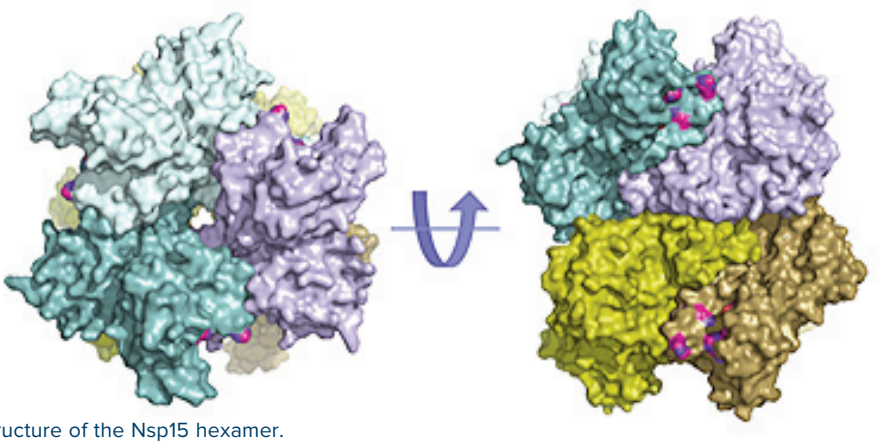
The Advanced Photon Source

Coronavirus Research at APS Beamlines

Research at the Advanced Photon Source (APS) into the molecular structure of the SARS CoV-2 virus is moving at an accelerated pace, as it is at many of the world's x-ray light sources. As a result, the content of this article will be outdated by the time you read it. Nevertheless, we offer here some pertinent information.

The SARS CoV-2 virus, which causes coronavirus disease 2019 (COVID-19), is composed of 28 unique proteins. Researchers using APS beamlines funded by the U.S. Department of Energy (DOE), by the National Institutes of Health, and the State of Michigan have to date determined structures of the main protease (NSP5), NSP3, NSP9, NSP15, NSP16/NSP10 complex, and the spike protein with an antibody and bound to the cell surface receptor. These are important targets for antiviral drug or vaccine development.

As of 4.8.20 at least 23 groups have used or expressed interest in using beamlines at the DOE's APS operated by four separate groups (the Structural Biology Center [SBC-XSD], the Life Sciences Collaborative Access Team [LS-CAT], the National Institute of General Medical Sciences and National Cancer Institute facility [GM/CA-XSD], and the Northeastern [NE] CAT). (This does not include the pharmaceutical companies performing proprietary research at the Industrial Macromolecular Crystallography Association CAT.) These beamlines have been used by researchers to determine a total of 16 structures (to date) of these proteins, which have been deposited in the Protein Data Bank. Several of these structures include a bound molecule providing critical insights for drug development.



Structure of the Nsp15 hexamer.

Y. Kim, R. Jedrzejczak, N. I. Maltseva, M. Endres, A. Godzik, K. Michalska, A. Joachimiak, "Crystal structure of Nsp15 endoribonuclease NendoU from SARS-CoV-2," bioRXiv preprint DOI: 10.1101/2020.03.02.968388 *Contact: andrzejj@anl.gov*

One of the first potential drug targets (above) was identified at SBC-XSD. The NSP15 protein of SARS CoV (the virus that causes SARS) and SARS CoV-2 are 89% identical, so drugs that had previously been in development to treat the SARS outbreak could be developed as effective drugs against COVID-19.

On March 30, 2020, Fang Li's group published an online "advanced preview" in *Nature* of the structure of the receptor-binding domain of the spike protein with the human receptor hACE2. They collected data at NE-CAT on March 5, 2020.

On April 3, 2020, Ian Wilson's group published online in *Science* the structure of the receptor-binding domain of the spike protein with the antibody CR3022. They collected data at GM/CA-XSD on February 15, 2020.

Three structures have been determined by Center for Structural Genomics of Infectious Diseases researchers using LS-CAT. Andy Mesecar's group determined the structure of the main protease with a broad-spectrum inhibitor, and Karla Satchell's group determined the structure of the NSP16-NSP10 complex with two different inhibitors.

Note: The Structural Biology Portal listing DOE-Basic Energy Sciences-funded capabilities that could be brought to bear on SARS CoV-2 is now posted on the home page of most of those light sources.

Further information: rfischetti@anl.gov

Call for APS General-User Proposals

The Advanced Photon Source is open to experimenters who can benefit from the facility's high-brightness hard x-ray beams.

General-user proposals for beam time during Run 2020-3 are due by Thursday, July 2, 2020.

Information on access to beam time at the APS is at http://www.aps.anl.gov/Users/apply_for_beamtime.html or contact Dr. Dennis Mills, DMM@aps.anl.gov, 630/252-5680.

Argonne National Laboratory is a U.S. Department of Energy (DOE) laboratory managed by UChicago Argonne, LLC
The Advanced Photon Source is a U.S. DOE Office of Science User Facility operated for the DOE Office of Science by Argonne National Laboratory under Contract No. DE-AC02-06CH11357

Advanced Photon Source
Bldg. 401/Rm A4113
Argonne National Laboratory
9700 S. Cass Ave.
Argonne, IL 60439 USA
aps.anl.gov
apsinfo@aps.anl.gov

U.S. Department of Energy
Office of Science
science.energy.gov/

Argonne National Laboratory
anl.gov