The Frederick National Laboratory for Cancer Research

We are a national laboratory and Federally Funded Research and Development Center dedicated to the application of biomedical science and technology to improve human health.

Our scientists conduct basic, translational and applied research, create new technologies, and collaborate with government, industry and academic colleagues. We support the National Cancer Institute, National Institute of Allergy and Infectious Diseases, and other institutes within the National Institutes of Health.

As a government-owned, contractor-operated scientific enterprise, the Frederick National Laboratory for Cancer Research efficiently addresses critical biomedical questions that no one else can readily do and rapidly responds to emerging health threats.

- Biomedical research institute focusing on cancer, HIV/AIDS and infectious diseases
- National resource for the scientific community
- One of 40 Federally Funded Research and Development Centers, designated private-public partnerships with the U.S. government
- The only one of 19 national laboratories exclusively dedicated to biomedical sciences
- Sponsored by the National Cancer Institute

This document provides images from just a few programs that make up the FNLCR:

RAS Initiative

AIDS & Cancer Virus Program

Standardized Organoid Modeling (SOM) Center

Cryo-Electron Microscopy Images

Clinical Monitoring Research Program

Nanotechnology Characterization Lab

DNA origami formulations (1 example nanoparticle)

Volume Electron Microscopy

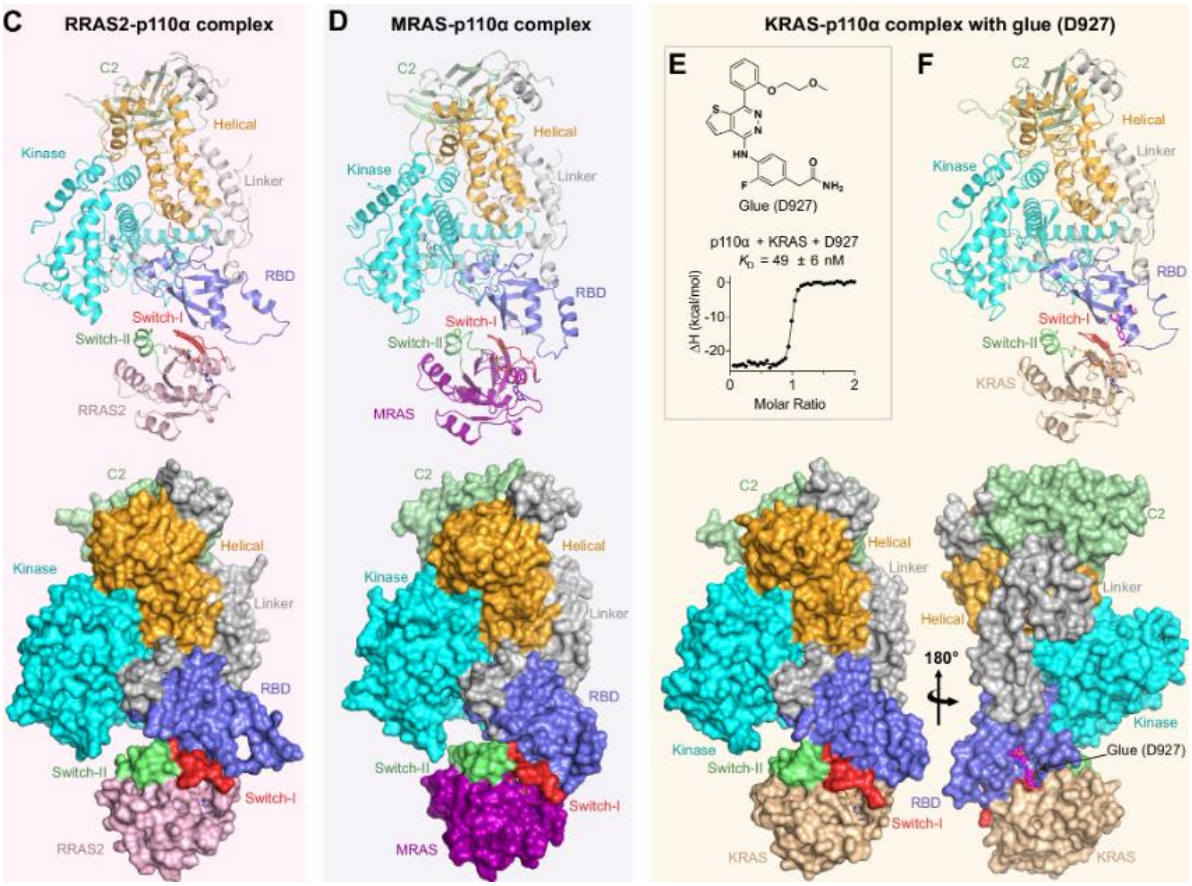
There are many additional cancer research images from NIH here:
https://www.flickr.com/photos/nihgov/albums/72157656657569008/with/20689855941

RAS Initiative

The RAS Initiative mobilizes the cancer research community to develop ways to treat cancers driven by the mutant RAS gene in an open model of collaboration among government, academic, and industry researchers. More than 30% of all human cancers are driven by mutations of RAS genes.

The Structural Biology Research Team at the RAS Initiative leads efforts to define the molecular architecture of RAS in complex with its effectors, regulators, and small molecules using NMR spectroscopy, X-ray crystallography, and cryo-electron microscopy. By elucidating these structures, the team seeks to uncover the mechanistic basis of RAS signaling and regulation. These insights not only deepen our understanding of RAS-driven biology but also enable the identification of novel targets and binding pockets for structure-guided drug discovery.

The Structural Biology Research Team Lead, Dhirendra Simanshu, Ph.D., spent years working with his team to determine the RAS-bound PI3Kα structure. With this "molecular glue" stabilizing RAS and PI3Kα during crystallization, Simanshu and his team solved the first structure of this complex.

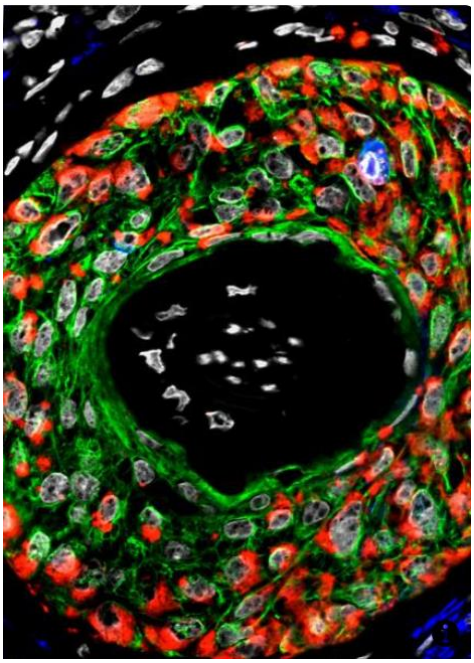


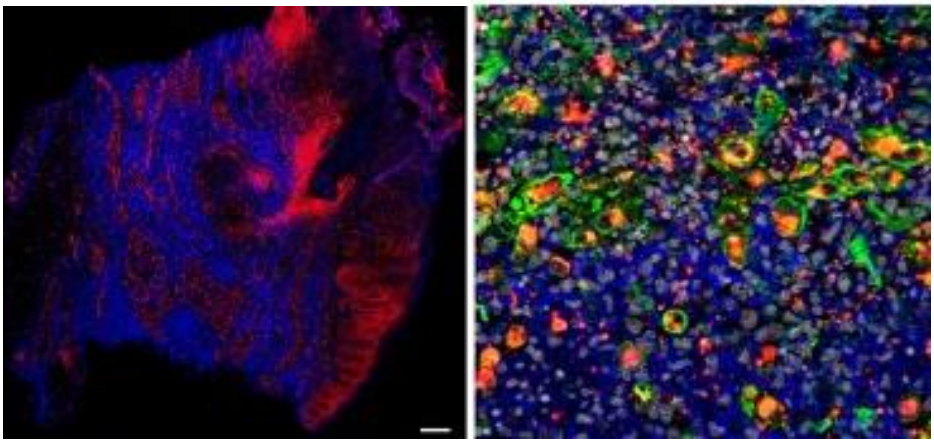
https://www.nature.com/articles/s41467-024-55766-x

C Overall structure of the RRAS2-p110α complex shown in cartoon and surface representations. **D** Overall structure of the MRAS-p110α complex depicted in cartoon and surface representations. **E** Chemical structure of the glue compound D927 and an ITC profile showing a significant increase in the binding affinity between KRAS (GMPPNP) and p110α-RBD in the presence of D927. **F** Overall structure of the KRAS-p110α complex in the presence of glue D927 is shown in cartoon and surface representations. RRAS2, MRAS, and KRAS are colored pink, purple, and wheat, respectively, with the switch-I and switch-II regions highlighted in red and green, respectively.

AIDS & Cancer Virus Program

The AIDS and Cancer Virus Program investigates ways to diagnose, prevent, and treat HIV infection and AIDS-related tumors associated with cancer viruses, such as Kaposi sarcoma–associated herpesvirus.



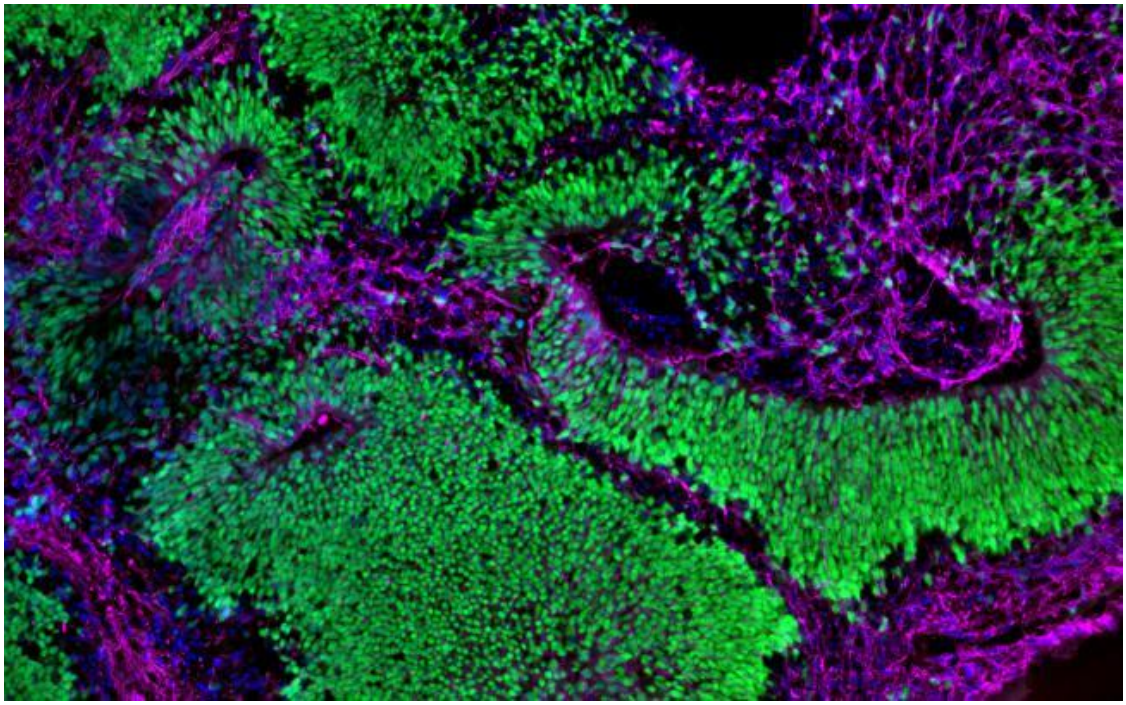


Immunofluorescence of skin biopsies demonstrated a dense immune infiltrate predominantly composed of myeloid and CD8+ T cells, with a strong type I interferon local response. RNAscope detected large amounts of monkeypox virus in epithelial cells (epithelium and hair follicles) and dendritic cells.
(https://pubmed.ncbi.nlm.nih.gov/38019806/)

Standardized Organoid Modeling (SOM) Center

Organoids are small, lab-grown models that mimic the structure and function of human organs and are transforming how researchers study disease and test treatments. Yet most organoid models today are created through trial-and-error, making them difficult to reproduce across labs and slowing their adoption across research and industry. The Standardized Organoid Modeling (SOM) Center will be the nation's first fully integrated platform dedicated to developing standardized organoid-based New Approach Methodologies (NAMs).

The SOM Center is supported by special authorities through the Frederick National Laboratory for Cancer Research (FNLCR), the nation's only Federally Funded Research and Development Center (FFRDC) dedicated exclusively to biomedical research. Using resources from the FNLCR, NCI will direct the in vitro organoid efforts for the SOM Center, while NIAID's Division of Intramural Research will drive in silico development through the Research Technologies Office, applying advanced machine learning (ML) and artificial intelligence (AI) tools to enable real-time optimization of organoid protocols.



Brain organoid depicting neural stem cells in green and neurons in magenta. Both cell types are abundant, showing normal development. Photo credit: NIAID

Cryo-Electron Microscopy Images

Cryogenic electron microscopy (cryo-EM) has rapidly emerged as a powerful tool to determine high resolution structures of biological molecules. However, the cost of the instrumentation is prohibitively expensive for many institutions, precluding more widespread adoption of the technique. At the Frederick National Laboratory, we develop methods for lower-voltage electron microscopes, which are significantly less expensive than the microscopes typically used for high-end data collection. The new data collection procedures have enabled these cheaper microscopes to produce high-resolution structures that show an unprecedented level of detail, including water molecules, metal ions, and bound drugs.

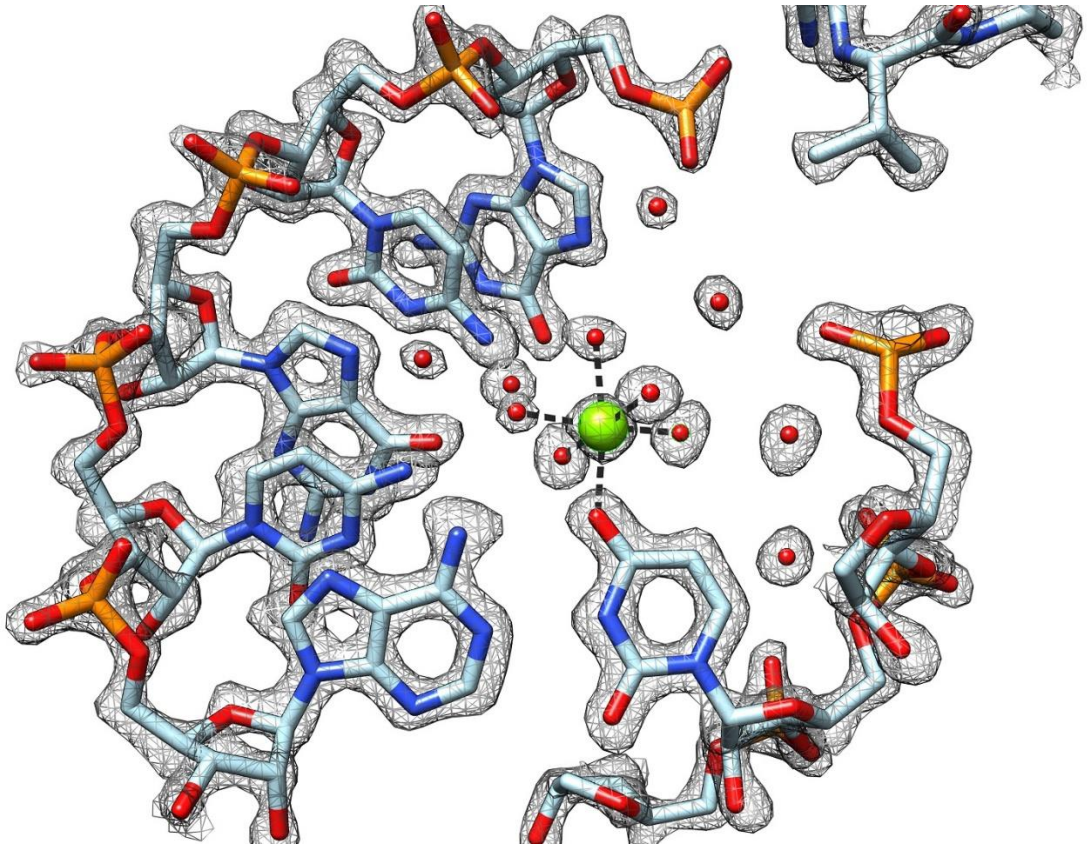
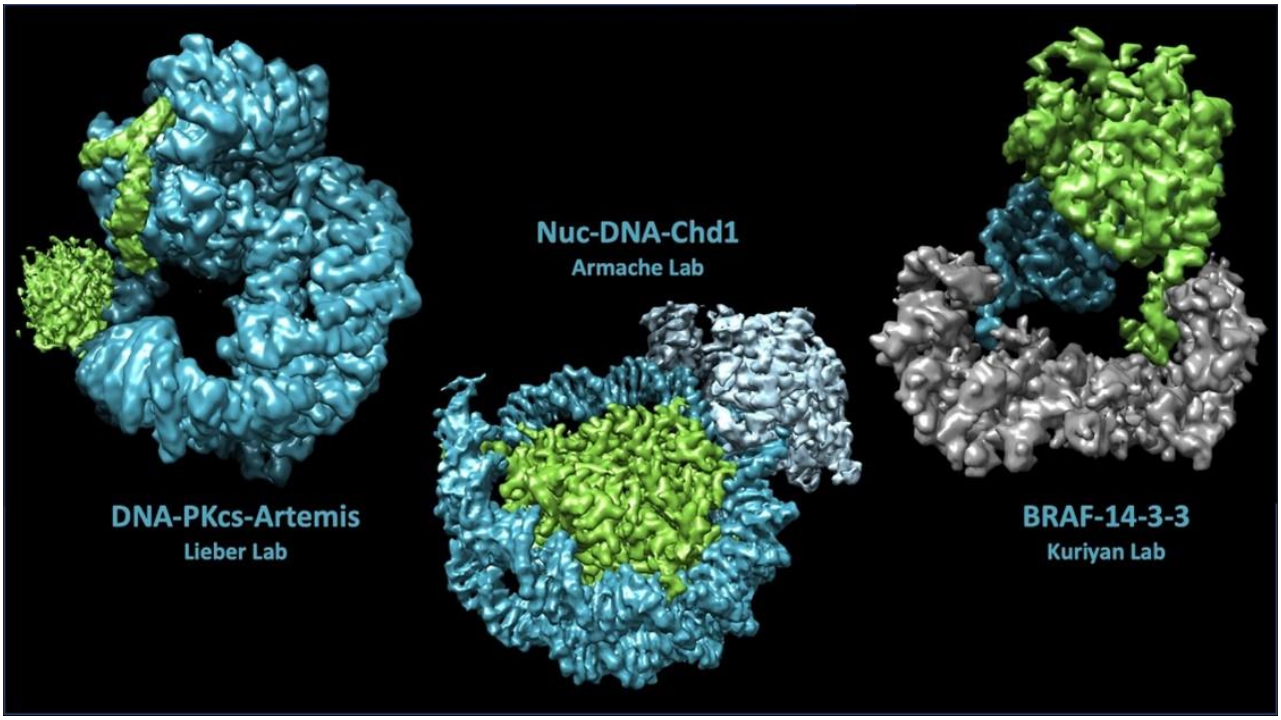


Photo credit: Alan Merk and Jana Ognjenović, Frederick National Laboratory



Cryo-EM density of three molecular complexes, segmented into individual components:

- Left: DNA-PKcs (blue) bound to Artemis (green) (Watanabe et al., *Nucleic Acids Res*. 2022, EMD-26192).
- Middle: Nucleosome (green) complexed with DNA (blue) and Chd1 (gray) (Nodelman et al., *Nat. Structu. Mol. Biol.* 2022, EMD-25480)
- Right: BRAF dimer (blue and green) bound to 14-3-3 (gray) (Kondo et al., *Science*. 2019, EMD-20708).

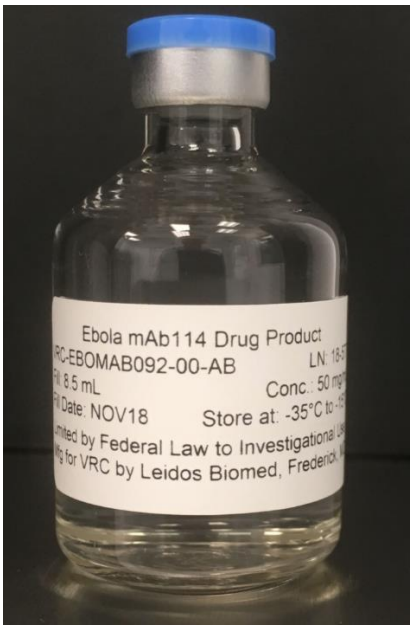
All structures were generated from datasets collected at the **National Cryo-EM Facility, located at the Frederick National Laboratory.**

This is the microscope, a Titan Krios transmission electron microscope, that produced these images →

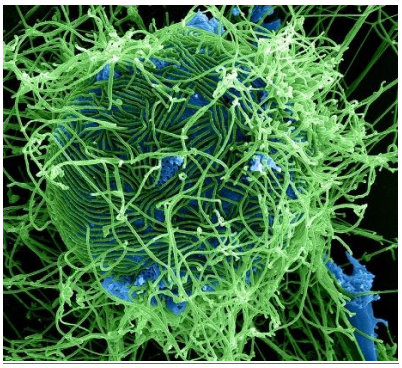
Clinical Monitoring Research Program

The Clinical Monitoring Research Program facilitates strategic support of global clinical research programs conducted by the National Institutes of Health by providing comprehensive clinical trials operations and project management services from concept to cure. The team response to urgent needs for clinical trials during times of crisis. For example, the team quickly launched critical clinical studies amid health emergencies such as the Ebola virus disease outbreak in West Africa and the worldwide COVID-19 pandemic.

Ebola



(Pic-Left) Ebola therapeutic produced at the Frederick National Lab for use in Ebola clinical trials. (Pic-Right) Dr. Marie-Claire Kolié of the World Health Organization (left) and Dr. Ian Crozier, Frederick National Laboratory/NIAID, deployed by WHO, at the Butembo Médecins Sans Frontières (Doctors Without Borders) Ebola Treatment Unit. [Credit: NIAID] Learn more about the Ebola study.



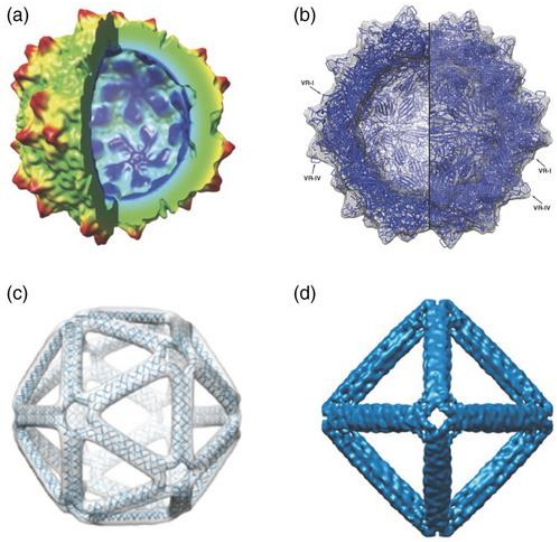
Ebola Virus Particles. Colorized scanning electron micrograph of filamentous Ebola virus particles (green) attached to and budding from a chronically infected VERO E6 cell (blue) (25,000x magnification). Credit: National Institute of Allergy and Infectious Diseases, National Institutes of Health

Nanotechnology Characterization Lab

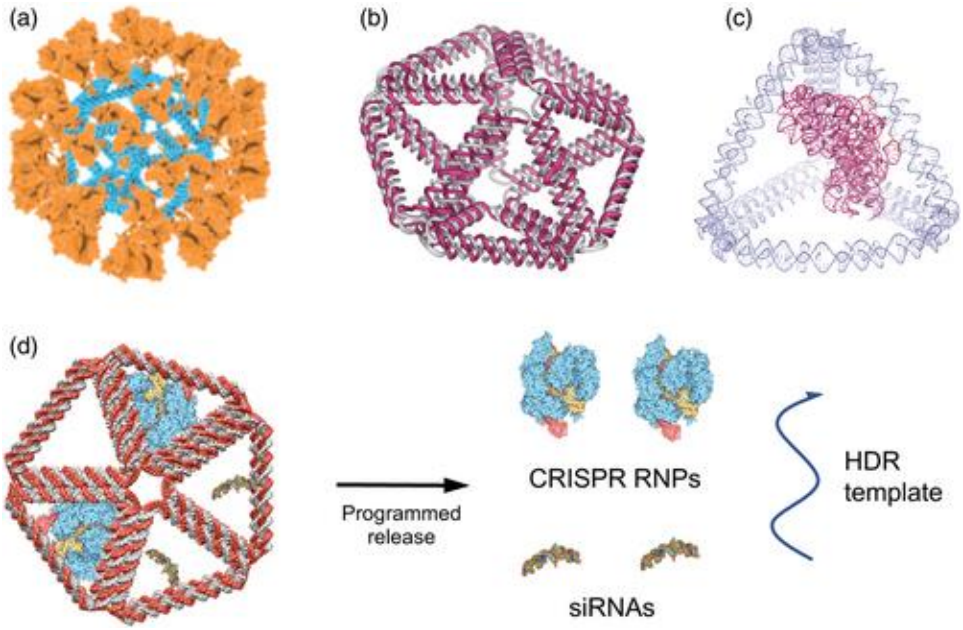
The Nanotechnology Characterization Lab provides comprehensive preclinical characterization of nanomedicine formulations. The lab serves as a resource and knowledge base for all cancer researchers in academia, industry and government to facilitate the development and clinical translation of nanotechnologies intended as cancer therapeutics and diagnostics. It has tested more than 550 unique nanomaterials and worked with more than 200 researchers.

Nanotechnology, which utilizes nanoparticles and nano-devices typically one hundred to ten thousand times smaller than human cells, enables researchers to address critical cancer-related challenges, such as developing diagnostic devices and sensors in vitro and achieving effective drug delivery to cancer targets in vivo.

DNA origami formulations (1 example nanoparticle)



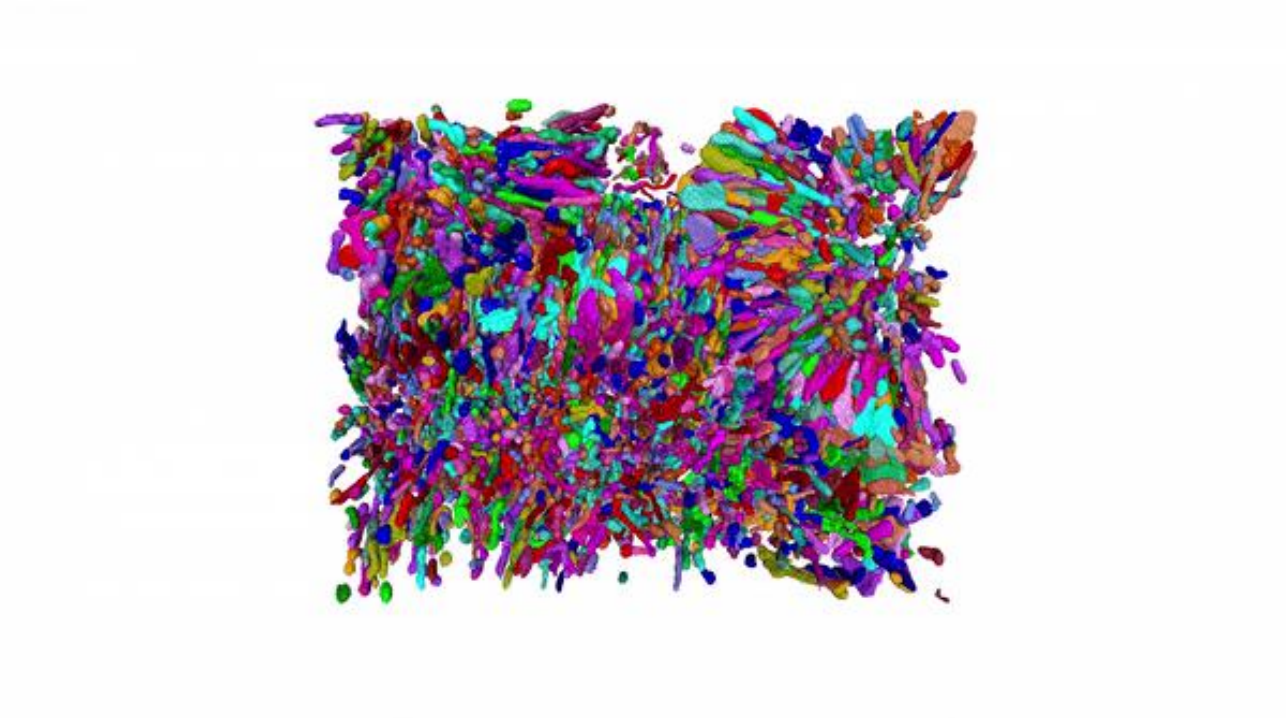
Structure-composition comparison of AAV9 and virus-like DNA assemblies fabricated using the scaffolded DNA origami approach.
(https://wires.onlinelibrary.wiley.com/doi/full/10.1002/wnan.1657)



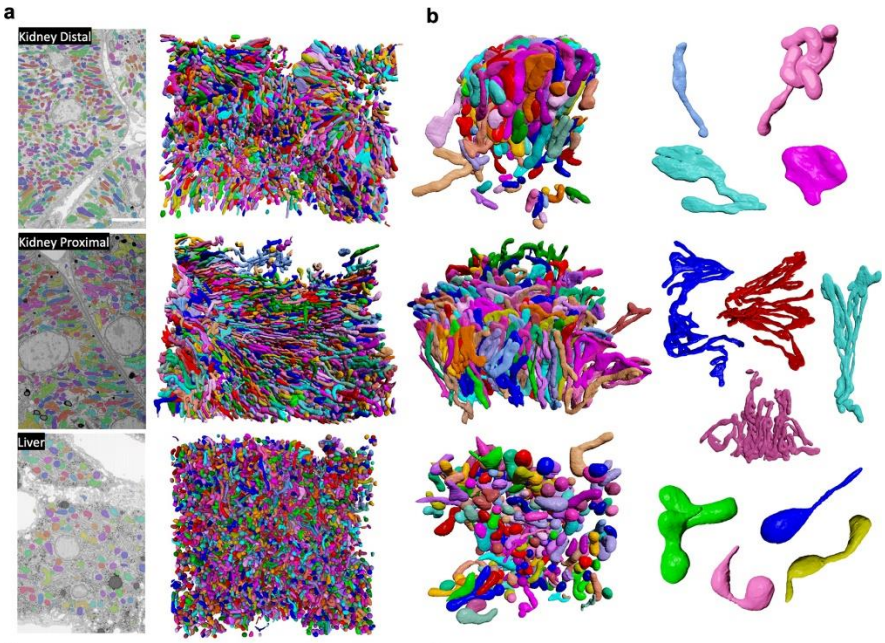
Virus-like nucleic acid nanoparticles can be programmed to deliver and release CRISPR ribonucleoprotein complexes (RNPs), homology directed repair (HDR) templates, and siRNAs either alone, or in combination, for next-generation in vivo gene therapeutic applications.

Volume Electron Microscopy

Volume electron microscopy (vEM) enables imaging of cells and tissues in 3D and at nanoscale resolution, revealing new and exciting biology. The group develops and deploys advanced volume EM techniques.



Mitochondrial segmentation of kidney distal tubule using Mitonet, generalist deep learning model that automatically segments mitochondrial instances using Empanada and a highly heterogeneous dataset of labeled mitochondria.



Results on volumes of mouse liver and kidney. **a.** Rows from top to bottom correspond to kidney distal tubule, kidney proximal tubule, and liver. Left column shows representative 2D images of MitoNet segmentation (scale bar, 5 µm); right column shows 3D predictions on the entire volume (small and boundary objects removed). **b.** Left column shows a zoomed in ROI of raw model predictions (basolateral surfaces of cells on top); right column shows representative mitochondrial models after manual cleanup. (https://www.sciencedirect.com/science/article/pii/S240547122200494X)