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

• Discuss our current and future work.

• Emphasize our partnership with the NCI, other Institutes, the extramural community and those patients who we serve.

• Answer your questions.
Frederick National Laboratory Serves the Public Interest

Frederick National Laboratory is a national resource that combats cancer, AIDS, infectious diseases and emerging challenges to the public’s health. We tackle problems that others do not.

This is done with the National Cancer Institute (NCI), National Institute of Allergy and Infectious Diseases (NIAID), and other NIH Institutes.

This mission is larger than anyone of us.

We serve in areas not readily addressed by others.
Bidirectional Hub and Spoke Model of Serving the Public’s Health

Intramural Laboratories

Extramural NCI-Supported Laboratories

FNLCR – The Hub

Biotech

Pharma

Contract Research

FNLCR

Extramural NCI-Supported Laboratories

Intramural Laboratories

Biotech

Pharma

Contract Research
# How We Do Our Work
## FY18 Awarded Task Orders

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>Total Awarded</th>
<th>Titles of the Major Initiatives (FY15-FY18)</th>
</tr>
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<tbody>
<tr>
<td><strong>National Cancer Institute</strong></td>
<td></td>
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<tr>
<td>CCG</td>
<td>3</td>
<td>Human Cancer Models Initiative, Refractory Cancers Biospecimens, HIV+ Tumor Characterization</td>
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<tr>
<td>CSSI</td>
<td>3</td>
<td>Lung Cancer Multiple Reaction Monitoring Assay, Multi-omics Analyses (CPTAC), Antibody Production and Characterization</td>
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<tr>
<td>OD</td>
<td>3</td>
<td>Replacement of the Animal Facility Colony, BIQSFP Precision Medicine Study, Bioequivalency Studies</td>
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<tr>
<td>DCP</td>
<td>1</td>
<td>Medicinal Chemistry Support for Chemopreventive Agent Development</td>
</tr>
<tr>
<td>DCTD</td>
<td>18</td>
<td>Monitor Circulating Tumor Nucleic Acid, MATCH, Epstein-Barr Virus-like Particles, Refractory Cancers Biospecimen Acquisition, Multi-omics Analyses for CPTAC, BIQSFP Precision Medicine</td>
</tr>
<tr>
<td>Facilities Refurbishment</td>
<td>14</td>
<td>Building Refurbishments to Buildings 433, 469, 538, 539, 560, and 1066, plus misc. infrastructure improvements</td>
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<tr>
<td><strong>Moonshot</strong></td>
<td></td>
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<tr>
<td>CCG</td>
<td>1</td>
<td>MasterLymph</td>
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<tr>
<td>DCEG</td>
<td>1</td>
<td>Accelerated Control of Cervical Cancer</td>
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<tr>
<td>CBIIT</td>
<td>2</td>
<td>Cancer Data Ecosystem, Data Commons</td>
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<tr>
<td>DCB</td>
<td>1</td>
<td>Human Tumor Atlas Pilot</td>
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<tr>
<td>DCTD</td>
<td>2</td>
<td>Retrospective Tumor Characterization, Biobank and Repositories</td>
</tr>
<tr>
<td>CGH</td>
<td>1</td>
<td>Development of Human Cancer Models Initiative Catalog</td>
</tr>
<tr>
<td><strong>National Institute of Allergy and Infectious Disease (NIAID)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIAID</td>
<td>30</td>
<td>Advance Universal Flu Vaccine, Ebolavirus Vaccines in W. Africa, HIV Clinical Research in West Africa, Zika Virus &amp; other Emerging Infectious Diseases</td>
</tr>
<tr>
<td><strong>Other NIH Institutes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIH (NCATS)</td>
<td>1</td>
<td>CMC Support for NCATS Gene Therapy for AADC Deficiency; Pompe Disease; DMD; Fuch Dystrophy</td>
</tr>
</tbody>
</table>
New Leaders at Frederick National Laboratory for Cancer Research

Beth Baseler
Clinical Monitoring Research Program Directorate

Leonard Freedman, PhD
Chief Science Officer

Eric Stahlberg, PhD
Biomedical Informatics and Data Science Directorate
Focus on the Frederick National Laboratory Community

FNLCR Leadership Team held a retreat. An outcome was an initiative to define core values to shape our identity as a national laboratory.

Dr. David Lindsay and Christopher March lead this effort that brought together colleagues from every part of FNLCR.

We will be rolling out the Workstride Program at FNLCR. This benefits program created by Johns Hopkins Cancer Center supports employees and their families and caregivers who are dealing with cancer.

Support is also provided to the employees’ supervisors so they can learn how best to assist colleagues with a cancer diagnosis in the workplace.

- Provides web-based tools and support of a nurse navigator.
- Maintains confidentiality and savings for FNLCR and our employees.
- We thank David Frick and Christopher March in HR and our medical carriers who provide this service at no cost to FNL employees.
Outreach to the Community

Listening and learning tour.

Executive leadership team held.

Reached out to local, national and international centers to establish collaborations.

Discussed Frederick National Laboratory at Frederick Rotary Club, University of Maryland Cancer Center, Georgetown University Lombardi Cancer Center, Lawrence Livermore Laboratory, National Academy of Medicine and Engineering, American Academy of Arts and Sciences, and elsewhere.

Recreated the popular NCI-Hood cancer meeting.

Launched the Frederick National Laboratory Director’s Distinguished Lecture Series.
New MOUs for Frederick National Laboratory

Hood College
Mount St. Mary’s University

President
Chapdelaine, Hood

President Trainor,
Mount St. Mary’s

Georgetown University
President DeGioia, Dr. Dimolitsas
Dr. Weiner, Dr. Quong and
Dr. Heimbrook

Howard University, iCURE,
NCI-Mexico, and CREST
Provost Wutoh, Howard University, Dr. Springfield, NCI, Dr. Herrera, NCI-Mexico,
Dr. Horn, Frederick CREST

Colleagues: Shannon Jackson, Beverly Hayes,
Richard Pendleton, Dr. Popov, Dr. Haywood,
Dr. Pannucci, Monica Slate, Dr. Quong,
Dr. Komschlies, and Lisa Coleman
Frederick National Laboratory Director’s Distinguished Lecture Series

Dr. Michael Sporn
Dartmouth

Dr. Ned Sharpless
National Cancer Institute

Dr. Doug Lowy
National Cancer Institute

Dr. James Allison
MD Anderson Cancer Center

Dr. Helen Piwnica-Worms
MD Anderson Cancer Center
Frederick National Laboratory and Hood College Cancer Science Symposium

- Annual meeting emphasizing interdisciplinary topics in cancer biology and oncology
- Hosted by Hood College and inaugural meeting is: “Imaging in Cancer Biology” June 21-23, 2019

Organizing Committee
- Ethan Dmitrovsky, M.D. (FNLCR)
- Andrew Quong, Ph.D. (FNLCR)
- Debbie Ricker, Ph.D. (Hood College)

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)
Types of Research

1. Discovery science.
2. Advanced core facility support.
3. Collaborative science in concert with NCI, NIAID, other Institutes.
4. Team science led by FNLCR (ie, RAS initiative).
5. Advanced technology support to extramural community.
Immune Response Genotypes Determine Survival of HIV Infected Cells

Genotype that causes inhibition of Natural Killer cells

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

Ramsuran et al, Science, 2018
Antiretroviral Therapy Begun Early After Infection Can Clear Initial HIV Infection

- 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.

Early antiretroviral therapy limits SIV reservoir establishment to delay or prevent post-treatment viral rebound
Management of 27 rodent and nonhuman primate research facilities (22 Frederick, 5 Bethesda).

Maintenance of 133,400 animals occupying 49,228 cages.

315 LASP associates (234 Frederick, 81 Bethesda)

Support of 206 investigators encompassing 551 active animal study protocols.

Provides support for Frederick and Bethesda ACUC.

LASP operates the NCI animal facilities and provides routine and specialized husbandry services for Investigators on the Bethesda and Frederick campuses.

LASP staffs and operates many state-of-the-art cores and other facilities to assist NCI Investigators in performing their animal-based cancer and AIDS research.

The NCI Mouse Repository is supported by the Division of Cancer Biology (DCB). Accepts submitted GEMs from the cancer community based on rigorous criteria (unique, not commercially availability, and value). The Repository expands strains, cryopreserves, archives, and ships frozen germplasm to the community. Available strains and shipment requests increased 15-20% since FY16.

The Genome Modification Core (GMC) is supported by the Center for Cancer Research (CCR). Provides expert advice on design and use of CRISPRs, TALENs, and other nucleases. Since inception only 10 months ago, the GMC served 44 CCR Investigators and completed 77 projects.

The Gnotobiotics Facility (GF) is funded by the Center for Cancer Research (CCR) and Office of Scientific Operations (OSO) to support research on the role of the microbiota in inflammation and anti-tumor response. Services include the rederivation, breeding, and conduct of experiments on germ-free (axenic) and gnotobiotic (defined microbiome) mice. GF doubled in size and usage over the past year.
NIH/NIAID Vaccine Research Center Development Cycle

**Basic Research** - VRC - NIH campus, Bethesda MD

**Clinical development cycle**
NIAID / Vaccine Research Center (VRC)

**Process development**
Analytical development
Formulation dev.

**Vaccine Production**
Program lab (VPPL)
Gaithersburg MD

**Clinical Trials**
US, global

NVITAL Immune Assessment
Gaithersburg, MD

Dr. David Lindsay, FNLCR
Public and Private Sector Leaders
Drug Discovery, High Performance Computing, Big Data Expertise

Joint Research Committee

Jim Brase
CTO | Co-Lead
LLNL

Stacie Calad-Thomson
COO | Co-Lead
GSK

Tom Rush
CSO | Co-Lead
GSK

Michelle Arkin
UCSF

Governing Board

John Baldoni
GSK

John MacWilliams
LLNL

Alan Ashworth
UCSF

Ethan Dmitrovsky
FNLCR

Amy Gryshuk
LLNL

Dwight Nissley
FNLCR

Patricia Falcone
LLNL

Jason Paragas
LLNL

Barry Selick
UCSF

Eric Stahlberg
FNLCR
Data and modeling groundwork

PK and safety data-driven models

Novel hybrid model development

Active learning integrated loop

Accelerating Therapeutics for Opportunities in Medicine (ATOM)
Support NCI Car-T Cell Trials

Internal Working Group
Stakeholders
Clinical staff

External Review Panel
Dry runs
Fresh Leukopacs from Healthy donors
Frozen Leukopacs from Hemacare

Phased Approach
I - Clinical Center
II - CHOP
III - NMDP sites (3-4)

All Sites will have prior experience with CART Cell Therapy
Ras Initiative: Progress

- RAS initiative continues to focus on two areas:
  - Directly targeting *KRAS*
  - Understanding the biology of *KRAS* in the context of the plasma membrane
- Developing a novel class of compounds that specifically target *KRAS*.
- Multiple screens to identify leads are ongoing.
- Working with Department of Energy to bridge experimental gaps using computation (JDACS4C).
- Partnering with biotech, Pharma and NIH to develop leads and push towards clinic.
Frederick National Laboratory brings cancer research to space by having a payload on the International Space Station to form enhanced Ras crystals for x-ray diffraction studies.
National Cryo-EM Overview and Team

• Mission is to address gap between need for cryo-EM and access to this expensive instrument.
• Opened in May 2017 with one Titan Krios microscope, with second in Winter 2018.
• Addition of third microscope in 2019 if demand grows.
• Over 145 cancer-related projects from 26 institutions across US have been completed; feedback is very positive.

National Cryo-EM Facility (NCEF) Personnel

- Ethan Dmitrovsky, Lab Director, FNLCR
- Dwight Nissley, Director, CRTP, FNLCR
- Ulrich Baxa, Senior Microscopist, NCEF
- Sriram Subramaniam, FNLCR Cryo-EM Program Advisor (Founding Director, NCEF)
- Thomas Edwards, Microscopist, NCEF
- Helen Wang, Project Manager, NCEF
- Matt Hutchison, IT Support, NCEF
National Cryo-Electron Microscopy Projects Since 2017 Launch
Conclusions

1. Frederick National Laboratory is a national resource focused primarily on biomedical research.

2. We work with the NCI and other Institutes on problems that are distinct from the academic community, industry and other national laboratories.

3. We are proud of this partnership and work with the NCI/NIH and the extramural community in service of the public’s health.