SSRL BL12-1 Commissioning

March 5th 2020 – First Diffraction Dataset Collected at SSRL BL12-1

Things on track to complete 12-1 commissioning

- Initial testing uncovered items in need of further alignment, troubleshooting or repair
- Work still necessary to complete our sample exchange robot
- Other systems also in need of final completion and testing, including systems that support our cryo-coolers and detectors

March 16th – San Mateo shelter-in-place order – SSRL shuts down

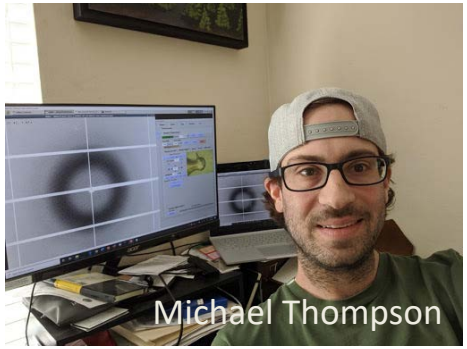
March 25th – BL 12-2 and 9-2 operations for Covid-19 related projects

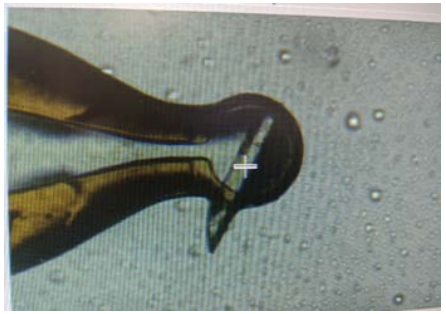
The intense X-ray micro-beams at SSRL BL12-1 would benefit challenging Covid-related projects

April 8th – Limited site access to complete BL12-1 commissioning!

May 5th – First Remote Users at BL12-1 – Fraser Group (UCSF)

- Studies of a conserved enzyme shown to promote virulence in the coronavirus family
- Measurements at physiological temperatures associated with infection in humans
- Understanding how temperature affects the enzyme structure and interactions may provide insight leading to the development of antiviral therapeutics





SSRL BL12-1 Commissioning

May 6th – 2nd User Group at BL12-1 – Cochran Group (Stanford) and Irimpan Mathews (SSRL)

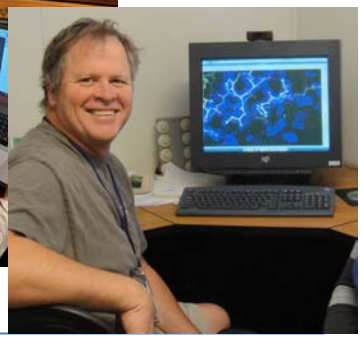
- Structural studies of engineered cell surface proteins targeted as an enhanced adjuvant for immunization against CoV proteins, information that could assist in vaccine development.

Irimpan Mathews

John Silberstein

Jennifer Cochran

Silvia Russi



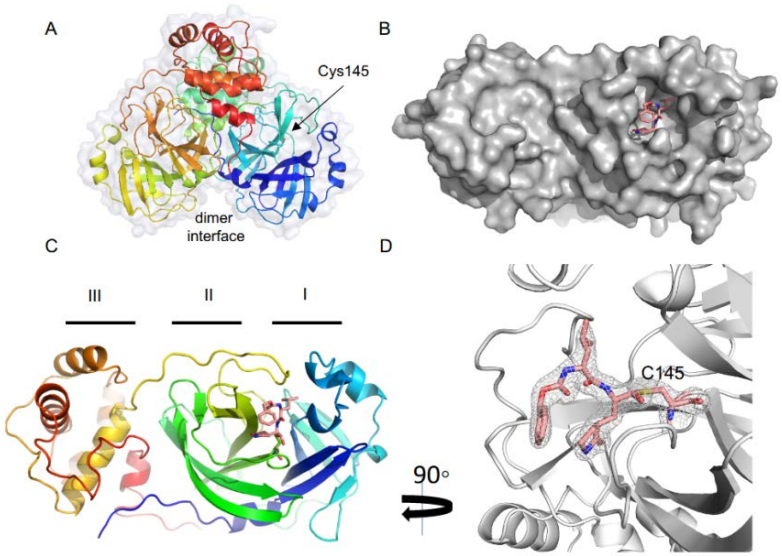
Clyde Smith

Covid-Operations of SSRL BL12-2 and 9-2

- 100s of datasets collected by remote users
- First publication online using data collected in April at BL12-2 – Lemieux (University of Alberta)

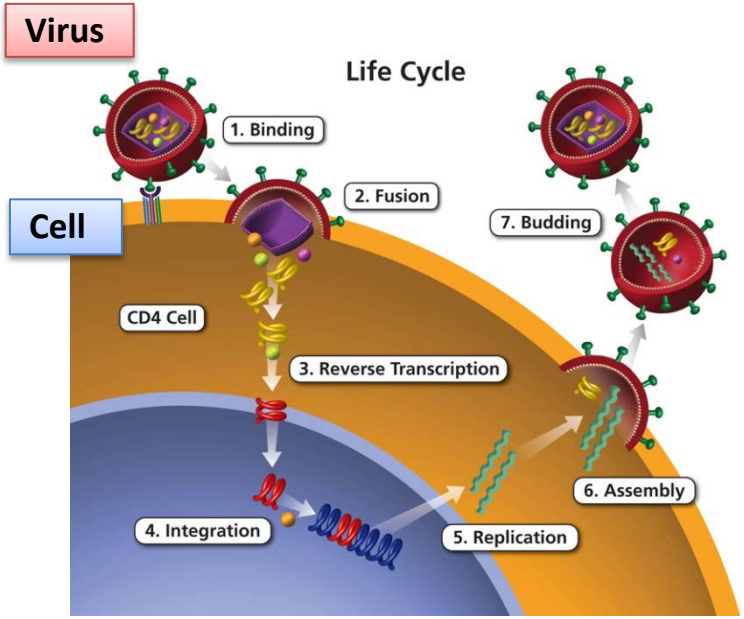
https://www.biorxiv.org/content/10.1101/2020.05.03.073080v1

The Lemieux group solved several structures of Corona virus drugs bound at the active site pocket of the main protease of SARS-CoV-2, to block virus replication. This may be a strong drug candidate for treatment of human coronavirus infections because it has already been successful treating SARS-CoV in animals.



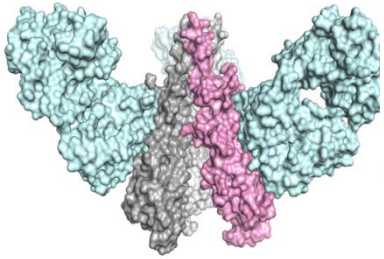
Structure Aided Rational Drug Design

- **Rational drug design** is the development of medications based on the structures and functions of target molecules.
- **Viral infections** comprise multiple steps, that involve interactions between viral and cellular molecules.
- **Structural knowledge** of virus and "helper" molecules during it's life cycle help locate **attack points**, often unique surface areas on viral structures accessible to our immune system.
- **SSRL Beamlines** and users produce structural data used in the development of **drugs and vaccines** to combat viral infections.



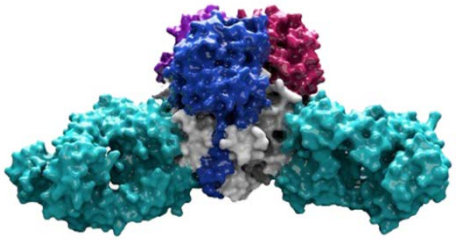
https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/1596/life-cycle

Flu



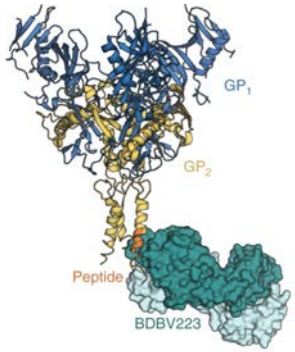
A broadly neutralizing antibody bound to the "invariable stem" of Flu virus hemagglutinin

Zika



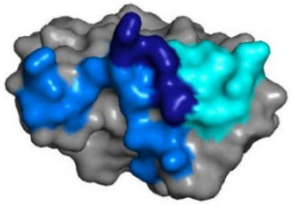
A human donor antibody bound to a ridge found in the binding domain of the Zika virus

Ebola



Antibody (teal) complexed with Ebola stalk epitope, with high sequence conservation among ebolaviruses

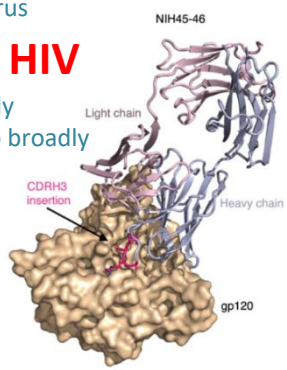
Lassa



Surface areas bound to antibodies recovered from a human survivor highlighted on the Lassa virus surface glycoprotein.

HIV

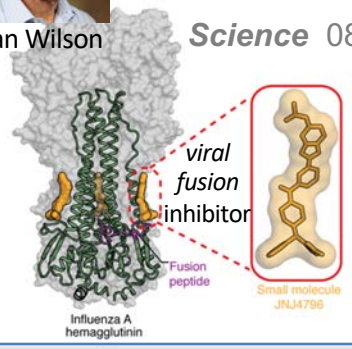
A new antibody rationalized to broadly neutralize HIV subtypes



Scientists Discover a Potential Strategy to Treat Influenza A

Ian Wilson

Science 08 Mar 2019



Mice infected with a lethal dose of H1N1 influenza survived when given JNJ-4796

Scripps janssen

Other Viral Therapeutics

- **Tamiflu®**: prevention and treatment of human influenza. FDA approved in 1999.
- **Retrovir®** (Zidovudine): treatment of human HIV. First FDA approval in 1987.
- **Zmapp®**: treatment for Ebola. 2019 trial during Ebola outbreak in the Congo.

Selected References and Science Highlights - SSRL Crystallography

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Highlight: https://www.caltech.edu/about/news/progress-toward-hiv-vaccine

EBOLA: Cross-reactive neutralizing human survivor monoclonal antibody BDBV223 targets the ebolavirus stalk. L.B. King, B.R. West, C.L. Moyer, P. Gilchuk, A. Flyak, P.A. Ilinykh, R. Bombardi, S. Hui, K. Huang, A. Bukreyev, J.E. Crowe Jr. & E.O. Saphire Nat Comms vol 10, 1788 (2019).

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