## Frederick National Laboratory Operations and Additional Updates

## Frederick National Laboratory for Cancer Research

sponsored by the National Cancer Institute



### Ethan Dmitrovsky, M.D.

President, Leidos Biomedical Research and Laboratory Laboratory Director, Frederick National Laboratory for Cancer Research

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

## **Session Objectives**

- Review the Frederick National Laboratory rapid response to the pandemic. This is a case study for a Federally Funded Research and Development Center.
- Show that this pivot did not prevent decisive quantitative or discovery science, translational research, and clinical trials.
- Cite NCI and NIAID programs with major recent progress.
- Answer your questions.

# Federally Funded Research and Development Center Operations



### Federally Funded Research and Development Center Contract

#### **Task Order Portfolio:**

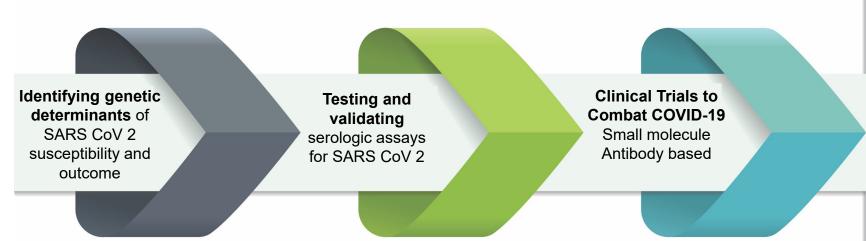
- 5 Operational Task Orders Benefits of services are recurring with annual funded appropriations.
- NCI Task Order, 3 NIAID Task Orders, 1 Lease Task Order
- 98 are Non-operational Task Orders
- 38 are in Clinical Group
- 47 are in Scientific Group
- 13 are Facility or Infrastructure Refurbishments Task Orders
- Extensive outreach to the broader research community is through subcontracting.

## Frederick National Laboratory Pivot with National Cancer Institute to Combat COVID-19

#### Frederick National Laboratory

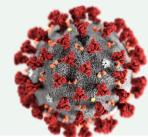
Tor Garice Hesearch

sponsored by the National Cancer Institute



Pivot to COVID-19 Response

- Identifying
- Testing
- Screening



Cancer Genomics
Research Laboratory

Pivot and sustain

Serology Laboratory of Vaccine, Immunity, and Cancer Program Protein Production

Identify space
Implement flexible
infrastructure and network
assess cyber security needs

Clinical Monitoring Research Program

**Pivot and sustain** 

#### **COVID-19 Publications**

- •Liu, G., et al. Cell Sys., In press, 2020.
- •Beigel, J.H. et al. New Engl. J. Med., 2020
- Hicks, J., et al. medRxivdoi: https://doi.org/10.1101/2020.06.22.20137695
- •Klumpp-Thomas C., et al. medRxivdoi: https://doi.org/10.110 1/2020.05.21.20109280.
- •Klumpp-Thomas C, et al, Nat. Commun. 2021
- •Kalil AC, et al, New Engl J. Med., 2020

## Recent Major Publications Beyond COVID-19

- •Petersdorf, E.W., et al, J. Clin. Oncol., 2020
- ●Li, Z., et al, Nat Struc. and Molec. Biol., 2020
- ●Pérez-Guijarro E, et al. Nat Med, 2020
- •Kriemer, A.R., et al. J Natl Cancer Inst, 2020.
- •Yan, W., et al. Cell Reports. In press.
- Liu J, et al. Cell, 2020.

## Does Recognition of Specific SARS CoV2 Peptides Result in Protection?

HLA region 6p21.1-21.3

HLA-DR 2478

HLA-DQ 1398

HLA-DP 1144





Specimens received: N ~2200

- Massachusetts General Hospital
- Brigham and Women's Hospital
- University of California-San Francisco
- **Emory University**

Specimens genotyped: N ~1607

HLA loci are highly polymorphic in humans and some allotypes of these genes appear better able to present peptides that elicit a protective immune response.

## SARS-CoV-2 Serology Protein Production for Collaborators

Frederick National Laboratory

for Cancer Researcl

Sponsored by the National Cancer Institut

- Produce >2 g spike, RBD (binds to ACE2 receptor) and nucleocapsid proteins.
- •Improved production yields for spike and RBD proteins.
- Published in Nat. Comm. and elsewhere on production and assay optimization.
- Proteins utilized for serology applications by multiple collaborators.

Dr. Dominic Esposito
Dr. Kaitlyn Sadtler



### Trans-NIH nationwide serosurvey for CoV-2 antibody detection

- 10,000 volunteers provided blood samples across the United States.
- Proteins used for high sensitivity ELISA-based serology study.
- Manuscript submitted.
- Follow-up longitudinal studies approved by NCI.







## Protein production for NCI SeroNet serology efforts

- Initial protein production used for internal development and validation of serology assays.
- Proteins provided to SeroNet collaborators at NIAID and NIST for assay validation.
- Proteins shared with extramural members of the SeroNet program.



### Rapid response for external serology needs from collaborators

- Proteins given to NIAID for critical Moderna vaccine trial serology.
- Proteins given to Mali scientists for serosurvey projects.
- Proteins to USUHS for multiplex Luminex serology assays.
- Serosurvey collaborations with NHTSA, NCATS and DoD.









### Serological Sciences Network (SeroNet): A View from Within

#### Frederick National Laboratory

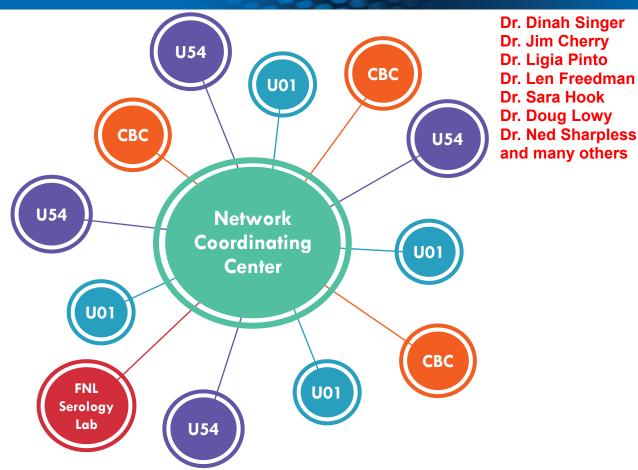
for Cancer Research

sponsored by the
National Cancer Institut

- Designed to be a highly interactive network.
- Sharing of data and resources within SeroNet.
- Open access publication.
- Data and resources made publicly available.

#### Frederick National Laboratory Serology Laboratory

- Implement and qualify SARS-CoV-2 assays.
- Develop qualified assay standards and generate novel reagents.
- •Procure and characterize serum samples from SARS-CoV-2 patients and controls and establish serum panels.
- •Share assays, reagents, and standards within SeroNet.



4-8 CBCs: Serological Sciences Capacity Building Centers (
4-8 U54s: Serological Sciences Centers of Excellence

5-10 U01s: Serological Sciences research projects

Frederick National Laboratory Serology Laboratory

**Network Coordinating Center Frederick National Laboratory** 

### **COVID-19 Clinical Trials with NIAID**



- ACTT: Adaptive COVID-19 Treatment Trial a Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in hospitalized patients.
- Four versions; 1-3 completed, 4 enrolling at US and international sites:
  - o **ACTT-1**: Remdesivir vs. placebo
  - ACTT-2: Remdesivir +/- Baricitinib/placebo
  - ACTT-3: Remdesivir +/- Interferon beta 1a/placebo
  - ACTT-4: Remdesivir + Dexamethasone/placebo vs. Baricitinib/placebo
- 3,500 subjects enrolled into four Phase 3 studies since February 2020.
- Studies Outcomes are:
   FDA Emergency Use Authorizations (EUAs) for Remdesivir and Baricitinib
  - FDA approval of Remdesivir for treatment of COVID-19

### **COVID-19 Clinical Trials in Concert with NIAID**

Frederick
National
Laboratory
for Cancer Research

sponsored by the

National Cancer Institute

Remdesivir International placebo-controlled trial of hospitalized COVID-19 patients on ventilators or oxygendependent.

60 sites and 1063 cases.
Completed accrual in ~2 months.

The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

### Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacio, S. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members\*

NIAID/DMID and CMRP
Beth Baseler
Laura McNay
Dr. Barry Gause
Dr. John Beigel



FDA-approved

Remdesivir +/- Baracitinib
International double-blind randomized placebocontrolled trial of hospitalized COVID-19 cases on
ventilators or oxygen-dependent.

71 sites and 1034 cases.
Completed accrual in ~1.5 months.

The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

#### Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19

A.C. Kalil, T.F. Patterson, A.K. Mehta, K.M. Tomashek, C.R. Wolfe, V. Ghazaryan,
V.C. Marconi, G.M. Ruiz-Palacios, L. Hsieh, S. Kline, V. Tapson, N.M. Iovine,
M.K. Jain, D.A. Sweeney, H.M. El Sahly, A.R. Branche, J. Regalado Pineda,
D.C. Lye, U. Sandkovsky, A.F. Luetkemeyer, S.H. Cohen, R.W. Finberg,
P.E.H. Jackson, B. Taiwo, C.I. Paules, H. Arguinchona, N. Erdmann, N. Ahuja,
M. Frank, M. Oh, E.-S. Kim, S.Y. Tan, R.A. Mularski, H. Nielsen, P.O. Ponce,
B.S. Taylor, L.A. Larson, N.G. Rouphael, Y. Saklawi, V.D. Cantos, E.R. Ko,
J.J. Engemann, A.N. Amin, M. Watanabe, J. Billings, M.-C. Elie, R.T. Davey,
T.H. Burgess, J. Ferreira, M. Green, M. Makowski, A. Cardoso, S. de Bono, T. Bonnett,
M. Proschan, G.A. Deye, W. Dempsey, S.U. Nayak, L.E. Dodd, and J.H. Beigel,
for the ACTT-2 Study Group Members\*

Emergency Use Authorization

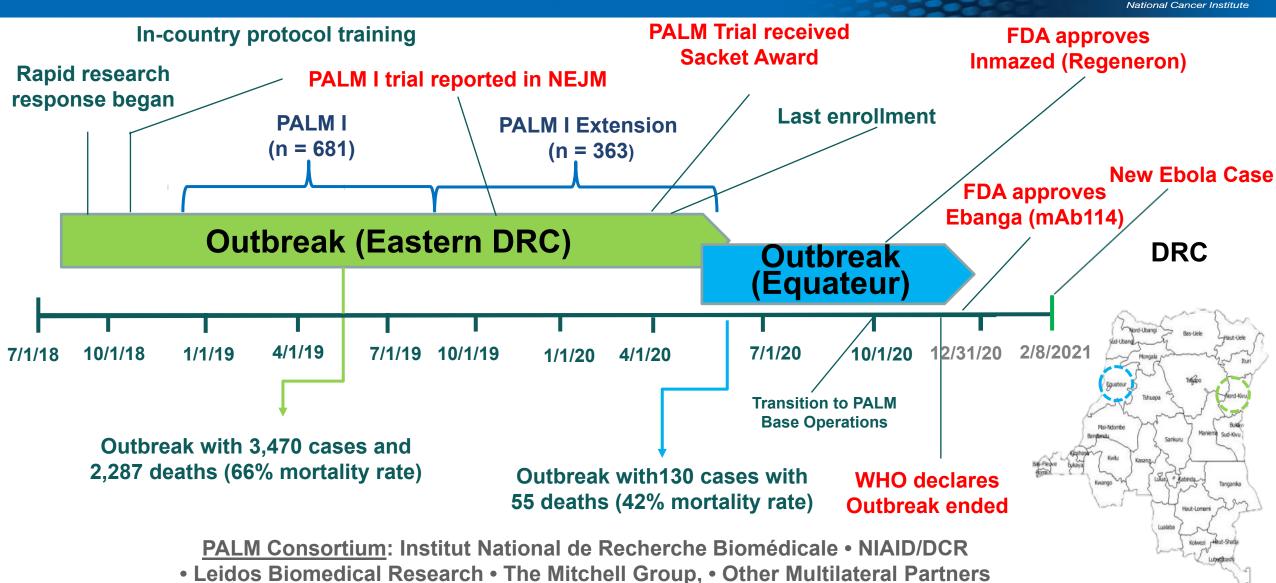
## 孠

## Democratic Republic of the Congo and Course of the Latest Ebola Virus Outbreaks

#### Frederick National Laboratory

for Cancer Research

sponsored by the National Cancer Institute



## NIAID and Frederick National Laboratory **Ebola Trial: A Cycle of Discovery**

**VCMP** 

Frederick **National** Laboratory for Cancer Research

sponsored by the National Cancer Institute

## PAI M



ESTABLISHED IN 1812

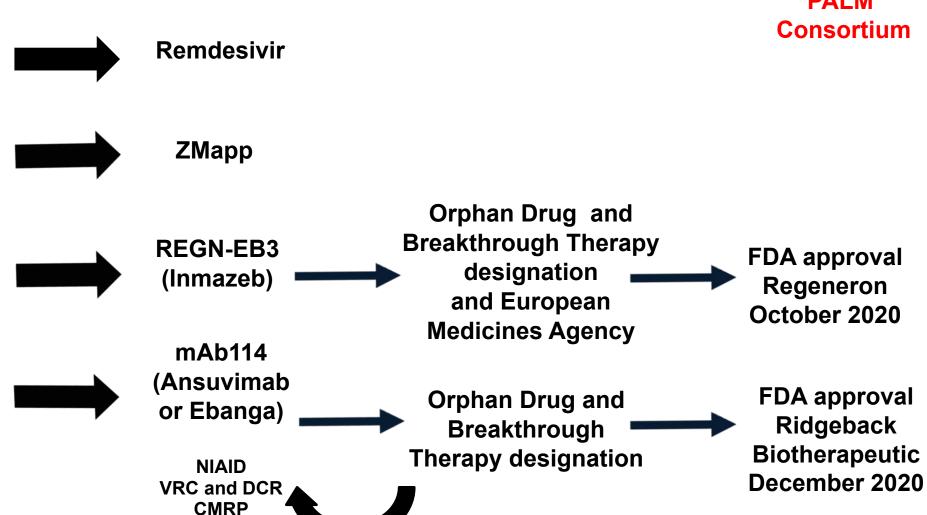
**DECEMBER 12, 2019** 

VOL. 381 NO. 24

A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

Sabue Mulangu, M.D., Lori E. Dodd, Ph.D., Richard T. Davey, Jr., M.D., Olivier Tshiani Mbaya, M.D., Michael Proschan, Ph.D., Daniel Mukadi, M.D., Mariano Lusakibanza Manzo, Ph.D., Didier Nzolo, M.D., Antoine Tshomba Oloma, M.D., Augustin Ibanda, B.S., Rosine Ali, M.S., Sinaré Coulibaly, M.D., Adam C. Levine, M.D., Rebecca Grais, Ph.D., Janet Diaz, M.D., H. Clifford Lane, M.D., Jean-Jacques Muyembe-Tamfum, M.D., and the PALM Writing Group, for the PALM Consortium Study Team®

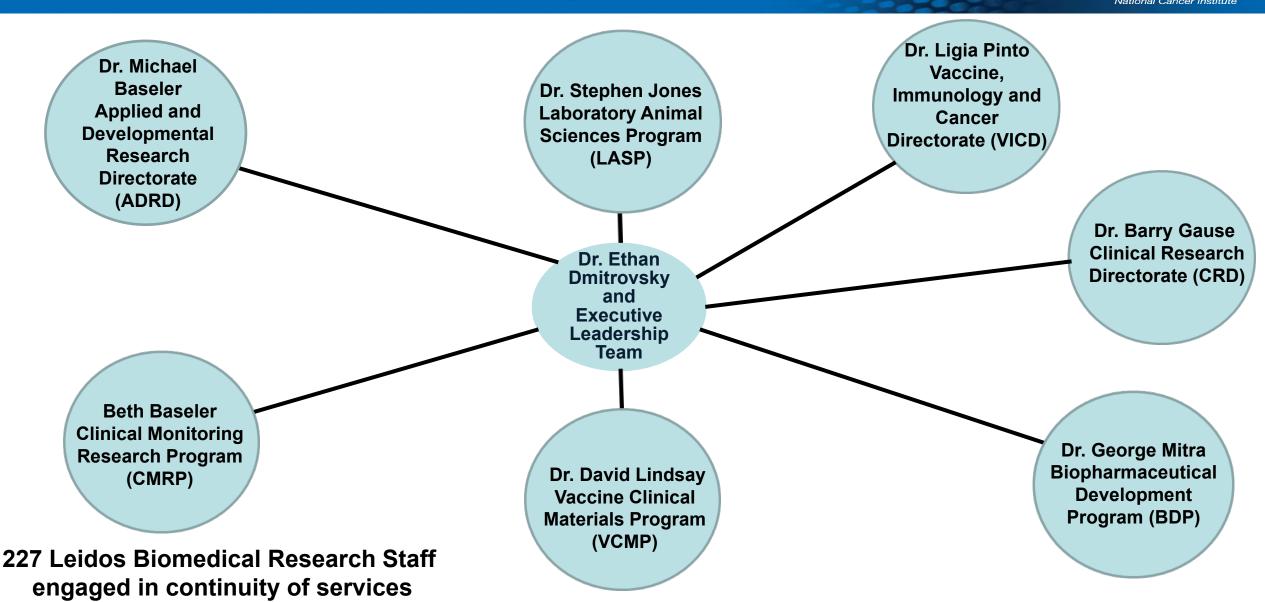
> **PALM** Consortium



# Continuity of Veterinary and Clinical Services During the Pandemic

Frederick National Laboratory

sponsored by the



## Case Study: Continuity of Essential Services for Laboratory Animal Sciences

Frederick **National** Laboratory

for Cancer Research

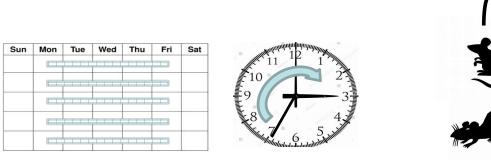
sponsored by the

**LASP** (pre-pandemic)



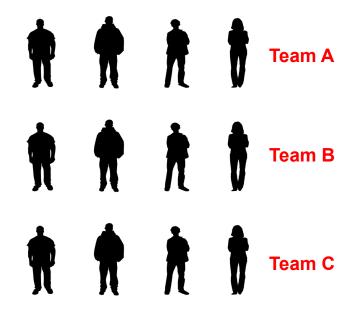


**NCI** vivarium (Bethesda and Frederick) essential veterinary and husbandry services





#### **LASP** (during pandemic)



Sun	Mon	Tue	Wed	Thu	Fri	Sa
ш		ш	ш		ш	
<del></del>	 					-
111	1 1 1 1					11
						-
ш						11



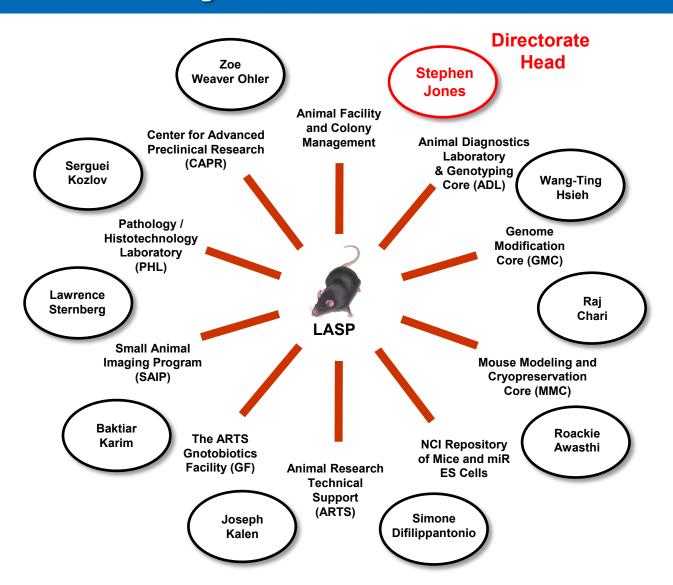


## Laboratory Animal Sciences Program (LASP)



for Cancer Research

sponsored by the National Cancer Institute



#### **Funding Source: NCI Office of the Director**

#### **Supports**

NCI Intramural
Center for Cancer Research
OD (Animal Health Monitoring)
Division of Cancer Epidemiology
and Genetics

NCI Extramural
NCI Division of Cancer Treatment
and Diagnosis
Division of Cancer Biology
NIAID, NIAMS, FNLCR
Interagency Agreements
cCRADAs

#### **Recent High-Impact Publications**

Choi et al., Nat Commun, 2020.
Ruiz-Rodado et al. Cancer Metab, 2020.
Buel et al., Nat Commun, 2020.
Chibaya et al. PNAS, 2021.
Torres-Ayuso et al., Cancer Disc, 2021.
Shrestha et al., J Cell Bio, 2021.

## 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

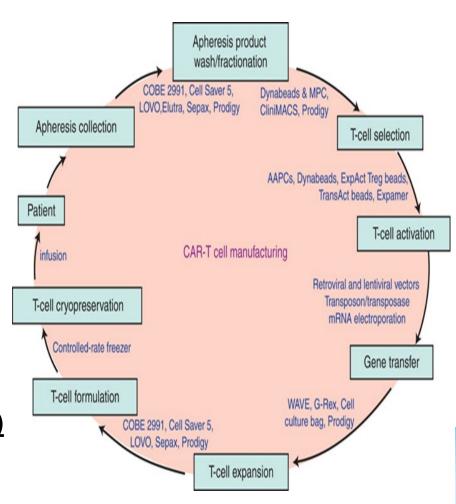
#### **Clinical Trial Phased Approach**

#### Pediatric AML (CD33)

- Manufactured by Biopharmaceutical Development Program (BDP).
- Clinical Trials with National Marrow Donor Program (NMDP).
- Three patients already treated at NIH and one at CHOP.

#### Pediatric Neuroblastoma/Osteosarcoma (GD2)

- Manufacture will be by BDP.
- Clinical Trials are with NMDP.
- Open first at Clinical Center later this year.



Dr. Ned Sharpless

**Dr. James Doroshow** 

**Dr. Anthony Welch** 

**Dr. Jason Yovandich** 

**Dr. Barry Gause** 

**Dr. George Mitra** 

#### **Prodigy System**

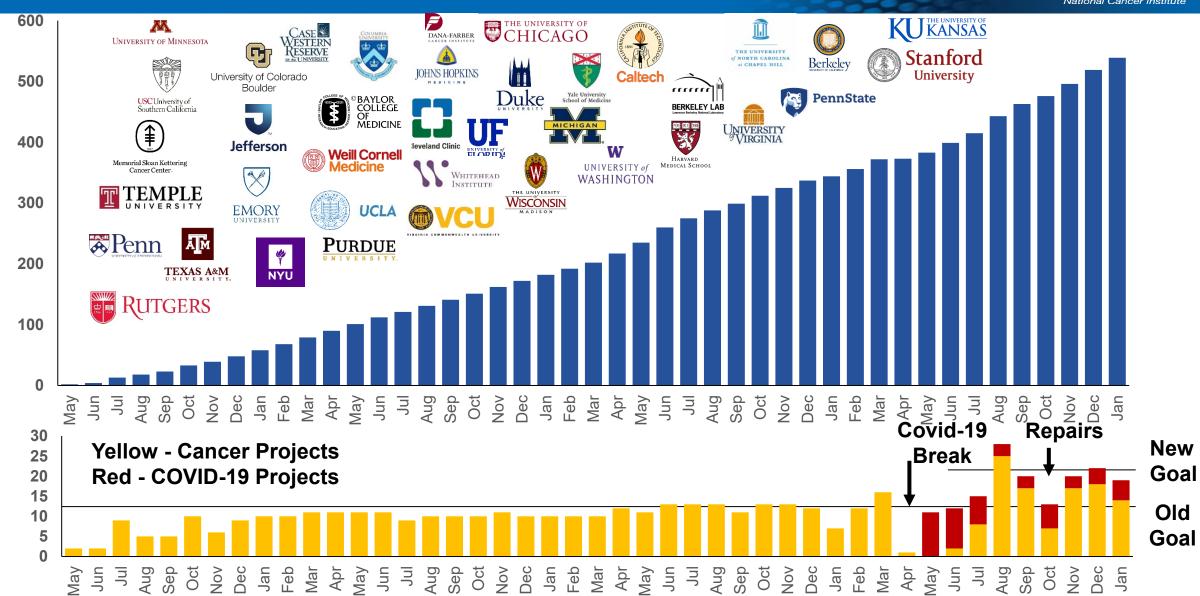


## NCI National Cryo-EM Facility The First Four Years



for Cancer Research

sponsored by the National Cancer Institute



## **Recent Honors and Recognitions**



sponsored by the National Cancer Institute





Ruth Nussinov, Ph.D.
2020 Fellow
American Physical
Society





Jeffrey Lifson, M.D.
2020 Fellow
American Association for
the Advancement of
Science





Mary Carrington, Ph.D.
2021 Fellow
American Academy of
Microbiology



## **Asymptomatic COVID Testing Program**



sponsored by the National Cancer Institute

Frederick National Laboratory has five asymptomatic COVID testing clinics sites. These were put in place within weeks and serve all NIH employees and contractors.

Four clinics are at three Frederick locations.
One clinic is at NCI Shady Grove.

Over 5,600 tests were conducted to date with a positivity rate of 0.2%.

Location	Tests Completed	Positive Results
Frederick Sites	5017	14
Shady Grove	640	0



# Support for Frederick National Laboratory Staff and Community



### **Concierge service:**

Child and elder care resources.

#### **Programs with Johns Hopkins Medicine:**

- Work Stride to help reduce cancer risk and to assist employees who are managing a cancer diagnosis or serving as a caregiver for someone battling cancer while continuing to work.
- DECIDE and Act 2: Diabetes management and prevention programs.
- HealthyWorks portal for access to healthy living and disease prevention information.
- Balance: a behaviorial health resource to improve health and overall well-being.

### **Community service:**

"Nourish our Neighbors"



# Frederick National Laboratory Academic Partnerships

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



- Reviewed Frederick National Laboratory's rapid response to this pandemic that threatened the public's health.
- Despite this pivot other essential work continued.
- This did not prevent decisive discovery, quantitative biology, translational and clinical science.
- Our public-private partnership is expected for a Federally Funded Research and Development Center.

## Acknowledgements



sponsored by the National Cancer Institute

## We thank our NCI, NIAID, and NIH colleagues along with the Key Staff, Directorate Heads and their teams for service during the pandemic.

Dr. Kathy Terlesky, Chief Operating Officer

Dr. Leonard Freedman, Chief Science Officer

Dr. Barry Gause, Chief Medical Officer

Beth Baseler, Clinical Monitoring Research Program

Dr. Michael Baseler, MS, Applied and Developmental

Research

Frank Blanchard, Public Affairs and Communications

**Terri Bray, Environment, Health and Safety** 

**Sue Bruce, MBA, Financial Operations** 

Dr. Mary Carrington, Basic Science Program

Dr. Bernard Courtney, Project Management Operations

**Beverly Hayes, Contracts and Acquisitions** 

Dr. Claudia Haywood, Esq., Intellectual Property and

**Strategic Agreements** 

**Shannon Jackson, Chief Ethics and Compliance Officer** 

Dr. Jeffrey Lifson, AIDS and Cancer Virus Program

Dr. Stephen Jones, Laboratory Animal Sciences

Program

Dr. David Lindsay, Vaccine Clinical Materials

**Program** 

**Chris March, Human Resources** 

Dr. George Mitra, Biopharmaceutical Development

**Program** 

Dr. Dwight Nissley, Cancer Research Technology

Program

Rich Pendleton, Business Service

Dr. Ligia Pinto, Vaccine, Immunology and Cancer

Dr. Vladimir Popov, Partnership Development Office

**Brett Smith, Business Enterprise Systems** 

Dr. Eric Stahlberg, Biomedical Informatics and Data

Science

Dr. Dante Tedaldi, Facilities Maintenance and

**Engineering**