



November 2020

The mission of NCCAT is twofold: to provide nationwide access to advanced cryoEM technical capabilities, and to assist users in the development of cryoEM skills needed for independent research. NCCAT provides access to state-of-the-art equipment required to solve structures to the highest possible resolution using cryoEM methods. Supported by the NIH Common Fund Transformative High Resolution Cryo-Electron Microscopy program (U24 GM-129539).

## Story of the Month: NCCAT Saves the Day



Larry Shapiro is a principle investigator at Columbia's Zuckerman Institute and has spent the last 15 years working in collaboration with the Vaccine Research Center at NIH on developing an HIV vaccine. Like many virologists Larry and his lab shifted most of their efforts this year to SARS-CoV-2, but he still considers HIV the world champion virus. "98% of people will clear COVID-19." He says, "Nobody clears HIV - HIV wins against the immune system." In 2019, there were few scientists working on coronavirus, so many critical contributions on COVID-19 right now, are coming from people who worked with HIV. This is part of why he believes

HIV is a model system. The key methods that allowed them to work quickly with COVID-19 were developed while investigating HIV. Comparatively, SARS-CoV-2 appears to be a more "normal" virus and Larry is optimistic about our ability to develop vaccines and anti-viral therapeutics. Larry was one of the investigators to submit a SARS-CoV-2 rapid access proposal to NCCAT and the data collected during that project resulted in a [paper in Nature](#) that was published in July.

### *The Project*

Larry jokes that David Ho actually started the pandemic when he moved with the Aaron Diamond AIDS Research Center to Columbia University in January of this year. It was excellent timing that enabled them to start a collaboration on SARS-CoV-2. Columbia University Medical Center had a number of coronavirus patients early on in the pandemic. Larry's and David Ho's groups looked at serum of the patients with the most severe cases of COVID-19. They found that the people who have the most challenging courses of the disease have by far the best antibodies, which is probably not surprising because they've had a long time for those antibodies to develop. When they characterized the antibodies from these patients they found some of the most potent antibodies that have been discovered to date. Larry's lab used cryoEM to map how the antibodies are interacting with the virus and determine the mechanisms of neutralization for each antibody. By looking at the structures of the antibodies from many patients they found there is a limited number of ways that humans neutralize coronavirus with antibodies that target the virus's spike protein. There are classes of antibodies that were found in many different donors showing their common elements to the human neutralizing response to coronavirus.

## NCCAT to the Rescue

Pursuing COVID-19 research, Larry's lab was one of the few that remained opened during the lockdown in New York City. With a skeleton crew they were able to collect and isolate samples from patient's serum. There was only one problem, under a citywide lockdown most of the microscopes in NYC were shutdown. But then NCCAT opened for COVID-19 research. "Before there was a lockdown ... we were making proteins, and once the lockdown started and we had samples it was NCCAT that came to the rescue" Larry said. The staff at NCCAT was absolutely critical in the beginning. There was a lot of focus on the spike protein which was very challenging at the time. The team at NCCAT worked with the members of the Shapiro lab to figure out ways to get stable samples so they could solve complexes with antibodies. Because of those advances it's now much easier to move things along. As an X-Ray crystallographer, Larry thought that CryoEM was the end of days, but it turns out it's actually a very good thing.

## Hope for the Future?

If there is a thin silver lining in the current dark cloud that is COVID-19, Larry believes that we will definitely learn from this crisis. Spending a few extra billion dollars for pandemic prevention and vaccine or treatment development against coronaviruses will save trillions in the long run. We used to understand that we have to make these investments and he thinks now that we will understand as a modern society that this is a core function of government.

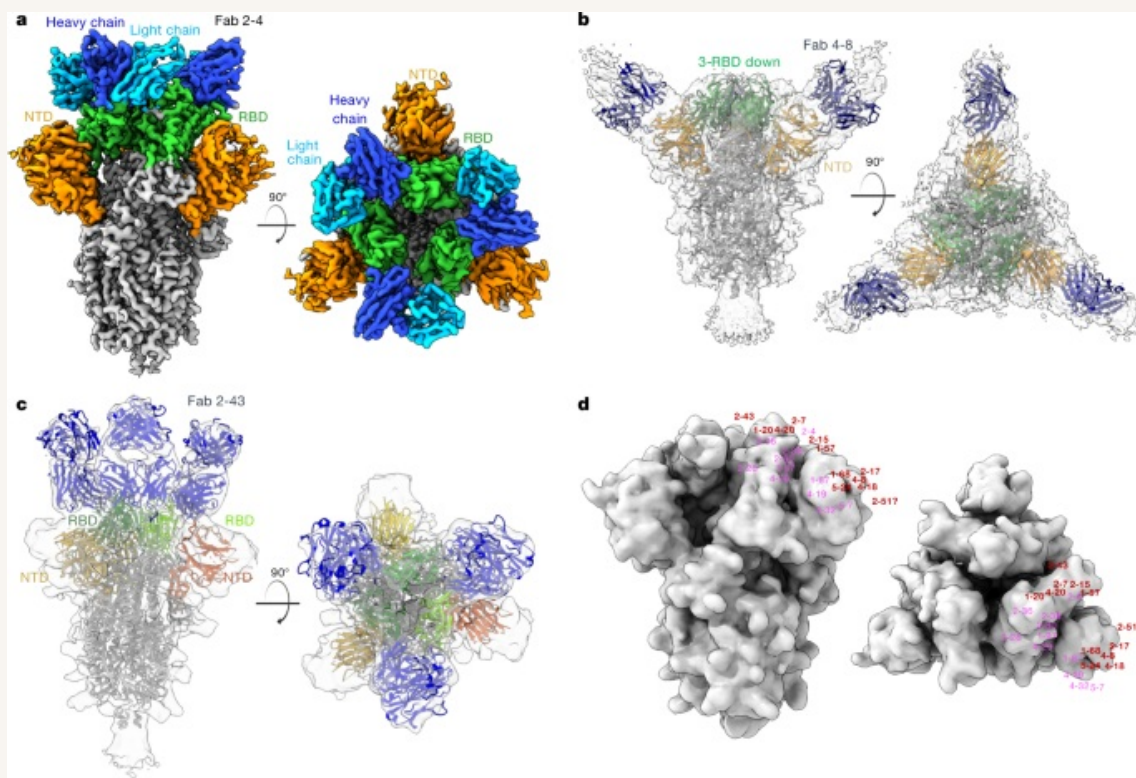


Figure 4 from Liu *et al.* "Cryo-EM reconstructions of Fab-spike complexes and visualization of neutralizing epitopes on the spike surface." [*Nature* 2020]

## Virtual Appion Workshop Part 2.5

Single Particle Analysis – 3D Reconstruction

November 16 & 18

**2:30pm - 5:00 EST**

The Appion Part 2.5 Workshop is a follow-up to the Part 2 workshop and will focus on 3D initial models and refinement. Utilizing AWS Cloud services and RELION this workshop will provide a foundation in not only the SPA workflow but current best practices in data processing and analysis. The workshop will be held over 2 afternoons with 2-3 hours of instruction and demonstration followed by self-paced individual practice. The first day will focus on a comparison of the SPA workflow between cryoSPARC and RELION. The second day will focus on refinements, validation, and additional tools. We will be using the same tutorial dataset as in Part 2 so you may compare workflows and outputs.

**[Register Now!](#)**

## **National Center for In-Situ Tomographic Ultramicroscopy**

NYSBC is one of **[four service centers](#)** funded by the NIH Common Fund's **[Transformative High Resolution Cryoelectron Microscopy \(CryoEM\) Program](#)**. The center at NYSBC will be called the National Center for In-Situ Tomographic Ultramicroscopy (NCITU).

The National Network for Cryoelectron Tomography will offer the biomedical community access to a specialized cryoelectron microscopy (cryoEM) technique that is uniquely capable of visualizing intact regions of cells and tissues at high resolution and with little perturbation. The network hub will be located at University of Wisconsin-Madison and led by Dr. Elizabeth Wright. The other three network service centers will be located at New York Structural Biology Center (contacts: Bridget Carragher, Clint Potter, Misha Kopylov), SLAC National Accelerator Laboratory-Stanford University (contact: Dr. Wah Chiu), and University of Colorado Boulder (contact: Dr. Andreas Hoenger).

The service centers will specialize in cryoET specimen preparation. The hub will perform cryoET data collection for all the user laboratories served by the network, in addition to its service center functions.

Read full announcement from **[NIH Common Fund](#)**

## **Job Opportunities**

### **Staff Microscopist**

We are seeking an electron microscopist to join the staff of the Simons Electron Microscopy Center (SEMC). This individual will primarily be a cryoEM specialist who will assist users of the facility to carry out service experiments and will also have opportunities to pursue collaborative research projects. The individual

### **Laboratory Technician**

We are seeking a laboratory technician to add to our expanding group. We are looking for a bright and enthusiastic individual to help out with various tasks to keep the lab running. Most important requirements are a good attitude, ability to learn, able to work independently, and willingness to do what needs to be done. Must be able to work in a multi-



should be capable of multitasking, enjoy working with other people, have a good working knowledge of electron microscopes, and a strong research background. Good communication skills are essential.

[Apply on Indeed](#)

tasking environment where priorities may change often and be able to work well with others. Previous electron microscope experience is not required, but is a plus.

[Apply on Indeed](#)

## Submit Your Proposal to NCCAT



### NCCAT GUP1 PROPOSAL SUBMISSION

The [GUP1 access program](#) supports single particle cryoEM data collection on one of our existing Titan Krios instruments using a Gatan K2 direct-electron detector.

[Submit Now!](#)



### NCCAT GUP2 PROPOSAL SUBMISSION

The [GUP2 access program](#) supports use of [Chameleon](#) (the commercialized version of [Spotiton](#)) and an exploratory screening microscope session.

[Submit Now!](#)



### NCCAT RAP1 PROPOSAL SUBMISSION

The [RAP access program](#) allows users with GUP proposals that have an active URC/UAC score to request additional time on their project without submitting an entirely new proposal.

[Submit Now!](#)



### NCCAT BAG PROPOSAL SUBMISSION

The [BAG access program](#) allows researchers greater flexibility in instrumentation access by combining General User Proposal (GUP) access proposals

[Submit Now!](#)

## VISIT OUR WEBSITE

FOLLOW NCCAT



NCCAT is supported by the NIH Common Fund Transformative High Resolution Cryo-Electron Microscopy program (U24 GM-129539).