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 cytosolic chaperone / mitochondrial outer membrane receptor complexes responsible for the targeting of mitochondrial preproteins through the outer membrane

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 interactions of the cytosolic chaperone complexes with proteins of the TOM receptor from the mitochondrial outer membrane, which is the central hub for protein import through the outer mitochondrial membrane. 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, how the chaperones can prevent their aggregation and how they are handed over to the Tom proteins. 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 different protein complexes, and will also provide an image of the assemblies at lower resolution. We want to understand the functional role of the different Tom constituents and how they are involved in the different sorting events at the outer 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:

Structural basis of membrane protein chaperoning through the mitochondrial intermembrane space.
Weinhäupl, K., Lindau, C., Hessel, A., Wang, Y., Schütze, C., Jores, T., Melchionda, L., Schönfisch, B., Kalbacher, H., **Bersch, B.**, Rapaport, D., Brennich, M., Lindorff-Larsen, K., Wiedemann, N., Schanda, P. Cell 2018, 175(5):1365-1379
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.