

Laboratoire d'accueil

Laboratoire de Biologie et de Modélisation de la Cellulaire (LBMC) – UMR 5239, ENS de Lyon 46 allée d'Italie, 69364 Lyon Cedex 07

Equipe d'accueil

Equipe Post-transcriptional Regulation in Infection and Oncogenesis (PRIO)

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Tuteur de stage

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Titre du projet de recherche / Research project title:

**INHIBITION OF NONSENSE MEDIATED mRNA DECAY (NMD)
BY HTLV-1 INFECTION**

KEYWORDS : retrovirus, RNA decay, viral replication, virus/host relation, RNA helicase UPF1

Description du projet / Project description:

The Nonsense mediated mRNA Decay is a cellular pathway degrading mRNA, triggered by translation termination and stimulated by the 3'UTR environment. Our lab works on the links between NMD and viral infection. This virus/NMD field is of growing importance and already led to the identification of several viruses interfering with RNA decay (Mocquet et al 2015). Concerning our model the Human T cell Leukemia/Lymphoma virus (HTLV), we already demonstrated that the viral Tax protein is able to inhibit NMD by interfering with the UPF1 RNA helicase (Mocquet et al 2012; Fiorini et al 2018).

A second viral protein from HTLV called Rex has also been associated with NMD inhibition. The project consists in deciphering the mechanism of NMD inhibition by Rex. A comparative approach with the other human retrovirus HIV already validated the preliminary results obtained by the team but we are still characterizing this mechanism. Especially we want to understand how UPF1 is hijacked in this process and characterize those consequences on the host transcriptome and the viral replication. To understand the overlapping action of Tax and Rex is another aspect of the project.

Methods: ELISA, cell culture, confocal microscopy, FACS, RTqPCR, cloning strategies, RNA and protein immunoprecipitation, long read nanopore sequencing.



Publications du laboratoire (5 max) / Lab publications (5 max):

-PROCHASSON L, JALINOT P, MOCQUET V, **2020** The Complex Relationship between HTLV-1 and Nonsense-Mediated mRNA Decay (NMD) **Pathogens**. 9(4):287.

-FIORINI F, ROBIN JP, KANAAN J, BOROWIAK M, LE HIR H, JALINOT P, MOCQUET V **2018** HTLV-1 Tax plugs and freezes UPF1 helicase leading to nonsense-mediated mRNA decay inhibition. **Nat Commun**, 9(1):431

-PERES, E, BLIN, J, RICCI, EP, ARTESI, M, HAHAUT, V, VAN DEN BROEKE, A, CORBIN, A, GAZZOLO, L, RATNER, L, JALINOT, P, AND DUC DODON, M **2018** .PDZ domain-binding motif of Tax sustains T-cell proliferation in HTLV-1-infected humanized mice. **PLoS Pathog**, 14(3):e1006933.

-MOCQUET V, DURAND S, JALINOT P **2015** How retroviruses escape the Nonsense Mediated mRNA Decay (NMD)? **AIDS Res Hum Retroviruses**. [Epub ahead of print]

-MOCQUET V, NEUSIEDLER J, RENDE F, CLUET D, ROBIN JP, TERME JM, DUC DODON M, WITTMANN J, MORRIS C, LE HIR H, CIMINALE V, JALINOT P. **2012** The human T-lymphotropic virus type 1 tax protein inhibits nonsense-mediated mRNA decay by interacting with INT6/EIF3E and UPF1. **J Virol**. 86(14):7530-43.