CRBM external seminar
BIOLuM
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Investigating the functions of histone ADP-ribosylation during the DNA damage response.

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Professor Sébastien Huet received initial training in physics and optics, owning an engineering degree from the Ecole Supérieure d'Optique in Orsay. During his PhD work at the Institut de Biologie Physico-Chimique in Paris, he got introduced to cell biology and studied regulated secretion of neuroendocrine cells under the supervision of Jean-Pierre Henry and Sophie Cribier. Then Sébastien moved to the European Molecular Biology Laboratory in Heidelberg for his post-doc. In the lab of Jan Ellenberg, he studied the impact of the chromatin architecture on target-search dynamics of nuclear factors. He got recruited in 2010 as associate-professor at the University of Rennes. As a member of the Institut de Génétique et Developpement de Rennes, Sébastien has been studying early steps of the DNA damage response, focusing on the repair of single-strand breaks and base oxidation. To monitor these processes, he developed a multiscale framework based on live-cell fluorescence imaging. Sébastien is also the scientific manager of the plateform MRic-photinic (Microscopy Rennes Imaging Center) of the UAR Biosit in Rennes.

Abstract

Besides PARP1 itself, histones appear as the second main target of ADP-ribosylation in the DNA damage context. Yet, the contribution of this histone mark during the DNA repair process remains poorly described. In this work, we used a multiscale live-cell imaging approach to characterize the specific contributions of histone ADP-ribosylation to chromatin remodeling events occurring in the vicinity of the DNA lesions as well as the timely release of PARP1 from these lesions. We demonstrate that histone ADP-ribosylation affect the dynamics of the nucleosomes along the chromatin fiber, which promotes the establishment of a open chromatin conformation. Furthermore, we propose that histone ADP-ribosylation, in addition to PARP1 automodification, facilitates the dissipation of the enzyme from DNA lesions, thus promoting cell resistance to PARP inhibitors. Therefore, our work contributes to a better understanding of the roles of histone ADP-ribosylation at early stages of the DNA damage response.

Selected publications

- García Fernández F. ,..., S. Huet*, J. Miné-Hattab* (2025) *Single nucleosome imaging reveals principles of transient multiscale chromatin reorganization triggered by histone ADP-ribosylation at DNA lesions.* **Nature Commun.** 16(1):6652.
- Zentout S., ..., R. Smith*, S. Huet* (2024) *Histone ADP-ribosylation promotes resistance to PARP inhibitors by facilitating PARP1 release from DNA lesions.* **Proc. Natl. Acad. Sci. USA.** 121(25):e2322689121.
- D'Augustin O., ..., A. Campalans*, S. Huet*. (2023) *Identification of key residues of the DNA glycosylase OGG1 controlling efficient DNA sampling and recruitment to oxidized bases in living cells.* **Nuc. Acid. Res.** 51(10):4942-4958.
- Longarini E.J., ..., S. Huet* and I. Matic* (2023) **Mol. Cell.** *Modular antibodies reveal DNA damage-induced mono-ADP-ribosylation as a second wave of PARP1 signaling.* 83(10):1743-1760.e11. (*co-corresponding authors)
- Smith R.*, …, Timinszky* and S. Huet* (2023) *HPF1-dependent histone ADP-ribosylation triggers chromatin relaxation to promote the recruitment of repair factors at sites of DNA damage.* **Nature Struct. Mol. Biol.** 30(5):678-691.

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