

Open PhD position:

The importance of mRNA subcellular localization and local translation in cell adhesion.

Actin-based adhesion structures, especially those involved in cell adhesion to the extracellular matrix via integrins are complex molecular assemblies with a wide range of shapes and dynamics. By participating in the cell adhesion to the extracellular matrix, extracellular matrix remodeling and cell migration, they perform essential functions in many biological processes such as embryonic development, tissue repair, immune response, angiogenesis and tissue invasion... The transport of mRNAs and their local translation participate in the spatial and temporal control of protein distribution, notably in the lamellipod, a well-known example of actin-based adhesion structures. However, very little is yet known about the diversity of mRNAs enriched in actin-based adhesion structures. Furthermore, the mRNAs whose local translation is required for their formation and maintenance are not known.

In the context of a collaborative project between our lab in Montpellier and teams located in Bordeaux and Toulouse, we have begun to establish and compare the local landscape of mRNAs and proteins in different types of actin-based adhesion structures, to characterize the local translation activity of mRNAs and establish the hierarchy of translation events during their formation, and to identify the specific translation factors that control protein synthesis in actin-based adhesion structures. Our aim is to discover mRNAs whose local translation is key to the maintenance of actin-based adhesion structures, and identify translation factors and locally translated mRNAs that are critical for their establishment and function.

Our team more specifically studies the actin ring of osteoclasts, a particular actin-based adhesion structures that supports their bone resorption apparatus. We have shown that the actin ring is a relevant target to control pathological osteoclast hyperactivity, which leads to osteoporosis associated with many metabolic disorders and the heavy bone loss and pain linked to bone metastases. One of the expected outcomes of the project is the identification of molecular target that could be valuable to counteract pathological bone loss.

Mission of the PhD student: The PhD student will be in charge of 1) characterizing the local proteome at the osteoclast actin ring, using subcellular microdissection, 2) develop tools to follow the local translation at the actin ring of candidate mRNAs we identified, using single molecule imaging approaches and 3) establish the mRNA translation events that occur during the formation of the actin ring, by time-resolved translatomics. The PhD student will benefit the direct technical and scientific guidance by experienced staff scientists, have access to the state-of-the-art Montpellier Ressources Imagerie imaging platform. She/he will also take advantage of the stimulating environment of the Montpellier Cell Biology Research center (CRBM) and institutes nearby, as well as the opportunity to visit and learn from our collaborators in Bordeaux and Toulouse.

<u>Requirements:</u> we are looking for a highly motivated student with a Master's degree or equivalent in a discipline relevant to cell biology and cell imaging.

Solid knowledge in cell biology, and previous experience in cell culture and cell imaging is required. Research experience with single molecule imaging would be most welcome.

Scientific curiosity and the desire to participate in the shaping of your own research project will be highly seen.

Excellent ability to work in team and excellent communication skill is required in English and/or French (level B2 or higher).

<u>Location:</u> The Montpellier Cell Biology Research center (CRBM) is located in Montpellier, south of France, in the CNRS campus and directly near the university.

Interested candidates should apply as soon as possible, with at least two contact references.

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