



Regulation and fidelity of the mitotic spindle positioning in *C. elegans* nematode



This project, for a Master M2 student (or equivalent level), aims to understand the key role of astral microtubules in the correct positioning of the mitotic spindle during cell division and in the detection and correction of its perturbations, using the model organism *C. elegans*. This internship will take place at the Institute of Genetics and Development of Rennes (IGDR, CNRS UMR 6290/Univ. Rennes 1, Brittany, France), and more precisely in the team CeDRE « Reverse engineering cell division ». The team CeDRE is composed of scientists with complementary expertise in biology, physics, images analysis, mathematics and statistics.

Background of the research project:

The ability of cancerous cells to divide despite accumulated defects suggests that some robustness mechanisms compensate for these defects and broadly that the cell can adapt to internal (chromosomal instability, aberrant number of centrosomes or chromosomes, e.g.) and external changes (temperature, antimitotic presence, e.g.), with mechanisms the remain to be discovered. We will further focus on the mitotic spindle positioning. This crucial event contributes to dictating the plane of division and, in case of asymmetric division, the correct daughter cell fates. We will use the one-cell embryo of nematode *C. elegans*, a well-established model organism of (asymmetric) division. During its division, spindle undergoes three phases of positioning: (1) in prophase, the complex formed by the *pronuclei* and the centrosomes migrates towards cell centre; (2) between the end of prophase until metaphase, the spindle is maintained at the centre of the cell; in anaphase, the mitotic spindle migrates towards the posterior side of the cell to reach its final position. These distinct steps in space and in time suggest distinct mechanisms featuring feedbacks to detect and correct errors. We hypothesize that the microtubules network, due to its dynamical behaviour, is appropriate for this task. Microtubules are semi-rigid and highly dynamic filaments that generate and transmit forces. Feedbacks and corrective mechanisms emerge from collective effects of the network of microtubules, their regulators and the molecular motors that are associated.

Goal of the project:

The chosen candidate will study the regulation in time and in space of the mechanical and dynamical properties of the astral microtubules (emanating from spindle poles), to understand the regulation of the forces transmitted to the mitotic spindle. This study will be performed using methods recently established in the team: we will measure and map spatially the dynamics of the astral microtubules (growth/shrinking rates, residency time) at the cell cortex and in the spindle plane, through optical microscopy. We also aim at measuring, through an in-progress analysis, the microtubules rigidity. The regulating role of some MAPs (Microtubule Associated Proteins) will be studied through a gene-candidate approach (RNA inferences or mutants). These results will be integrated into bottom-up physical models and numerical simulations of cell division, which are developed by the team.

Position details:

The candidate, of M2 or equivalent level, will have an education in molecular cell biology. Some knowledge/experience in optical microscopy will be an advantage. The candidate will join an interdisciplinary team including scientists expert in biology, physics, image analysis or statistics. Candidate is expected to be open-minded to these fields and show some curiosity, although to prior knowledge is required. The student will gain training in fluorescent microscopy, quantitative analysis of images, molecular biology (cloning) and Mendelian genetics (crossing of nematode strains). According to candidate skills and motivation, a PhD student position can be offered at the end of the internship and the candidate will receive support to obtain scholarships. The candidate must be regularly registered at a university or education institution and will receive a stipend of ca 529 €. Application should include a curriculum vitae, if possible marks and rankings of current and two previous semesters and a cover letter detailing the motivation of the candidate. Application, as a single pdf, or informal enquiries should be sent to:

Hélène Bouvrais – helene.bouvrais@univ-rennes1.fr

Team CeDRE (Jacques Pécreaux : jacques.pecreaux@univ-rennes1.fr)

Team website: <http://pecreaux.openwetware.org/>

IGDR, CNRS-UMR 6290 – Faculté de Médecine (Université de Rennes 1)

2 Avenue du Pr. Léon Bernard, 35000 Rennes Cedex, France