

## iNEXT workshop on Integrated methodologies and approaches for structural biology

Name of Speaker: **Irina Cornaciu**

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Title of Lecture: **Automated, Remote Controlled Protein to Structure Pipelines for Drug Design**

### Abstract:

The evolution of automation in structural biology over the last decade has facilitated the study of challenging targets and enabled the use of protein crystallography in drug discovery. However, manual crystal mounting and processing are resource-intensive and time-consuming, thus limiting the capacity and efficiency of small molecule screening in the context of drug design. We have developed a novel approach called CrystalDirect™, enabling automated crystal harvesting and cryo-cooling. This technology offers an unprecedented level of control during sample processing, making crystal mounting a systematic and more reliable operation that can easily deal with problematic crystal morphologies and sizes. The approach also enables the delivery of small molecules and other chemicals to crystals by diffusion, providing an alternative to manual crystal soaking experiments (1). Thanks to this technology, we are providing access to an integrated pipeline including high-throughput crystallization, crystal soaking and mounting, and synchrotron data collection into a fully automated and continuous workflow. This pipeline can support very-fast analysis of small molecule-target complexes as well as high-throughput large-scale fragment screening and is available to scientists from both industry and academia (the later through the E.C. funded iNEXT project). Results, along with all the experimental details are made available in real-time through the web interface of CRIMS (the Crystallization Information Management System). Automated data processing through the Global Phasing Pipedream software suite - including data reduction, phasing, refinement, and ligand fitting - enables efficient data processing (2). The experience from the use of these automated pipelines for fragment screening in the context of the iNEXT academic projects, as well as the new opportunities enabled will be discussed.

### References:

- 1) Zander *et al.* Automated harvesting and processing of protein crystals through laser photoablation *Acta Cryst.* D72, 454-466
- 2) Sharff A, Keller P, Vonrhein C, Smart O, Womack T, Flensburg C, Paciorek C and Bricogne G (2011). Pipedream, version 1.2.1, Global Phasing Ltd, Cambridge, United Kingdom.

## Research Profile:

Dr. Irina Cornaciu is a Staff Scientist in the Marquez Team at EMBL Grenoble. She did her PhD in Molecular Biosciences at the University of Graz (Austria), within the DK program, in the laboratory of Dr. Monika Oberer. Since 2013, she joined EMBL as a Postdoctoral Fellow with a Marie Curie Fellowship within the EIPOD program. In the Marquez Team at EMBL Grenoble, she has contributed to the set-up and development of a new generation of integrated and fully automated ligand screening pipelines with crystallography. From 2017, she is a Staff Scientist in the Marquez Team, where she is coordinating the high-throughput, automated fragment screening pipelines for both academia and industry.

## Selected publications:

1. Bezerra GA, Ohara-Nemoto Y, Cornaciu I, Fedosyuk S, Hoffmann G, Round A, Márquez JA, Nemoto TK, Djinović-Carugo K. (2017) **Bacterial protease uses distinct thermodynamic signatures for substrate recognition.** *Sci Rep* 7(1) doi: 10.1038/s41598-017-03220-y
2. Zander U, Hoffmann G, Cornaciu I, Marquette JP, Papp G, Landret C, Seroul G, Sinoir J, Röwer M, Felisaz F, Rodriguez-Puente S, Mariaule V, Murphy P, Mathieu M, Cipriani F, Márquez JA. (2016) **Automated harvesting and processing of protein crystals through laser photoablation.** *Acta Crystallogr D Struct Biol* 72(Pt 4):454-466. doi: 10.1107/s2059798316000954