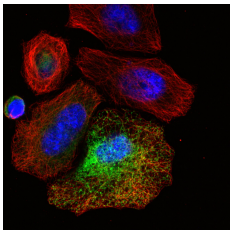

Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - UFR Sciences du Vivant
Parcours : **Biologie et Développement Cellulaires 'BDC'**
https://master2bdc.ijm.fr/
Fiche de Projet de Stage de M2, 2026-2027

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| **Unité INSERM ou CNRS ou Université :** Unité CPCV (Chime Physique Chimie du vivant), Ecole Normale supérieure, CNRS UMR8228, SU<br><br>**Intitulé Equipe :** METHROX (METaux et Homéostasie RedOX)<br>**ED d'appartenance :** ED515 Complexité du vivant<br>**Responsable de l'Equipe :** Clotilde Policar et Nicolas Delsuc | **Responsables du Stage :**<br>Christine Rampon et Alice Balfourier<br><br>**Contacts**<br>christine.rampon@u-paris.fr<br>alice.balfourier@ens.psl.eu |

**Titre du projet** : **Iron and $H_2O_2$ dialog during zebrafish development**

**Human embryo development is severely impacted by endogenous iron imbalance**. iron exhibits a U-shaped risk curve. At one side deficiency impairs haematopoiesis, cardiovascular system formation and sex determination; at the other, overload leads to hepatic iron accumulation, oxidative stress and ferroptosis in offspring [1]. Despite these effects, the exact role of iron during embryogenesis remains unclear. A general overview of the localization and dynamics of this metal during embryogenesis, is missing even in unperturbed environment. Furthermore, iron acts as a double sword regarding reactive oxygen species regulation; it is a known cofactor of enzymes that regulate ROS level in tissues, and it is capable of generating oxidative damage via Fenton-like reactions [2]. ROS were originally described as toxic by-products of aerobic cellular energy metabolism, however, recent findings have shown that ROS can also contribute to bona fide physiological processes [3]. Amongst ROS, hydrogen peroxide ($H_2O_2$) best fits the properties of a signaling molecule, and is at the same time recognized as the major ROS in the oxidative regulation of physiological activity. Less is known about the iron homeostasis modulation by ROS, giving rise to a possible feedback loop which would impact embryogenesis. Bridging this gap is thus a challenge we are tackling in the Methrox team. This internship project aims to complete the **distribution of the iron labile pool**, during the first hours post fertilization, with a new genetically encoded ratiometric probe that we obtained recently [4]. Then, iron distribution will be analysed after ROS modulation. Furthermore, **$H_2O_2$ levels** after iron supplementation or chelation will be monitored using the HyPer probe [5]. All the necessary tools are available in the lab. Expression of the redox machinery or iron storage proteins will be studied to complete this project. We chose the **zebrafish as a vertebrate model organism**. It offers a number of advantages, including scale, high fecundity, optical clarity enabling non-invasive live imaging. It is often used in embryogenesis studies to bypass mammalian constraints as it displays rapid and external development in controllable environment.

[1] 10.3390/biom10081176, [2] 10.1016/j.tox.2011.03.001, [3] 10.1038/s41580-020-0230-3, [4] 10.1021/acssensors.5c01165, [5] 10.1016/j.cmet.2020.02.003

**Techniques or methods :** zebrafish spawning and egg collection, *in vitro* transcription, RNA microinjection, morphological analyses, molecular analyses (*in situ* hybridization, RT-qPCR, whole-organism immunolabeling), confocal and spinning-disk imaging (time-lapse or on fixed embryos), image analysis using Fiji, XRF session (if obtained)

## Publications de l'équipe relatives au projet de stage (max 5) :

1. Pak VV et al. (2020) Ultrasensitive genetically encoded indicator for intracellular hydrogen peroxide identifies novel roles for cellular oxidants in cell migration and mitochondrial function. ***Cell Metabolism***, *32*, 642-53. https://doi.org/10.1016/j.cmet.2020.02.003
2. Vincent A et al. (2021) Evaluation of the compounds commonly known as superoxide dismutase and catalase mimics in cellular models. ***J. Inorg. Biochem.*** *219*, 111431. https://doi.org/10.1016/j.jinorgbio.2021.111431
3. Coulibaly K, et al. (2021) A di-copper peptidyl complex mimics the activity of catalase, a key antioxidant metalloenzyme. ***Inorg. Chem.*** *60*, 9309-9319. https://doi.org/10.1021/acs.inorgchem.0c03718
4. Thauvin M, et al. (2022) Reciprocal Regulation of Shh Trafficking and $H_2O_2$ Levels via a Noncanonical BOC-Rac1 Pathway. ***Antioxidants*** *11*, 718. https://doi.org/10.3390/antiox11040718
5. Thauvin M, et al. (2022) An early Shh-$H_2O_2$ feedback loop controls the progression of the regenerative program during adult zebrafish fin regeneration. ***J Cell Sci*** (6): jcs259664. https://doi.org/10.1242/jcs.259664