Frederick National Laboratory: Current Work and Future Directions

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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 30th, 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

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

ODF Office of the Director, NCI-Frederick: includes funding from Institutes outside of the National Cancer Institute (excluding NIAID).
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

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

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(Leidos Biomedical Research scientists underlined).
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
Two Ebola Outbreaks in One Year

Consecutive Outbreaks

Bikoro
2018

May 7: EVD confirmation by qPCR
April 3: Death of index case

Béni
2018

July 31: EVD confirmation by qPCR
May: Community Deaths

Dr. Cliff Lane and NIAID colleagues Beth Baseler and Clinical Monitoring Research Program (CMRPT)

Enrollment to the PALM RCT study stopped on August 9th with 681 participants enrolled at the Data Safety and Monitoring Board (DSMB) recommendation.
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.
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.

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)
- Basic Science Program (BSP)
- Cancer Research and Technology Program
- Bioinformatics and Data Science (BIDS)
- Laboratory Animal Science Program (LASP)

*40% to extramural community (via subcontracts and procurement)
AIDS and Cancer Virus Program (ACVP)

Collaborations

Intramural
NIAMID
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

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

Dr. Jeff Lifson, ACVP
Antiretroviral Therapy Begun Early After Infection Can Clear Initial SIV 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.
Basic Science Program (BSP) Collaborations

Intramural
- NIAID
- NIDDK
- NCI

Extramural
- Harvard
- MIT
- Oxford Univ.
- Cambridge Univ.
- Fred Hutchinson
- Vanderbilt Univ.
- Johns Hopkins
- University of Colorado Denver
- University of Kansas
- Karolinska Institute
- Hebrew Univ.
- 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

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

Recent High Impact Publications
Immune Response Genotypes Determine Survival of HIV Infected Cells

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

Genotype that causes inhibition of Natural Killer cells

Strong inhibition

Poor HIV control

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)
NIAID, NIAMS, FNLCR
Interagency Agreements
FDA, U.S. Army
cCRADAs

Recent High-Impact Publications
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.

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

#### Social media activity from FNL and FNL PDO:
- 400 flyers circulated at AACR (NCI booth, ATOM event, and meet the experts meetings)
- 20 Twitter posts:
  - 11,836 views
  - 141 engagements (clicks, retweets, likes)
- 3 Facebook posts:
  - 481 people reached

- 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
To significantly accelerate the development of more effective therapies for patients

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

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

OUTREACH
- National
  - Scientific Conferences
  - SBIR/STTR Workshops
- Regional
  - Business Development Partnering Conferences
  - Networking Events
- Local
  - Panels
  - Forums

…and more

- Technical services
- Research Collaboration Agreements
- Beta Testing Agreements

Material Transfer Agreements
Confidentiality Disclosure Agreements
Memoranda of Understanding
Recent Academic Partnerships with Frederick National Laboratory

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

2019:
- 1 postdoc fellow
- 1 graduate trainees
- 2 faculty appointments (processing)
- Seminar series
- Imagining Science and Cancer Biology Symposium
- 1 undergrad trainee
- 1 undergrad trainee
- 1 MSMU professor conducting research
- Teacher-in-training cohort
Who Are Our Partners?

- 149 unique partners
- 48 executed cCRADAs

Connect with us at 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.