Fiche proposition de stage - *Internship offers*

Offre pour / Offer for (you can make offers for both level, if the subjects are different, please use a new form)

Master 2

Parcours concerné(s) :EpiGenBio

Intitulé du stage *Title*	**Molecular Determinants of Topoisomerase Inhibitor Toxicity Involving Transcription- and Replication-Dependent DNA Damage**
Laboratoire d'accueil *Host laboratory*	Institut de Génétique Humaine (IGH), Montpellier Maintien de l'intégrité du génome au cours de la réplication
Nom du responsable *Name of the PI*	Philippe PASERO
Nom d'encadrant *Supervisor*	Benjamin PARDO
Description (3 phrases) *Description (3 sentences)*	The alkaloid drug camptothecin (CPT) has been used in the clinics for the last two decades to induce DNA damage and trigger the apoptosis of highly proliferative cancer cells. First, the cytotoxicity of CPT has been linked to the occurrence of replication-dependent DNA double-strand breaks (DSBs). DSBs have been proposed to originate from the conversion of single-strand breaks at Top1ccs into DSBs when the DNA strands are separated during DNA replication (replication run-off model). More recently, we have observed that Top1ccs induce the DNA damage response (DDR) in non-replicating cells or cells in the G_1 phase of the cell cycle. DDR activation was dependent on transcription, consistent with the stalling RNA polymerase II (RNAPII) elongation by Top1ccs. Thus, it appears that DNA damage caused by CPT may be related to collisions between replication forks and Top1ccs-stalled RNAPII, rather than a simple replication run-off. By using genetic, genomic and single-cell microscopy approaches, we are currently addressing this hypothesis in yeast *Saccharomyces cerevisiae* cells by assessing the impact of Top1ccs on genome stability during the G1 and S phases of the cell cycle. This research project is suitable for a Ph.D. program.
Durée prevue (2 à 6 mois) Duration (2 to 6 months)	6 months
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