



Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - UFR Sciences du Vivant

Parcours : **Biologie et Développement Cellulaires 'BDC'**

<https://master2bdc.ijm.fr/>

Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : CNRS-Université Paris Cité	Responsable du Stage : Nicolas Joly
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Titre du projet : Functional Study of Katanin (Microtubule-Severing Enzyme) under Physiological and Pathological Conditions

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

The precise spatiotemporal regulation of the microtubule (MT) cytoskeleton is fundamental to essential cellular processes, including **mitotic spindle assembly, chromosome segregation, and directed cell migration**. Among the key players in this regulation is Katanin, a member of the AAA+ ATPase family specialized in MT severing. While **Katanin** is essential for genomic stability during cell division, its dysregulation is increasingly linked to disease. Specifically, Katanin overexpression has been observed in several cancers, such as prostate and lung cancer, where it contributes significantly to increased cellular motility and the formation of metastases.

Beyond its role in migration, Katanin is a conserved regulator required for meiotic spindle assembly and proper chromosome segregation across various species, including in human, *C. elegans* and *Drosophila*. As Katanin emerges as a pivotal controller of both division and movement, a comprehensive understanding of its mechanism in both physiological and pathological contexts is a prerequisite for developing innovative therapeutic approaches. This Master 2 project aims to decipher the functional duality of Katanin—balancing normal developmental homeostasis with the molecular changes that drive disease progression. This project integrates two synergistic axes:

- **Biochemical Reconstitution** (in Vitro): To isolate Katanin's intrinsic properties, we will utilize single-molecule **TIRF microscopy**. This approach allows for the real-time visualization of individual severing events, free from indirect cellular interference, to determine the enzyme's precise kinetic parameters.
- **Cellular biology** (in Vivo): To capture the global impact on development and tissue integrity, we will employ the *C. elegans* model system. The student will use **CRISPR/Cas9** for endogenous **GFP-tagging** at the locus and perform high-resolution live-cell imaging (**Spinning Disk**) to track Katanin's behavior and its impact on the development of a living individual.

Publications de l'équipe relatives au projet de stage (max 5)

- Joly N & Pintard L. (2026) Intramolecular Regulation of the MT-Severing Enzyme Katanin Prevents Futile ATP Hydrolysis. *J Cell Biol.* 225, no 2. *J Cell Biol.* 2026 Feb 2;225(2):e202506192. doi: 10.1083/jcb.202506192. Epub 2025 Nov 19. PMID: 41258800.
- Beaumale E, Van Hove L, Pintard L, Joly N. (2024) Microtubule-binding domains in Katanin p80 subunit are essential for severing activity in *C. elegans*. *J Cell Biol.* 2024 Apr 1;223(4):e202308023. doi: 10.1083/jcb.202308023. Epub 2024 Feb 8. PMID: 38329452
- Joly N, Beaumale E, Martino L, Van Hove L, Pintard L. (2020) Phosphorylation of the Microtubule-Severing AAA+ Enzyme Katanin regulates *C. elegans* embryo development. *J Cell Biol.* 2020 Jun 1;219(6):e201912037. doi: 10.1083/jcb.201912037. PMID: 32412594
- Joly N, Martino L, Gigant E, Dumont J, Pintard L. (2016) Microtubule-severing activity of AAA-ATPase Katanin is essential for female meiotic spindle assembly. *Development.* 2016 Oct 1;143(19):3604-3614. doi: 10.1242/dev.140830. Epub 2016 Aug 30. PMID: 27578779.