Internship project Master 2
Year 2017-2018

Laboratory: Institut de Biologie Structurale (IBS) **Director:** Prof Winfried Weissenhorn
Team: Protein Dynamics and Flexibility by NMR (FDP)
Head of team: Dr. Martin BLACKLEDGE
Name and status of scientist in charge of the project: Dr. Martin BLACKLEDGE **HDR yes** X **no** ☐
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http://www.ibs.fr/groups/protein-dynamics-and-flexibility/?lang=en

Program the Master's degree in Biology:

☐ Neurosciences and Neurobiology ☐Immunology, Microbiology, Infectious Diseases
X Integrative Structural Biology ☐ Physiology Epigenetics Development Differentiation

Title of project: Characterisation of the role of intrinsic conformational disorder in Measles virus replication machinery using NMR spectroscopy

Objectives (up to 3 lines):

The aim is to study, at atomic resolution, the interactions between the intrinsically disordered Phospho- and Nucleoproteins of measles virus both in their monomeric and multi-megadalton nucleocapsid forms, in order to understand the molecular basis of viral replication. The project combines NMR with EM and FRET.

Abstract (up to 10 lines):

Measles virus (MeV) belongs to the *Paramyxoviridae* family, negative strand RNA viruses that encode their own transcription and replication machinery. Many MeV proteins have complex domain architectures comprising folded domains and functionally important intrinsically disordered regions that are characterised by ensembles of rapidly interconverting conformations rather than a single structure. This is the case for MeV nucleoprotein (N) and phosphoprotein (P), that play essential roles in viral replication and dynamically interact to form a complex that exhibits chains comprising over 500 disordered amino acids. The investigation of such complexes represents a new challenge for structural biology, and their analysis requires fundamentally new approaches. We will use high field NMR spectroscopy, in combination with cryo-EM and FRET to develop atomic resolution descriptions of the complex formed between N and P, both in its chaperoned heterodimer, and in the context of self-assembling multimegadalton nucleocapsids.

Methods (up to 3 lines):

Preparation of isotopically labelled recombinant protein NMR samples representing the biological paradigm. Development and application of NMR-based approaches to study the different molecular interactions at atomic resolution. Combination of the experimental results with molecular simulation.

Up to 3 relevant publications of the team:

Plasticity of an Ultrafast Interaction between Nucleoporins and Nuclear Transport Receptors. Milles S, Mercadante D, Aramburu IV, Jensen MR, Banterle N, Koehler C, Tyagi S, Clarke J, Shammas SL, **Blackledge M***, Gräter F*, Lemke EA*. ***Cell***. 163, 734-45 (2015)

Large Scale Conformational Dynamics Control H5N1 Influenza Polymerase PB2 Binding to Importin α. Delaforge E, Milles S, Bouvignies G, Bouvier D, Boivin S, Salvi N, Maurin D, Martel A, Round A, Lemke EA, Jensen M, Hart D, **Blackledge M*** ***J Am Chem Soc*** 137,15122-34 (2015)

Visualizing the molecular recognition trajectory of an intrinsically disordered protein using multinuclear relaxation dispersion NMR. Schneider R, Maurin D, Communie G, Kragelj J, Hansen F, Ruigrok R, Jensen M, **Blackledge M*** ***J. Am. Chem. Soc.*** *137*, 1220-1229 (2015)

Requested domains of expertise (up to 5 keywords):

Biophysics, molecular biology, biochemistry, physical chemistry, NMR.