Internship in Chemical Biology

DNA scaffolds for tunable spatiotemporal control over receptor kinase assemblies.

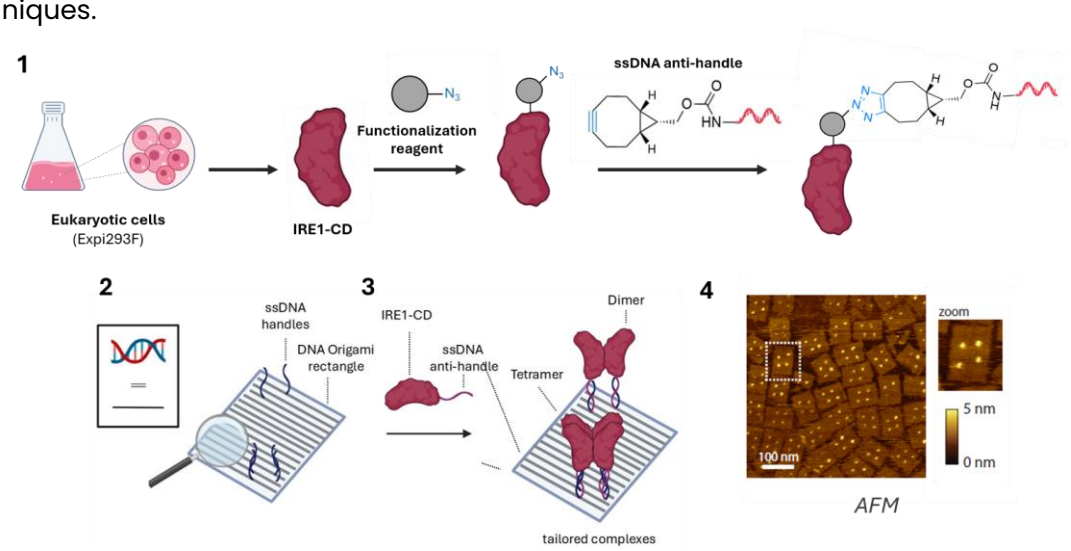
Supervisors: Dr X. Guillory (PI), C. Walter (PhD); *Remuneration:* 580€ net/month; *Duration:* **6 months** between January and July 2027

Scientific background – Cellular stress induced by the abnormal accumulation of improperly folded proteins in the endoplasmic reticulum (ER) is emerging as a major actor in disease development and an appealing actionable target.[1] ER stress levels are under constant surveillance by the unfolded protein response (UPR), a major adaptive mechanism that lies at the core of cellular homeostasis and is responsible for cellular life-or-death decisions. The Inositol-requiring enzyme 1 (IRE1), the most evolutionary conserved UPR transducer, is an ER-resident transmembrane protein with a cytosolic dual kinase/RNase activity controlling pro-survival or pro-death signals. Yet, despite >20 years of investigations, the precise molecular mechanisms by which IRE1 is activated and exerts its catalytic and scaffolding functions still remain unclear and a subject of debate.[2] The group aims at deciphering the molecular mechanisms of IRE1 activation through a unique and novel prism at the interface of chemical biology, supramolecular chemistry and structural biology.

Description of the project & duties - This internship is in support of a PhD project focusing on using a programmable synthetic platform made of DNA structures (*i.e.* DNA origami) to control the nanoscale organization and nature of different complexes of a kinase protein.[3]

As part of this internship, you will focus on:

1 –Expressing, purifying and functionalizing the protein kinase *N*-terminus using a small molecule reagent.
2 - Assembling and purifying DNA origami structures.
3 - Bioconjugating proteins on the DNA origami using DNA hybridization principles.
4- Validating by AFM microscopy the functionalized Protein-DNA nanostructure obtained.
5 – Evaluating the enzymatic activities of the protein using established biochemical assays and molecular biology techniques.



Main activities and techniques involved –
• Molecular biology (design and conception of plasmids).
• Protein expression in eukaryotic cells.
• Protein engineering, bioconjugation, purification (affinity & SEC chromatography).
• Structural characterization of protein-DNA conjugates (AFM, CryoEM).

Applicant profile – We encourage applications from highly motivated students from the national and international community with a background in chemical biology, biochemistry, biophysics, molecular biology, or other life sciences and with outstanding qualifications.

Please send CV, cover letter, M1/4th year transcripts and at least one contact likely to provide a recommendation to: Dr. Xavier Guillory - xavier.guillory@univ-rennes.fr & Chloé Walter chloe.walter@etudiant.univ-rennes.fr

DEADLINE – 18th September 2026

References: [1] *iScience* **2023**, 106687. https://doi.org/10.1016/j.isci.2023.106687; [2] *Biomedicines 9, 156.* https://doi.org/10.3390/biomedicines9020156; [3] *Nat. Catal.* **2020**, *3*, 295–306. https://doi.org/10.1038/s41929-019-0403-7.