

April 21, 2020  
Revised April 23, 2020

# Promising Applications of Synchrotron Radiation to Fight Against COVID-19

Task Force for COVID-19  
International Center for Synchrotron Radiation Innovation Smart (SRIS),  
*Tohoku University*

# 1. Application to Supporting Technology for Drug Discovery

## Phase III

**Establish measurements and analyses to visualize structural mutations at in-vivo state and predict potential mutation sites**

- R&D target: Structure analysis of virus, development of quick method for structural dynamics of virus.

(ex.) Visualization of dynamics of structures and chemical states of virus

## Building innovative analytical method

## Phase II

**Construction of measurement protocol that contributes to development of new antiviral agents**

- R&D target: Development of simulations such as high throughput measurement and structure prediction

(ex.) Visualization and understanding of unknown mechanism of interaction between antiviral drug and target

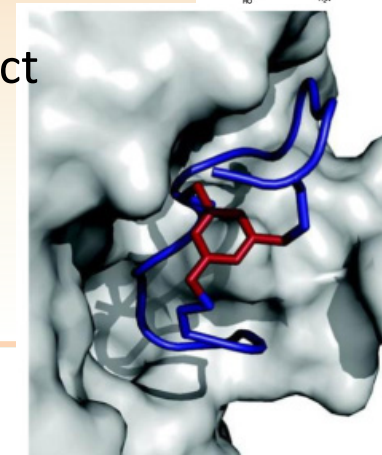
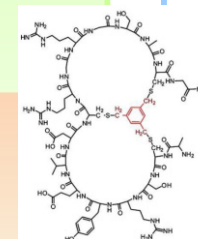
## Sophistication of prior analytical process

## Phase I

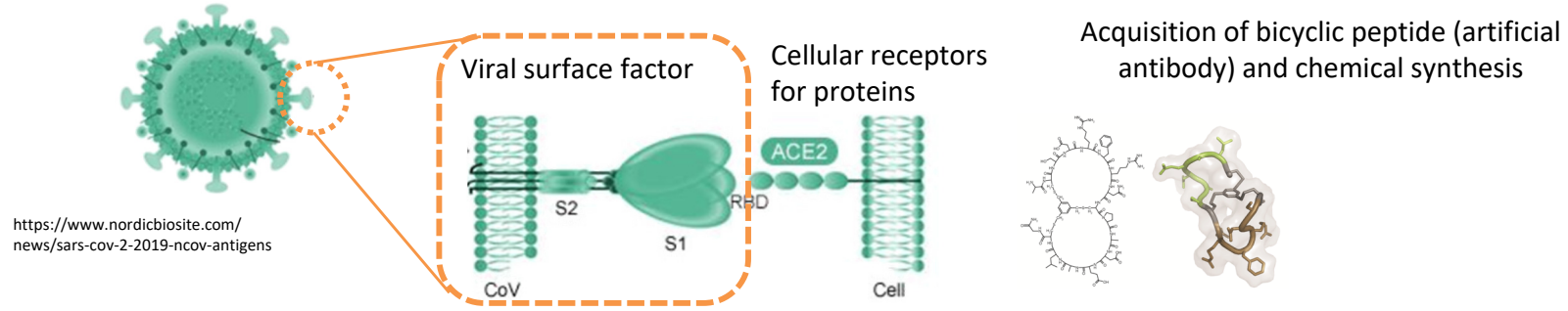
**Structural biology of interactions between existing antiviral drugs and viruses**

- R&D target: Establishment of measurement technology of indirect evidence for clinical research

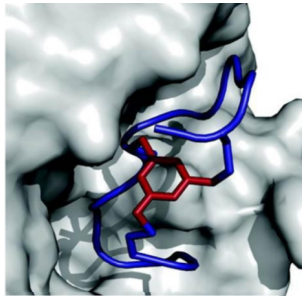
(ex.) Development of artificial antibody against COVID-19 protein and analysis of intracellular element dynamics (infectious / non-infectious) contributing to it



# (ex.A) Structural biological analysis of the interaction between antibody drug that inhibits viral infection and viral surface factor



## Present Task



https://www.efmc.info/medchemwatch-2011-3/researcher.php

### Next Generation SR Facility

Precise analysis of Infection reaction trigger

Sample selection  
Detailed structure

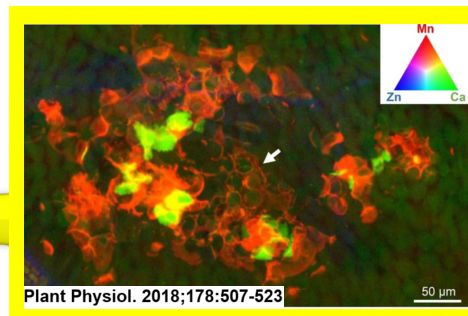
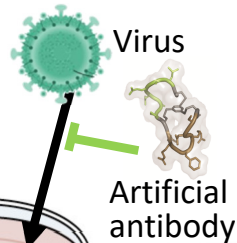
- Precisely visualize the state in which the antibody drug reaction site surely inhibits the functional expression of the infection control factor.
- Based on precise structural information, simulations will be carried out to optimize drug efficacy and develop into more powerful drug development.

### Laboratory

X-ray fluorescence imaging



## Task for the Next Generation SR



Structural evaluation, Fitting analysis

Improvement of artificial antibody

Next-generation SR measurement combined with high-throughput technology and computational science accelerates the development of virus mutation prediction technologies and related drug discovery.

Visualization by next generation SR

Mutation Prediction

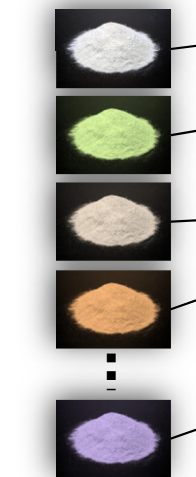
# (ex.B-1) Challenge to predict variation of virus accelerating procedure for clinical trials

## Present Task: Rapid development of medicines and vaccines

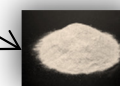
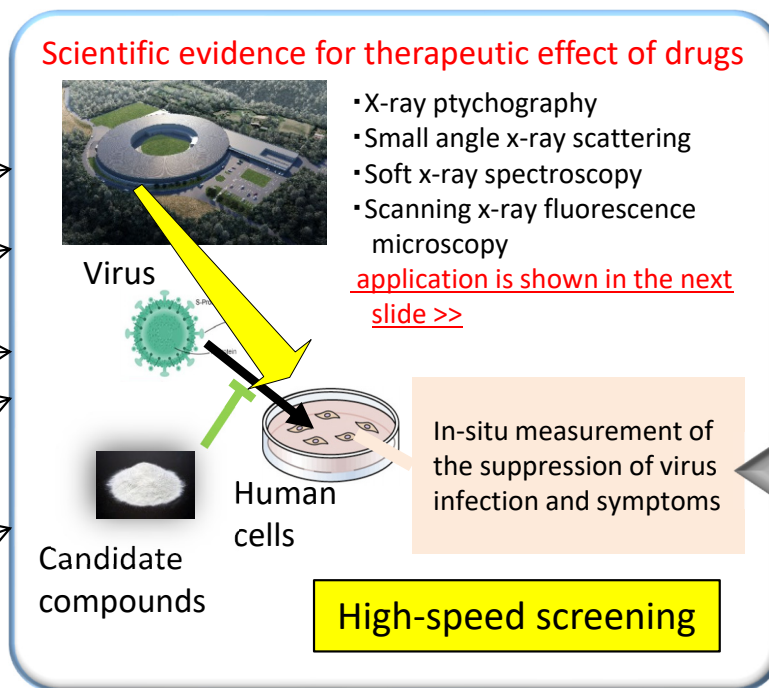
Immediate delivery of drugs to over 2 million infected people, followed by vaccination of approximately 8 billion people worldwide.

## Task for the Next Generation SR

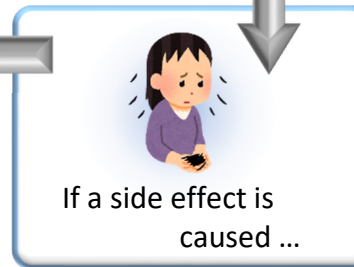
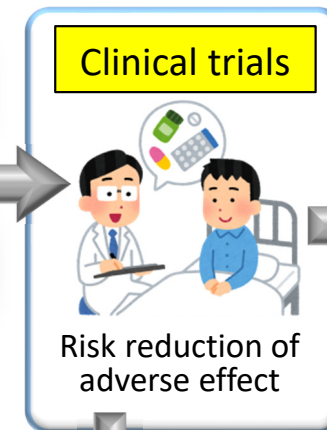
- Over 650 drugs registered in the world
- Others, candidate compounds



$N > 10,000$



$N < 10$

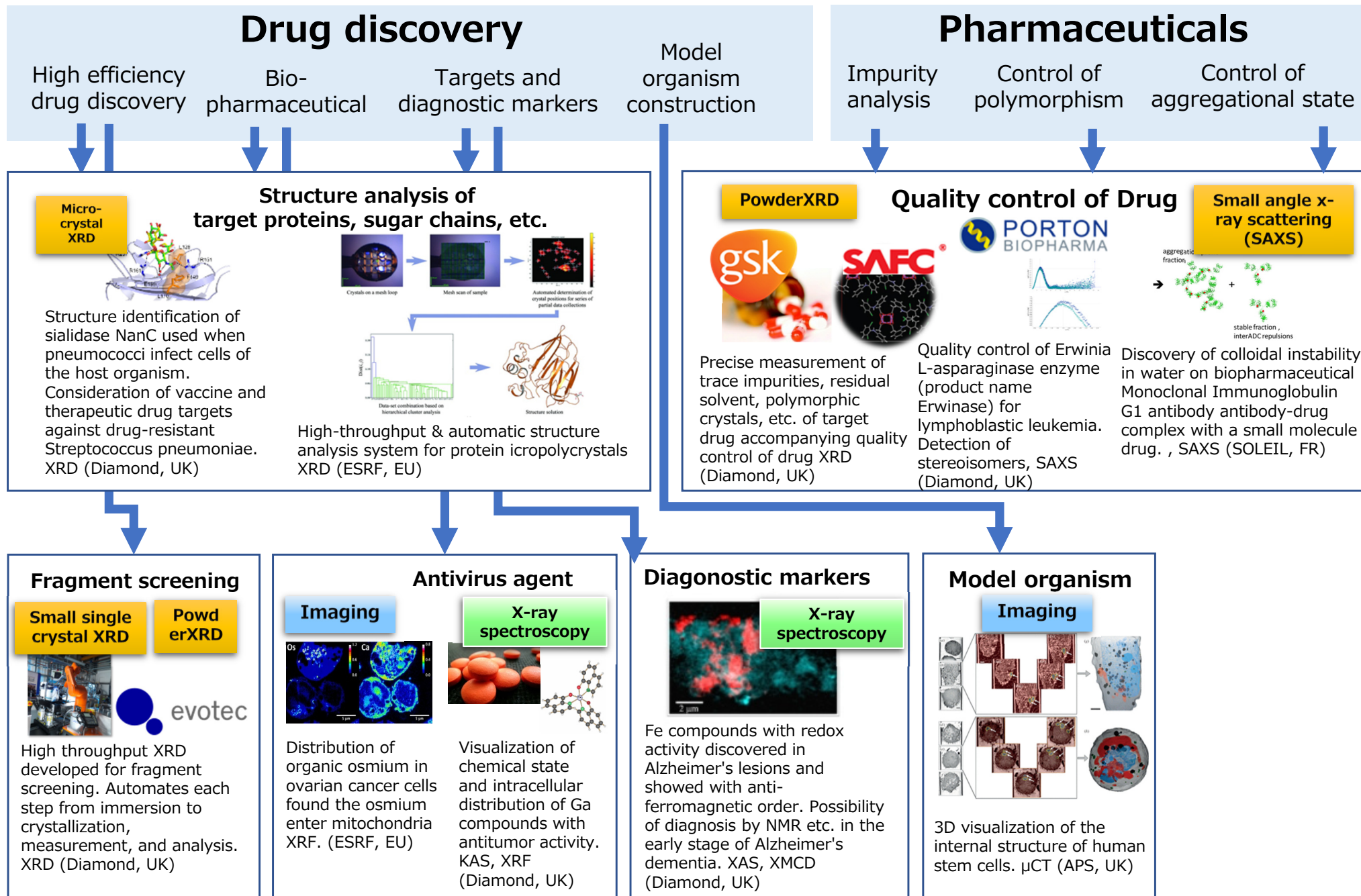


Mass production of drugs

drug discovery & development process

Pharmaceutical process

# (ex.B-2) Utilization of synchrotron radiation facilities expected in drug discovery / pharmaceuticals





## 2. Materials Development for Life Support & Cure, Diagnostics, and Preventing Infection

### **Material for life support & cure**

(ex.) R&D of ECMO materials

- high-functional membrane/filter
- biocompatible material preventing blood coagulation
- Sensor build in ECMO

### **Disinfectant process & material**

(ex.) disinfectant absorption of surfactant

(ex.) disinfectant effect of nano-bubble

- chemical-state imaging of virus at 100 nm scale
- Visualization of adsorption states of virus and surfactant

### **Filter material**

(ex.) nano-micro filter material

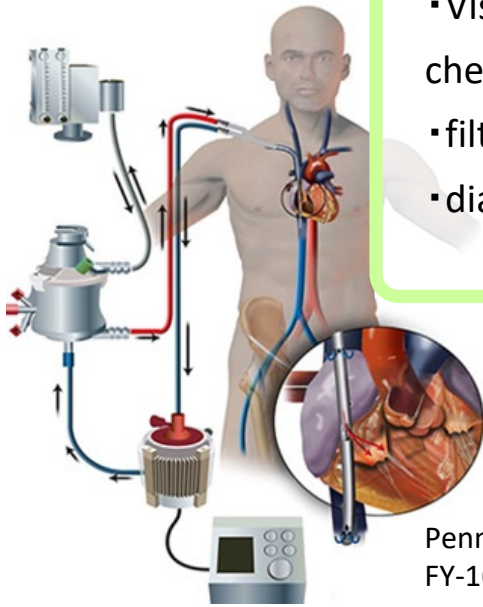
- Visualization of aerosol behavior with chemical state
- filter manufacturing process
- diagnostic kit

### **Photocatalyst decomposes virus**

(ex.) application to clothes, living material,

hygienic goods, vehicular interior material

- coating technology
- manufacturing process of thin-film
- in-situ catalytic reaction
- durability evaluation (shape / chemical state)



PennMedicine.org/clinical-briefings  
FY-16\_10007 05.16

<https://newswitch.jp/p/21589>



## (Reference) Actions in SR facilities to fight against COVID-19 (1/2)

### Diamond Light Source, DLS (UK)

■ **Diamond Light Source** (UK) has created a specific website “Coronavirus Science” with platforms for various audience.

#### For Journalists

• Published their latest news updates, as well as key information on resources, interview opportunities and press relations contacts

#### For Scientists

• Introduces some background about SARS-CoV-2: Understanding the biochemical and structural makeup of the virus is absolutely crucial for the development of drugs and tremendously helpful for the design of vaccines  
• Call for chemists to contribute to the fight against COVID-19

#### For the Public

• Published the article: How is Diamond Light Source helping global efforts to combat the current COVID-19 pandemic?  
• Making results available and sharing information as early and as rapidly as possible to help inform the scientific community and wider public  
• Explanation of technical terms  
• **Crowdfunding**

<https://www.diamond.ac.uk/covid-19.html>

### Paul Scherrer Institute, PSI (Switzerland)

■ Formed interdisciplinary teams comprising physicists, molecular and structural biologists, chemists and beamline scientists

• **X-ray Imaging for Biomedicine**: Lung Imaging

• The **macromolecular crystallography** (MX) group at the Swiss Light Source operates three beamlines (PXI, PXII and PXIII), which allow study of biological molecules such as proteins, viruses and nucleic acids (RNA and DNA).

• **Photonics for Biomedicine**: a novel strategy for the detection of very small amounts of substances, such as toxins or viruses, has recently been developed (Hales et. al. 2019, Nat Commun 10:3594).

• **Molecular Biology**: design of protein nanoparticles, using building blocks found in nature (molecular biomimetics)

• **Micro- and Nanofabrication**: Sensor devices based on microfluidics may significantly improve the rapid diagnosis of biologically relevant species including the SARS-CoV-2 virus.

<https://www.psi.ch/de/psd/research-areas>

## (Reference) Actions in SR facilities to fight against COVID-19 (2/2)

### Brookhaven Lab (NSLS-II) (USA)

#### ■ Brookhaven Lab Mobilizes Resources in Fight Against COVID-19:

Scientists and staff combine expertise across disciplines to address drug development, medical supplies, information processing, and more

- **Deciphering protein structures**: fielding requests to pursue COVID-19 protein studies at its new cryo-electron microscopy (cryoEM) facility which is currently under construction adjacent to NSLS-II
- **Computational approaches**: computational scientists at Brookhaven, working in partnership with colleagues at Stony Brook University, Argonne National Laboratory (ANL), Rutgers University, Oak Ridge National Laboratory (ORNL), the University of Texas, and elsewhere—currently around 160 scientists, 25 at Brookhaven—are helping to speed up the search for drugs

- **virtual screening using these “molecular dynamics” simulations**: refine the machine learning and AI approaches so that successive rounds of evaluations create a list of potentially viable small-molecule drug candidates
- **COVID-19 science and technology working group is also exploring other ways the Lab can contribute at the local hospital level**: the Laboratory has been working with the DOE to gather and distribute the Lab’s excess personal protective equipment (PPE) to health care workers on the front lines.
- Look at ways one’s might **sterilize masks or other critical equipment**
- **Exploring options for using the Lab’s 3-D printers** to make components for face shields, or possibly even ventilators
- They’ve deployed a **shipping container outfitted with a Critical Care Decontamination System** to Stony Brook Hospital. According to Battelle, the system uses hydrogen peroxide vapor to clean tens of thousands of pieces of PPE at a time.

<https://www.bnl.gov/newsroom/news.php?a=117162>

#### ■ Attacking the COVID-19 research head-on

- 3D structural analysis on proteins
- fragment screening
- high-throughput analysis
- fielding multidisciplinary researchers cooperation

#### ■ Logistics support

- measuring devices in Laboratory (ex. cryo-EM)
- computational science
- regional alliances for conducting clinical studies