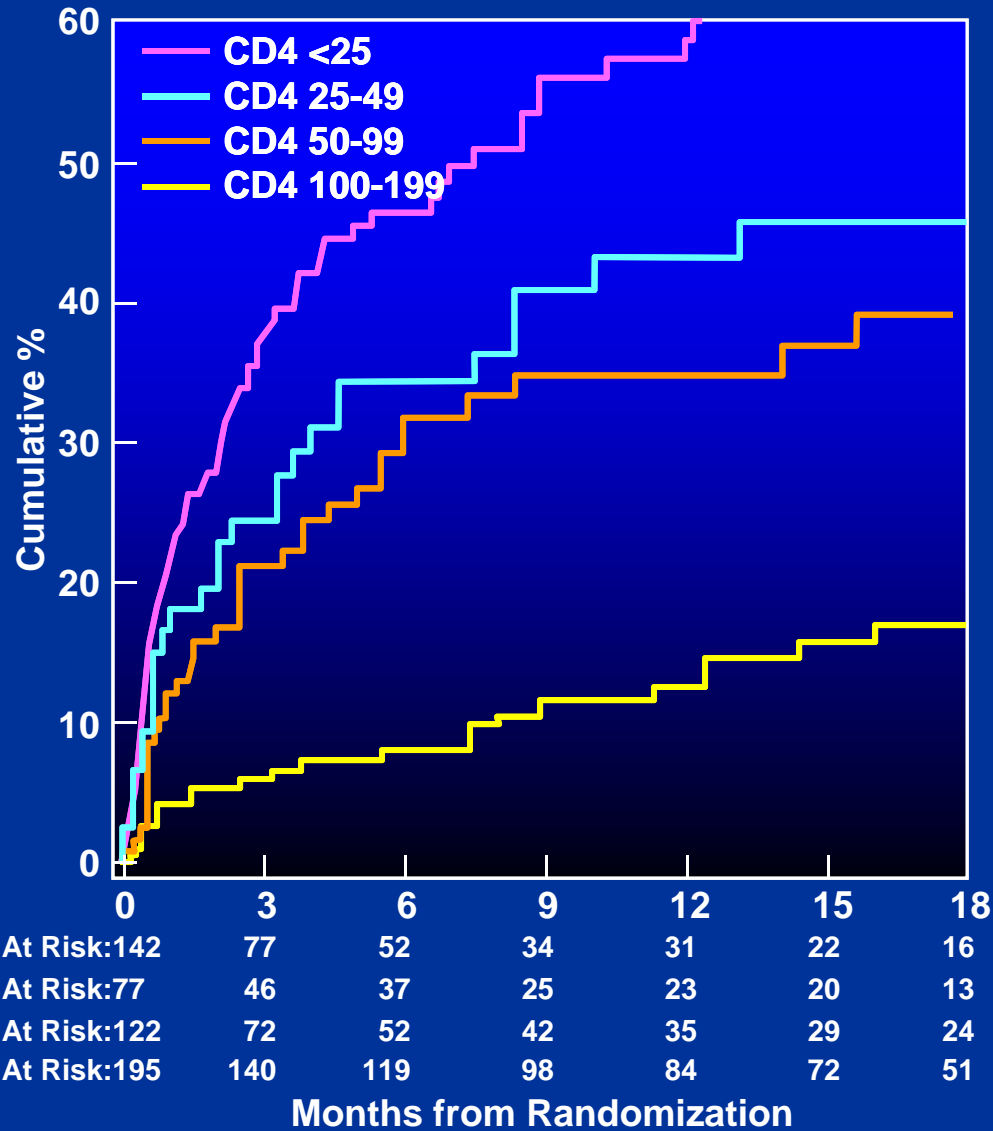


DCM La Lime and MG Motumi
October 5, 2010



Comparison of Outcomes in Untreated vs. Treated Pts.

K-M Estimates of Mortality Rates Over Follow-up by CD4; $p < 0.0001$



Special Project- DC PFAP

Launch of D.C. Partnership for HIV/AIDS Progress, Jan. 12, 2010



Photos: V. Aiyer/Executive Office of the D.C. Mayor (L); J. Marquardt (R)



Carl Dieffenbach, PhD
Director, Division of AIDS
National Institute of Allergy and
Infectious Diseases



Henry Masur, MD
Chief
Critical Care Medicine
Department
NIH-Clinical Center



Gregory Pappas, MD, PhD
Senior Deputy Director for HIV/AIDS,
Hepatitis, STD, and TB Administration,
Department of Health
District of Columbia

The mission of DC PFAP Sub specialty Clinics is to reduce the burden of HIV in DC by developing an innovative community-based clinical research program that will inform health care strategies and impact the AIDS epidemic and create a model for other urban areas and globally.

DCPFAP Steering Committee

NIAID Review of Projects Supported by NCI- Frederick

- **Board of Scientific Counselors for Projects led by Intramural Investigators**
- **For Special Projects there are Two Levels of Review**
 - **NIAID Research Initiative Committee**
 - **Project-Specific External Scientific Advisory Committees**

Summary

- **NCI-Frederick is a critical component of the NIAID clinical research effort**
- **This is especially true for the support of intramural investigators and “Special Projects”**
- **Consistency, flexibility and rapid response time are key factors in choosing NCI-Frederick for select activities within the NIAID portfolio**