Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2025-2026

Laboratory/Institute: Institut de Biologie Structurale (IBS) **Director:** Winfried WEISSENHORN
Team: SIGNAL, IBS **Head of the team:** Malene R. Jensen
Name and status of the scientist in charge of the project:
Dr. Malene R. Jensen, CNRS research director (DR1) **HDR: yes** X **no** ☐
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Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology X Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology

Title of the project:

Structural snapshots of a substrate in the active site of a mitogen-activated protein kinase

Objectives (up to 3 lines):

The project aims to capture high-resolution structures of substrates in their pre-catalytic, transition, and post-catalytic states within the active site of a mitogen-activated protein kinase.

Abstract (up to 10 lines):

Mitogen-activated protein kinases (MAPKs) are central signaling hubs that orchestrate critical cellular processes, including apoptosis. Their dysregulation underlies a wide spectrum of human diseases, notably cancer and neurodegeneration. Despite extensive studies of MAPK activation and catalytic mechanisms, one key aspect of their function remains poorly understood: how do MAPKs achieve substrate specificity at the structural level? This project aims to address this gap by determining high-resolution structures of MAPKs bound to their substrates, capturing the molecular details of substrate engagement at the active site. By combining nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography with biochemical and biophysical approaches, we will elucidate the structural principles underlying substrate recognition and phosphorylation by MAPKs. These insights will transform our understanding of MAPK signaling specificity and open new avenues for targeting kinase-substrate interactions in disease contexts.

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:

Orand, Delaforge, Lee, Kragelj, Tengo, Tengo, Blackledge, Boeri Erba, Davis, Palencia, Jensen.
Bipartite binding of the intrinsically disordered scaffold protein JIP1 to the kinase JNK1.
PNAS (2025) 122, e2419915122.

Mariño Pérez, Ielasi, Lee, Delaforge, Juyoux, Tengo, Davis, Palencia, Jensen.
Structural basis of homodimerization of the JNK scaffold protein JIP2 and its heterodimerization with JIP1
Structure (2024) 32, 1394-1403.

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.

Requested domains of expertise (up to 5 keywords):

Biochemistry, NMR spectroscopy, X-ray crystallography, biophysics