Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : Inserm U944 - CNRS/P7 UMR 7212 **Intitulé Equipe :** ER stress and nuclear mRNA biogenesis (équipe émergente attachée à l'équipe Genome Biology) https://gencelldis.fr **ED d'appartenance :** HOB **Responsable de l'Equipe :** Anna Babour	**Responsable du Stage :** Anna Babour **Adresse :** Institut de Recherche Saint Louis (ex-IUH) Hôpital St Louis 16 rue de la Grange aux Belles, 75010 Paris **Email** : anna.babour@inserm.fr **Tel :** 01 53 72 40 86

Titre du projet : Quality control of gene expression: nuclear-ER cross-talks

Résumé du Projet de Stage

Cellular homeostasis is maintained by surveillance mechanisms that intervene at virtually every step of gene expression. While individual signaling pathways are well described, their integration into a single cellular network that coordinates a multi-faceted response is poorly understood. Our lab is interested in deciphering **molecular cross-talks** between **nuclear** and **Endoplasmic Reticulum (ER) quality control (QC)** pathways.

The ER is the main subcellular compartment involved in protein folding and QC, representing a central node of the proteostasis network. The **unfolded protein response** (UPR) is a specialized mechanism to cope with the accumulation of unfolded protein in the ER lumen (=ER stress). UPR dysregulation has been associated with pathological conditions including viral infection, diabetes, cancer, and neurodegenerative diseases. Although the molecular mechanisms of UPR induction are well characterized, less is known about the processes that drive its deactivation or modulate its duration and intensity, although they determine cell fate. We identified a novel mechanism of UPR attenuation (1), guided from the nucleus by a chromatin remodeler, Isw1, that we previously reported to act as an mRNA biogenesis QC factor (3). Isw1 exerts it nuclear mRNA QC activity in cooperation with Rrp6, a catalytic subunit of a multi-subunit complex involved in RNA degradation, QC, and termination of short RNAs. We now aim at further exploring how nuclear mRNA biogenesis processes influence the cell's response to ER stress. For this purpose, genome-wide and single-molecule imaging approaches will be combined with mechanistic studies, using primarily budding yeast as a model system. In particular, the influence of **Rrp6** on the intensity and duration of the UPR, ER fitness and global cell physiology will be analyzed during this internship. This work is expected to shed light on the mechanisms that drive the shift from an adaptive to pro-apoptotic UPR.

Publications de l'équipe relatives au projet de stage

1. Matabishi L, Challal D, Barucco M, Libri D and **Babour A**. Termination of the unfolded protein response is guided from the nucleus by ER stress induced *HAC1* mRNA nuclear retention. *Submitted*.
2. Dargemont C, **Babour A.** (2017) Novel functions for chromatin dynamics in mRNA biogenesis beyond transcription. *Nucleus*. **8**: 482-488.
3. Babour A, Shen Q, Dos-Santos J, Murray S, Gay A, Challal D, Fasken M, Palancade B, Corbett A, Libri D, Mellor J, Dargemont C.The Chromatin Remodeler ISW1 Is a Quality Control Factor that Surveys Nuclear mRNP Biogenesis. (2016). *Cell*. 167:1201-1214.
4. Vitaliano-Prunier, A*, **Babour A.*,** Hérissant, L.*, Apponi, L., Margaritis, T., Holstege, FCP, Corbett, AH, Gwizdek, C. and Dargemont, C. (2012). H2B ubiquitylation controls the formation of export-competent mRNP. *Mol Cell.* **1**: 132-139.
5. Babour, A., Bicknell, AA., Tourtelotte, J. Niwa, M. A surveillance pathway monitors the fitness of the endoplasmic reticulum to control its inheritance. (2010). *Cell*. 142:256-69.