Characterising the division of cancerous colorectal cells displaying perturbed DCLK1 expression level

This internship offer is for students in Master or equivalent, who have a background in cellular and molecular biology and ideally some basic knowledge in human cell culture and fluorescence microscopy.

Host laboratory:
The internship will be carried out within the Rennes Institute of Genetics and Development (IGDR, UMR 6290), and more specifically in the CeDRE team "Reverse Engineering of the Cell Division".
Our team – which has the specificity of being an **interdisciplinary team** made up of specialists in biology, physics, image analysis, artificial intelligence and bioinformatics – **studies cell division robustness using a cell biophysical approach**. For this, we use the first division of the *Caenorhabditis elegans* nematode, an established model of cell division, and then validate our findings in Human cells. We aim to understand the robustness of cell division by studying and modeling the biophysical and mechanical interactions between the molecular actors of mitosis, which are the microtubules and their regulators, as well as the molecular motors.

Internship project:
The proteins of the **doublecortin family** (DCX) are capable of **associating with microtubules** by binding to the interface of 4 tubulin dimers. This ability would allow them, among other things, to **stiffen these fibers** by likely preventing the sliding of the protofilaments that constitute them or by bundling the micortubules.
Interestingly, **the expression of DCLK1** (doublecortin-like kinase 1), a DCX member, is **deregulated in many human solid tumors** (e.g. colorectal, pancreatic, breast and kidney cancers). In particular, in colorectal tumors, the isoform capable of binding to microtubules, noted DCLK1-L, is inhibited. This likely leads to microtubules less rigid, which perturb the microtubule-mediated pushing forces. Importantly, pushing forces are key for a proper positioning of the mitotic spindle and may participate in chromosome congression to the metaphase plate. Defects in any of these stages of division can lead to aneuploidy, a major mechanism of carcinogenesis.
We therefore hypothesize that the deregulation of DCLK1, observed in solid tumours, affects the rigidity of microtubules, disrupting the proper course of cell division.
The objective of the internship is to characterize the cell division of colorectal cancerous cell lines (HCT116, SW480) and compare them with the cell division of healthy cell line (CCD841CoN).
For that, the student will first quantify the level of expression of DCLK1 isoforms in the different cell lines, since we expect a deregulation of DCLK1. Then, he/she will transfect the cell lines to have a fluorescent labelling of the centrosomes and the chromosomes, and he/she will acquire movies of cell division. Using home-made image-analysis tools, he/she will track the positions of the chromosomes and the centrosomes, which will permit to reveal potential defects in spindle positioning and chromosome segregation. Last, by modulating the level of DCLK1-L expression, he/she will decipher whether the defects may be correlated to DCLK1 expression level.

This internship in an interdisciplinary team will allow the student to acquire skills in cell culture, cell transfection, fluorescence microscopy, cell and molecular biology and image and data analysis. Besides, he/she will improve his/her English and teamwork skills.

Contact:
Dr Hélène Bouvrais – helene.bouvrais@univ-rennes.fr / Louis Cueff – louis.cueff@univ-rennes.fr
Team CeDRE (Leader: Dr Jacques Pécréaux: Jacques.pecreaux@univ-renne.fr)
Websites: http://pecreaux.openwetware.org/ and https://igdr.univ-rennes.fr/en/cedre-lab