2020-11-30

EuReCa International PhD Program

PhD thesis project

2021 Call for application

Comparative mechanisms of spindle assembly dynamics and scaling

General information

Call	2021
Reference	2021-12-TRAN_NEDELEC
Keyword(s)	Spindle; Scaling; Kinesin; Yeast; Modeling

Director(s) and team

Thesis director(s)	Phong Tran & François Nedelec
Research team	Cytoskeletal Architecture and Cell Morphogenesis
Research department	UMR144-Cell Biology and Cancer

Description of the PhD thesis project

Project: Cells proliferate by duplicating and segregating their chromosomes into daughter cells.

In eukaryotic cells, chromosome segregation is accomplished by the spindle – a dynamics structure composed of microtubules (MTs), motors, non-motor microtubule-associated proteins (MAPs), and other regulatory proteins.

The spindle size is precisely controlled by the cell, and scales with cell size – small cells have small spindles, big cells have big spindles. Defects in spindle assembly dynamics and spindle size can lead to errors in chromosome segregation, which result in aneuploidy and can give rise to developmental defects such as trisomy or diseases such as cancer.

Using the model organism fission yeast (S. pombe), the Tran team showed that the mechanism of spindle assembly is controlled by kinesin-5 Cut7 (Rincon et al, 2017), and spindle scaling is controlled by kinesin-6 Klp9 (Kruger et al, 2019). Is this mechanism conserved?

The potential student will compare S. pombe to S. japonicus, a related fission yeast. These rod-shaped yeasts have 3 similar-sized chromosomes, and ~90% of their genes are similar.

However, S. japonicus is ~10x larger by volume than S. pombe, and has a longer spindle. Importantly, whereas S. pombe has one kinesin-5, S. japonicus has 2 kinesin-5s. These key differences enable us to determine which motors function in spindle assembly and size control, to reveal potential diverse mechanisms.

Objective: The potential student will carry out experiments to compare spindle assembly and spindle scaling in S. pombe and S. japonicus.

Generally, experiments involve constructing gene-deletion, gene-mutation, or gene-tagging with fluorescent protein; live-cell imaging of spindle dynamics; and image analysis and Cytosim modeling of spindle dynamics.

International, interdisciplinary & intersectoral aspects of the project

The project has interdisciplinary and international components.
The student will perform experimental work at the Institut Curie supervised by Phong Tran.
Theoretical and modeling work will be done through visits to Cambridge University supervised by Francois Nedelec.

Recent publications

1. Loncar A, Rincon SA, Lera Ramirez M, Paoletti A, **Tran PT** (2020). Kinesin-14 family proteins and microtubule dynamics define S. pombe mitotic and meiotic spindle assembly, and elongation. J Cell Sci 133(11):jcs240234.

2. Loiodice I, Janson ME, Tavormina P, Schaub S, Bhatt D, Cochran R, Czupryna J, Fu C, **Tran PT** (2019). Quantifying Tubulin Concentration and Microtubule Number Throughout the Fission Yeast Cell Cycle. Biomolecules 9(3):86.

3. Krüger LK, Sanchez JL, Paoletti A, **Tran PT** (2019). Kinesin-6 regulates cell-size-dependent spindle elongation velocity to keep mitosis duration constant in fission yeast. Elife 8:e42182.

4. Lin L, Chen L, **Tran PT** (2017). Fission yeast neddylation ligase Dcn1 facilitates cohesin cleavage and chromosome segregation at anaphase. Biol Open 6, 844-849.

5. Rincon SA, Lamson A, Blackwell R, Syrovatkina V, Fraisier V, Paoletti A, Betterton MD, **Tran PT** (2017). Kinesin-5-independent mitotic spindle assembly requires the antiparallel microtubule crosslinker Ase1. Nat Commun 8, 15286.

Expected profile of the candidate

The potential student should have a strong interest in cell biology and with university degrees in either biology, physics, bioengineering, or computer science.