Czech Infrastructure for Integrative Structural Biology (CIISB)

The Czech Infrastructure for Integrative Structural Biology (CIISB) is a distributed Czech national infrastructure, which consists of two nodes, one represented by CEITEC (Central European Institute of Technology, Brno) and one by BIOCEV (Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University, Vestec near Prague).

CEITEC location: Kamenice 753/5, Brno 625 00

BIOCEV location: Průmyslová 595, Vestec 252 50

CIISB provides expertise and access to technologies used for integrative approaches to the structural analysis of biologically important cellular components and macromolecules - proteins, nucleic acids, and their complexes. Equipped with cutting-edge technologies CIISB offers access to equipment and expertise in the following fields: high-field NMR spectroscopy; high throughput crystallization of biological macromolecules; X-ray diffraction and scattering techniques; AFM imaging and nanomechanical studies; characterization of proteins, nucleic acids and complexes by biophysical methods including microcalorimetry, dynamic light scattering, analytical ultracentrifugation, and surface plasmon resonance; high-end cryo-electron microscopy and tomography allowing studies of cellular structures, organelles, and biomacromolecular complexes; high-end mass spectrometry characterization of biomacromolecules including determination of post-translational modifications, peptide mapping/sequencing, high throughput sequencing and proteomic services.

CIISB offers access to **10 core facilities** - six of them belonging to CEITEC, four to BIOCEV. Full details are provided at the CIISB website www.ciisb.org.

Flagship technologies: CIISB FLAGSHIP TECHNOLOGY

- **Cryo-electron Microscopy and Tomography:** provides access and support with acquisition of cryo-electron microscopy images for both single particle and cryo-electron tomography applications, plunge freezing of in vitro purified samples, and cryo-FIB lamella micromachining of cells for tomography applications.

- **Josef Dadok National NMR Centre:** Core Facility of High Field NMR Spectroscopy provides access to NMR spectrometers in the range of proton frequencies from 500 MHz to 950 MHz. The equipment is suited mainly

to the studies of structure, dynamics and interactions of biomacromolecules, i.e. proteins, nucleic acids and carbohydrates and their complexes.

- **Structural Mass Spectrometry:** provides access and support to structural proteomics to determine the composition of molecules (metabolites, nucleic acid, proteins, and carbohydrates) based on accurate mass measurements and fragment patterns to analyze post-translational modifications, and structural states of proteins and complexes in solution.

- **Diffraction Techniques:** provides assisted use of all experimental equipment for x-ray diffraction and SAXS measurements, hosting prolonged experiments (in-house experimental phasing), "service" data collection at synchrotron sources of radiation in individual cases, capacity dedicated to methods development, and long-term documented cryo-storage.

Here you can see our promotional **video**: https://www.youtube.com/watch?v=G4wT9ldbZ4A

Contact us via email ceitec@ciisb.cz

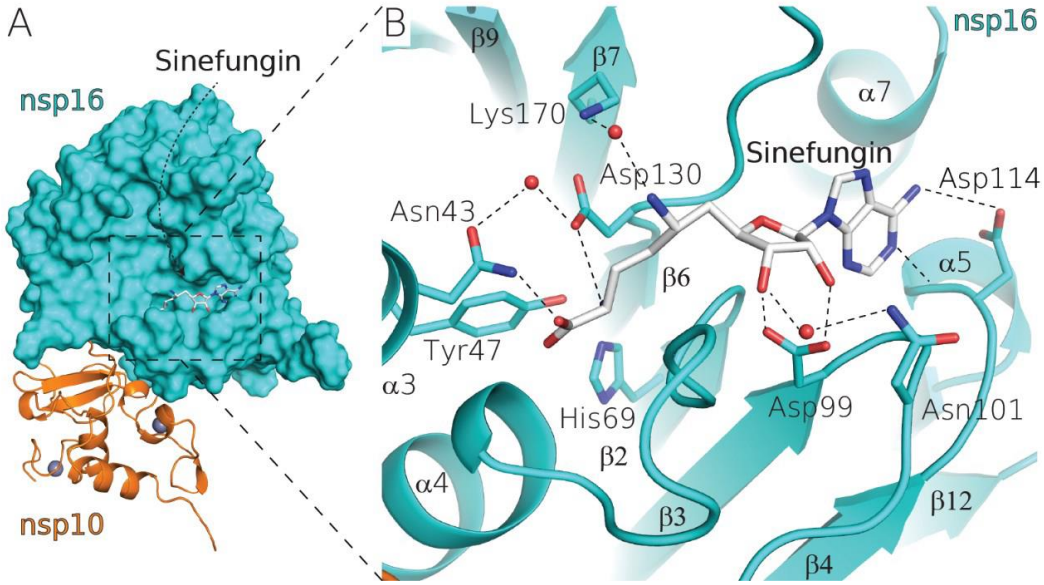
Contribution of CIISB to the Covid-19 pandemic

CIISB is committed to use its resources in response to the emergency situation of the COVID-19 virus pandemic, which has developed during 2020. CIISB ensures that available technologies support primarily researchers in their efforts to study the SARS-CoV-2 virus and projects aiming to the development of an effective vaccine or treatment. In this context, we are offering priority access to groups that need to use CIISB structural biology services for projects directly related to COVID-19 virus particles. Priority access ensures a faster review of research proposals relating to COVID-19. Successfully accepted proposals are served free of charge, and no financial contribution is requested for the measurement/service.

Research Highlights in Coronavirus Structural Studies

As an example, one study that benefited from the adopted Covid-19 Measures and from the preferential access offered to groups that use CIISB services for projects directly related to studies of the SARS-CoV-2 virus and projects aiming at development of an effective vaccine or treatment is described below.

Nat. Commun. 2020



Sinefungin recognition by the nsp16 MTase. A) SARS CoV-2 nsp10-nsp16 protein complex bound to sinefungin (white sticks), nsp16 in surface representation (cyan), nsp10 in cartoon representation (orange) and zinc ions as gray spheres. B) Detailed view of sinefungin recognition, important amino acid residues are shown in stick representation, water as red spheres and hydrogen bonds are shown as dashed lines.

Evžen Bouřa and Radim Nencka Research Groups

Significance

COVID-19 pandemic is caused by the SARS-CoV-2 virus that has several enzymes that could be targeted by antivirals including a 2'-O RNA methyltransferase (MTase) that is involved in the viral RNA cap formation; an essential process for RNA stability. This MTase is composed of two nonstructural proteins, the nsp16 catalytic subunit and the activating nsp10 protein. We have solved the crystal structure of the nsp10-nsp16 complex bound to the pan-MTase inhibitor sinefungin in the active site. Based on the structural data we built a model of the MTase in complex with RNA that illustrates the catalytic reaction. A structural comparison to the Zika MTase revealed low conservation of the catalytic site between these two RNA viruses suggesting preparation of inhibitors targeting both these viruses will be very difficult. Together, our data will provide the information needed for structure-based drug design.

Krafčíková, P., Šilhan, J., Nencka, R., and Bouřa, E.: **Structural analysis of the SARS-CoV-2 methyltransferase complex involved in coronaviral RNA cap creation**, *Nat. Commun* (2020) 11, 3717.

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