

Frederick National Laboratory for Cancer Research



FNLCR Update Progress and Programs

David Heimbrook, Ph.D.

Laboratory Director & President of Leidos Biomedical Research, Inc.

FNLAC

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The Frederick National Laboratory is a federally funded research and development center operated by SAIC-Frederick, Inc., for the National Cancer Institute
DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Cancer Institute

Overview of Frederick National Laboratory for Cancer Research

FNLCR is the only Federally Funded Research and Development Center (FFRDC) dedicated exclusively to biomedical research

- Proudly operated in the public interest by **Leidos Biomedical Research, Inc** (formerly SAIC-Frederick) on behalf of the National Cancer Institute

Main campus located on 70 acres at Ft. Detrick, MD

- Leidos Biomed employees co-located with NCI researchers and other contractors on the NCI Campus at Frederick
- Additional Leidos Biomed scientists at Bethesda, Rockville and other sites



Mission

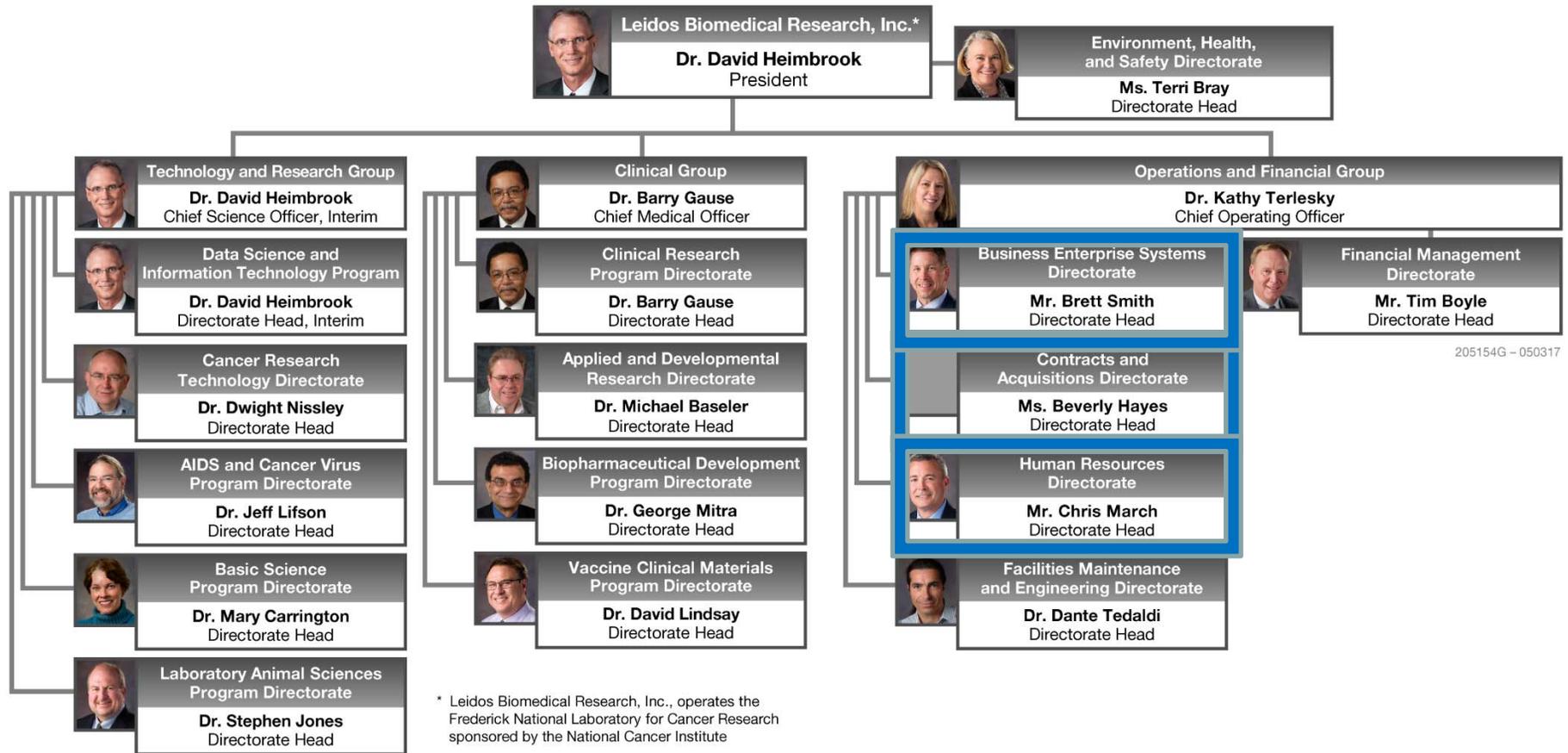
Provide a unique national resource for the development of new technologies and the translation of basic science discoveries into novel agents for the prevention, diagnosis and treatment of cancer and AIDS.

FNCLR – Why an FFRDC?

- **The FFRDC provides the NCI unique technical and response capabilities, including:**
 - **Flexibility** – due to the broad charter and use of contractor staff
 - **Rapid Response** – new or cutting edge projects can be accomplished more expeditiously.
 - **Increased Efficiency** – due to :
 - familiarity with the Government's needs and access to Government expertise and resources beyond what is common in a normal contract; *and*
 - technical expertise aligned with Government's mission
- **The FFRDC designation requires FNCLR to meet the NCI's rapidly changing needs that cannot be achieved *as effectively* by other NCI components or through other government mechanisms.**

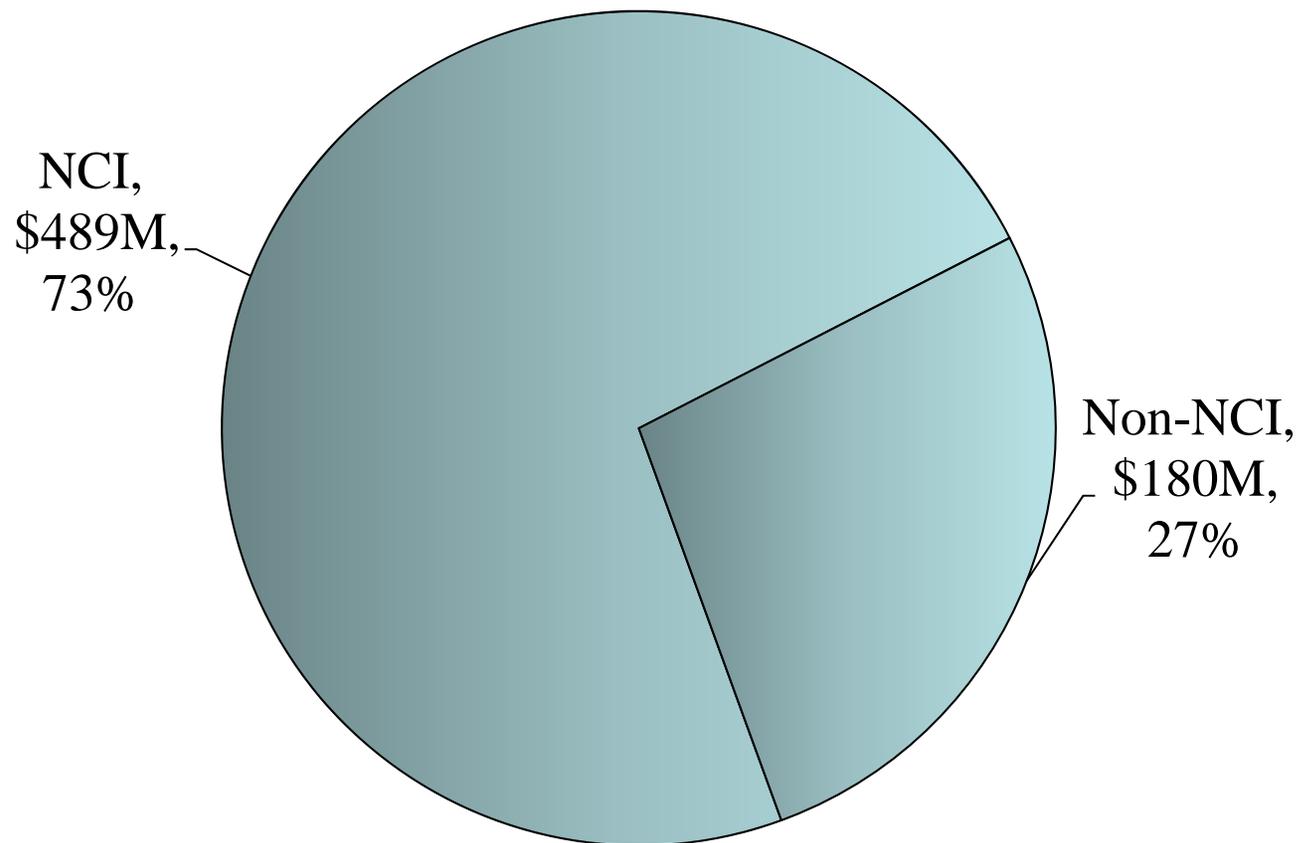
Leidos Biomedical Research Organizational Chart

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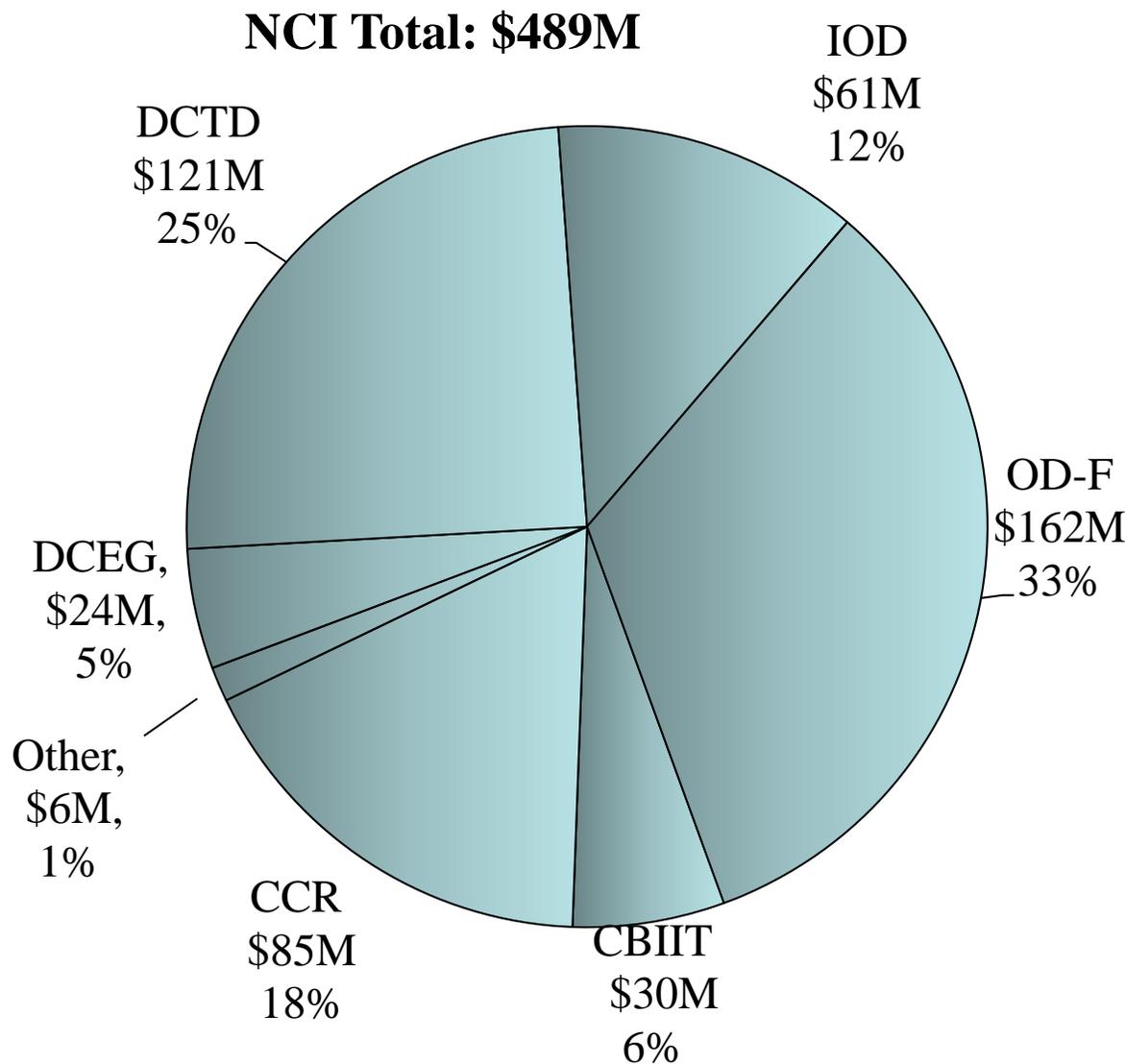


NCI Operations and Technical Support / IDIQ Contracts FY 2016 Obligated Funding

FNLCR Total: \$669M



NCI Operations and Technical Support/IDIQ Contracts FY 2016 Obligated Funding



CBIIT – Center for Biomedical Informatics and Information Technology
CCR – Center for Cancer Research
DCEG – Div. of Cancer Epidemiology and Genetics
DCTD – Div. of Cancer Treatment and Diagnosis
IOD – Immediate Office of the Director
OD-F – Office of the Director - Frederick
Other – **DCB** – Division of Cancer Biology, **DCCPS** – Division of Cancer Control and Population Sciences, **DCP** – Division of Cancer Prevention

Programs and Project Updates

- **Continued growth in support of NIAID**
 - Zika vaccine manufacture and clinical trial support
- **Renewal of the RAS Initiative (FNLAC – 2016)**
- **Direct Partnering authorities (FNLAC - 2012)**
- **Nanotechnology Characterization Laboratory 2.0 (FNLAC - 2015)**
- **Laboratory-Directed Exploratory Research (FNLAC - 2015)**

NIH /NIAID Vaccine Research Center *Development cycle*

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Basic Research—VRC -NIH campus, Bethesda MD



Process development
Analytical development
Formulation dev.

Vaccine Production
Program lab (VPPL)
Gaithersburg MD

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



NVITAL Immune
Assessment
Gaithersburg, MD



Clinical Trials: US, global



cGMP pilot scale production
Pilot Plant, Frederick MD

- Design/build: 2003-2004
- Commissioned: Dec 2005
- In operation 2006

ZIKV DNA Vaccine Discovery

- Vaccination with DNA expressing the prM and E proteins of ZIKV
- Immunogenic in mice and nonhuman primates
- Protection against viremia after ZIKV challenge correlated with serum neutralizing activity



Rapid Development of a DNA Vaccine for Zika Virus

Dowd *et al.*, *Science*
10.1126/science.aai3197
(2016)

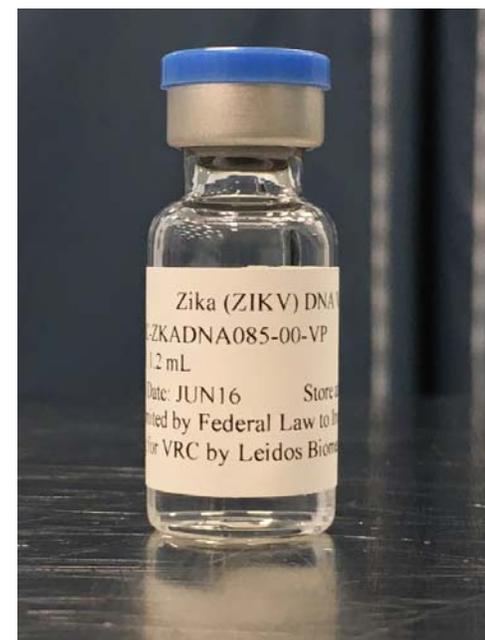
Supporting NIAID ZIKA rapid response

DNA Vaccine candidate 1

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VCMP Zika Manufacturing, Testing & Release

- Plasmid was received on 15 April 2016
 - Drug Substance (DS) Manufacture
 - **Completed on 27 May 2016**
 - Drug Product (DP) Manufacture
 - **Completed on 15 Jun 2016 : 664 vials**
 - QC testing completed 28 June
 - Sterility testing completed mid-July
- **Target release met: 21 July 2016**



Phase 1 - First vaccination 02 Aug 2016

Ongoing ZIKA pDNA clinical supply activities (Candidate 2)

- **Completed testing and release of 7000+ vial lot DP completed March 23, 2017**
 - 1.5 ml fill configuration in 3 ml vials
 - Released May 2017
- Executing contingency bulk drug substance manufacture, testing and release (tentative fill slot into vialled DP in Q2 2017)
- Produce additional PBS placebo vials
- Continue stability testing on all DS and DP batches produced at the pilot plant over the course of clinical trials per approved protocol



Clinical Monitoring Research Program Support for NIAID Zika DNA Vaccine Trials

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A Phase 2/2b, Randomized Trial to Evaluate the
Safety and Immunogenicity of a Zika Virus DNA
Vaccine

Healthy Volunteers Ages 15-35



20 sites in the US,
Caribbean, Central
and South America

VRC 705 Phase 2b							
Part A							
Group	n=	Total Dose	Number of Injections	Number of Limbs	Day 0	Week 4	Week 8
1	30	4 mg	2	2 limbs (both arms)	DNA	DNA	DNA
2	30	4 mg	4	4 limbs (arms and legs)	DNA	DNA	DNA
3	30	8 mg	4	4 limbs (arms and legs)	DNA	DNA	DNA
Total	90	<i>Part B proceeds if Phase 1 and Part A results promising</i>					
Part B (To begin accrual following analysis of preliminary data from Part A)							
Group	n=	Total Dose	Number of Injections	Number of Limbs	Day 0	Week 4	Week 8
4	1200	TBD	TBD	TBD	DNA	DNA	DNA
5	1200	N/A	TBD	TBD	Placebo	Placebo	Placebo
Total	2400	<i>Blinded evaluation of case rates to increase sample size as needed</i>					

Protocol Chairs: Julie Ledgerwood and Grace Chen
IND Sponsor: VRC/NIAID

Julie Ledgerwood / VRC

CMRP : Support to the Division of Clinical Research, NIAID

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Launch and conduct a portfolio of clinical research studies to better understand Zika virus (ZIKV) and to improve outcomes for patients afflicted with ZIKV

- **Established new sites in Tapachula, Chiapas**
 - Central lab in Mexico City
- **Developed natural history study (Zik01)**
 - Febrile Rash Cohort
- **Zika vs. Dengue vs. Chikungunya**
 - Guillain-Barre Cohort
 - Asymptomatic household members Cohort
- **Began June 2016**
- **First enrollment October 2016**



RAS Initiative

Follow-up to FNLAC Feedback

Immediate follow up to FNLAC guidance (Nov 2016):

- Emphasis on partnerships that give the RAS Initiative significant influence on inhibitor development priorities
- Develop in house medicinal chemistry capability
- Develop *in silico* screening capabilities
- Develop models for RAS activation of effectors

RAS Initiative Post-renewal strategy will be presented in detail following discussions with the expanded RAS *ad hoc* working group

Partnering Update

Expanding access to FNLCR Resources

- **Contractor Cooperative Research and Development Agreements (cCRADA)**
 - Research collaboration involving intellectual and material contributions by FNLCR scientists and external partner(s), with no participation in the joint work statement by government personnel
 - Useful for projects of significant scope and duration, specifically translational research and technology development, with defined resource commitments and future intellectual property (IP) considerations
 - Can include co-location and additional staffing
 - Commonly used by DOE FFRDCs, and designed to foster strategic technology-based partnering

Contractor partnering authorities approved in 2012

FNLCR Partnerships

cCRADA Program Overview FY13-FY17

Total of **28** cCRADAs executed from FY13 to FY17

- Approval times: 1-12 months
- *Median time from Concept Approval to Signature: 6 months*

Total Partner Contribution: \$6.8 million

Employee Invention Reports (EIR)s (to date): 6

Patent applications resulting from cCRADAs (to date): 2

Also completed : 3 materials cCRADA's and 2 collaboration agreements

FNLCR Partnership Pipeline

Approved cCRADAs for FY17 - to date

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FNLCR	Partner	Subject	Duration	Approval
CRTP (Nissley)	Eli Lilly	Identification of KRAS allele-specific complexes	2 yrs	Oct 2016
BSP (Matsuo)	Univ. of Mass	Dissecting APOBEC3's for HIB-1 restriction	5 yrs	Dec 2016
CRTP (Holderfield)	Novartis	Identify anti-RAF-dimerization compounds	1 yr	Dec 2016
ADRD (Pinto)	Moffitt Cancer Center	Evaluation of HPV-specific antibody and B cell response	2 yrs	Dec 2016
ACVP (Estes)	Boston Children's Hospital	Characterization of FDCs as a reservoir for HIV	1 yr	Mar 2017
CRTP (Nissley)	TheRas	Dev. and characterization of KRAS targeting compounds.	2 yrs	Mar 2017
CRTP (Holderfield)	Beatson Institute	Developing Kras/Raf effector binding assay	2 yrs	Mar 2017

Median time from Concept Approval to Signature: 7 months

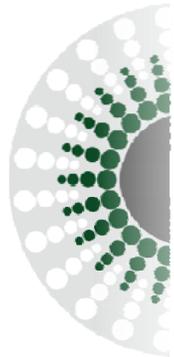
FNL CR contractor CRADAs in progress

FNL LEAD	Partner	Subject	Duration
BSP (Carrington)	Cancer Center	The role of HLA-A expression levels in defining permissible HLA mismatches in hematopoietic stem cell and cord blood transplantation	2 yrs
ADRD (Pinto)	Foundation + Institute	A dose Reduction Immunobridging and Safety Study of two HPV vaccines in Tanzanian girls	6 yrs
CRTP (Stephen)	Research Institute	Identification of small molecules that bind or modulate KRAS4b using in silico docking.	2 yrs
CRTP-NCL (McNeil)	Major Corp	Characterization and Formulation of Nanomaterials	4-5 yrs

FNLCR Technical Services

- **Technical Service Agreement (TSA)**
 - Streamlined agreement executed under CRADA statute allowing FNLCR labs to provide well-defined and validated research services to the scientific community. Pre-approved services are authorized for provision by Contracting Office.
- FY16 Total Partner Contributions : ~ \$ 2.1 million
- FY17 Partner Contributions to date: ~ \$ 1.3 million
- **Partner Contributions to date : ~ \$ 6.7 million**
- **Over 200 agreements and 85 partners to date**
- **23 Technical Services are available from many directorates:**
 - The AIDS and Cancer Virus Program (ACVP) and Laboratory Animal Services Program (LASP) services are most requested
- **New Technical Services are constantly in development**
<http://frederick.cancer.gov/Services/TSA.aspx>

Nanotechnology Characterization Lab



NCL
Nanotechnology
Characterization
Laboratory

Assay Cascade

- Provides “pharmaceutical mentorship” for materials scientists and engineers



Reformulation

- Collaborations with Pharma, CMOs & industry consortia



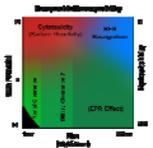
Non-Oncology Nanomaterials

- Other indications, EHS, etc.



Metrology & New Methods

- Working with instrument manufacturers; keeping pace with the growing complexity of nanotech



Basic Research & Grand Challenges

- Immunotoxicology; active targeting



Informing Regulatory Agencies

- Addressing FDA’s scientific questions
- Equivalence testing for nanosimilars



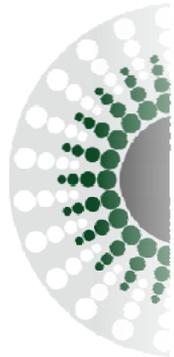
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

NCL 2.0 presented
2015

Transnational Collaboration

- EU-NCL

Implementation of NCL 2.0



NCL
Nanotechnology
Characterization
Laboratory

Assay Cascade

- Provides “pharmaceutical mentorship” for materials scientists and engineers



Reformulation



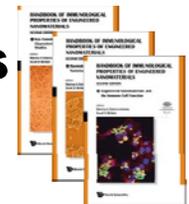
Non-Oncology Nanomaterials



Metrology & New Methods



Basic Research & Grand Challenges



Informing Regulatory Agencies



Transnational Collaboration

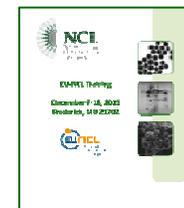
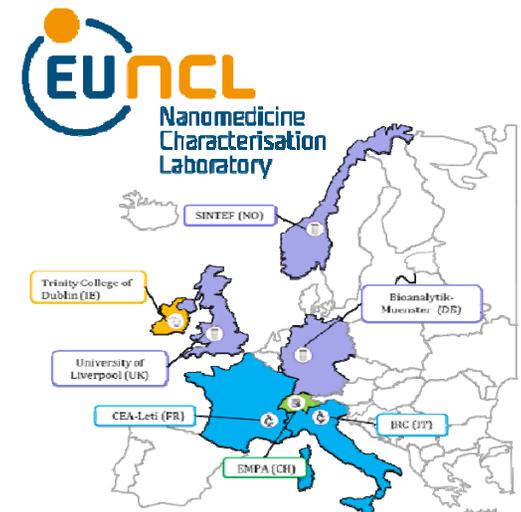
- EU-NCL fully operational March 2017



NCL - International Collaborations

NCL is a partner in the establishment of a multi-national NCL-like entity in Europe

- Advised the set up of the EU-NCL, a consortia of 8 labs across 7 countries. ***Expands much-needed access to nanomaterial characterization for developers.***
- Provided intensive training at FNLCR for members of EU-NCL Core Expert Team.
- Afforded EU-NCL assay qualification by comparing characterization data for ONIVYDE (irinotecan liposome injection, for advanced pancreatic cancer).
- Tested EU-NCL with “bugged” samples
 - The “bugs” were selected to reflect issues common with samples in early development that would not be present in commercial samples.



EU-NCL fully operational March 2017

Innovation : Lab-Directed Exploratory Research (LDER) fund at FNLCR

Emulating a Cornerstone of DOE FFRDC Success

- **Virtually all significant new projects at the DOE FFRDCs visited started with Lab-Directed R and D, funded by a DOE Lab-specific “tax” on all funding**
 - Varying levels of government involvement in project approval in different Labs
- **Emulating FFRDC Best Practice : LDER Fund Objectives**
 - Enhance the innovation, creativity, originality, and quality of its research activities
 - Facilitate collaborations within FNLCR
 - Engage local universities to encourage collaboration and strategic interactions
 - Enable demonstration of exploratory “proof of concept” projects which will lead to durable funding through contract or grant mechanisms
- **The Laboratory Director of FNLCR is responsible for the overall execution and management performance of the LDER program**

Status : NCI committed up to \$1 Million to this effort for FY 2016

(renewed for FY2017)

Laboratory Directed Exploratory Research Funded Projects

FY2016

Investigator	Title	Program	FY16 Budget
Ligia Pinto	Oral Immune Profiles in HPV-Related Oral Cancers	Applied and Developmental Research	\$176,039
Xiaolin Wu	Genomic analysis of NCF1 and its pseudogenes in p47phox CGD	Cancer Research and Technology Program	\$108,000
Stephen Lockett	Modeling Cell Heterogeneity Dynamics in Tumors in Response to Drugs	Cancer Research and Technology Program	\$23,657
Zoe Weaver Ohler	Identification of EGFR tyrosine kinase inhibitor drug resistance and development of models to improve therapeutic efficacy	Laboratory Animal Sciences Program	\$106,145
Mary Carrington	KIR/HLA interaction: influence on risk of nasopharyngeal carcinoma (NPC) in China	Basic Sciences Program	\$70,000

New FY2017

Investigator	Title	Program	FY17 Budget
Stephen Adler	The Development of a Micro-Dose Calibrator	Clinical Research Program	\$21,656
Eckart Bindewald	Targeting KRAS-Expressing Cancers with Conditional RNA Activation	Basic Science Program	\$94,884
Tommy Turbyville	3D Micro-printed Tissue and High Content Imaging as a Predictive Model for Evaluating Targeted Drug Therapies	Cancer Research and Technology Program	\$29,578
Nazzarena Labo	Development of a Multiplexed Isotype Specific Serological Assay for Kaposi's Sarcoma Herpesvirus (KSHV)	AIDS and Cancer Virus Program	\$87,378

2017 Awards to FNLCR Staff

- **Dr. Claudia Haywood – 2017 “Excellence in Technology Transfer” from the Federal Laboratory Consortium for Technology Transfer**

- With a team from NIAID for a cooperative effort to hasten the delivery of a safe and effective Ebola vaccine during the 2014 outbreak in West Africa



- **Dr. Eric Stahlberg – selected as one of FCW’s 2017 Federal 100**
 - For his “vision...leadership,... and determination...” leading to the DOE / NCI collaboration to apply High-Performance Computing capabilities to daunting challenges in Cancer Research

Thank you for your attention

Questions?