Frederick National Laboratory Operations Update

Frederick National Laboratory
for Cancer Research

sponsored by the National Cancer Institute

Ethan Dmitrovsky, M.D.

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

1. Update Frederick National Laboratory's rapid response to the pandemic.

2. Show that this activity did not delay progress in quantitative, discovery, translational or clinical science.

3. Cite NCI and NIAID projects that exemplify federally-funded research and development center efforts and how we share our expertise with the extramural scientific community.

4. Answer your questions.

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
- 104 are Non-operational Task Orders
- 74 are in Clinical Group
- 13 are in Scientific Group
- 17 are Facility or Infrastructure Refurbishments Task Orders
- Extensive outreach to the broader research community is through subcontracting.

Asymptomatic COVID Testing Program
A Case Study for Rapid Response and Partnership

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Terri Bray, Dr. Kristin Komschlies, EHS, OHS, Sam Denny, Eric Cole, Donna Siegle, and many others at NCI and LBR

Frederick National Laboratory has four asymptomatic COVID testing clinics that were stood up within weeks. They serve NIH employees and contractors.

Three clinics in Frederick and one at NCI Shady Grove. They monitor employees' health independent of employer by daily health surveys and tracking of exposures and illnesses.

Over 10,300 tests were performed to date with a positive rate of 0.2%.

Location	Tests Completed	Positive Results
Frederick Sites	8208	18
Shady Grove	2099	2

Continuity of Veterinary, Scientific and Clinical Services During the Pandemic

Frederick National Laboratory for Cancer Research
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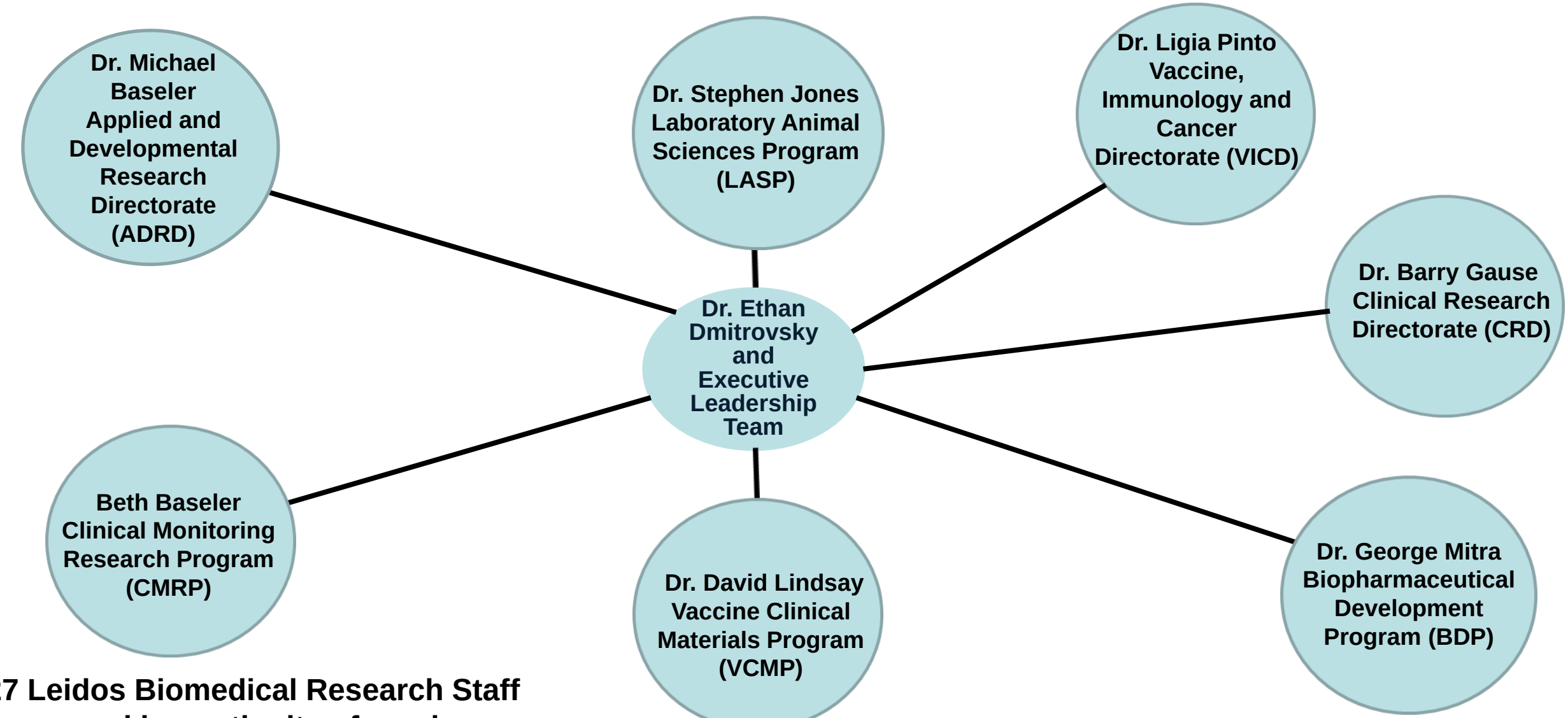

227 Leidos Biomedical Research Staff engaged in continuity of services

Laboratory Animal Sciences Program (LASP)

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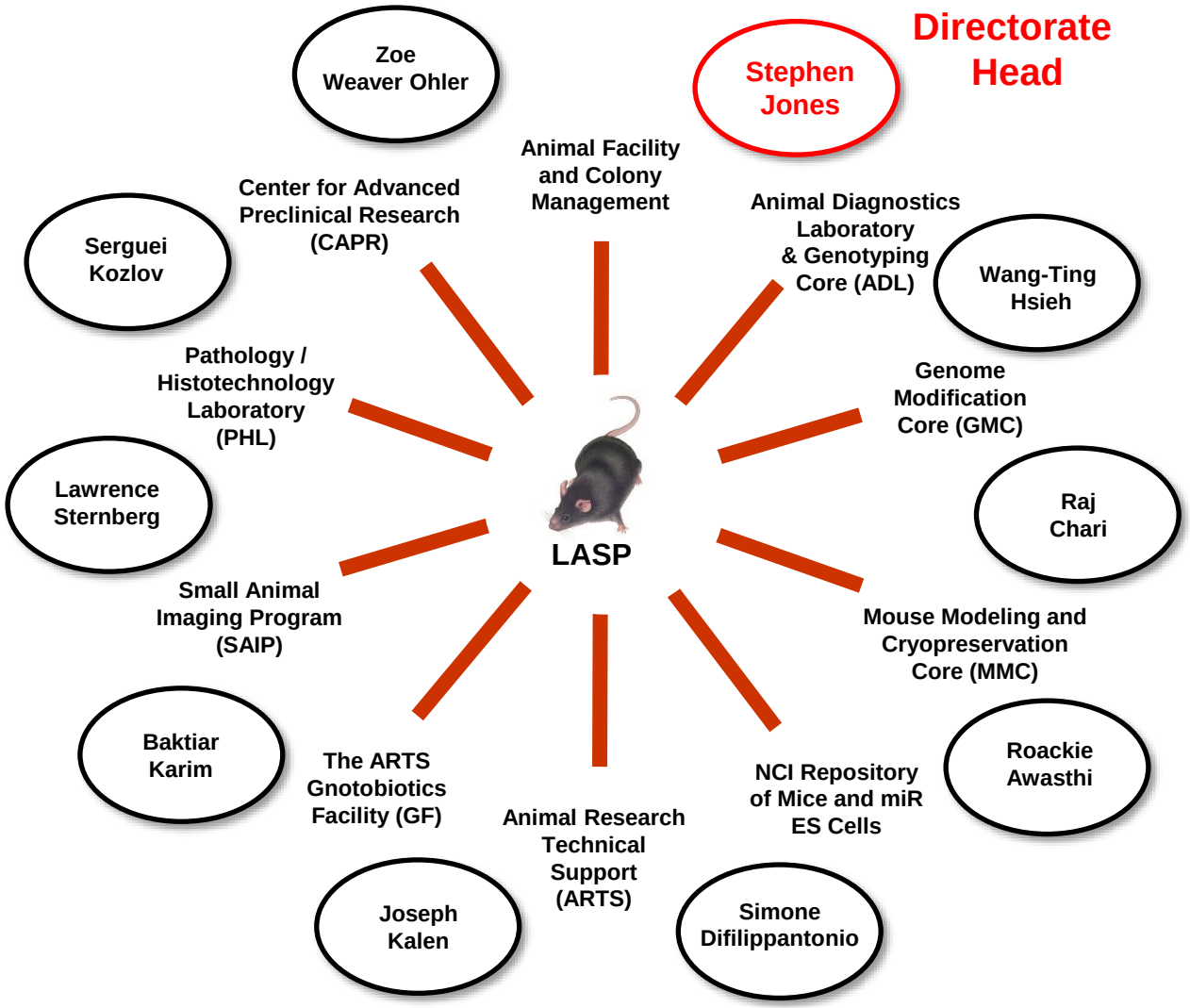
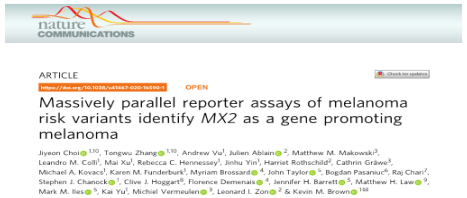


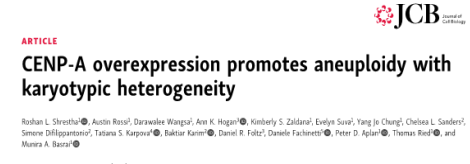
Funding Source: NCI Office of the Director

Supports NCI Intramural (CCR and DCEG) and extramural research (DCTD and DCB), NIAID, NIAMS, FNLCR, Interagency Agreements and cCRADAs.

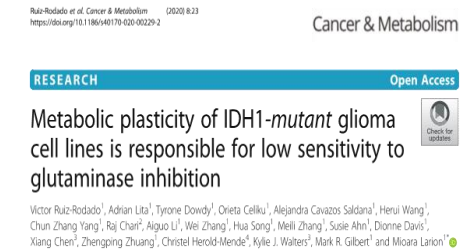
Recent High-Impact Publications


nature COMMUNICATIONS
ARTICLE
Massively parallel reporter assays of melanoma risk variants identify *MX2* as a gene promoting melanoma


RESEARCH BRIEF
TNIK Is a Therapeutic Target in Lung Squamous Cell Carcinoma and Regulates FAK Activation through Merlin


JCB
ARTICLE
CENP-A overexpression promotes aneuploidy with karyotypic heterogeneity


Mdm2 phosphorylation by Akt regulates the p53 response to oxidative stress to promote cell proliferation and tumorigenesis


Cancer & Metabolism
RESEARCH Open Access
Metabolic plasticity of IDH1-*mutant* glioma cell lines is responsible for low sensitivity to glutaminase inhibition


nature COMMUNICATIONS
ARTICLE
Structure of E3 ligase E6AP with a proteasome-binding site provided by substrate receptor hRpn10

Support for NCI CAR-T Cell Trials
With the Division of Cancer Treatment and Diagnosis (DCTD)

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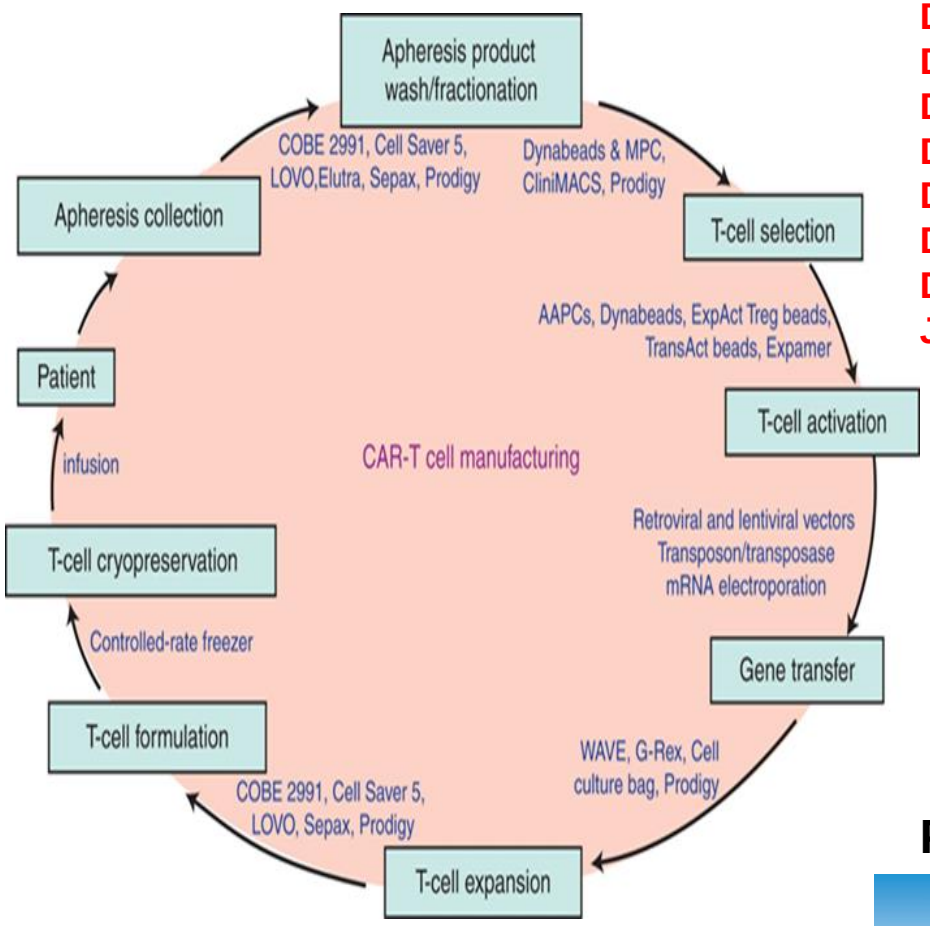
Phased Clinical Trial Approach

Pediatric AML (CD33)
- Manufactured by Biopharmaceutical Development Program (BDP)
- Trials with National Marrow Donor Program (NMDP)
- Seven patients treated (5 at NCI and 2 at CHOP)

Pediatric Neuroblastoma/Osteosarcoma (GD2)
- Manufacture at BDP
- Open at Clinical Center and Stanford in July and then Children's Immuno-Therapy Network (CITN)

CART Gene Transfer at BDP
- Lentiviral Vector is current technology
- CRISPR-Cas 9 knock in/out under development
- Planned: Mesothelin-expressing cancers (hYP812-CART): mesothelioma, ovarian, pancreatic lung adenocarcinoma and cholangiocarcinoma



Dr. Ned Sharpless
Dr. James Doroshow
Dr. Kristin Komschlies
Dr. Anthony Welch
Dr. Jason Yovandich
Dr. Barry Gause
Dr. George Mitra
Joy Beveridge

Prodigy System

SeroNet Initiative Objectives and Components

Frederick National Laboratory for Cancer Research
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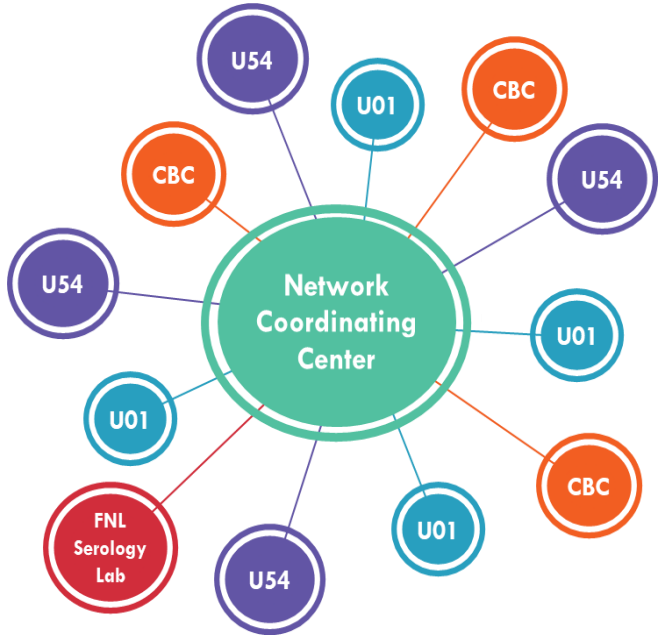
Dr. Doug Lowy
Dr. Sharpless
Dr. Kristin Komschlies
Dr. Dinah Singer
Dr. Jim Cherry
Dr. Ligia Pinto
Dr. Len Freedman
Dr. Sara Hook
and many others



- **Develop and standardize novel serological assays and deploy them to the extramural community.**
- **Elucidate biological and mechanisms driving innate, humoral and cellular responses to SARS-CoV-2.**
- **Discover modulators for this immune response.**

Investigator Initiated Research

- **8 U54s: Serological Sciences Centers of Excellence**
- **13 U01s: Serological Sciences Research Projects**
- **4 Serology Testing Capacity Building Centers (CBCs)**
- **FNL Serology Laboratory**
- **FNL Network Coordinating Center**

Highlights from SeroNet Coordinating Centers:
Role of Frederick National Laboratory

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- **Manage contracts with SeroNet Serology Testing Capacity Building Centers: Arizona State University, University of Minnesota, Mount Sinai and Feinstein Institutes for Medical Research.**

- **Project Management for meetings, operations and monthly Newsletter.**

- **Distributed serology and viral proteins reagents, US Standard and assay evaluation for SeroNet investigators and scientific community.**

- **Storage, coordination, sharing, curation and deployed Go Live for serology data upload. Independently evaluated ~100 commercial serology tests for FDA.**

- **EIT team installed and implemented LIMS LabVantage system at the Frederick National Laboratory Serology Laboratory**

COVID-19 Clinical Trials with NIAID

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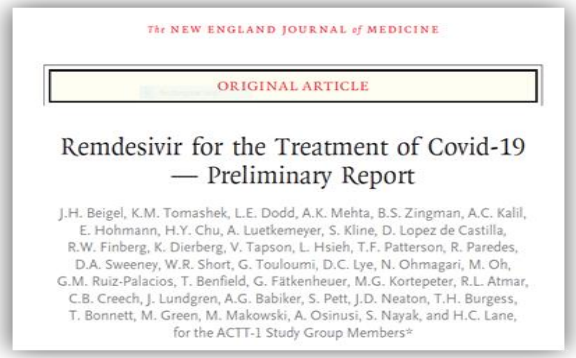
Remdesivir international placebo-controlled trial hospitalized COVID-19 patients on ventilators or oxygen-dependent.

60 sites, 1063 cases and ~ 2 months accrual


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-Palacios, T. 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 CMRPD
Beth Baseler
Theresa Engel
Laura McNay
Dr. John Beigel

Emergency Use Authorization FDA-approved

Remdesivir +/- Baracitinib: international double-blind randomized placebo-controlled 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

Remdesivir +/- LY-CoV555 Monoclonal Antibody
Randomized trial of hospitalized COVID-19 patients +/- oxygen and steroids

31 sites, 314 untreated patients randomized (LY-CoV555 vs. placebo)


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

ACTIV-3/TICO LY-CoV555 Study Group*

ABSTRACT

Study closure for futility

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

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

In-country protocol training

Rapid research response began

PALM I Trial published in NEJM

Sacket Award

FDA approves Inmazeb (Regeneron)

PALM I (n = 681)

PALM I Extension (n = 363)

Last enrollment

WHO declares Outbreak ended

FDA approves Ebanga (mAb114)

Outbreak (Eastern DRC)

Outbreak (Equateur)

Outbreak (Eastern DRC)

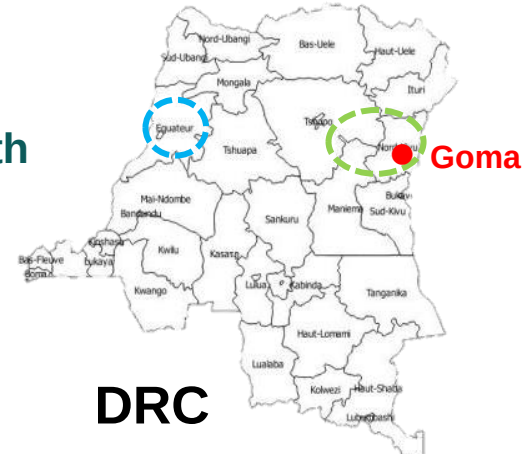
7/1/18 10/1/18 1/1/19 4/1/19 7/1/19 10/1/19 1/1/20 4/1/20 7/1/20 10/1/20 12/31/20 2/7/21 5/3/21

Transition to PALM Base Operations

Outbreak with 3,470 cases and 66% mortality rate

Outbreak with 130 cases with 42% mortality rate

Outbreak with 12 cases with 50% mortality rate



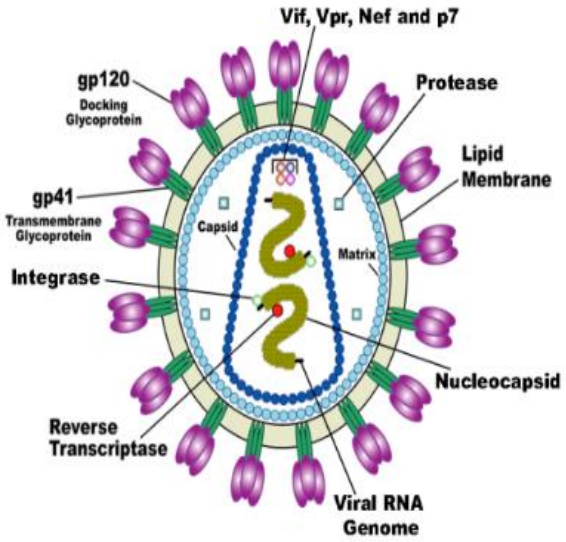
PALM Consortium: Institut National de Recherche Biomédicale • NIAID/DCR • Leidos Biomedical Research • The Mitchell Group, • Other Multilateral Partners

Management of Diverse Projects Related to Vaccine Development and Manufacturing

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

Dr. Jason Gall, VPP
Dr. Kevin Carlton, VPP
Dr. Shanker Gupta, VRC
Dr. John Mascola, VRC
Dr. David Lindsay, VCMP

HIV



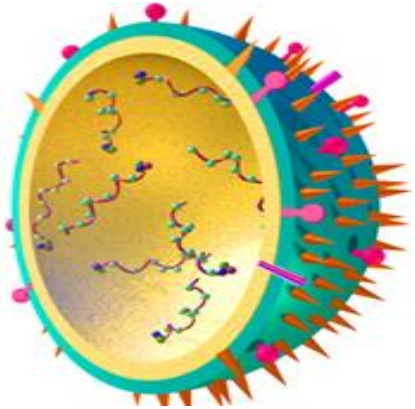
Neutralizing monoclonal antibody

Trimer vaccine

Filovirus (Ebola)

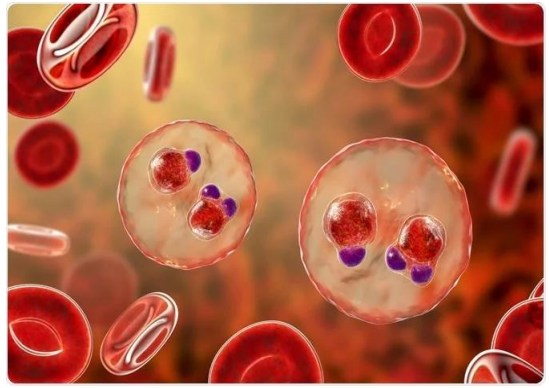
Bispecific and monoclonal

Influenza



Nanoparticle Influenza vaccine

Malaria



Monoclonal antibody

VCMP Clinical Manufacturing Support to the Vaccine Research Center

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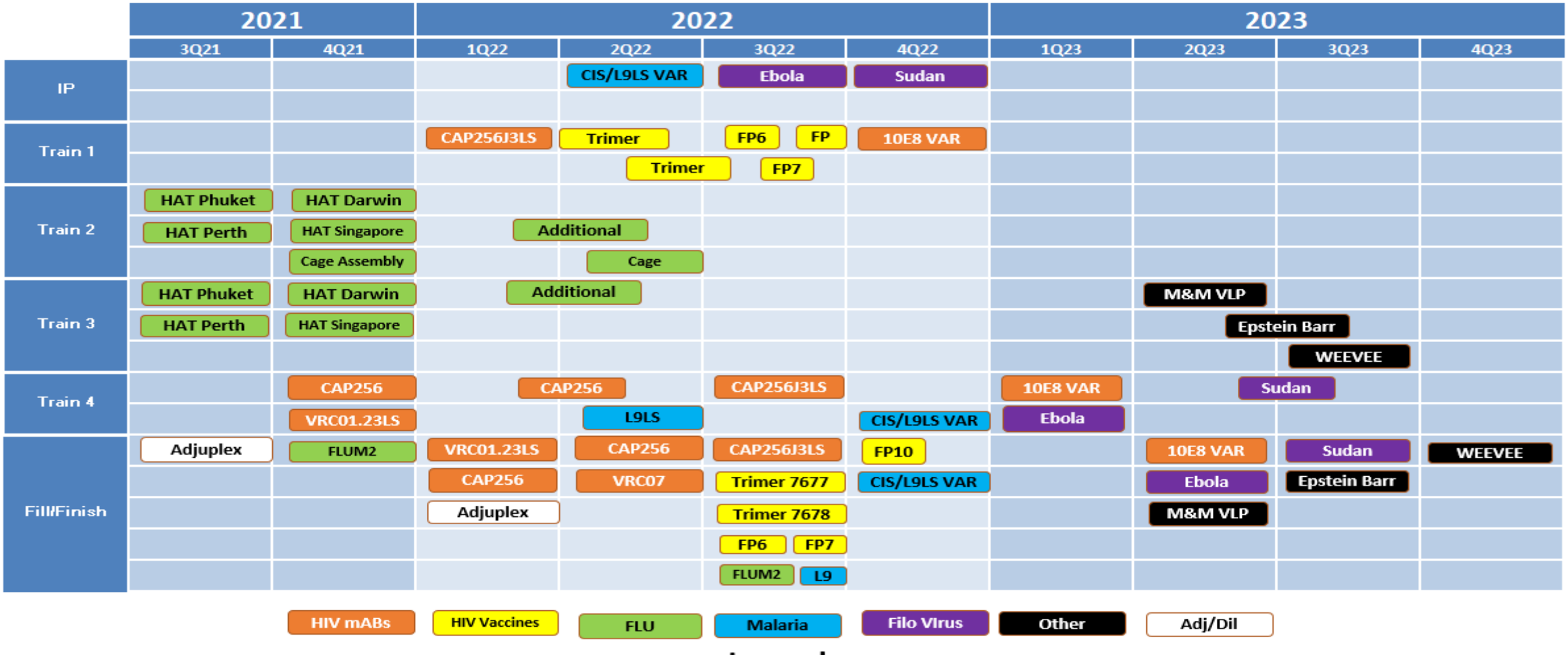
sponsored by the National Cancer Institute

Dr. Jason Gall, VPP
Dr. Kevin Carlton, VPP
Dr. Shanker Gupta, VRC
Dr. John Mascola, VRC
Dr. David Lindsay, VCMP



NCI National Cryo-EM Facility: the First Four Years of Operations

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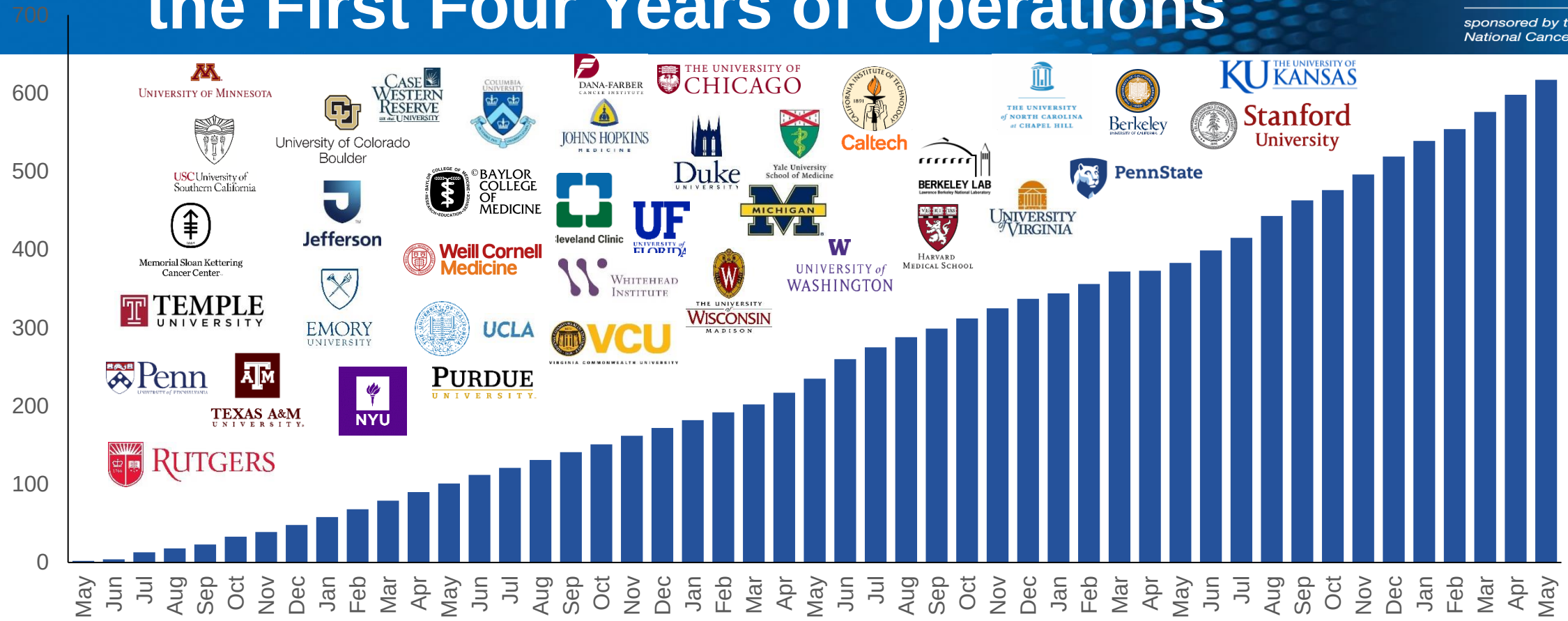

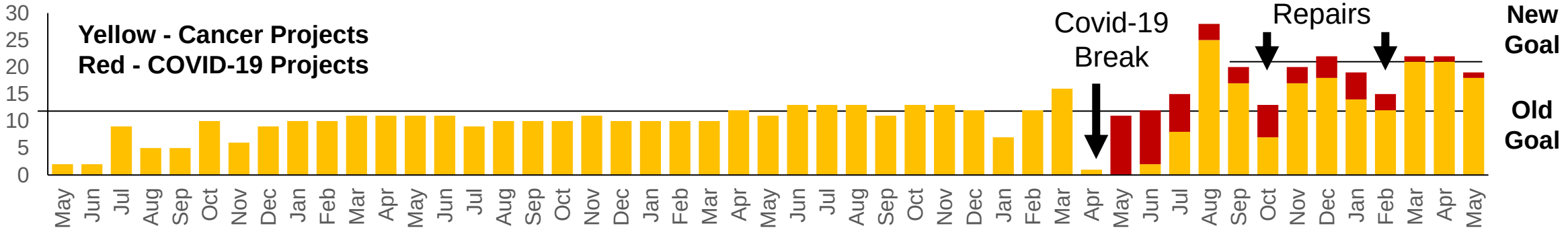

NCI National Cryo-EM Facility Associated Publications Since April 2020

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

Cell

Selective PP2A Enhancement through Biased Heterotrimer Stabilization

Daniel Leonard [16] • Wei Huang [16] • Sudeh Izadmehr • Caitlin M. O'Connor • Danica D. Wiredja • Zhizhi Wang • Nilesh Zaware • Yinghua Chen • Daniela M. Schlatzer • Janna Kiselar • Nikhil Vasireddi • Stefan Schüchner • Abbey L. Perl • Matthew D. Galsky • Wenqing Xu • David L. Brautigan • Egon Ogris • Derek J. Taylor • Goutham Narla

Show less • Show footnotes

Published: April 20, 2020 • DOI: https://doi.org/10.1016/j.cell.2020.03.038

nature COMMUNICATIONS

ARTICLE OPEN

Alternative splicing controls teneurin-latrophilin interaction and synapse specificity by a shape-shifting mechanism

Jingxian Li[1,2,5], Yuan Xie[1,5], Shaleeka Cornelius[3,4], Xian Jiang[3,4], Richard Sando[3,4], Szymon P. Kordon[1,2], Man Pan[1], Katherine Leon[1,2], Thomas C. Südhof[3,4], Minglei Zhao[1] & Demet Araç[1,2]

nature

Article | Published: 27 May 2020

Electromechanical coupling in the hyperpolarization-activated K^+ channel KAT1

Michael David Clark, Gustavo F. Contreras, Rong Shen & Eduardo Perozo

Nature **583**, 145–149 (2020) | Cite this article

nature communications

Article | Open Access | Published: 09 July 2020

The structures of two archaeal type IV pili illuminate evolutionary relationships

Fengbin Wang, Diana P. Baquero, Zhangli Su, Leticia C. Beltran, David Prangishvili, Mart Krupovic & Edward H. Egelman

Nature Communications **11**, Article number: 3424 (2020) | Cite this article

SCIENCE ADVANCES | RESEARCH ARTICLE

CELL BIOLOGY

Cryo-EM structure of NPF-bound human Arp2/3 complex and activation mechanism

Austin Zimmet[1], Trevor Van Eeuwen[2], Malgorzata Boczkowska[1], Grzegorz Rebowski[1], Kenji Murakami[2], Roberto Dominguez[1]*

nature

Nanobodies from camelid mice and llamas neutralize SARS-CoV-2 variants

Jianliang Xu, Kai Xu, Seolkyoung Jung, Andrea Conte, Jenna Lieberman, Frauke Muecksch, Julio Cesar Cetrulo Lorenzi, Solji Park, Fabian Schmidt, Zijun Wang, Yaoxing Huang, Yang Luo, Manoj Nair, Pengfei Wang, Jonathan E. Schulz, Lino Tessarollo, Tatsiana Bylund, Gwo-Yu Chuang, Adam S. Olia, Tyler Stephens, I-Ting Teng, Yaroslav Tsybovsky, Tongqing Zhou, Vincent Munster, David D. Ho, Theodora Hatziioannou, Paul D. Bieniasz, Michel C. Nussenzweig, Peter D. Kwong & Rafael Casellas -Show fewer authors

Nature (2021) | Cite this article

SCIENCE ADVANCES | RESEARCH ARTICLE

STRUCTURAL BIOLOGY

Structural mechanism of two gain-of-function cardiac and skeletal RyR mutations at an equivalent site by cryo-EM

Kavita A. Iyer[1], Yifan Hu[1], Ashok R. Nayak[1], Nagomi Kurebayashi[2], Takashi Murayama[2], Montserrat Samsó[1]*

nature COMMUNICATIONS

ARTICLE OPEN

Mechanisms of activation and desensitization of full-length glycine receptor in lipid nanodiscs

Arvind Kumar[1], Sandip Basak[1], Shanlin Rao[2], Yvonne Gicheru[1], Megan L. Mayer[3], Mark S. P. Sansom[2] & Sudha Chakrapani[1,4]

Science AAAS

CORONAVIRUS

Structure-based design of prefusion-stabilized SARS-CoV-2 spikes

Ching-Lin Hsieh[1], Jory A. Goldsmith[1], Jeffrey M. Schaub[1], Andrea M. DiVenere[2], Hung-Che Kuo[1], Kamyab Javanmardi[1], Kevin C. Le[2], Daniel Wrapp[1], Alison G. Lee[1], Yutong Liu[2], Chia-Wei Chou[1], Patrick O. Byrne[1], Christy K. Hjorth[1], Nicole V. Johnson[1], John Ludes-Meyers[1], Annalee W. Nguyen[2], Juyeon Park[1], Nianshuang Wang[1], Dzifa Amengor[1], Jason J. Lavinder[1,2], Gregory C. Ippolito[1,3], Jennifer A. Maynard[2]*, Ilya J. Finkelstein[1,4]*, Jason S. McLellan[1]*

Cell Host & Microbe

Volume 28, Issue 6, 9 December 2020, Pages 867-879.e5

Article

Cryo-EM Structures of SARS-CoV-2 Spike without and with ACE2 Reveal a pH-Dependent Switch to Mediate Endosomal Positioning of Receptor-Binding Domains

Tongqing Zhou[1,7], Yaroslav Tsybovsky[2,7], Jason Gorman[3], Micah Rapp[3], Gabriele Cerutti[3], Gwo-Yu Chuang[1], Phinikoula S. Katsamba[3], Jared M. Sampson[3,5], Arne Schön[4], Jude Bimela[3], Jeffrey C. Boyington[2], Alexandra Nazzari[1], Adam S. Olia[1], Wei Shi[1], Mallika Sastry[1], Tyler Stephens[2], Jonathan Stuckey[1], I-Ting Teng[1], Pengfei Wang[1], Shuishu Wang[1], Baoshan Zhang[1], Richard A. Friesner[4], David D. Ho[6], John R. Mascola[1], Lawrence Shapiro[3,4,6], Peter D. Kwong[1,3,6]

Molecular Cell

Volume 80, Issue 3, 5 November 2020, Pages 501-511.e3

Article

Structures of a Complete Human V-ATPase Reveal Mechanisms of Its Assembly

Longfei Wang[1,2], Di Wu[3], Carol V. Robinson[3], Hao Wu[1,2], Tian-Min Fu[1,2,4,5,6]

eLife

An ER translocon for multi-pass membrane protein biogenesis

Philip T McGilvray[#1], S Andrei Anghel[#1,2], Arunkumar Sundaram[1], Frank Zhong[1,2], Michael J Trnka[3], James R Fuller[3], Hong Hu[4], Alma L Burlingame[3], Robert J Keenan[1]

Structures of filamentous viruses infecting hyperthermophilic archaea explain DNA stabilization in extreme environments

Fengbin Wang[a,1], Diana P. Baquero[a,b,1], Leticia C. Beltran[a], Zhangli Su[a], Tomasz Osinski[a], Weili Zheng[a], David Prangishvili[b,c], Mart Krupovic[b,2], and Edward H. Egelman[a,2]

[a]Department of Biochemistry and Molecular Genetics, University of Virginia, Charlottesville, VA 22908; [b]Archaeal Virology Unit, Department of Microbiology, Institut Pasteur, 75015 Paris, France; [c]College Doctoral, Sorbonne Universités, 75005 Paris, France; and [d]Academia Europaea Tbilisi Regional Knowledge Hub, Ivane Javakhishvili Tbilisi State University, 0179 Tbilisi, Georgia

This contribution is part of the special series of Inaugural Articles by members of the National Academy of Sciences elected in 2019.

Contributed by Edward H. Egelman, June 26, 2020 (sent for review June 1, 2020; reviewed by Tammay A. M. Bharat and Jack E. Johnson)

nature COMMUNICATIONS

ARTICLE OPEN

Structural basis of ribosomal RNA transcription regulation

Yeonoh Shin[1,3], M. Zuhaib Qayyum[1,3], Danil Pupov[2], Daria Esyunina[2], Andrey Kulbachinskiy[2] & Katsuhiko S. Murakami[1]

Structural and Functional Diversity of Resistance–Nodulation–Cell Division Transporters

Philip A. Klenotic, Mitchell A. Moseng, Christopher E. Morgan, and Edward W. Yu*

Cite this: *Chem. Rev.* 2021, 121, 9, 5378–5416
Publication Date: November 19, 2020
https://doi.org/10.1021/acs.chemrev.0c00621
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Article Views 637 | Altmetric 5 | Citations 4

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nature COMMUNICATIONS

ARTICLE OPEN

Structural analysis of cross α-helical nanotubes provides insight into the designability of filamentous peptide nanomaterials

Fengbin Wang[1], Ordy Gnewou[2], Charles Modlin[2], Leticia C. Beltran[3], Chunfu Xu[2], Zhangli Su[3], Puneet Juneja[3], Gevorg Grigoryan[4,5], Edward H. Egelman[3] & Vincent P. Conticello[2]

nature COMMUNICATIONS

ARTICLE OPEN

Seesaw conformations of Npl4 in the human p97 complex and the inhibitory mechanism of a disulfiram derivative

Man Pan[1,4], Qingyun Zheng[2,4], Yuanyuan Yu[1,4], Huasong Ai[2], Yuan Xie[1], Xin Zeng[3], Chu Wang[3], Lei Liu[2] & Minglei Zhao[1]

Molecular Cell

Volume 81, Issue 3, 4 February 2021, Pages 599-613.e8

Article

Structural analysis of RIG-I-like receptors reveals ancient rules of engagement between diverse RNA helicases and TRIM ubiquitin ligases

Kazuki Kato[1,2], Sadeem Ahmad[1,2], Zixiang Zhu[3], Janet M. Young[4], Xin Mu[1,2,4], Sehoon Park[2], Harmit S. Malik[4,5], Sun Hur[1,2,7]

CSH Cold Spring Harbor Laboratory **bioRχiv** THE PREPRINT SERVER FOR BIOLOGY

Antibodies with potent and broad neutralizing activity against antigenically diverse and highly transmissible SARS-CoV-2 variants

Lingshu Wang, Tongqing Zhou, Yi Zhang, Eun Sung Yang, Chaim A. Schramm, Wei Shi, Amarendra Pegu, Olamide K. Oloninyi, Amy Ransier, Samuel Darko, Sandeep R. Narpala, Christian Hatcher, David R. Martinez, Yaroslav Tsybovsky, Emily Phung, Olubukola M. Abiona, Evan M. Cale, Lauren A. Chang, Kizzmekia S. Corbett, Anthony T. DiPiazza, Ingelise J. Gordon, Kwanyee Leung, Tracy Liu, Rosemarie D. Mason, Alexandra Nazzari, Laura Novik, Adam S. Olia, Nicole A. Doria-Rose, Tyler Stephens, Christopher D. Stringham, Chloe Adrienna Talana, I-Ting Teng, Danielle Wagner, Alicia T. Widge, Baoshan Zhang, Mario Roederer, Julie E. Ledgerwood, Tracy J. Ruckwardt, Martin R. Gaudinski, Ralph S. Baric, Barney S. Graham, Adrian B. McDermott, Daniel C. Douek, Peter D. Kwong, John R Mascola, Nancy J. Sullivan, John Misasi

doi: https://doi.org/10.1101/2021.02.25.432969

nature methods ARTICLES

A 'Build and Retrieve' methodology to simultaneously solve cryo-EM structures of membrane proteins

Chih-Chia Su[1], Meinan Lyu[1], Christopher E. Morgan[1], Jani Reddy Bolla[2], Carol V. Robinson[2] and Edward W. Yu[1]*

nature COMMUNICATIONS

ARTICLE OPEN

Distinct axial and lateral interactions within homologous filaments dictate the signaling specificity and order of the AIM2-ASC inflammasome

Mariusz Matyszewski[1,3], Weili Zheng[2], Jacob Lueck[1], Zachary Mazanek[1], Naveen Mohideen[1], Albert Y. Lau[1], Edward H. Egelman[2] & Jungsan Sohn[1]

nature

Article | Published: 17 March 2021

DPP9 sequesters the C terminus of NLRP1 to repress inflammasome activation

L. Robert Hollingsworth, Humayun Sharif, Andrew R. Griswold, Pietro Fontana, Julian Mintseris, Kevin B. Dagbay, Joao A. Paulo, Steven P. Gygi, Daniel A. Bachovchin & Hao Wu

Nature **592**, 778–783 (2021) | Cite this article

STAR Protocols

Volume 2, Issue 1, 19 March 2021, 100350

Protocol

Purification and cryoelectron microscopy structure determination of human V-ATPase

Longfei Wang[1,2,5], Zhenhang Chen[3,4], Hao Wu[1,2], Tian-Min Fu[1,2,3,4,6]

nature communications

Article | Open Access | Published: 10 February 2021

Cryo-EM structures of engineered active bc_1-cbb_3 type $CIII_2CIV$ super-complexes and electronic communication between the complexes

Stefan Steimle, Trevor van Eeuwen, Yavuz Ozturk, Hee Jong Kim, Merav Braitbard, Nur Selamoglu, Benjamin A. Garcia, Dina Schneidman-Duhovny, Kenji Murakami & Fevzi Daldal

Nature Communications **12**, Article number: 929 (2021) | Cite this article

Frederick National Laboratory: Spotlighting Extramural Collaborations

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

- **The AIDS and Cancer Virus Program led by Dr. Jeff Lifson is collaborating with Dr. Louis Picker (OHSU) on a novel CMV-vectored AIDS virus vaccine that provides unique "control and clear" vaccine protection.**

- **This paper and a companion study** *(Malouli et al, Science Immunology, 2021)***, help to define the mechanism of action of the vaccine acting partly through novel unconventionally restricted (MHC-E) CD8+ T cell responses.**

- **This work is supported by a cCRADA through the NIAID funded *"Consortium for Innovative AIDS Research in Nonhuman Primates"*, led by Dr. Picker (OHSU), Dr. Lifson (Frederick National Laboratory) and Dr. Dan Barouch (Harvard/BIDMC/Ragon Institute).**

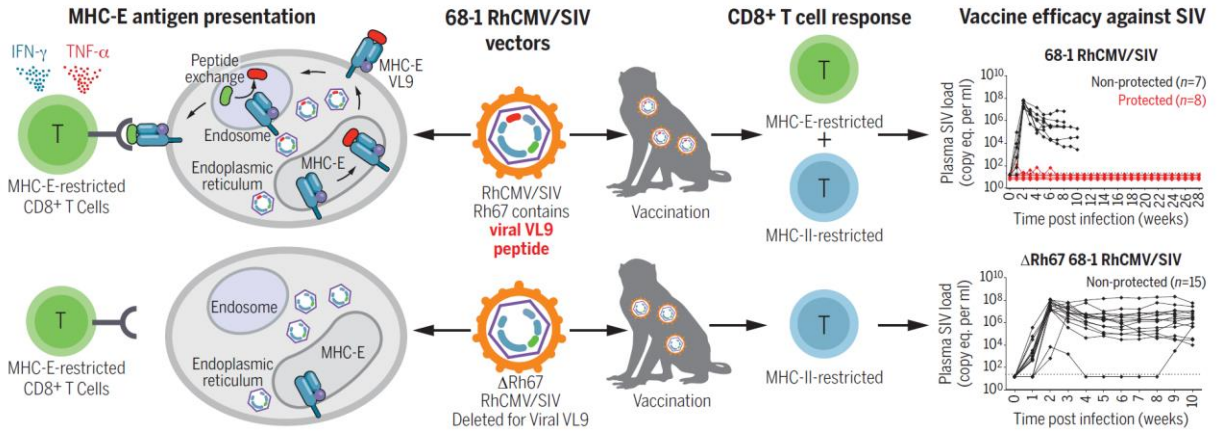
RESEARCH ARTICLE

Science 372, eabe9233 (2021)

VACCINES

Modulation of MHC-E transport by viral decoy ligands is required for RhCMV/SIV vaccine efficacy

Marieke C. Verweij[1]†, Scott G. Hansen[1]†, Ravi Iyer[1]†, Nessy John[1]†, Daniel Malouli[1], David Morrow[1], Isabel Scholz[1], Jennie Womack[1], Shaheed Abdulhaqq[1], Roxanne M. Gilbride[1], Colette M. Hughes[1], Abigail B. Ventura[1], Julia C. Ford[1], Andrea N. Selseth[1], Kelli Oswald[2], Rebecca Shoemaker[2], Brian Berkemeier[2], William J. Bosche[2], Michael Hull[2], Jason Shao[3], Jonah B. Sacha[1], Michael K. Axthelm[1], Paul T. Edlefsen[3], Jeffrey D. Lifson[2], Louis J. Picker[1]*, Klaus Früh[1]*



Frederick National Laboratory Gives Back to the Extramural Science and Cancer Care Community

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

Frederick National Laboratory as a Federally-Funded Research and Development Center serves the extramural community and public health through its science as well as its education and training efforts.

These efforts take advantage of the distinct research programs underway with the National Cancer Institute and the National Institute of Allergy and Infectious Diseases

MAY 24TH - 26TH, 2021

The Third RAS Initiative Symposium

Dr. Sharpless NCI Director

Dr. Frank McCormick RAS Scientific Consultant

Dr. Charles Swanton Francis Crick Institute

Virtual Symposium

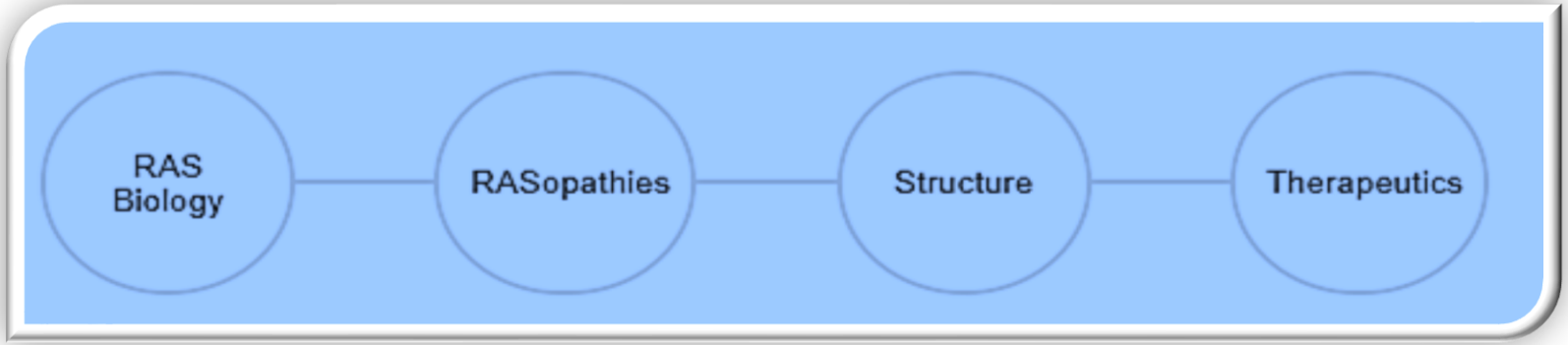
1,792 Attendees and 126 submitted abstracts
9 Short Talks selected by peer review from abstracts
103 posters shared for Poster Session

29 Invited Speakers, including:

- **NCI Director, Dr. Ned Sharpless**
- **RAS Scientific Consultant, Dr. Frank McCormick**
- **Keynote Speaker, Dr. Charles Swanton**

Topics were RAS Biology, Structure, Therapeutics, and RASopathies.

Milestone FDA-approval of a KRAS G12C-targeting agent.



LETTER

doi:10.1038/nature12796

K-Ras(G12C) inhibitors allosterically control GTP affinity and effector interactions

Jonathan M. Ostrem[1]*, Ulf Peters[1]*, Martin L. Sos[1], James A. Wells[2] & Kevan M. Shokat[1]

- KRAS G12C inhibitor clinical trials
- RGS3 acts as a GAP for oncogenic KRAS G12C
- Resistance to KRAS G12C inhibitors
- G12C-GTP (on) inhibitors
- Structure of full-length BRAF kinase in complex with 14-3-3
- Combinatorial regimens for RAS-driven cancers
- Tipifarnib therapy for HRAS head and neck squamous cell carcinoma
- Degradation of KRAS
- New RAS effectors in pancreatic cancer

Leidos Biomedical Research and Hood College Life Science Symposium

Dr. Leonard Freedman
Chief Science Officer

Dr. Eric Stahlberg
Director, Biomedical Informatics & Data Science

Artificial Intelligence in Cancer Research and Clinical Care: Turning Promise into Reality

April 26-28, 2022 - Hood College, Frederick, MD

Keynote Speaker
Dr. Keith Yamamoto
University of California San Francisco

Dr. Amber Simpson; Queen's University

Dr. Fred Streitz; Lawrence Livermore National Laboratory

Dr. Rachael Callcut, University of California San Francisco

Dr. Ron Kikinis; Brigham and Woman's Hospital; Dana-Farber/Harvard Cancer Center

Dr. Robert Gillies; Moffitt Cancer Center

Dr. Michael Green; Queen's University

Dr. FayanjuOluwadamilola "Lola"; Penn Medicine, University of Pennsylvania Health System

Dr. Ulas Bagci; University of Central Florida

Dr. Fabio Moraes; AI Kingston Health Sciences Centre, Queens University

Dr. Corey Arnold; University of California Los Angeles

Dr. Anant Madabhushi; Case Western Reserve University

Dr. Stephanie Harmon, National Cancer Institute

Dr. Thomas Fuchs, Icahn School of Medicine at Mount Sinai

Dr. Jonathan Green, National Institute of Health

Dr. Barbara Evans; University of Florida

Dr. Stephanie Russo Carroll, University of Arizona; Native Nations Institute

International Clinical Trials Training Modules

Leidos Biomedical Research (Beth Baseler and CMRPD) is launching educational modules (at no cost to the government) for extramural investigators in conduct of international clinical trials in resource constrained and politically unstable countries. Trainees will receive CEU or CME credit and a certificate of completion.

Dr. Ian Crozer and Team

Frederick National Laboratory deployed Dr. Crozier (Ebola survivor) to DRC in February 2021 at the request of WHO to combat recent outbreak.

MODULES

- Introduction to Clinical Trials (Clinical Trials 101)
- Partnering with international clinical researchers
- Governance Models
- Protocol Development
- Regulatory Approvals and Oversight
- Clinical Trials Monitoring
- Pharmacovigilance
- IT Infrastructure
- Data Management
- Cold-Chain Management
- Inventory management
- Logistics
- Clinical Laboratories
- Biorepository
- Community Engagement/Good Participatory Practices
- Data reporting
- Legal considerations
- Inspections and Audits
- Summary of Lessons Learned

Conclusions

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

- Reviewed Frederick National Laboratory's rapid response to the COVID-19 pandemic that disrupted society.

- Despite this pivot other essential science continued.

- This did not prevent decisive discovery, quantitative biology, translational and clinical science. That scholarship extensively engages the extramural biomedical community.

- Our public-private partnership and educational efforts seek to advance the public's health.