M1-Molecular and Cellular Biology (MCB)
Internship Proposal Form
Chemistry-Biology Department

Laboratory/Company Address and Affiliation:

Institut de Biologie Structurale (UMR5075, UGA-CNRS-CEA)
71, avenue des Martyrs, CS 10090, 38044 Grenoble, France

Laboratory/Team Research/Company area (Keyword)

SIGNAL group – IBS (Malene R. Jensen)
Structural biology, NMR spectroscopy, X-ray crystallography, intrinsically disordered proteins, protein dynamics, cell signaling, enzyme kinetics

Summary of the Proposed Internship Project

Title:

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

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.

Methodologies and/or Techniques to be used

Biochemistry (expression and purification of proteins), NMR spectroscopy, X-ray crystallography and biophysical methods for probing protein-protein interactions

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Additional information

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