Centre de Recherche de Biologie cellulaire de Montpellier
CRBM / CNRS – Université de Montpellier
1919 Route de Mende, 34293 Montpellier Cedex 05

# 2027 Internship Offer

**Master 1**: YES/NO – Duration: **Master 2**: YES/NO – Duration:

| | |
|---|---|
| Team, Contact | Thierry Lorca: thierry.lorca@crbm.cnrs.fr |
| Title | How CSF and SAC activities regulate the arrest of oocytes in metaphase II of meiosis |
| Research Themes and questions | The meiotic progression of Xenopus oocytes serves as a fundamental model for studying the regulation of cell division and the establishment of arrest mechanisms in metaphase II. In these oocytes, meiotic maturation is triggered by progesterone and progresses from prophase I to metaphase II, the stage at which the cell remains arrested, awaiting fertilization. This arrest, long attributed to the activity of the CSF (Cytostatic Factor) pathway, involves in particular the Mos-MAPK-P90Rsk cascade, which ensures the stabilization of the activity of the Cdk-Cyclin (MPF) complex and the inhibition of subsequent cell cycle transitions.<br>At the same time, the Spindle Assembly Checkpoint (SAC) pathway has been recognized for its crucial role in monitoring spindle assembly and preventing meiotic progression in the presence of misassembled microtubules. Previous studies have shown that key SAC proteins, such as Mps1, Mad1, and Bub1, contribute to the arrest at metaphase II. However, these findings were obtained in a reconstituted system using Xenopus egg extracts supplemented with the Mos protein, which, although highly informative, does not fully replicate the intact cellular context of the oocyte. This situation raises the question of the functional interaction between the CSF pathway and the SAC in the establishment and maintenance of meiotic arrest in metaphase II. More specifically, it remains to be clarified whether the SAC and CSF act strictly independently or whether they cooperate to stabilize the metaphase II arrest. This question warrants further investigation in the context of the whole oocyte, in order to better understand the physiological mechanisms governing meiotic arrest and preparation for fertilization.<br>The emergence of the Trim-Away technique offers a unique opportunity to address this question. This approach allows for the rapid and specific removal of endogenous proteins from the intact oocyte, without resorting to exogenous transcription or translation, and thus enables the study of the role of Mps1, Mad1, and Bub1 directly within the physiological context of metaphase II. By combining Trim-Away with the analysis of MPF and MAPK markers, as well as with the observation of spindle dynamics, it becomes possible to re-examine the role of the SAC and its interaction with the CSF pathway in maintaining meiotic arrest, overcoming the limitations of the reconstituted systems used to date. This project thus aims to clarify the potential cooperation between SAC and CSF in the Xenopus oocyte, providing a more integrated view of the control of metaphase II and paving the way for a more detailed understanding of the regulatory mechanisms of meiotic division. |
| Methods and experimental approaches | The project is based on an experimental approach that combines Trim-Away, a technique enabling the rapid and specific elimination of endogenous proteins in the intact oocyte (mastered in the laboratory), with biochemical analyses to measure MPF activity, the MAPK pathway, and key regulators of meiotic maturation. It also includes microscopy to observe meiotic spindle dynamics as well as chromosome condensation and segregation, alongside functional approaches involving the targeted disruption of SAC proteins and the analysis of their effects on metaphase II arrest. |
| Illustration | |

| | |
|---|---|
| | https://www.crbm.cnrs.fr/anna-castro-thierry-lorca/ |
| 2-3 Publications | 1. Greatwall depletion from Xenopus oocytes reveals a key role of the cyclin B/CDK1-PP2A-B55 balance in the coordination of meiotic events. Sylvain Roque , Célia Ben Choug, Cedric Hassen Khodja , Suzanne Vigneron, Véronique Legros, Guillaume Chevreux, Benjamin Lacroix, Anna Castro and Thierry Lorca. Nature Communication (2026) PMID: 42129183 DOI: 10.1038/s41467-026-73011-5<br>2. The MAST kinase KIN-4 carries out mitotic entry functions of Greatwall in C. elegans. Roumbo L, Ossareh-Nazari B, Vigneron S, Stefani I, Van Hove L, Legros V, Chevreux G, Lacroix B, Castro A, Joly N, Lorca T, Pintard L. EMBO J. 2025 Feb 17. Pubmed<br>3. Increases in cyclin A/Cdk activity and in PP2A-B55 inhibition by FAM122A are key mitosis-inducing events. Lacroix B, Vigneron S, Labbé JC, Pintard L, Lionne C, Labesse G, Castro A, Lorca T. EMBO J. 2024 Feb 20. Pubmed |