

# Frederick National Laboratory: Current Work and Future Directions

Frederick National Laboratory  
for Cancer Research

*sponsored by the National Cancer Institute*



**Ethan Dmitrovsky, M.D.**  
American Cancer Society Professor  
President, Leidos Biomedical Research and Laboratory  
Director, Frederick National Laboratory for Cancer Research

DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Cancer Institute

Frederick National Laboratory is a Federally Funded Research and Development Center operated by Leidos Biomedical Research, Inc., for the National Cancer Institute

# Session Objectives

- **Review advances since the last FNLAC meeting; cite future directions of Frederick National Laboratory.**
- **Provide updates into NCI and NIAID programs that have made recent substantial progress.**
- **Describe efforts to reach out broadly to the NIH and external academic and biomedical communities to enable partnerships that advance the public's interest.**
- **Answer your questions.**

# How Frederick National Laboratory Works to Serve the Scientific Community

## FFRDC Contract Portfolio

- The legacy contract ended. All work transitioned to NCI or NIAID Task Orders on September 30<sup>th</sup>, 2019.
  - 5 Operational Task Orders
  - 95 Non-operational or Moonshot Task Orders
  - Extensive outreach to the broader research community is via subcontracting.

## Operational Task Orders

- Benefits of services are recurring with annual funded appropriations.
- The RAS Initiative is funded as an example of operational work.

## Long Term Projects

- Benefits of work are received upon completion of the work.
- Examples include Ebola or Zika trials and facility refurbishment projects.

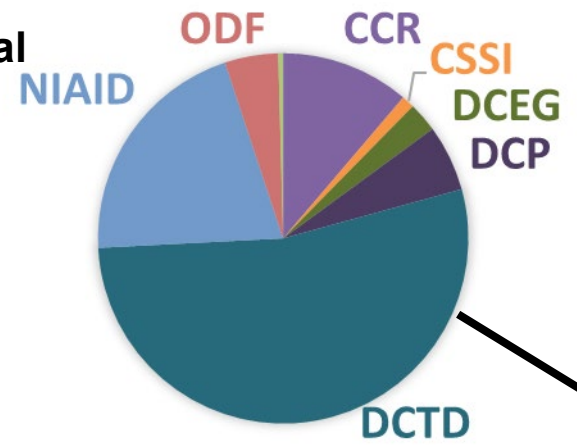
# National Cancer Institute and National Institutes of Health: Guide to Useful Abbreviations

<b>CBIIT</b>	<b>Center for Bioinformatics and Information Technology</b>
<b>CCCT</b>	<b>Coordinating Center for Clinical Trials</b>
<b>CCG</b>	<b>Center for Cancer Genomics (NCI)</b>
<b>CCR</b>	<b>Center for Cancer Research (NCI)</b>
<b>CGH</b>	<b>Center for Global Health (NCI)</b>
<b>CSSI</b>	<b>Center for Strategic Scientific Initiatives (NCI)</b>
<b>DCB</b>	<b>Division of Cancer Biology (NCI)</b>
<b>DCEG</b>	<b>Division of Cancer Epidemiology and Genetics (NCI)</b>
<b>DCP</b>	<b>Division of Cancer Prevention (NCI)</b>
<b>DCTD</b>	<b>Division of Cancer Treatment and Diagnosis (NCI)</b>
<b>IOD</b>	<b>Immediate Office of the Director (NCI)</b>
<b>NCI</b>	<b>National Cancer Institute</b>
<b>NIAID</b>	<b>National Institute of Allergy and Infectious Disease</b> <b>Includes three Divisions in NIAID: Division of Clinical Research, Vaccine Research Center and the Division of Intramural Research.</b>
<b>ODF</b>	<b>Office of the Director, NCI-Frederick: includes funding from Institutes outside of the National Cancer Institute (excluding NIAID).</b>

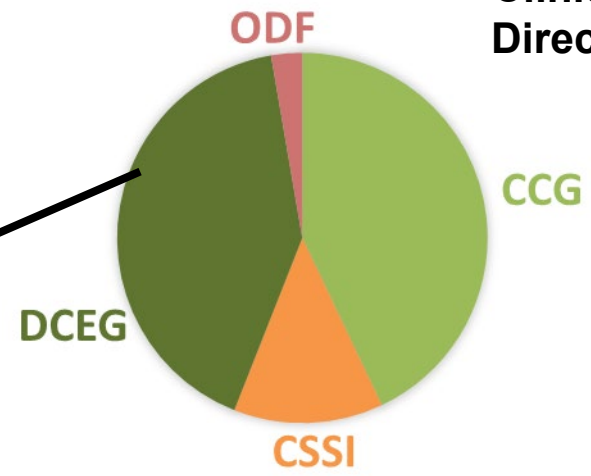
# Breadth of Support at Frederick National Laboratory: Chief Medical Officer Dr. Barry Gause

**Annual Appropriated Funding Sources for Each Directorate**

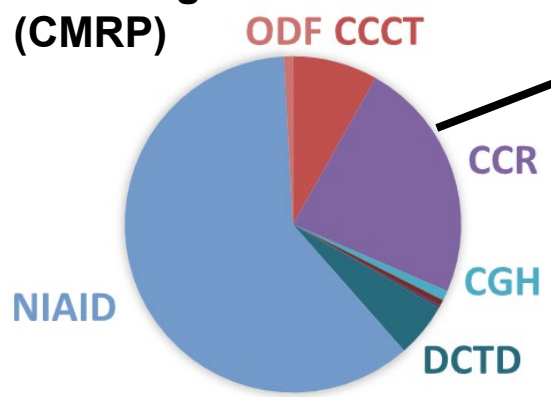
**Applied and Developmental Research Directorate (ADRD)**



**Clinical Research Directorate (CRD)**

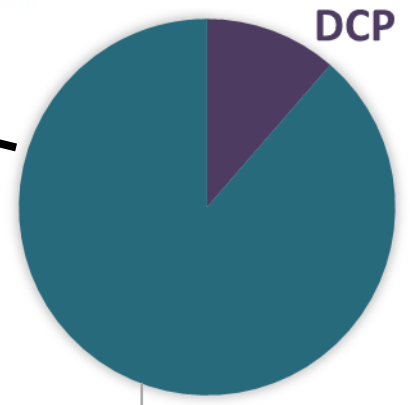
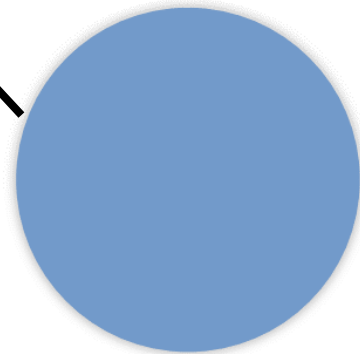


**Clinical Monitoring Research Program (CMRP)**



**Chief Medical Officer**

**Vaccine Clinical Materials Program (VCMP)**



**Biopharmaceutical Development Program (BDP)**

**\*60% to extramural community (via subcontracts and procurement)**

# Support for NCI CAR-T Cell Trials

With the Division of Cancer Treatment and Diagnosis (DCTD)

Frederick  
National  
Laboratory  
for Cancer Research

sponsored by the  
National Cancer Institute

## Internal Working Group

Stakeholders

Clinical staff

Trial: pediatric AML

## Infrastructure

Dry runs

Fresh Leukopacs from healthy donors

Frozen Leukopacs from Hemacare

## Phased Approach

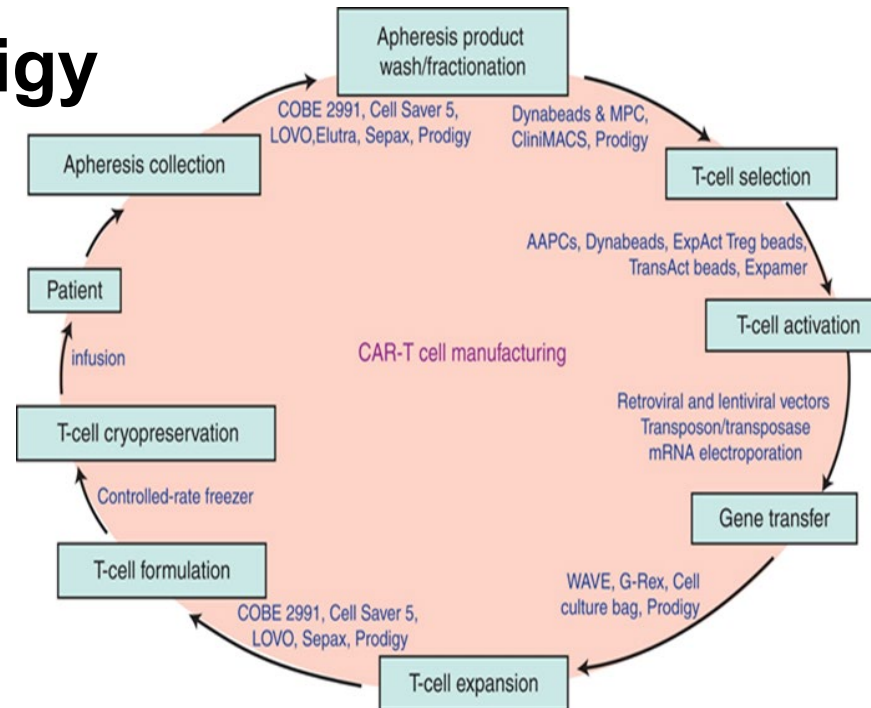
I Clinical Center (summer 2019)

II CHOP

III NMDP sites (3-4)

All Sites will have prior experience  
with CART Cell therapy

## Prodigy



**Dr. James Doroshov, NCI**  
**Dr. Anthony Welch, NCI**  
**Dr. Jason Yovandich, NCI**  
**Dr. Barry Gause, FNLCR**  
**Dr. George Mitra, FNLCR**

- Ferry-Galow KV, Datta V, Makhlof HR, Wright J, Wood BJ, Levy E, Pisano ED, Tam AL, Lee SI, Mahmood U, Rubinstein LV, Doroshow JH, Chen AP. J Oncol Pract, 2018.
- Burton JH, Mazcko C, LeBlanc A, Covey JM, Ji J, Kinders RJ, Parchment RE, Khanna C, Paoloni M, Lana S, Weishaar K, London C, Kisseberth W, Krick E, Vail D, Childress M, Bryan JN, Barber L, Ehrhart EJ, Kent M, Fan T, Kow K, Northup N, Wilson-Robles H, Tomaszewski J, Holleran JL, Muzzio M, Eiseman J, Beumer JH, Doroshow JH, Pommier Y. Clin Cancer Res 24(23): 5830-5840, 2018.
- Fischer WA, Crozier I, Bausch DG, Muyembe JJ, Sabue M, Diaz JV, Kojan R, Wohl DA, Jacob ST: N Engl J Med 380(15): 1389-1391, 2019.

(Leidos Biomedical Research scientists underlined).

# CART Cell Manufacture at the Biopharmaceutical Development Program (BDP)

**Background:** CART cells is an immunotherapy for specific relapsed malignancies. This therapy needs to be democratized. With DCTD we seek to address this need.

**Goals:** Democratize this technology by providing support that does not compete with private sector.

**Approach:** FNLCR will be the central manufacturing site for rare tumor trials. Patients are apheresed at home institution and cells transferred to BDP for transfection and expansion.

**Note:** BDP may also provide Vector Production and distribution to the extramural community for other DCTD-approved projects.

## **CD33 CART Cells**

**Pediatric AML (40 patients)**

**Sponsor/IND: National Marrow Donor Program (NMDP)**

**6 sites: initially at NCI POB and CHOP then extended to 4 other sites**

**Accrual: mid November 2019 - 2022**

## **GD2 CART Cells**

**Neuroblastoma or Osteosarcoma recurrent, refractory, or unresectable metastatic cases, 30 patients will be accrued may expand to 58 cases.**

**Sponsor/IND: CTEP/DCTD**

**Initially at Stanford then to sites in the Pediatric Cancer Immunotherapy Trials Network (CITN).**

**Timeline: December 2020 - 2024**





# The HPV Serology Laboratory

(Sponsored by NCI and The Bill and Melinda Gates Foundation)



**Dr. Ligia Pinto**

## Mission:

- To partner with the international HPV serology community to advance standardization, harmonization and proficiency of HPV serology assays to assess vaccine immunogenicity in vaccine trials through:
  - development of qualified assay standards, critical reagents (HPV Virus-Like Particles), multiplex assays and guidelines that will be made available to the scientific community.

## Impact:

- Enable comparisons of data between different vaccines and studies.
- Accelerate implementation of new vaccines and new vaccine recommendations.

## Partners:

Frederick National Laboratory: Ligia Pinto, Troy Kemp  
NCI: Drs. Doug Lowy, John Schiller, Sean Hanlon  
The Bill and Melinda Gates Foundation: Dr. Peter Dull  
CDC: Dr. Elizabeth Unger

Karolinska Institute: Dr. Joakim Dillner  
Public Health England: Dr. Simon Beddows  
Biostat Consulting, LLC: Dr. Brian Plikaytis  
Global Health Network

Collaborators: Academic Laboratories, Vaccine Industry Laboratories, NIBSC, NIFDC, and WHO.

# Genetics of Human Papillomaviruses (HPVs)

*Cancer Genomics Research Laboratory in support of DCEG*

## Goals:

HPV program was developed in 2014 to study the genetics of HPV and identify the viral genetic basis of HPV carcinogenicity

- Determine which SNPs or sequence specific differences make an HPV type more or less carcinogenic.
- Develop high-throughput methods to allow sequencing of large numbers of HPV genomes.
- Determine risk related to host genome variation and integrate with viral genetic variation.
- Determine the HPV natural history and epidemiologic patterns related to HPV variant lineages and isolates.
- **Model of partnership between NCI and the FNL.**

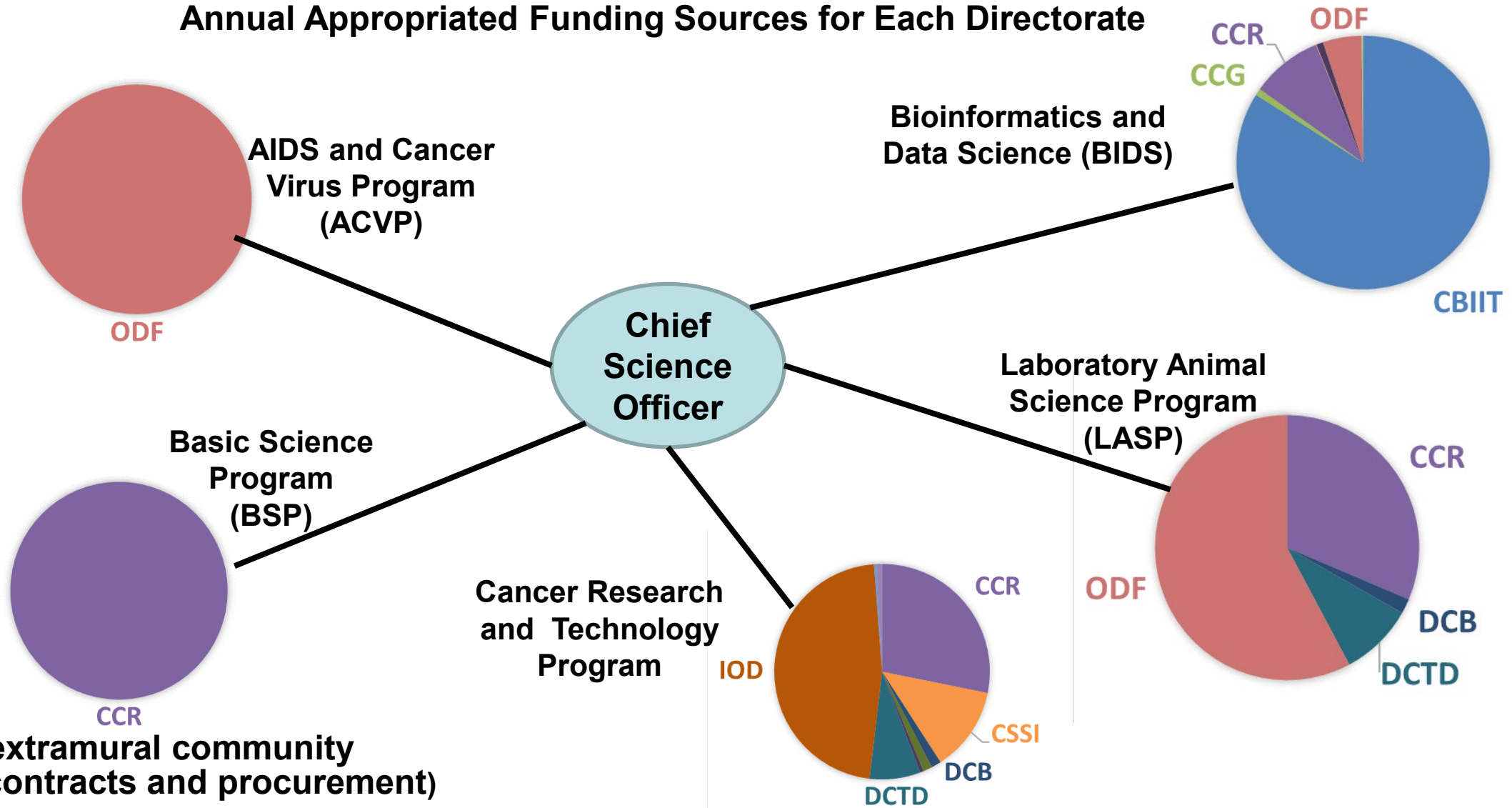
**Dr. Stephen Chanock, DCEG**

## Key Outcomes:

- Developed a next-generation whole-genome sequencing (WGS) assay for HPV16 for clinical specimens that allowed pre-cancer/cancer risk estimates for HPV16 sub-lineages.
- Built bioinformatic and analytic infrastructure for HPPV analyses.
- Develop a low-cost HPV typing assay.
- A deep-sequencing panel of multiple frequently somatically driver mutations in cervical cancer.
- Initiated HPV natural history studies to query clinical biology and epidemiology related to viral lineages.
- These findings led to new studies and collaborations between DCEG, LBR, Cancer Genomics Research Laboratory, and external investigators.

# Breadth of Support at Frederick National Laboratory: Chief Science Officer Dr. Leonard Freedman

Annual Appropriated Funding Sources for Each Directorate



# AIDS and Cancer Virus Program (ACVP) Collaborations

## Intramural

NIAID  
NCI

## Extramural

Boston Children's  
Beth Israel  
Brigham and Women's  
Boston College  
CHOP  
Emory  
Gilead  
MD Anderson  
Oregon Health  
Population Council  
Scripps Research Institute  
Temple University  
UC-Davis  
UCSF  
University of Melbourne  
University of Miami  
University of Nebraska  
UNC  
University of Pennsylvania  
UT-Health  
University of Wisconsin

## cCRADAs

Rockefeller University  
UCSF  
Gilead  
Beth Israel Deaconess

**Dr. Jeff Lifson, ACVP**

## Major Contributions

- Diagnostic tools
- Facilitated HIV testing to secure blood supply
- Non-human primate models
- Innovative therapy
- Disseminated tools and reagents to the community

## Recent High Impact Publications

Iwamoto N et al, Science, 2019.

Di Mascio M et al, Science, 2019.

Hansen SG et al, Sci. Trans. Med., 2019.

Gardner MR et al, Sci. Trans. Med., 2019.

# Antiretroviral Therapy Begun Early After Infection Can Clear Initial SIV Infection

Dr. Jeff Lifson, FNLCR

- Antiretroviral drug therapy initiated at different times post-SIV infection of rhesus macaques.
- Outcome depended on timing of treatment initiation.
- Early treatment for ~ 2 years → eventual decline or clearance of infection without recurrence after stopping treatment begun within 5 days of initial infection.
- The window of opportunity to prevent full systemic AIDS virus infection may be longer than once thought with implications for treatment and prevention.

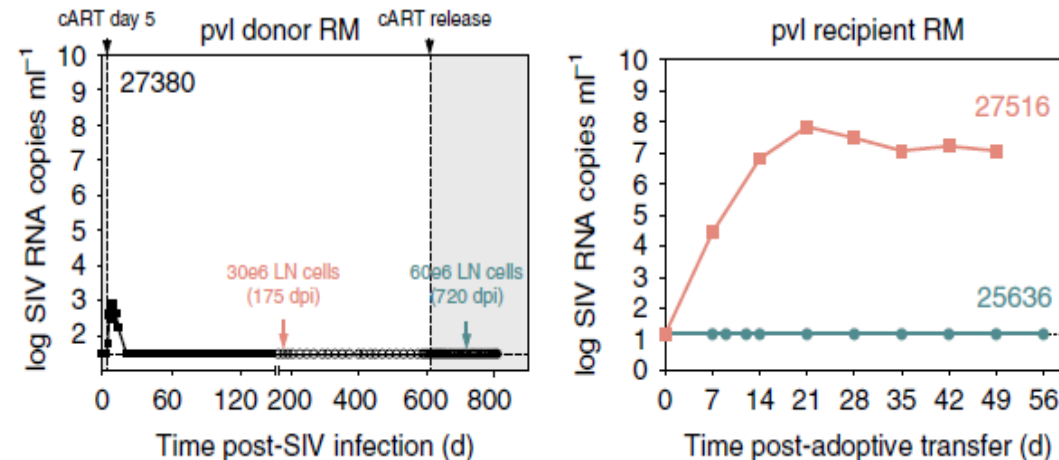
ARTICLES

NATURE MEDICINE | VOL 24 | SEPTEMBER 2018 | 1430-1440 |

nature  
medicine

## Early antiretroviral therapy limits SIV reservoir establishment to delay or prevent post-treatment viral rebound

Afam A. Okoye<sup>1</sup>, Scott G. Hansen<sup>1</sup>, Mukta Vaidya<sup>1</sup>, Yoshinori Fukazawa<sup>1</sup>, Haesun Park<sup>1</sup>, Derick M. Duell<sup>1</sup>, Richard Lum<sup>1</sup>, Colette M. Hughes<sup>1</sup>, Abigail B. Ventura<sup>1</sup>, Emily Ainslie<sup>1</sup>, Julia C. Ford<sup>1</sup>, David Morrow<sup>1</sup>, Roxanne M. Gilbride<sup>1</sup>, Alfred W. Legasse<sup>1</sup>, Joseph Hesselgesser<sup>2</sup>, Romas Geleziunas<sup>2</sup>, Yuan Li<sup>3</sup>, Kelli Oswald<sup>3</sup>, Rebecca Shoemaker<sup>3</sup>, Randy Fast<sup>3</sup>, William J. Bosche<sup>3</sup>, Bhavesh R. Borate<sup>4</sup>, Paul T. Edlefsen<sup>4</sup>, Michael K. Axthelm<sup>1</sup>, Louis J. Picker<sup>1\*</sup> and Jeffrey D. Lifson<sup>3\*</sup>



# Basic Science Program (BSP) Collaborations

## Intramural

NIAID  
NIDDK  
NCI

## Extramural

Harvard

MIT

Oxford Univ.  
Cambridge Univ.  
Fred Hutchinson  
Vanderbilt Univ.  
Johns Hopkins  
University Kansas  
Karolinska Institute  
Hebrew Univ.

University of Colorado Denver

Ohio State University

Stanford University

Central South University, China

University of Illinois

University of Maryland

Cleveland Clinic

UCSF

Mount Sinai School of Medicine

## cCRADAs

Fred Hutchinson  
Univ. of Massachusetts

**Dr. Mary Carrington**

## Major Contributions

- Investigator-initiated research
- Cohort development (disease, therapeutic, vaccine)
- NGS for HLA and KIR
- Procurement for CCR and BSP

## Recent High Impact Publications

Ramsuran V, et al. Science 359: 86, 2018.

Singh SK, et al. Cell Stem Cell 23: 252, 2018.

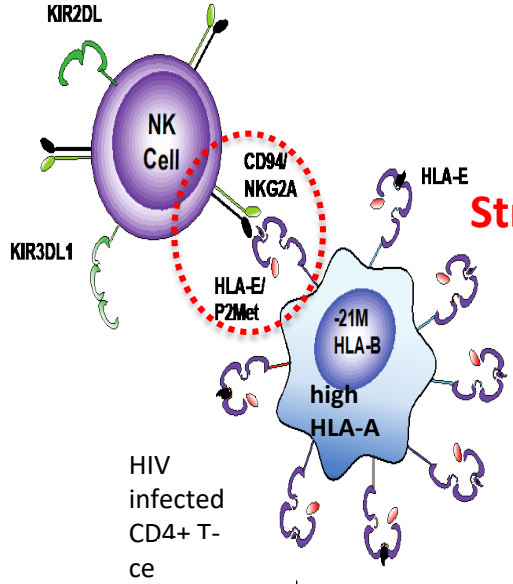
Kulkarni S, et al, Nature Immunol, 2019.

Petersdorf E, et al. Lancet Haematol, 2019.

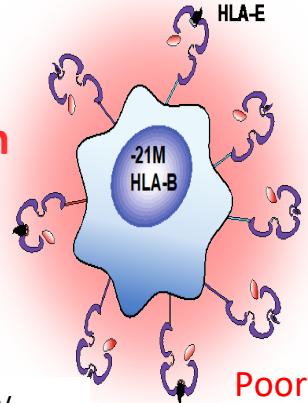
# Immune Response Genotypes Determine Survival of HIV Infected Cells

Dr. Mary Carrington, FNLCR

Genotype that causes inhibition of Natural Killer cells

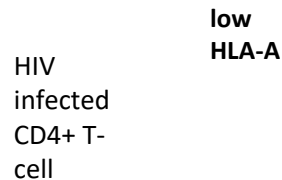


Strong inhibition



Poor HIV control

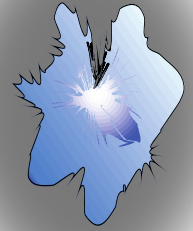
Genotype that enhances killing of HIV infected cells by Natural Killer cells



Activation



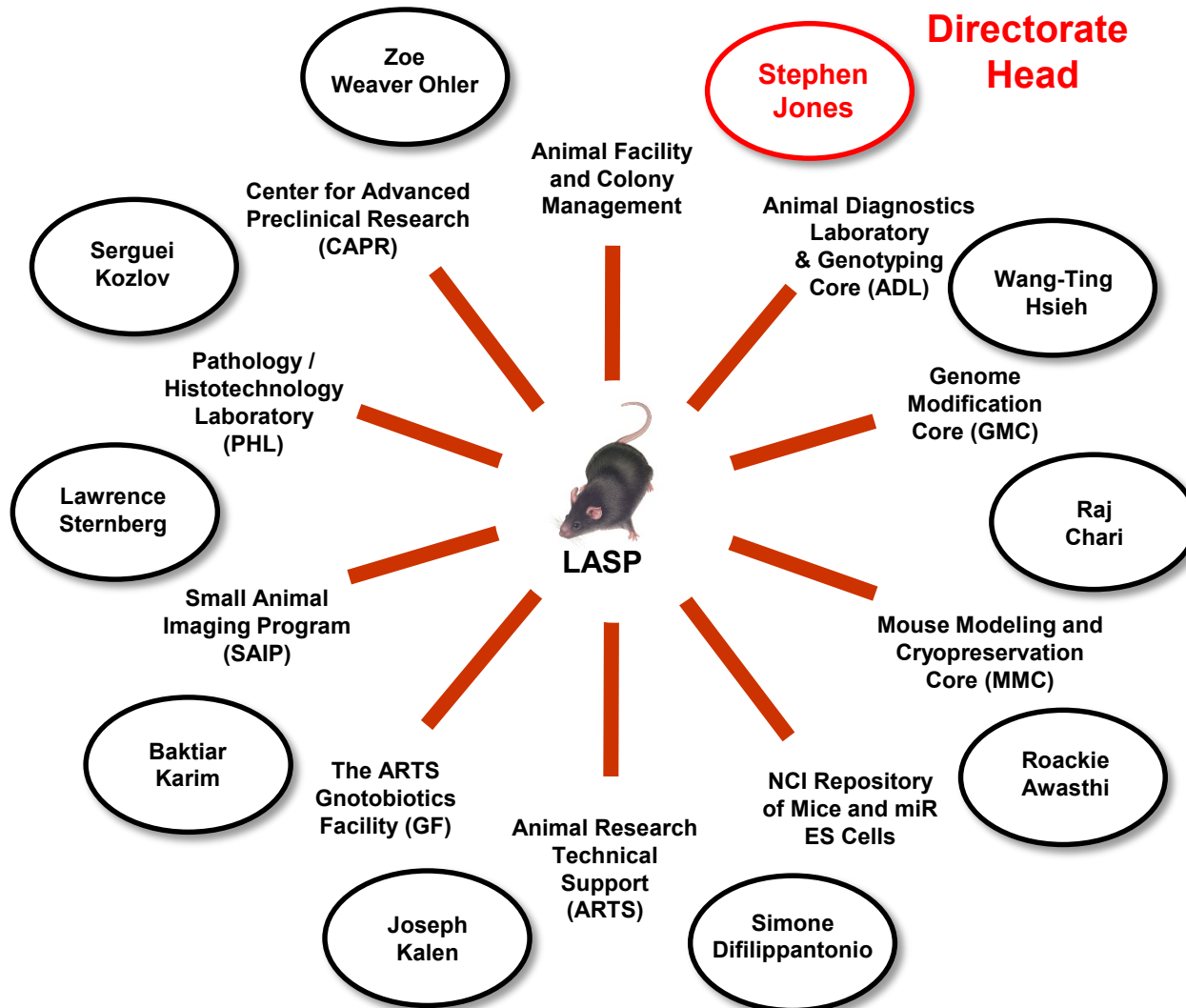
IFN-gamma  
 Perforin  
 Granzymes



Good HIV control

Ramsuran et al, Science, 2018

# Laboratory Animal Sciences Program (LASP)



## Funding Source: NCI Office of the Director

### Supports

NCI Intramural

Center for Cancer Research (CCR)  
OD (Animal Health Monitoring)  
Division of Cancer Epidemiology  
and Genetics (DCEG)

NCI Extramural

NCI Division of Cancer Treatment  
and Diagnosis (DCTD)  
Division of Cancer Biology (DCB)  
NIAID, NIAMS, FNLCR

Interagency Agreements

FDA, U.S. Army

cCRADAs

## Recent High-Impact Publications

Gril et al., Nat Commun. 9:2705, 2018.  
Szot et al., J Clin Invest. 128:2927, 2018.  
Yohe et al., Sci Transl Med. 10:441, 2018.  
Siddiqui et al., Sci Rep. 9:2084, 2019.  
Zong et al., Mol Cell 73:1267, 2019.



# NCI National Cryo-EM Facility and Collaborating Institutions



**Dr. Sriram Subramaniam**

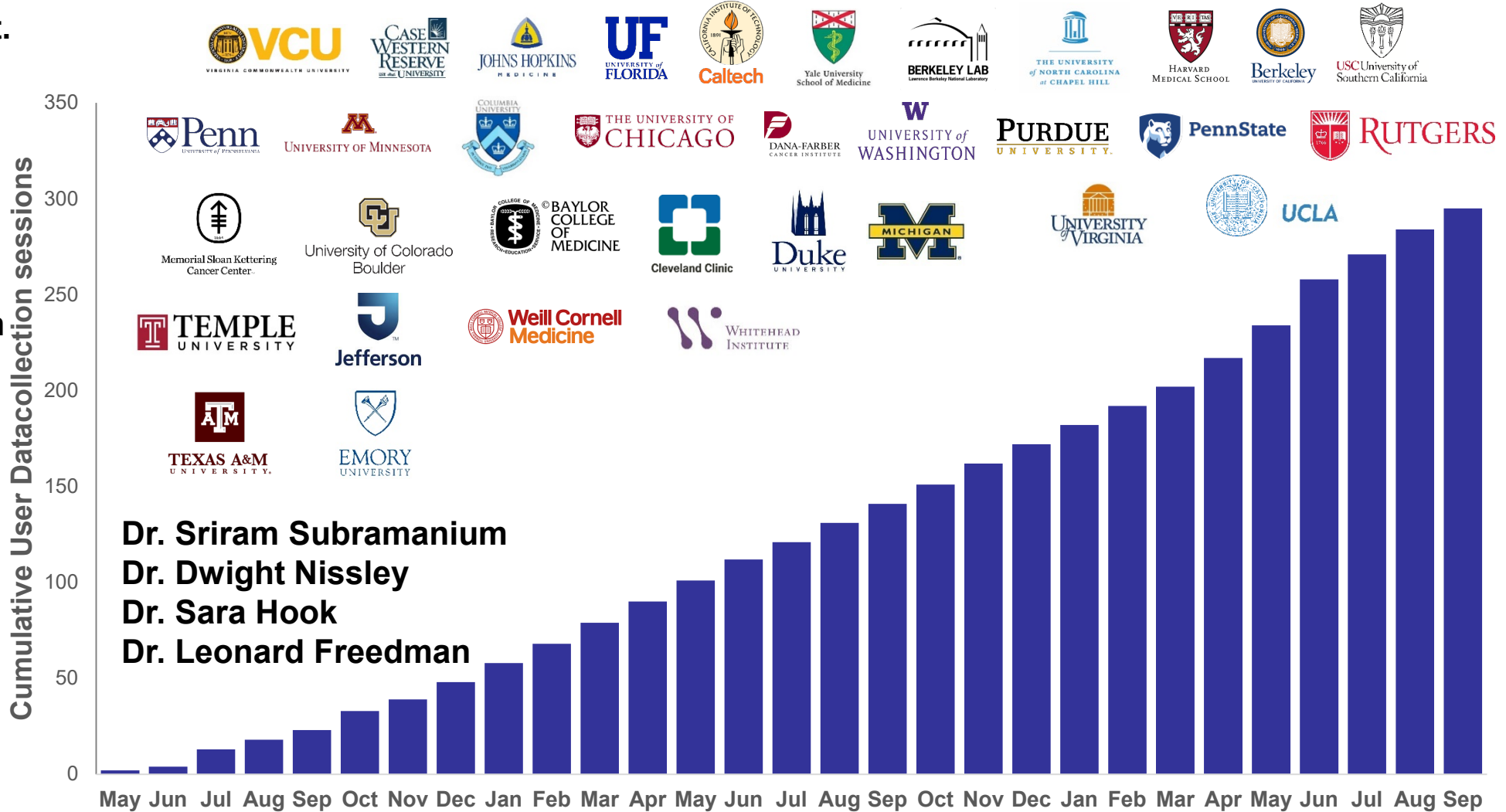
Address gap between need for cryo-EM and access to this instrument.

Opened in May 2017 with one Titan Krios microscope, with second in Winter 2018.

Addition of third microscope in 2019 given growing demand.

Over 300 cancer-related projects from 34 institutions. Feedback is very positive.

First publications in Nature, Cell, Nature Communications, PNAS, Nature Structural and Molecular Biology, Science and elsewhere.



**Dr. Sriram Subramaniam**  
**Dr. Dwight Nissley**  
**Dr. Sara Hook**  
**Dr. Leonard Freedman**

# External Partnerships and Contractor Responsibilities

- **“The Contractor maintains relationships with the broader research community to enhance the intellectual vitality and research relevance of the Laboratory.”**
- **“The Contractor actively develops and pursues collaborative engagement with public and private partners... with the goals of discovery, innovation and improvement of human health. The Contractor is to work with civic, academic and private organizations to advance biomedical research, scientific discovery, and the mission of the Frederick National Laboratory.”**

# Extensive ATOM Outreach Efforts



## Emails sent to:

- 515** pharma contacts from FNL and UCSF Strategic Alliances
  - 69** Cancer center directors
  - 50** NCI academic collaborators
  - 6** national labs directly invited (ANL, ORNL, PNNL, BNL, LANL, and Sandia)
- Additional invites circulated through DOE HQ to DOE system-wide users.

## Online presence across multiple websites and platforms:

- FNL website
- ATOM website
- ATOM LinkedIn
- Personal LinkedIn accounts
- FNL, FNL PDO, ATOM, and NCI NCIP Twitter accounts
- FNL Facebook account

**400**

flyers circulated at AACR (NCI booth, ATOM event, and meet the experts meetings)



• National Academies of Sciences, Engineering and Medicine. Engineering and General Accountability Office (GAO)

• Lawrence Livermore National Laboratory

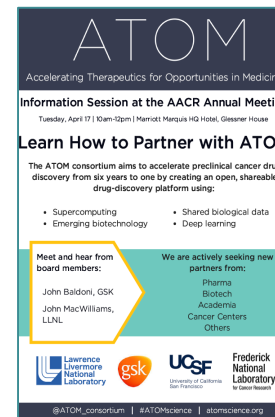
• Oak Ridge National Laboratory

• Argonne National Laboratory

• Purdue University

• Brookhaven National Laboratory

• NCI-Designated Cancer Center Directors' meeting



## Social media activity from FNL and FNL PDO:

### 20 Twitter posts:

- **11,836** views
- **141** engagements (clicks, retweets, likes)

### 3 Facebook posts:

- **481** people reached

# Accelerating Therapeutics for Opportunities in Medicine

## Mission and Vision



**Mission**

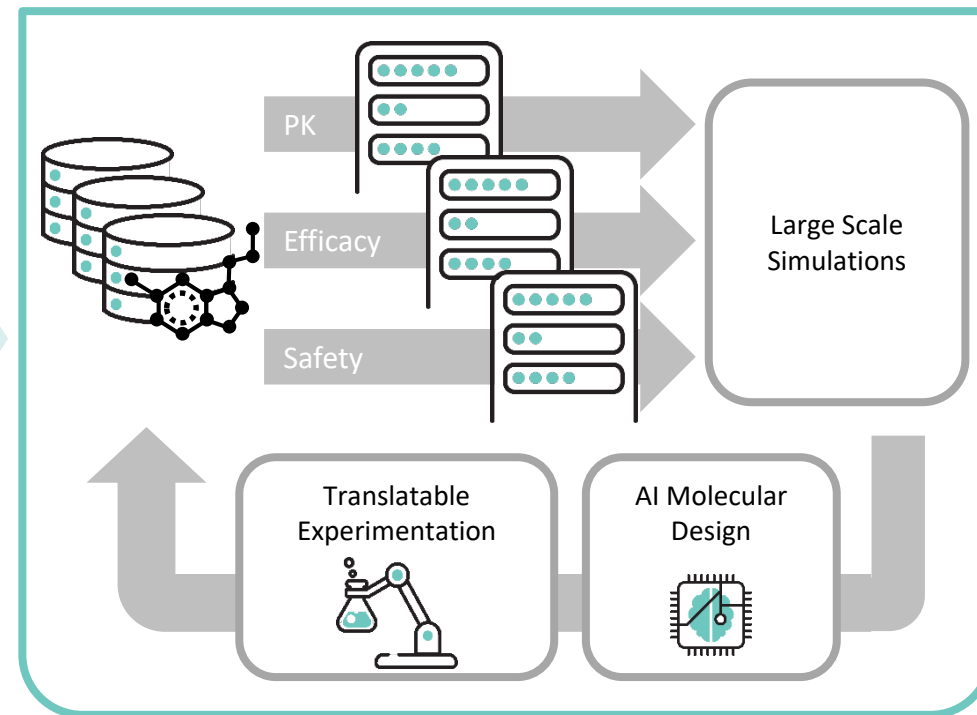
To significantly accelerate the development of more effective therapies for patients



**Vision**

A new starting point:  
Transform drug discovery from a slow, sequential, and high-failure process into a rapid, integrated, and patient-centric one.

How?



Join Us

Lawrence Livermore  
National Laboratory



Frederick National Laboratory  
for Cancer Research

sponsored by the National Cancer Institute



ATOM

# Leidos Biomedical Research and Hood College Cancer Science Symposium

Frederick  
National  
Laboratory  
for Cancer Research

sponsored by the  
National Cancer Institute

**Symposium: interdisciplinary topics in cancer science and cancer medicine  
Hosted by Hood College and inaugural meeting was:  
“Imaging Science in Cancer Biology” June 21-23, 2019**

**Distinguished Speakers (included a keynote public lecture by Dr. Otis Brawley)**

## **Organizing Committee**

Ethan Dmitrovsky, M.D. (FNLCR)  
Andrew Quong, Ph.D. (FNLCR)  
Debbie Ricker, Ph.D. (Hood College)  
Leonard Freedman, Ph.D. (FNLCR)

## **Advisory Committee**

Sriram Subramanian, Ph.D. (UBC)  
Frank McCormick, Ph.D. (UCSF)  
Sara Hook, Ph.D. (NCI)  
Valda Vinson, Ph.D. (Science)  
Ines Chen, Ph.D. (Nature)  
Jean-Charles Soria, M.D., Ph.D. (Medimmune)



# Frederick National Laboratory Director's Distinguished Lecture Series Speakers

Frederick  
National  
Laboratory  
for Cancer Research

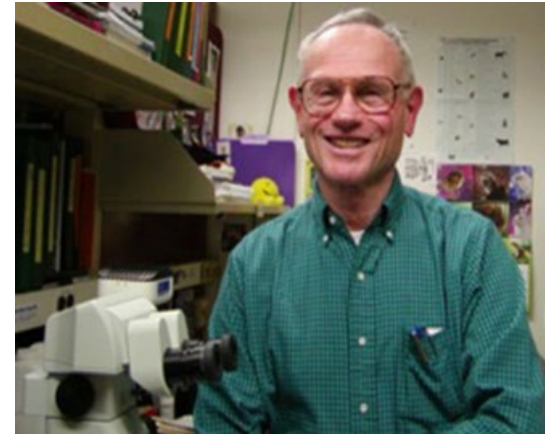
sponsored by the  
National Cancer Institute



**Nancy Speck, Ph.D.**  
Perelman School of Medicine  
University of Pennsylvania



**Jay Dunlap, Ph.D.**  
Dartmouth Geisel School of Medicine



**Michael Sporn, M.D.**  
Dartmouth Geisel School of Medicine



**Helen Piwnica-Worms, Ph.D.**  
MD Anderson Cancer Center



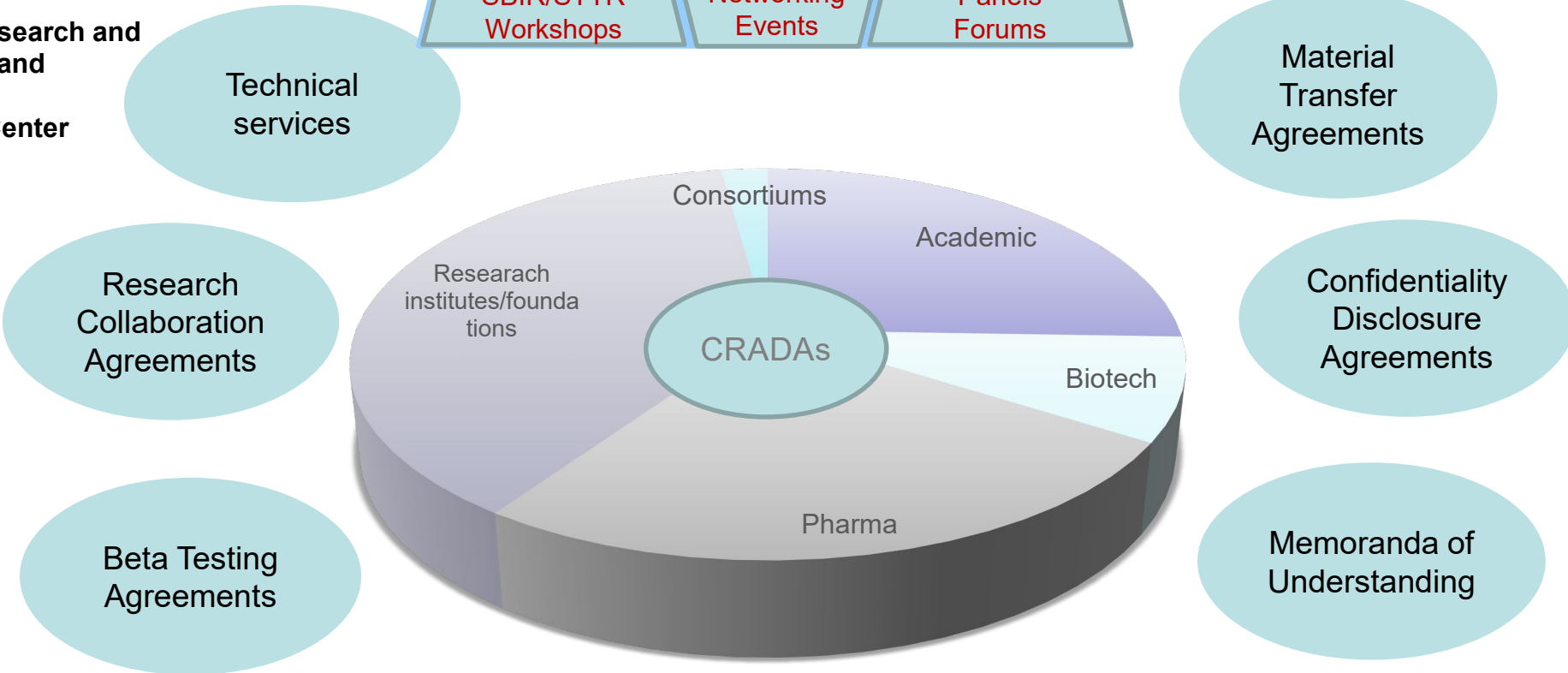
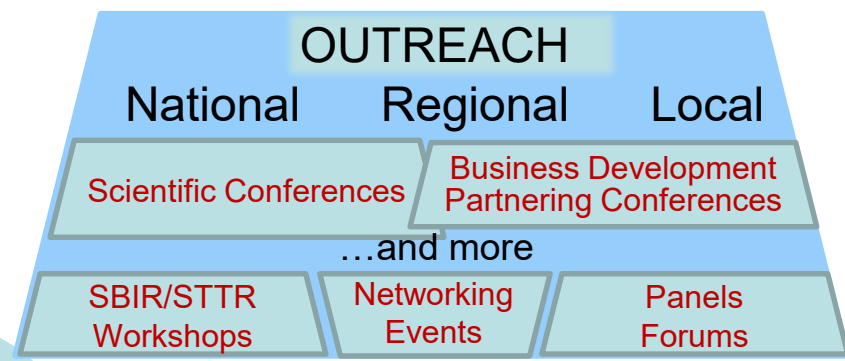
**Doug Lowy, M.D.**  
National Cancer Institute



**James Allison, Ph.D.**  
MD Anderson Cancer Center

# Outreach and Partnerships

- Hood College
- Mount St. Mary's University
- Howard University
- Georgetown University
- University of Maryland
- Morgan State University
- American Academy of Arts and Sciences
- Purdue University
- NCI-Mexico
- CREST (Center for Research and Education in Science and Technology)
- Dartmouth's Cancer Center
- Lawrence Livermore National Laboratory
- Oak Ridge National Laboratory
- Hood College-Leidos Biomedical Research Life Science meeting

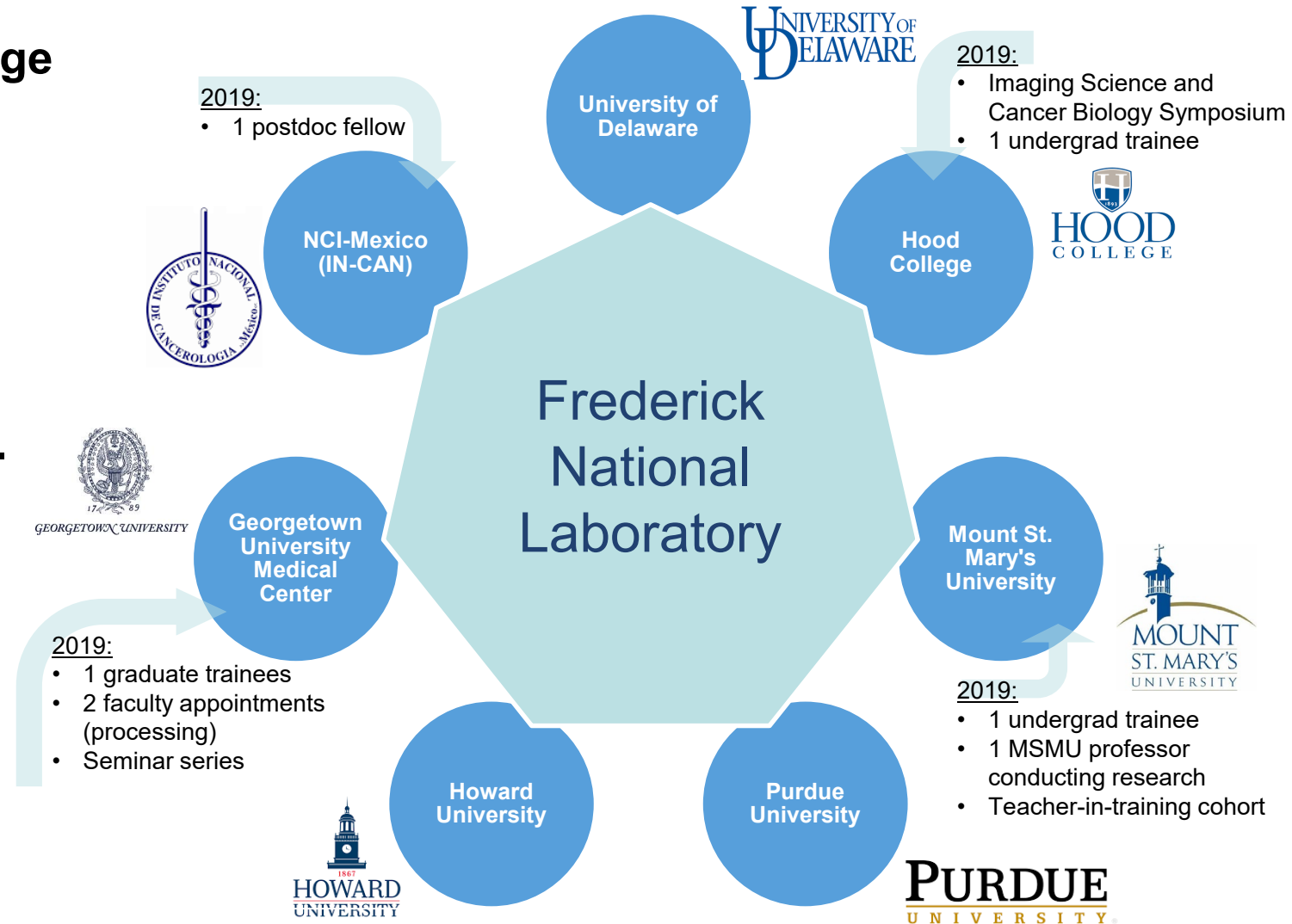


# Recent Academic Partnerships with Frederick National Laboratory

Frederick National Laboratory  
for Cancer Research

sponsored by the  
National Cancer Institute

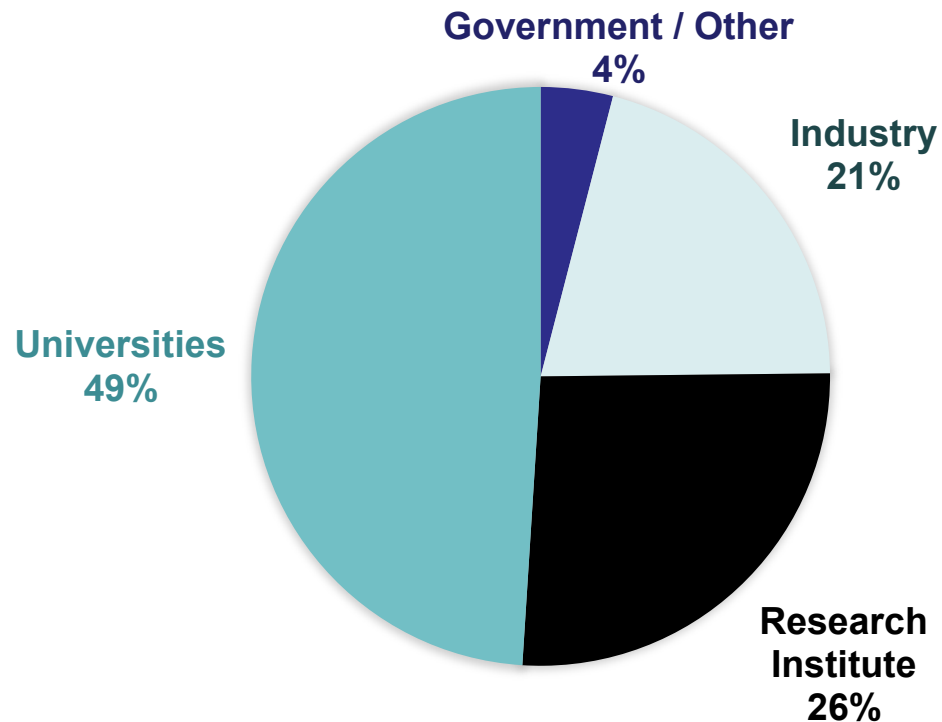
- Appointment and exchange of scientific staff.
- Sabbatical opportunities
- Student training.
- Postdoctoral fellowships.
- Student internships.
- Scientific projects.
- A collaborative model of partnerships.



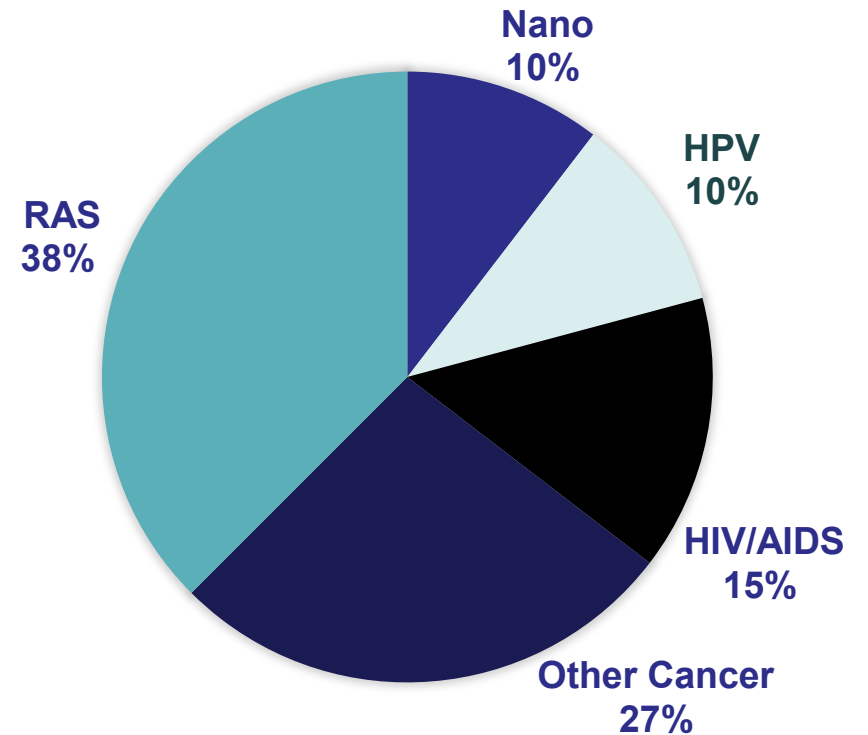


# Who Are Our Partners?

**cCRADA, mcCRADA, MOU, and  
TSA Partners**



**cCRADAs by Research Area**



- 149 unique partners
- 48 executed cCRADAs

Connect with us at [Frederick.Cancer.gov/WorkWithUs](https://Frederick.Cancer.gov/WorkWithUs)

# Conclusions

- **Cited projects at the Frederick National Laboratory having substantial progress since the last FNLAC meeting.**
- **Reviewed how we perform our work at FNLCR.**
- **Provided an update of both NCI and NIAID projects.**
- **Emphasized our partnership with the NCI, other Institutes, government agencies and the extramural community. We work collaboratively to improve the public's health.**