Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
Valentin Gordeliy, valentin.gordeliy@ibs.fr

Host laboratory:
Institut de Biologie Structurale
https://www.ibs.fr/spip.php?lang=en

Title of the M2 research internship:
Structural studies of SARS-CoV-2 Envelope protein

Project summary:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes an ongoing pandemic of coronavirus disease 2019 (COVID-2019). The viral particles of SARS-CoV-2 consist of four proteins: S ("Spike"), M ("Membrane"), E ("Envelope"), and N ("Nucleocapsid"). These proteins not only constitute the viral particle but also play a role in the viral life cycle. In this project, we propose to perform structural studies of protein E which is a small membrane protein that is known to be able to form pentameric ion channels inside the membrane of infected cells and involved in the virion assembly and the release of
viral particles from the surface of the cell. Proteins with the same ion channel activity were called "viral porins" and were found in different viruses. The following proteins were identified as viral porins: Vpu from HIV, M2 from influenza A and p7 from the hepatitis C virus. Some viral porin inhibitors happen
to be antiviral drugs such as M2 channel inhibitors rimantadine, which is an FDA-approved drug. In the case of SARS-CoV, inhibition of the channel activity of protein E resulted in inhibition of the viral reproduction in the cell culture. Also blocking the protein E may help in preventing activation of inflammasome – a protein complex responsible for the inflammatory response, which eventually causes lung injury during infection. This shows that this protein is an important drug target. Unfortunately, for today high-resolution structural data on protein E is quite limited. In this project, we suppose to obtain first X-ray structure of protein E ion channel in apo form and in comples with known inhibitors.

Keywords:
SARS-CoV-2, X-ray crystallography, in meso crystallization

Relevant publications of the team:
Bratanov, D., Kovalev, K., Machtens, J. P., Astashkin, R., Chizhov, I., Soloviov, D., ... & Gordeliy, V. (2019). Unique structure and function of viral rhodopsins. Nature communications, 10(1), 1-13.

Zabelskii, D., Alekseev, A., Kovalev, K., Rankovic, V., Balandin, T., Soloviov, D., ... & Gordeliy, V. (2020). Viral rhodopsins 1 are an unique family of light-gated cation channels. Nature communications, 11(1), 1-16.

Volkov, O., Kovalev, K., Polovinkin, V., Borshchevskiy, V., Bamann, C., Astashkin, R., ... & Gordeliy, V. (2017). Structural insights into ion conduction by channelrhodopsin 2. Science, 358(6366).