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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université :	**Responsable du Stage : Paul Conduit**
Intitulé Equipe : **Microtubule Regulation in Multi-cellular Animals** **ED d'appartenance :** **BioSPC** **Responsable de l'Equipe :** **Paul Conduit**	**Contacts** Adresse : Institut Jacques Monod, CNRS - Université de Paris, 15 rue Hélène Brion, 75013 Paris Email : paul.conduit@ijm.fr Tel : 01 57 27 80 95

Titre du projet : Investigating the regulation of microtubule nucleation within neurons

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

A highly polarised **microtubule** cytoskeleton is essential for **neuronal development and function**. Within axons, microtubule plus ends point away from the soma (plus-end-out), while within dendrites the minus ends predominantly point away (minus-end-out). This **polarity** difference is essential for neurons and is established in part via regulation of **microtubules nucleation**. Microtubules are nucleated by multi-protein **γ-tubulin ring complexes (γ-TuRCs)**, which are normally recruited and activated at **microtubule organising centres (MTOCs)** within cells. We use ***Drosophila* dendritic arborisation (da) neurons** as a model system to study how microtubule nucleation is regulated within neurons. These neurons can be imaged directly in living larvae or in fixed and stained larval preparations.

We recently showed that γ-TuRCs are asymmetrically localised to the somatic Golgi in da neurons and that they nucleate microtubules that grow preferentially towards axons (Mukherjee et al., 2020, eLife). We proposed that this helps to maintain overall microtubule polarity. We now have preliminary data showing that this directionally microtubule growth is lost when γ-TuRCs are depleted. The student will use **genetics** and **fluorescent imaging** to investigate which molecules recruit γ-TuRCs asymmetrically to the Golgi and what effect losing directional microtubule nucleation has on overall microtubule polarity within axons and dendrites. The student will also help investigate putative MTOCs that we have discovered within dendrites. These are regions of dendrites that have expanded to form what we call **dendritic bubbles**; these bubbles contain γ-TuRCs and other microtubule regulating factors (Mukherjee et al., 2020, eLife). The student will use genetic and live cell imaging to characterise these bubbles, discovering how they form and what happens when they are disrupted.

By the end of the M2 the student will have acquired training in fly husbandry, genetics, molecular biology, and fluorescent imaging (including confocal). The student will be encouraged to be proactive, coming up with ideas and taking initiative. There is potential for the student to return as a PhD student.

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

Tovey T, Tsuji C, Egerton A, Bernard F, Guichet A, Roche MA, Conduit PT*. Auto-inhibition of Cnn binding to γ-TuRCs prevents ectopic microtubule nucleation and cell division defects. JCB, in press. BioRxiv.
doi: https://doi.org/10.1101/2020.10.05.326587

Mukherjee A, Brooks P, Bernard F, Guichet A, Conduit PT*. (2020). Microtubules originate asymmetrically at the somatic Golg and are guided via Kinesin2 to maintain polarity in neurons. eLife. DOI: 10.7554/eLife.58943

Tovey CA, Tubman CE, Hamrud E, Zhu Z, Dyas AE, Butterfield AN, Fyfe A, Johnson E, Conduit PT*. (2018). γ-TuRC heterogeneity revealed by analysis of Mozart1. Current Biology 28, 2314-2323.

Tovey CA and Conduit PT*. (2018). Microtubule nucleation by γ-tubulin complexes and beyond. Essays in Biochemistry. DOI: 10.1042/EBC20180028

Feng Z, Caballe A, Wainman A, Johnson S, Haensele AFM, Cottee MA, Conduit PT, Susan M. Lea, Jordan W. Raff. (2017). Structural Basis for Mitotic Centrosome Assembly in Flies. Cell 169, 1078–1089.