Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: IBS, Biomolecular NMR spectroscopy group

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Research project title:

Atomic-resolution insight into dynamics and structure of chaperone complexes responsible for the transport of membrane proteins from the cytosol into organelles

5 Keywords to describe the project:

chaperone, NMR, SAXS, protein dynamics, protein import into mitochondria and chloroplasts

Description of the project (aims, experimental techniques, recommended background):

Most proteins present in mitochondria and chloroplasts are synthesized on cellular ribosomes in the cytoplasm and require targeting to their final compartment. Chloroplasts and mitochondria therefore developed dedicated protein import machineries and associated chaperones. While the "part list" of these import systems is known to large part, very little is known about atomistic and mechanistic details. In this project we want to study the main chaperone complex of the mitochondrial inter-membrane space, the "small Tims" that are the central hub for protein import into both mitochondrial membranes. We will combine several biophysical and biochemical techniques to determine how preproteins (i.e. the membrane proteins on the way to their membrane) bind to these chaperones, and how the chaperones can prevent their aggregation. High-resolution solution-state NMR on isotopically labelled proteins will be used in order to obtain structural and dynamical information on an atomic level. SAXS, native mass-spectrometry and electron microscopy data will inform on the composition and stoichiometry of the chaperone assemblies with and without substrate, and will also provide an image of the chaperone assemblies at lower resolution. We want to understand how very different membrane proteins can bind to these chaperones, and what determines specificity. We also want to investigate how these membrane proteins are then transferred further from the chaperone to the insertion machineries in the membrane.

Justification that the internship's subject fits with the general theme of GRAL:

The present research project addresses structural and dynamical properties of protein machineries that are very important for overcoming limits imposed by one central property of life: compartmentalization. Therefore, it fits well with the general priority but also with Research Axis 2.

Relevant publications of the team (3 max):

Slow conformational exchange and overall rocking motion in ubiquitin protein crystals.
Kurauskas V, Izmailov SA, Rogacheva ON, Hessel A, Ayala I, Woodhouse J, Shilova A, Xue Y, Yuwen T, Coquelle N, Colletier JP, Skrynnikov NR, Schanda P. Nat Commun. 2017, 8(1):145.
Proton-Detected Solid-State NMR Spectroscopy of a Zinc Diffusion Facilitator Protein in Native Nanodiscs.
Bersch B, Dörr JM, Hessel A, Killian JA, **Schanda P**. Angew Chem Int Ed Engl. 2017, 56(9):2508-2512.
RNA binding and chaperone activity of the E. coli cold-shock protein CspA.
Rennella E, Sára T, Juen M, Wunderlich C, Imbert L, Solyom Z, Favier A, Ayala I, Weinhäupl K, **Schanda P**, Konrat R, Kreutz C, Brutscher B. Nucleic Acids Res. 2017, 45(7):4255-4268.