### Proposition de Stage de Master (M2)

# Master BMC

### Université de Paris - UFR des Sciences du Vivant

***Conventions : Sorbonne Université, Université Sorbonne Paris Nord, Université Paris Saclay,***

***Muséum National d’Histoire Naturelle, Institut Pasteur***

Equipe d’Accueil : DNA Repair and Chromosome Stability Team

Intitulé de l’Unité : UMR Stabilité Génétique, Cellules Souches et Radiations

Nom du Responsable de l’Unité : François Boussin

Nom du Responsable de l’Équipe : Stéphane MARCAND

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**9 Parcours de M2**

**(plusieurs parcours peuvent être choisis)**

###### **- Biologie moléculaire, cellulaire et fonctionnelle de l'hématopoïèse** 🞎

Responsables: S. Giraudier, N. Dulphy, E. Lauret

**- Biomolécules, biologie et pathologie moléculaires** ✓

Responsables: JM. Dupret, F. Rodrigues-Lima

**- Biologie et développment cellulaires : contactez directement les responsables**

Responsables: A. Guichet, A. Benmerah

**- Inflammation et maladies inflammatoires** 🞎

Responsables: R. Monteiro, L. Mouthon

**- Biothérapeutiques: Conception et applications** ✓

Responsables: I. Garcia-Verdugo, JM. Sallenave

**- Immunologie et Immunopathologies** 🞎

Responsables: M. Viguier, E. Tartour, D.Ledoux

**- Microbiologie** ✓

Responsables: I. Martin-Verstraete, X. Nassif

**- Virologie** 🞎

Responsables: S. van der Werf, F. Rozenberg

**- Microbiologie et génie biologique** ✓

Responsables: O. Dussurget

**Titre du sujet de recherche : Telomere protection and its impact on genome stability**

**Résumé du projet**

Telomeres cap native chromosome ends by preventing them from being recognized and processed as chromosomal break ends. In addition, telomeres length homeostasis avoids the occurrence of excessively short or long telomeres. These ubiquitous core telomere functions are a cornerstone of chromosome stability. Furthermore, in most human somatic tissues, telomeres shorten with age, leading to replicative senescence, a major tumour suppressor mechanism limiting cell division potential but also a contributor to ageing. Failure to cap telomeres results in chromosome fusions whose mitotic instability leads to catastrophic pro-oncogenic mutational processes, namely dicentric chromosome breakage-fusion-bridge cycles and chromothripsis. The rarity of these events is key to genome integrity.

Full telomere protection is the result of a synergy between several co-existing mechanisms that buffer each other. Key molecular mechanisms acted by telomere factors are still poorly understood today. This is problematic since addressing the roles of telomeres in ageing and oncogenesis and future attempts at targeting telomeres in therapeutic approaches must rely on a deeper knowledge of how telomere capping operates at a molecular and mechanistic level. To tackle this central issue of chromosome biology, our laboratory address the individual molecular mechanisms of telomere protection using the experimentally amenable unicellular eukaryote Saccharomyces cerevisiae as a model system. Check our recent papers for an overview of the current context.

The specific goal of this internship will be to unravel the mechanism established by a telomere factor to protect telomeres against NHEJ-mediated fusions. We will do this by (i) dissecting this pathway in isolation from the others and (ii) combining a large set of complementary state-of-the-art in vivo and in vitro approaches, several previously developed in the laboratory. The expected outcome of this work is to improve our knowledge of telomeres and of DNA repair mechanisms. As in the past, the gain of knowledge acquired with the yeast system will have general significance and will open the path for equivalent findings in other model systems and species. Please contact us for more information.

**Dernières Publications en lien avec le projet :**

* Guerin T. M., C. Beneut, ... and S. Marcand (2019) Condensin-Mediated Chromosome Folding And Internal Telomeres Drive Dicentric Severing By Cytokinesis. *Molecular Cell* 75:131-144.

<https://www.cell.com/molecular-cell/fulltext/S1097-2765(19)30393-4>

Roisné-Hamelin F., Pobiega S., ... and S. Marcand (2021) Mechanism of Rad50 Inhibition by Rif2 at Telomeres. *Nature Communications* 12:2763.

<https://www.nature.com/articles/s41467-021-23035-w>

Pobiega S., Alibert O. and S. Marcand (2021) A New Assay Capturing Chromosome Fusions Shows a Protection Trade-off at Telomeres and NHEJ Vulnerability to Low Density Ionising Radiation. *Nucleic Acids Research*, *in press.*

**Ce projet s’inscrit-il dans la perspective d’une thèse :**

**oui** ✓ **non** 

**si oui type de financement prévu : CEA ou ANR**

**Ecole Doctorale de rattachement : Paris-Saclay SDSV**

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**oui** ✓ **non** 