MASTER 2 BMC
PARCOURS GENOPATH
ANNÉE 2021-2022

Titre du sujet de stage :
Transgenerational memory of environmental stress in *Caenorhabditis elegans*

Nom, adresse de l'Unité d'accueil / Nom du responsable de l'unité :

Laboratoire de Biologie Et Modélisation de la Cellule, 46 Allée d'Italie, 69007 Lyon. Responsable : Didier Auboeuf

Nom, adresse de l'Equipe d'accueil / Nom du responsable d'équipe :

Epigenetic regulation of cell identity and environmental stress responses. Responsable d'équipe : Francesca Palladino

Nom, tel, adresse e-mail de l'encadrant de stage :

Valérie Robert, 0472728126, valerie.robert@ens-lyon.fr

Sujet de stage :

Epigenetic regulation influences gene expression and cellular homeostasis in response to environmental stress, and contributes to the inheritance of environmentally-induced changes across generations [1]. *C. elegans* has become an organism of choice to study how epigenetic regulation contributes to the transgenerational inheritance of environmentally-induced changes [2]. One of the most well studied example of this phenomenon is memory of RNAi-induced silencing [3], in which RNAi silencing induced on endogenous genes or single-copy transgenes is maintained for many generations after elimination of the initial dsRNA trigger. This process relies on the nuclear RNAi machinery that generates small RNAs homologous to the silenced locus and targets repressive histone post-transcriptional modifications to it [4]. While it is widely accepted that small RNAs are agents of heritability, the roles of histone modifications in transgenerational epigenetic inheritance is still debated.

Our lab is interested in the germline functions of H3K4 methylation, a histone modification found at promoters and catalyzed by the evolutionary conserved Set1/MLL family of histone methyltransferase (HMTase). SET-2 is one of the 2 Set1/MLL HMTase encoded by the *C. elegans* genome [5,6]. We have shown that, in the germline, SET-2 is required to maintain cellular identity [7], genome stability [8] and chromatin organization [9]. More recently, we have also observed that animals lacking SET-2 activity have a longer memory of RNAi-induced silencing, suggesting that H3K4 methylation may play a role in limiting transgenerational memory of RNAi-induced silencing.

We are looking for a M2 student to investigate how H3K4 methylation interferes with the duration of transgenerational memory. Specifically, the student will ask how the pool of

small RNA generated during RNAi-induced silencing is affected in *set-2* mutants and how the absence of H3K4 methylation influences the deposition of others histone marks at the silenced locus.

Technologies utilisées : RNA-seq, TaqMan, qRT-PCR, ChiP-qPCR, microscopie, génétique classique (croisements, interférence par ARN)

Mots clés : epigenetic, histone post-transcriptional modifications, small RNA, gene silencing, transcriptional regulation, transgenerational memory, *Caenorhabditis elegans*

Publications d'intérêt :

[1] G. Cavalli, E. Heard, Advances in epigenetics link genetics to the environment and disease, Nature. 571 (2019) 489–499. https://doi.org/10.1038/s41586-019-1411-0.

[2] M.F. Perez, B. Lehner, Intergenerational and transgenerational epigenetic inheritance in animals, Nature Cell Biology. 21 (2019) 143–151. https://doi.org/10.1038/s41556-018-0242-9.

[3] N.L. Vastenhouw, K. Brunschwig, K.L. Okihara, F. Muller, M. Tijsterman, R.H.A. Plasterk, Gene expression: Long-term gene silencing by RNAi, Nature. 442 (2006) 882. https://doi.org/10.1038/442882a.

[4] R.M. Woodhouse, A. Ashe, How do histone modifications contribute to transgenerational epigenetic inheritance in C. elegans?, Biochemical Society Transactions. 48 (2020) 1019–1034. https://doi.org/10.1042/BST20190944.

[5] T. Simonet, R. Dulermo, S. Schott, F. Palladino, Antagonistic functions of SET-2/SET1 and HPL/HP1 proteins in C. elegans development, Developmental Biology. 312 (2007) 367–383. https://doi.org/10.1016/j.ydbio.2007.09.035.

[6] Y. Xiao, C. Bedet, V.J.P. Robert, T. Simonet, S. Dunkelbarger, C. Rakotomalala, G. Soete, H.C. Korswagen, S. Strome, F. Palladino, Caenorhabditis elegans chromatin-associated proteins SET-2 and ASH-2 are differentially required for histone H3 Lys 4 methylation in embryos and adult germ cells, Proceedings of the National Academy of Sciences of the United States. (2011) 8305.

[7] V.J. Robert, M.G. Mercier, C. Bedet, S. Janczarski, J. Merlet, S. Garvis, R. Ciosk, F. Palladino, The SET-2/SET1 histone H3K4 methyltransferase maintains pluripotency in the Caenorhabditis elegans germline, Cell Reports. 9 (2014) 443–450. https://doi.org/10.1016/j.celrep.2014.09.018.

[8] M. Herbette, M.G. Mercier, F. Michal, D. Cluet, C. Burny, G. Yvert, V.J. Robert, F. Palladino, The C. elegans SET-2/SET1 histone H3 Lys4 (H3K4) methyltransferase preserves genome stability in the germline, DNA Repair. 57 (2017) 139–150. https://doi.org/10.1016/j.dnarep.2017.07.007.

[9] M. Herbette, V. Robert, A. Bailly, L. Gely, R. Feil, D. Lleres, F. Palladino, A Role for Caenorhabditis elegans COMPASS in Germline Chromatin Organization, Cells. (2020). https://doi.org/10.3390/cells9092049.