**Master 2 internship project**

**Year 2023-2024**

**Laboratory/Institute:** IAB **Director:** P. Hainaut

**Team:** Hainaut **Head of the team:** P. Hainaut

**Name and status of the scientist in charge of the project:** H. Menoni **HDR: yes ☐ no ☐**

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**Program of the Master’s degree in Biology:**

**☐** Microbiology, Infectious Diseases and Immunology **☐** Structural Biology of Pathogens

**☐** Physiology, Epigenetics, Differentiation, Cancer **☐** Neurosciences and Neurobiology

**Title of the project:**

**Unraveling in human cells the consequence of an acute depletion of the essential Base Excision Repair (BER) factor XRCC1 with live cell imaging and “seahorse” approaches**

Objectives (up to 3 lines):

To investigate whether an acute depletion of XRCC1 factor can influence the cell metabolism circuit (e.g. suppression of mitochondrial respiration) and the recruitment of CSB (Cockayne syndrome protein B) or other DNA repair factors.

Abstract (up to 10 lines):

The project will combine living cell imaging approaches with laser micro-irradiation to generate in the nucleus of living cells oxidative DNA damages. Thanks to this technological breakthrough (Menoni et al., 2012), we paved the way to study in living cells BER of oxidative DNA lesions in a unique way.

A recent development of new cell lines in the group allowed for the first time a rapidly induced depletion of XRCC1 (within ≈ 30 minutes) to study the effect of this essential protein (leading to early embryonic lethality in mice, and hypersensitivity to various DNA damaging agents in cultured cells). With this unique cells (unpublished), we can study immediate effect of XRCC1 depletion. We hypothesize that cells without XRCC1 i) will influence the recruitment of BER factors and ii) can reversibly suppress mitochondrial respiration in an attempt to reduce DNA damage stress generated by XRCC1 depletion.

Methods (up to 3 lines):

Living cell imaging combined with laser micro-irradiation, cell culture, western-blotting, seahorse experiment. Acute depletion of protein with temporal resolution regarding the DNA damage formation. Possibility to establish new CRISPR cell line.

Up to 3 relevant publications of the team:

Menoni, H., Wienholz, F., Theil, A.F., Janssens, R.C., Lans, H., Campalans, A., Radicella, J.P., Marteijn, J.A., and Vermeulen, W. (2018). The transcription-coupled DNA repair-initiating protein CSB promotes XRCC1 recruitment to oxidative DNA damage. **Nucleic Acids Res***46*, 7747-7756.

Menoni, H., Di Mascio, P., Cadet, J., Dimitrov, S., and Angelov, D. (2017). Chromatin associated mechanisms in base excision repair - nucleosome remodeling and DNA transcription, two key players. **Free Radic Biol Med** *107*, 159-169.

Menoni, H., Hoeijmakers, J.H., and Vermeulen, W. (2012). Nucleotide excision repair-initiating proteins bind to oxidative DNA lesions in vivo. **J Cell Biol** *199*, 1037-1046.

Requested domains of expertise (up to 5 keywords):

DNA Repair, Live cell imaging, CRISPR, High motivation, high organization skills.

**d’ici le Jeudi 20 Juillet 2023, 9H**,

en utilisant la **fiche ci-jointe dûment remplie**,

**et à l'adresse suivante :**

**ufrchimiebiologie-stages-bio-m2@univ-grenoble-alpes.fr**