2021/2022 Internship proposal (M1/M2) + possible PhD project

Institut Jacques Monod, Université de Paris, CNRS
Team : Regulation of Actin Assembly Dynamics - website
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Funding : available in the team

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Disassembling actin filament networks through biochemical modifications

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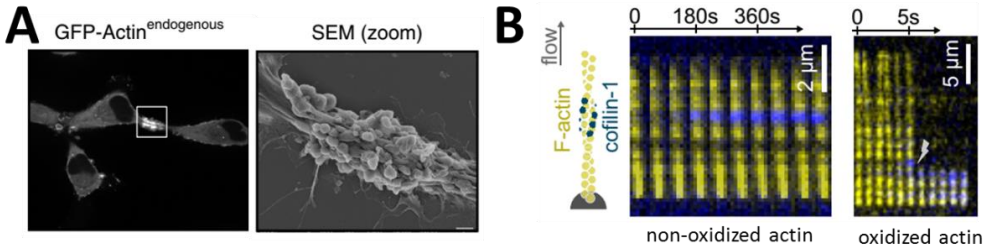
In cells, actin filaments form networks with different architectures and different dynamics, to perform a variety of important tasks. A key question is to understand how these networks are regulated, allowing them to coexist with such differences. Post-translational modifications (PTMs) of actin, which have been overlooked for decades, are now emerging as key biochemical factors that can change the filaments' ability to be regulated by proteins.

The oxidation of actin by the enzyme MICAL1 (counterbalanced by the action of the reductase MsrB2) is a PTM required to disassemble actin filaments in the cytokinetic bridge, which connects the two daughter cells, thereby allowing the bridge to be cut [1, 2]. We have recently shown that the oxidation of actin filaments by MICAL1 makes it much easier for the protein cofilin to fragment and depolymerize them [3], confirming that this PTM is enough to alter the regulatory scheme of actin.



A. MICAL1-depleted cells accumulate actin filaments in their cytokinetic bridge, delaying abscission [1]. **B.** single filaments in vitro, illustrating that oxidized filaments are more rapidly decorated and fragmented by cofilin [3].

The objective of this project is to understand how the redox state of actin filaments impacts the action of other regulatory proteins, and how it relates the specific network organization of the filaments. To do so, experiments will be carried out on single filaments and on different filament networks, which will be exposed to solutions of purified proteins, and monitored using optical microscopy combined with micropatterning and microfluidics.

We seek motivated and talented students with a background in biochemistry or biophysics, and an interdisciplinary mindset. Candidates should be curious, and eager to discover original experimental approaches.

Practical aspects: Institut Jacques Monod is a major research center for fundamental biology in Paris. With its strong student community, it is a very dynamic and friendly working environment. The host team is internationally recognized in the cytoskeleton field. It is composed of physicists and biologists of different nationalities, who work *in vitro* using purified proteins and develop new experimental tools. This project is part of an ongoing collaboration with the lab of Arnaud Echard (Institut Pasteur).

References (from our lab, full texts accessible via our website)

1. Frémont et al., *Nature Communications* (2017)
2. Bai et al., *P.N.A.S.* (2020)
3. Wioland et al., *EMBO Reports* (2021)