

Postdoc to study microtubule regulation



CONDUIT LAB PARIS

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The Conduit lab studies how microtubule nucleation is regulated in a cell-specific manner to allow different cells to form their specialised microtubule arrays.

Regulation of γ -TuRC activation

Microtubules are essential cell components linked to many human pathologies. They are nucleated by multi-protein **gamma-tubulin ring complexes (γ -TuRCs)**, which are themselves potential targets for cancer therapy. Microtubule nucleation needs to be tightly controlled to allow cells to form their complex microtubule networks. For this, γ -TuRCs remain inactive in the cytosol and are activated only after recruitment to centrosomes during mitosis. This activation step appears to be mediated by the binding of CM1 domain proteins, but the activation mechanism remains unknown. In *Drosophila*, the CM1 domain protein **Centrosomin (Cnn)** binds and recruits γ -TuRCs to centrosomes during mitosis. We recently showed that Cnn is auto-inhibited from binding γ -TuRCs in the cytosol, but that disrupting this auto-inhibition resulted in ectopic microtubule nucleation throughout the cytosol and to cell division defects (Tovey et al., 2021, JCB). The successful applicant will now explore how the binding of Cnn's CM1 domain activates γ -TuRCs. The project will involve purification of γ -TuRCs and Cnn fragments for processing by Cryo-EM and analysis by single molecule microtubule nucleation assays.

This position is funded by an Agence Nationale de la Recherche (ANR) grant for 3 years in first instance.

Required to apply:

- PhD (or close to completing a PhD)
- A published (or "in progress" first author paper)
- Interest in microtubule biology
- Good team player



Applicants should send a CV, cover letter and contact information for two referees to Paul Conduit (paul.conduit@ijm.fr).

Informal enquiries about the project and job responsibilities are welcome.

Details of our work can be found on the IJM website: <https://www.ijm.fr>

Zhu Z, Tovey CA, Yen EC, Bernard F, Guichet A, Conduit PT. (2022) Multifaceted modes of γ -tubulin complex recruitment and microtubule nucleation at mitotic centrosomes. *BioRxiv*. doi: 10.1101/2022.09.23.509043

Cunningham N, Bouhrel I, Conduit PT. (2022) Daughter centrioles assemble preferentially towards the nuclear envelope in *Drosophila* syncytial embryos. *Open Biol*. 12(1):210343. doi: 10.1098/rsob.210343. PMID: 35042404.

Mukherjee A and Conduit PT. (2021). γ -TuRCs are required for asymmetric microtubule nucleation from the somatic Golgi of *Drosophila* neurons. *BioRxiv*. doi:10.1101/2021.09.24.461707.

Tovey CA, Tsuji C, Egerton A, Bernard F, Guichet A, de la Roche M, Conduit PT. (2021) Autoinhibition of Cnn binding to γ -TuRCs prevents ectopic microtubule nucleation and cell division defects. *J Cell Biol*. 220(8):e202010020. doi: 10.1083/jcb.202010020. PMID: 34042945.

Mukherjee A, Brooks P, Bernard F, Guichet A, Conduit PT. (2020) Microtubules originate asymmetrically at the somatic golgi and are guided via Kinesin2 to maintain polarity within neurons. *Elife*. 9:e58943. doi: 10.7554/eLife.58943. PMID: 32657758

Tovey C, Conduit PT. (2018) Microtubule nucleation by γ -tubulin complexes and beyond. *Essays Biochem*. 62(6):765-780. doi: 10.1042/EBC20180028. PMID: 30315097.

Tovey C, Tubman C, Hamrud E, Zhu Z, Dyas A, Butterfield A, Fyfe A, Johnson E, Conduit PT. (2018) γ -TuRC Heterogeneity Revealed by Analysis of Mozart1. *Curr Biol*. 28(14):2314-2323.e6. doi: 10.1016/j.cub.2018.05.044. PMID: 29983314