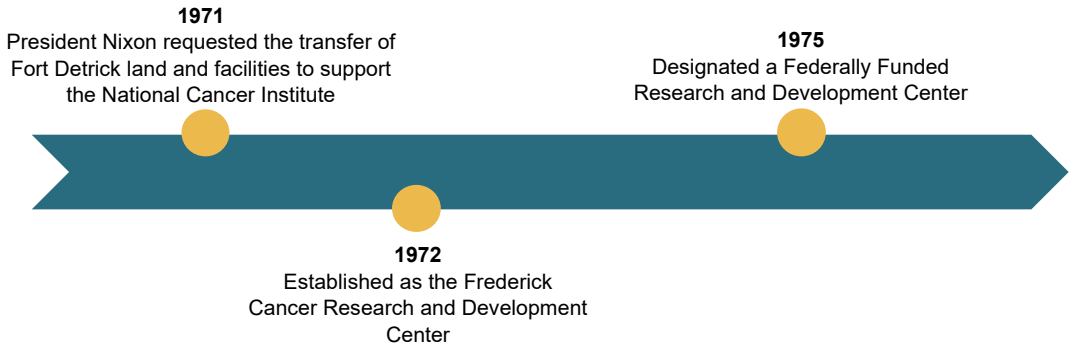
Work with Us!

PARTNERSHIP OPPORTUNITIES
with the
Frederick National Laboratory

Frederick National Laboratory
for Cancer Research



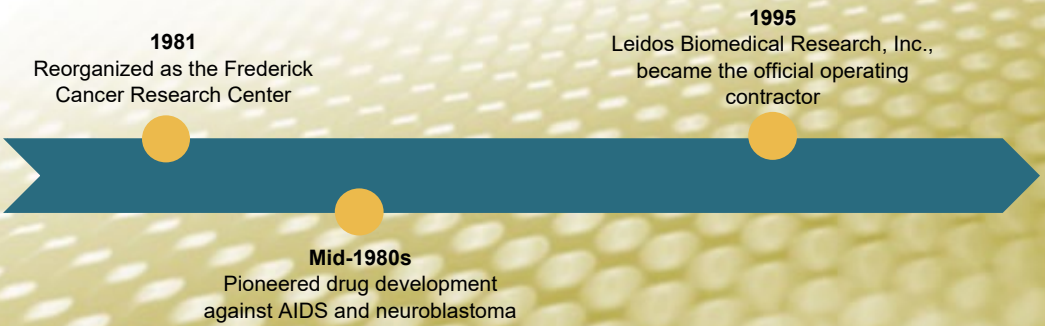
"Here we have previously had scientists—some of the best people that we could possibly find in the United States—working on weapons of war, we now have scientists devoting their efforts toward saving life."

– President Richard Nixon

Frederick National Laboratory for Cancer Research

The Frederick National Laboratory for Cancer Research is dedicated to improving human health through discovery and innovation in the biomedical sciences, focusing on cancer, AIDS, and emerging infectious diseases.

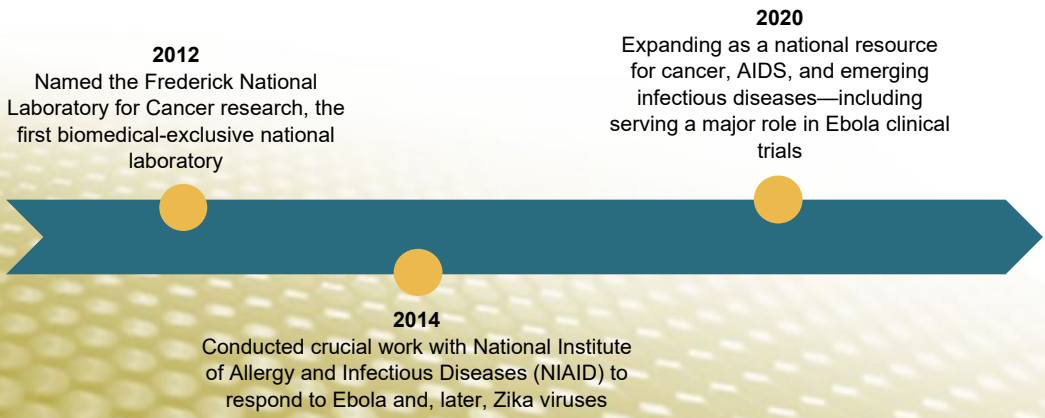
We are a Federally Funded Research and Development Center (FFRDC) operated by Leidos Biomedical Research, Inc., for the National Cancer Institute (NCI), part of the U.S. National Institutes of Health (NIH). As such, the Frederick National Laboratory is the only U.S. national laboratory exclusively devoted to biomedical research.



Our campus is spread across multiple locations:

- The Advanced Research Technology Facility in Frederick, MD, has served as our headquarters since 2012.
- Fort Detrick in Frederick, MD, served as the original home of the national laboratory, and it is still home to many of our laboratories and facilities.
- The Vaccine Clinical Materials Program, also in Frederick, MD, produces clinical-stage vaccine candidates for infectious diseases of global significance.
- At the NCI at Shady Grove Campus in Rockville, MD, Frederick National Laboratory staff work closely with their NCI colleagues.
- Additional satellite sites are located throughout the country and around the world to support clinical research trials.

As a shared national resource, we offer access to a suite of advanced biomedical technologies, engage in highly collaborative research, provide select science and technology services, and maintain vast repositories of research materials available to biomedical investigators worldwide. Our core values of accountability, compassion, collaboration, dedication, integrity, and versatility serve as a guidepost for how we do our work every day in serving the public's interest.



Work with Us!

Partnerships and collaborations play an integral role in advancing cancer and HIV/AIDS research at the Frederick National Laboratory. The Partnership Development Office spearheads these efforts. We offer a variety of partnership mechanisms that allow our scientists and their partners to solve common problems collaboratively and accelerate progress against cancer and related diseases.

By working together, we accelerate progress against cancer and AIDS.

Our goal is to develop new scientific capabilities at Frederick National Laboratory and make our expertise available to others to advance cancer research discoveries worldwide. Our partners gain access to an exceptionally wide range of advanced technologies and scientific expertise, covering such areas as laboratory animal sciences, preclinical model development, nanotechnology, proteomics research, molecular analysis, advanced biomedical computing, AIDS and cancer virus research, and high-resolution imaging technologies.

Who are our partners?

We collaborate with scientists and external researchers in government, academia, industry, and the nonprofit research sector, as well as neighbors in our community. Our partners range from one-person start-up companies to international organizations.

How can we partner?

The Frederick National Laboratory offers a range of contractual agreement options to fit a variety of partners and projects. Our agreement options include contractor Cooperative Research and Development Agreements (cCRADAs), Memorandums of Understanding (MOUs), Material Transfer Agreements, Beta-Testing Agreements, and Collaborative Agreements. We also offer a range of unique laboratory services on a reimbursable basis via our Technical Services Program.

Meet our Labs

The Frederick National Laboratory comprises multiple programs and laboratories. The following pages highlight some of the programs that engage in collaborative research.

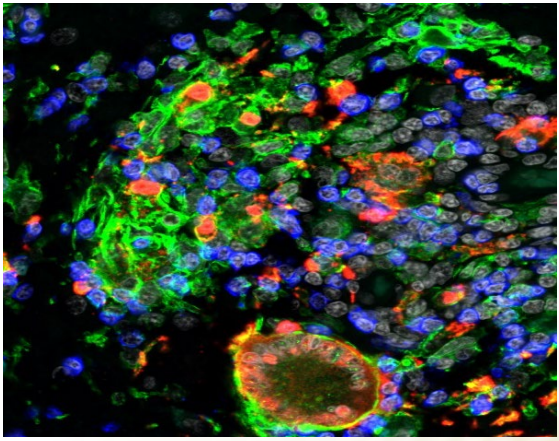
- AIDS and Cancer Virus Program
- Basic Science Program
- Biomedical Informatics and Data Science
- Laboratory Animal Sciences Program
- Molecular Characterization Laboratory
- Nanotechnology Characterization Laboratory
- National Cryo-Electron Microscopy Facility
- RAS Initiative
- Vaccine, Immunity, and Cancer Directorate
- Standards References and Training Research Committee

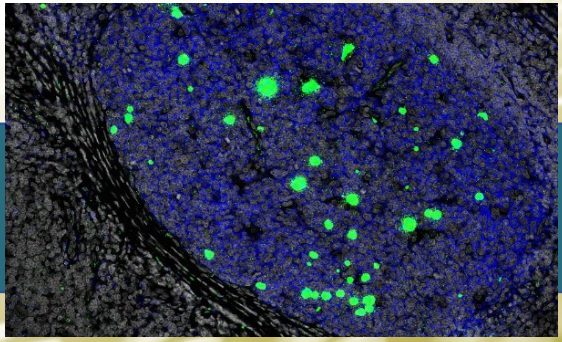
AIDS and Cancer Virus Program

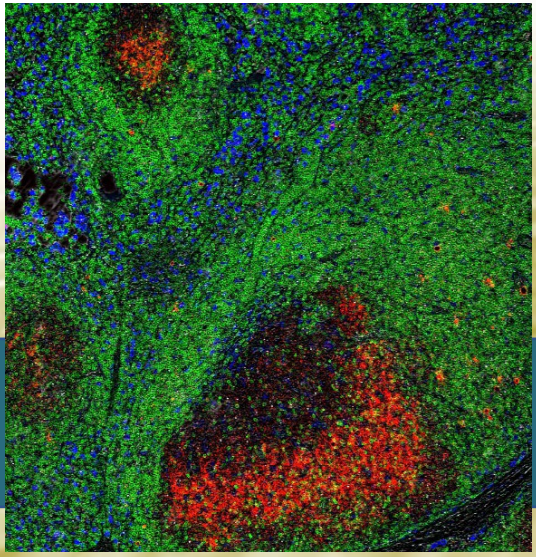
Developing new approaches against HIV and cancer-causing viruses

The AIDS and Cancer Virus Program (ACVP) conducts investigator-initiated basic and applied research to improve the diagnosis, prevention, and treatment of HIV infection, AIDS, and AIDS-related tumors. The ACVP's work includes fundamental molecular virology, non-human primate (NHP) model development and *in vivo* studies, and viral epidemiology. ACVP researchers are leading experts in conducting *in vivo* NHP studies and the virologic and immunologic analyses of specimens derived from these experiments.

The ACVP also develops novel research methods, analytical techniques, and reagents and makes these available to the research community. The program today directly stems from the scientists who, in 1984, contributed to the first-generation AIDS blood screening tests that helped prevent further spreading of the newly identified AIDS virus throughout the U.S. blood supply.







Images: (Top left) SIV-infected rhesus macaque cerebellum assayed with RNAscope; (Below) rhesus lymphocryptovirus infected lymph node; (Right) SIV-infected lymph node.
Image credit: Claire Deleage, Ph.D., Frederick National Laboratory.

The ACVP offers a robust portfolio of services to external researchers through the Technical Services Program:

- Quantitative PCR SIV viral load analyses
- Cell-associated SIV/SHIV RNA and DNA analyses on cell/tissue specimens
- SIV/HIV single-genome amplification and analyses
- Next-generation sequence analyses of barcoded SIV/SHIV/HIV
- Novel CD4+ T cell specific immunohistochemistry detection and analysis
- Quantitative assessment of lymphoid tissue fibrosis
- Quantitative assessment of HIV/SIV viral DNA in laser capture micro-dissected CD4+ T cell and/or macrophage populations
- Next-generation lineage-specific multiplex in situ hybridization for HIV/SIV RNA and DNA

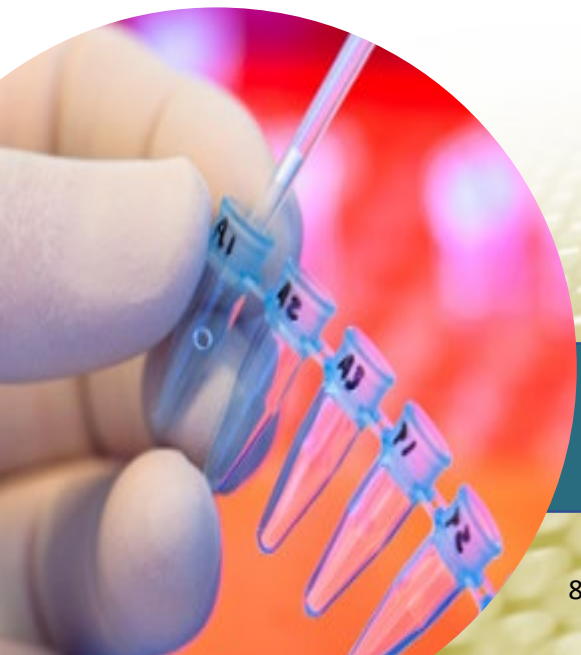
Partnership Highlights

- As part of two multi-collaborator consortia, the ACVP is conducting studies aimed at improving understanding of the virus that persists despite effective suppressive antiretroviral drug treatment and constitutes the major barrier to more definitive treatment of HIV infection.
- The ACVP partnered with Gilead Sciences to study the mechanism of action of an investigational toll-like receptor 7 agonist in SIV-infected NHPs.
- Through a cCRADA, researchers from the ACVP, Aaron Diamond AIDS Research Center, and the Rockefeller University used *in vitro* design and engineering and *in vivo* adaptation to develop a minimally chimeric virus that uses 95% HIV-1 gene sequence but can replicate well and cause AIDS in pigtail macaques. The model is being developed for certain applications to test HIV-1 specific targeted interventions.

Basic Science Program

Improving understanding of biological processes involved in cancer and other diseases

The Basic Science Program (BSP) is mission orientated in its research goals to improve our current understanding of biological processes involved in cancer and other diseases. This is achieved through independent multidisciplinary research programs focusing on basic science as well as developing new tools and methodologies that can further improve existing research strategies. The BSP team encompasses scientists from varied backgrounds, such as molecular biology, immunology, retrovirology, structural biology, cancer biology, and genetics. With six independent principal investigators, collaboratively aligned in the NCI Center for Cancer Research (CCR) laboratories or programs, research efforts are focused on immunology, epidemiology, epigenetics, hematology, and computational/structural biology. Dedicated research support embedded in more than 60 CCR laboratories provides scientific and technical expertise in pursuit of the research goals defined by each laboratory's scope of work and studies. In the past several months, BSP staff have co-authored more than 25 papers in high impact peer-reviewed scientific journals, such as *Nature*, *Science*, and the *Journal of Immunology*.



Partnership Highlights

- Patients with hematologic disorders can be cured by blood, marrow, and cord blood transplantation—but without compatible donors, life-threatening post-transplant complications can occur. To help improve donor selection and increase the availability of lifesaving transplantations, a cCRADA between the BSP and Fred Hutchinson Cancer Research Center enabled joint research exploring the role of human leukocyte antigen (HLA) expression in defining permissible HLA mismatches for donors.
- Through a cCRADA with the University of Massachusetts, Worcester, the BSP is working to understand the structural relationship of APOBEC3 proteins and their complexes on HIV infection to identify target sites for future therapeutic development.

Biomedical Informatics and Data Science

Accelerating biomedical innovations

Through collaborative efforts across the biomedical, computational, and research communities, the Biomedical Informatics and Data Science (BIDS) group brings creativity and spurs innovation to advance disease research. Supported by agencies across the community such as the NCI, NIAID, National Center for Advancing Translational Sciences (NCATS), and others, BIDS engages with and bridges these communities to deliver cutting-edge research insights, define frontier challenges, and advance innovations needed in the areas of informatics, computational and data science, and artificial intelligence.

Throughout BIDS, cross-cutting teams provide services in biomedical data management; research applications; cutting-edge technology development; and education, outreach, and training. Highlights of capabilities and key projects appear below.

Biomedical Data Management

BIDS delivers data resources that provide critical building blocks for the cancer data ecosystem, including the Integrated Canine Data Commons, the NCI data vault and data management environment supporting intramural investigators, clinical trials reporting program, a systems biology exploration environment, laboratory animal management systems, and custom-tailored data resources.

Key Resources

- Cancer Research Data Commons – data resources for cancer research.
- Biological DataBase network (BioDBnet) and Annotation, Visualization, and Impact Analysis (AVIA) – biomedical data resources for annotation and public data discovery.
- Clinical Trials Reporting Program – software systems enabling NCI-supported clinical trials.

Research Applications

BIDS operates core facilities for next-generation sequence analysis, bioinformatics analysis, and clinical data analysis. Scientists in BIDS collaboratively engage and support the biomedical research community across all scales with expertise in computational chemistry, drug discovery, structural biology, image analysis, systems biology, statistical modeling, data visualization, and more.

Cutting-Edge Technology Development

BIDS pushes the frontiers for data science, advancing machine learning, reducing barriers to adoption, and enabling broad use of this critical data analysis technique. BIDS is pioneering robust ways to utilize web applications and "the cloud" to enable advanced clinical trials and deliver new data and research resources. State-of-the-art capabilities are being developed in areas including digital pathology, cellular imaging, systems biology, predictive oncology, and accelerated drug discovery.

Education, Outreach and Training

BIDS develops collaborative learning programs around high-performance and scientific computing, data science, and artificial intelligence in biomedical applications that provide the foundation for scientific research. Workshops, seminars, and individual consulting are organized and offered in key areas, including deep learning, bioinformatics applications and workflow development, and new software packages.

Partnership Highlights

- Co-founded the **Accelerating Therapeutics for Opportunities in Medicine (ATOM) Consortium**, the active learning public-private partnership to accelerate drug discovery
- Co-developed the **CANcer Distributed Learning Environment (CANDLE)** working with the U.S. Department of Energy, an open-source environment for large-scale machine learning
- Collaboratively launched the **Joint Design of Advanced Computing Solutions for Cancer (JDACS4C)**, creating new research capabilities with large-scale high-performance computing and artificial intelligence as part of an NCI-Department of Energy collaboration
- Led development of **Molecular Analysis for Therapy Choice (MATCH)** precision medicine clinical trials software

Laboratory Animal Sciences Program

The Laboratory Animal Sciences Program (LASP) is a comprehensive resource for animal-based research. The program's expertise stretches from pathology and histotechnology to small animal imaging to the development of genetically engineered mouse (GEM) models. LASP leverages its expertise to partner with the external research community and support basic and translational cancer research around scientifically intriguing questions.

The program specializes in the design and utilization of reproducible preclinical studies toward the development of effective therapeutics and diagnostics for human cancers. This includes the evaluation of preclinical compounds or existing drugs or biologics in GEM models, GEM-derived allograft models, or patient-derived mouse xenografts. The program also provides support for animal health monitoring, biomarker discovery/validation, drug development, genomics, and proteomics.

Resource Highlights

- The NCI Mouse Repository is an NCI-funded resource for mouse cancer models and associated strains. The repository makes strains available to all members of the scientific community (academic, non-profit, and commercial). The strains are cryoarchived and distributed as frozen germoplasm (embryos and/or sperm). Additionally, 1501 genetically engineered mouse embryonic stem cells (mESCs) lines were produced, harboring conditional microRNA transgenes to enhance novel information obtained on their role in cancer. MicroRNAs play an important role in fundamental cellular processes through negative post-transcriptional regulation of gene expression. By generating these genetically engineered mESCs, the role of microRNAs in human cancer, their use as diagnostic tools, and their potential function as new targets for therapeutic intervention in the treatment of cancer can be addressed. The cell lines are available through the Technical Services Program.

Image: (Left) LASP technician working in an isolator. (Top) A chimera mouse.

Molecular Characterization Laboratory

Comprehensive characterization of molecular alterations in tumors

The Molecular Characterization Laboratory (MoCha) is a CLIA-certified laboratory that provides state-of-the-art genomic assay technologies, including multiple next-generation sequencing platforms, to analyze clinical and pre-clinical specimens. MoCha consists of histotechnologists, molecular biologists, bioinformaticians, and scientists who support NCI-sponsored clinical studies and precision medicine initiatives, including the NCI Molecular Analysis for Therapy Choice (NCI-MATCH) and Pediatric MATCH clinical trials. Both trials leverage cutting-edge precision medicine tools to determine the effectiveness of treating cancer based on specific genetic mutations, instead of cancer type. For these studies, MoCha developed a next-generation sequencing test to screen for alterations in 143 genes associated with cancer. The laboratory is committed to the improvement and incorporation of new genomic assay technologies for use in prospective and retrospective clinical studies.

Image: MoCha scientist examines a sample.

MoCha is also responsible for performing all genetic sequencing and gene expression profiling of models in the Patient-Derived Models Repository. It has a full pathology group responsible for reviewing the histology of all patient-derived xenograft models created for the repository.

Partnership Highlights

- MoCha is a key partner in the Foundation for the National Institutes of Health Biomarkers Consortium project to standardize the measurement of genetic blood tests to track cancer. Specifically, the project is developing tools to enable clinicians to measure and compare circulating tumor DNA test results across U.S. laboratories.
- Through a cCRADA with Illumina, MoCha is optimizing and validating Illumina's TruSight Oncology assay, a blood-based test that can identify cancer-related mutations in minute amounts of circulating tumor DNA. Once validated for clinical use, the assay will support future NCI trials.

Nanotechnology Characterization Laboratory

Expediting the translation of nanomedicine therapeutics and diagnostics

The Nanotechnology Characterization Laboratory (NCL) is a resource for all researchers developing nano-based therapies or diagnostics.

In partnership with U.S. federal labs—the NCI, National Institute of Standards and Technology, and Food and Drug Administration (FDA)—the NCL performs preclinical studies on nanomedicine candidates to facilitate their translation into the clinic. The NCL's mission is to expedite and de-risk the clinical translation of nanomedicine therapeutics and diagnostics. It does this by helping researchers move their nano-based products from the discovery phase to clinical trials, and it conducts studies, including physicochemical characterization and *in vitro* and *in vivo* studies to assess, toxicity, immunotoxicity, and pharmacokinetics. The NCL partners with the global research community, from academic groups to large pharmaceutical companies.

For researchers developing lead oncology nanomedicines, NCL offers free preclinical characterization to expedite translation to clinical trials through its Assay Cascade characterization program. The NCL Assay Cascade is a tailored set of analytical tests that assess physicochemical properties, *in vitro* toxicity, immunological effects, and pharmacokinetics. This service is available to candidates via an application process, and applications are accepted four times per year. In addition, many of the Assay Cascade protocols are free to download from the NCL website.

For non-oncology product characterization and other development needs, the NCL leverages its nanotechnology expertise to conduct sponsor-funded research and development. These projects are customized based on the partner's individual needs and are open to all nanotech strategies. This includes formulation, optimization, lead selection, assay development, instrumentation optimization, and more. Work is initiated through a negotiated cCRADA.

Through the Technical Services Program, the NCL offers two pre-defined services. These services utilize an analytical method invented at the NCL, called the Stable Isotope Tracer Ultrafiltration Assay (SITUA), that can measure critical nanomedicine fractions in plasma.

- Nanomedicine drug release study in human plasma using SITUA
- Nanomedicine pharmacokinetics in rats evaluated by SITUA

Partnership Highlights

- With the influx of generic versions of nanomedicines, these formulations pose unique regulatory hurdles. To help address these challenges, the NCL entered into a collaboration with the FDA to evaluate the bioequivalence of marketed nanomedicines. The NCL conducted *in vitro* and *in vivo* head-to-head comparisons of innovator and approved generic nanomedicines, using the SITUA developed at the NCL. These studies were then used to assess the potential of this bioanalytical assay as a new tool to determine the bioequivalence of nanomedicines.
- As part of the pre-IND process for Rhenium Nanoliposomes, the FDA requested validation of manufacturing and additional drug characterization. NCL was pivotal in addressing these regulatory questions for the drug developers. NCL characterization served as part of the chemistry, manufacturing, and controls section of the IND application. Rhenium Nanoliposomes are now completing a phase 1 clinical trial for patients with malignant glioma, with phase 2 planned.

Image: NCL scientist prepares a mass spectrometer for sample analysis.

National Cryo-Electron Microscopy Facility

High-resolution imaging to support cancer research

Cryo-electron microscopy (cryo-EM) is a biophysical technique used to visualize proteins, protein complexes, and cells in a near native state—without requiring structure-altering dyes, fixatives, or crystallization. Over the past decade, the field of cryo-EM has made unprecedented gains in resolving protein structures to near atomic resolution on almost a routine basis.

Improvements in the field have pushed the achievable resolution beyond the "atomic" threshold.

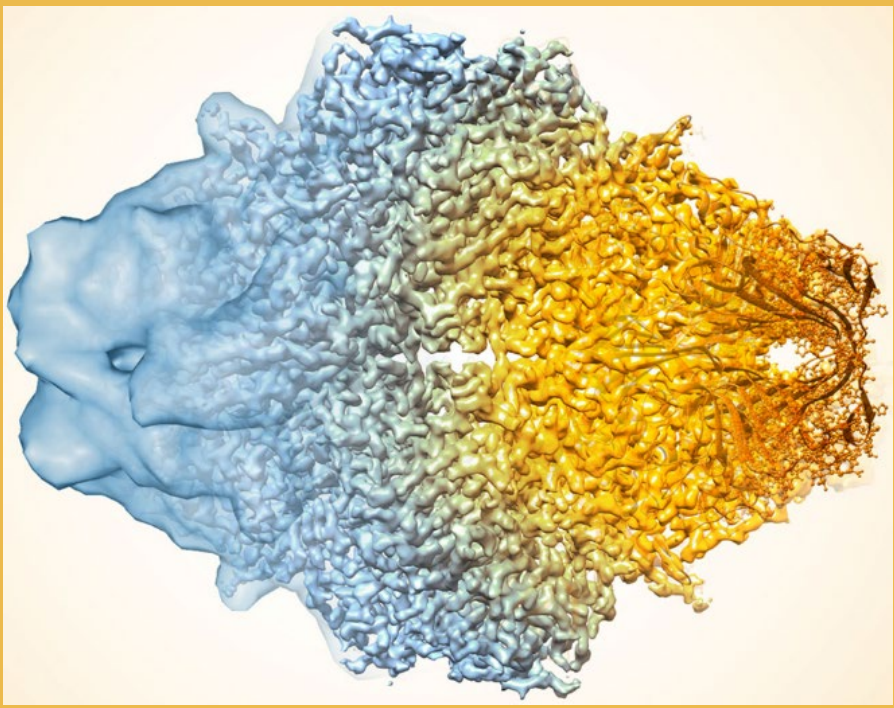
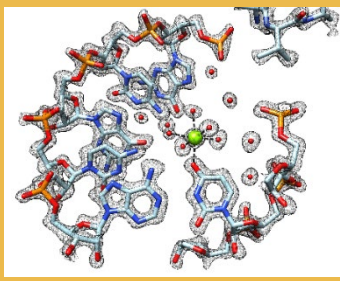


Image: Improvements in imaging over 10 years. Image credit: Veronica Falconieri, Sriram Subramaniam, NCI, NIH.

The National Cryo-EM Facility (NCEF) at the Frederick National Laboratory provides expertise in data collection and access to advanced instrumentation for cryo-EM. At the NCEF, two Titan Krios instruments equipped with Falcon 3EC and K3-BioQuantum direct electron detectors are fully dedicated to serving cancer researchers at nonprofit and academic institutions. Applicants for this no-cost service do not need to be NIH grant holders. Accepted samples undergo an automated two-day data collection that captures an average of 6,000 movies.



Potential applicants can submit a NCEF Sample Information Form through the online portal at apply.cancer.gov/login or contact the NCEF via email at NCI-NCEF@nih.gov.

Partnership Highlights

- In its first two years, NCEF helped more than 100 collaborators.
- Studies using the structures obtained from the facility have been published in high-impact journals, including *Science, Nature, Nature Communications, Nature Structural and Molecular Biology, Cell,* and *Proceedings of the National Academy of Sciences of the USA.*

NEW

NCEF Cryo-EM Training Program

Applications are open through May 1 for the first NCEF Cryo-EM Training Program, which will be held September 12–16, 2022.

The week-long event will provide 12 attendees with extensive classroom learning and hands-on training from Frederick National Laboratory and invited experts. It will be a comprehensive, full-lifecycle training opportunity for novice cryo-electron microscopy users. The workshop is free, but the application process is competitive. Apply here.

Images: (Top) Betta galactosidase. Image credit: Alan Merk, Ph.D., and Jana Ognjenović, Ph.D., Frederick National Laboratory. (Bottom) Titan Cryo-EM operated by the NCEF.

RAS Initiative

Researching novel strategies to target RAS-driven cancers

More than 30% of all human cancers, including 95% of pancreatic cancers and 45% of colorectal cancers, involve mutations in the RAS family of genes. Because of its significant impact on many forms of cancer, the NCI established the RAS Initiative in 2013. As part of this initiative, scientists at Frederick National Laboratory are engaged in cutting-edge research to identify novel strategies targeting RAS-driven cancers. The multi-disciplinary team at the RAS Initiative encompasses scientists from varied technical backgrounds—biologists, chemists, computational biologists, imaging experts, and data scientists. They are involved in leading key pillars that support the RAS Initiative—tools and reagents, structural biology, biochemistry and biophysics, and data informatics.

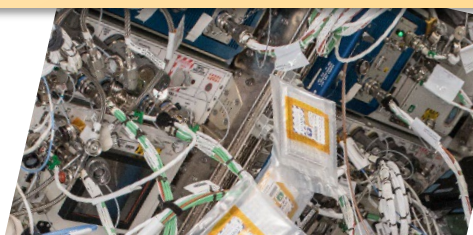
The overarching goal of the RAS Initiative is to mobilize the cancer research community to develop ways to understand and target cancers driven by mutant RAS in an open model of collaboration among government, academic, and industry researchers. This approach is called a “hub and spoke” model. The RAS Initiative at the Frederick National Laboratory acts as the hub that connects to the broader community of RAS researchers around the world, combining efforts and creating new ways to approach the complex issue of RAS.

Image: “Hub and spoke” model. Image credit: NCI, NIH.

Partnership Highlights

- The RAS Initiative has numerous cCRADAs for screening, characterization, and assay development projects to identify new strategies, tools, and compounds to treat RAS-mutated cancers. Past and current partners include Sanofi U.S.; Eli Lilly and Company; Daiichi-Sankyo; TheRas, Inc.; University of California at San Francisco; Weizmann Institute; Genomic Institute of the Novartis Research Foundation; Beatson Institute; and many more.
- Through a collaboration with the Center for the Advancement of Science in Space, the RAS Initiative sent KRAS proteins to the International Space Station to be crystalized in a micro-gravity environment, which can yield better quality crystals to aid in imaging efforts.

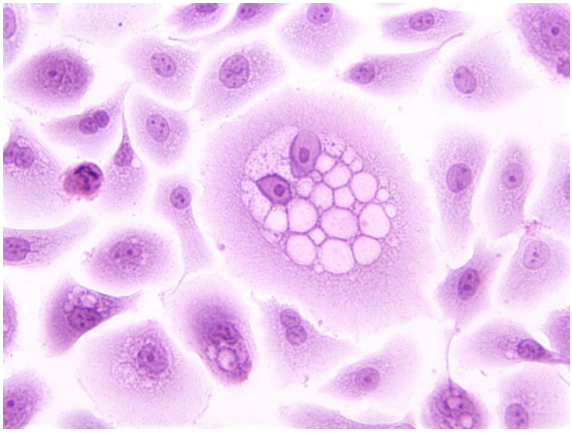
Images: (Right) KRAS protein samples crystallized in the microgravity of space during a five-week experiment aboard the International Space Station. Photo credit: Center for the Advancement of Science in Space.
(Below) SpaceX's Falcon 9 rocket CRS-16 lifts off from the Space Launch Complex 40 on Dec 5, 2018, carrying KRAS samples. Photo credit: Airman 1st Class Zoe Thacker, U.S. Air Force.



Vaccine, Immunity, and Cancer Directorate

Evaluation of immune responses to HPV and new cancer prevention vaccines

The Vaccine, Immunity, and Cancer Directorate (VIC) investigates immune responses to vaccines and viral infections with a main interest on human papillomavirus (HPV), and more recently on SARS-CoV-2. In addition, VIC has been involved in a number of preclinical studies involving new cancer preventive vaccine candidates as well as cancer biomarker studies to assess immune/inflammatory markers associated with an increased risk of cancer in different cancer types.



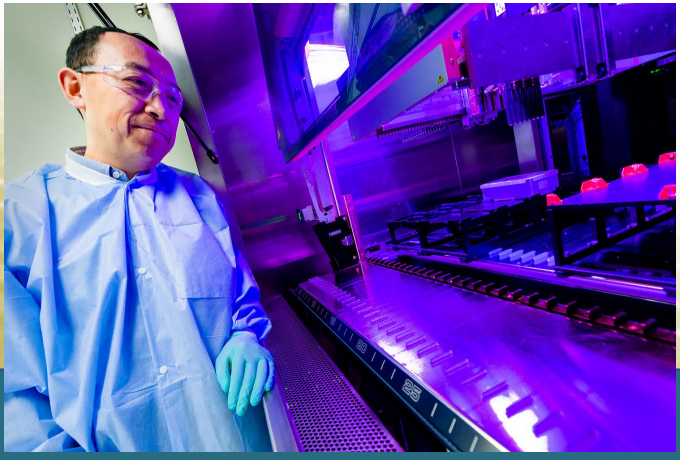
VIC includes the HPV Serology Laboratory at the Frederick National Laboratory, which standardizes assays and procedures, and makes reagents accessible to the scientific community to enable scientists to compare data across different HPV vaccines and different studies. To meet these goals, the HPV Serology Laboratory is focused on development and validation of high-throughput multiplex assays to measure antibody responses to the current multivalent HPV vaccines, both systemically and at mucosal sites, as well as standards to compare serological immune responses to multivalent HPV vaccines and other second-generation vaccines to licensed products. Standard Operating Procedures can be accessed on our website.

Images: (Top) HPV-infected cell. Image credit: NCI/Georgetown Lombardi Comprehensive Cancer Center, Ewa Krawczyk.
(Right): VIC scientist watches the robot that performs automated testing for anti-HPV antibodies.

Opportunities for collaboration include immunological studies in new cohorts of HPV infection and associated cancers and studies of immunogenicity of HPV vaccines and new vaccine candidates in clinical and preclinical studies.

Partnership Highlights

- The HPV Serology Laboratory was created in January 2017 as part of an international initiative on HPV serology standardization, and it is co-funded by NCI and the Bill & Melinda Gates Foundation.
- Through cCRADAs with the H. Lee Moffitt Cancer Center, VIC evaluated HPV-specific antibodies at the oral cavity among males vaccinated with the quadrivalent HPV vaccine, the associations with serum antibody levels, and the factors associated with oral HPV-16 and HPV-18 antibody levels. This was the first study demonstrating that vaccinating males with Gardasil® induces HPV antibody levels at the oral cavity that correlate with circulating levels.

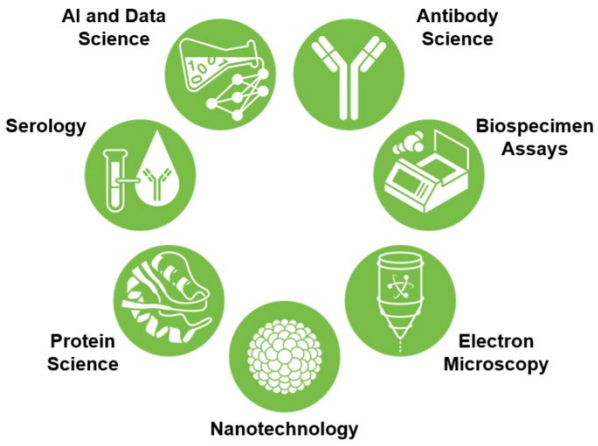


Standards References and Training Research Committee (STAR TREC)

Central hub for standards and references in biological research

STAR TREC strives to increase the reproducibility of data in the scientific community. By establishing and sharing standards and reference reagents for various scientific disciplines, we hope to encourage the adoption of these benchmarks among researchers.

Our scientists have provided standard operating procedures, assay validations, and other reference materials for several fields of research. We seek to leverage our areas of advanced technology and scientific expertise to spearhead collaborative engagement with the academic community and private sector.



Content on our site is meant to be a tool to help bridge gaps in scientific reproducibility. You may access reference material on our webpages, for each of the subgroups, by clicking the link below.

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