

**Master 2 internship project  
Year 2023-2024**

**Laboratory/Institute:** Institut de Biologie Structurale (IBS) **Director:** Winfried Weissenhorn  
**Team:** SIGNAL, IBS **Head of the team:** Dr. Malene R. Jensen

**Name and status of the scientist in charge of the project:**

Dr. Malene R. Jensen, CNRS research director (DR1)

**HDR:** yes  no

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**Program of the Master's degree in Biology:**

- Microbiology, Infectious Diseases and Immunology       Structural Biology of Pathogens  
 Physiology, Epigenetics, Differentiation, Cancer       Neurosciences and Neurobiology

**Title of the project:**

**Structural basis for the hijacking of MAPK cell signaling pathways by viral kinases**

**Objectives:**

The project aims at using solution NMR spectroscopy and X-ray crystallography for revealing the structural basis for subversion of signaling pathways by viral genome-encoded kinases.

**Abstract:**

Viruses have designed ingenious methods for hijacking cellular pathways to prevent host apoptosis in the early steps of infection. One example is vaccinia virus for which the viral genome encodes a serine-threonine protein kinase (termed B1R) that mimics human kinases of the VRK-family. B1R interacts with protein targets to activate signaling pathways, and prevents host apoptosis by phosphorylating transcription factors. In particular, it has been shown that B1R interacts with the JNK-interacting protein 1 (JIP1), which is an intrinsically disordered scaffold protein that coordinates the simultaneous assembly of specific kinases to activate the JNK signaling pathway. In this project, the candidate will express and purify the B1R kinase for structural biology studies, obtain its high-resolution crystal structure, map its precise binding site on the JIP1 scaffold protein using NMR spectroscopy and solve the structure of the B1R-JIP1 complex. The overall goal is to reveal the structural basis for subversion of the JNK signaling pathway by the B1R kinase.

**Methods:**

Biochemistry (expression and purification of proteins), NMR spectroscopy, X-ray crystallography and biophysical methods for protein-protein interactions such as isothermal titration calorimetry (ITC).

**Up to 3 relevant publications of the team:**

(1) Mariño Pérez, Ielasi, Bessa, Maurin, Kragelj, Blackledge, Salvi, Bouvignies, Palencia, Jensen.  
"Visualizing protein breathing motions associated with aromatic ring flipping".

**Nature (2022) 602, 695-700.**

(2) Delaforge, Kragelj, Tengo, Palencia, Milles, Bouvignies, Salvi, Blackledge, Jensen.

"Deciphering the dynamic interaction profile of a disordered protein using NMR exchange spectroscopy".

**J. Am. Chem. Soc. (2018) 140, 1148-1158.**

(3) Kragelj, Palencia, Nanao, Maurin, Bouvignies, Blackledge, Jensen.

"Structure and dynamics of the MKK7-JNK signaling complex".

**Proc. Natl. Acad. Sci. U.S.A. (2015) 112, 3409-3414.**

**Requested domains of expertise:**

Structural biology, (bio)chemistry, biophysics