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S E M I N A I R E

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"Modeling the regulation of DNA compaction by redox modifications"

Gene activity is tightly controlled by reversible chemical modifications called epigenetic marks, which are of various types and modulate gene accessibility without affecting the DNA sequence.
Major advances come from investigations of such structural regulation at the first level of compaction of DNA, the so-called nucleosome, that is composed of ~146 base pairs of DNA wrapped around an octamer of histone proteins [1]. Indeed, post-translational modifications of histone proteins play are major epigenetic mechanisms (e.g. lysine methylation mostly promotes gene silencing while acetylation are marks of gene expression).
Despite an increasing body of evidence demonstrating the role of oxidative-type modifications of histones (S-glutathionylation, S-nitrosylation...) in the regulation of DNA compaction [2], there remains a complete absence of structural data at the atomistic level to understand the molecular mechanisms behind their regulatory action.

In this talk, I will present our latest results on oxidative post-translational modifications of histone proteins structural impact on the nucleosome structure. Owing to MD simulations and advanced structural analysis tools, we described the impact of histone H3 hyperoxidation (i.e., S-sulfonylation) on the nucleosome dynamics [3]. Our results reveal the atomic-scale details of the intrinsic structural networks within the canonical histone core and their perturbation by hyperoxidation of the histone H3 C110. We show that this modification involves local rearrangement of the communication networks and destabilizes the dyad, which could be important for nucleosome disassembly process.
I will further discuss preliminary results we recently obtained on other types of cysteine modifications and the methodological struggles we are facing.

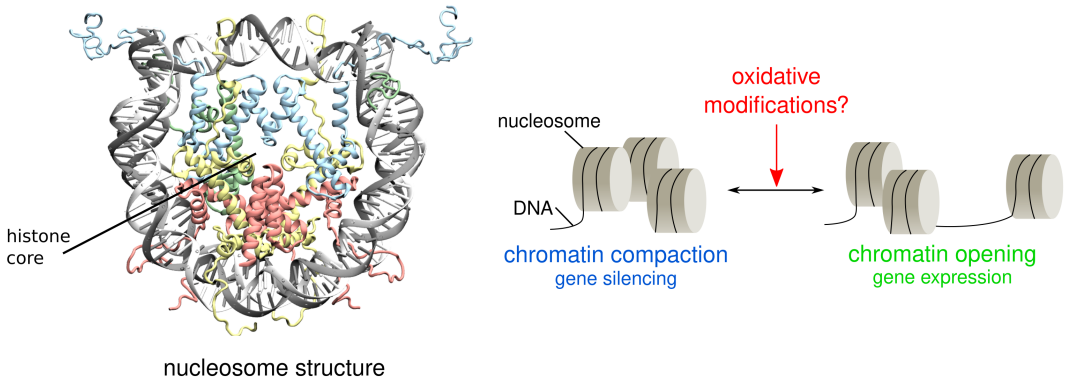

Figure The first level of DNA compaction is composed of DNA wrapped around a histone core (left).,We investigate how oxidative modifications of histones can impact the nucleosome structure, hence chromatin compaction and gene expression (right).

[1] Tsunaka, Yasuo, Ayako Furukawa, and Yoshifumi Nishimura. "Histone tail network and modulation in a nucleosome." *Current Opinion in Structural Biology* 75 (2022): 102436.
[2] García-Giménez, José-Luis, et al. "Oxidative stress-mediated alterations in histone post-translational modifications." *Free Radical Biology and Medicine* 170 (2021): 6-18.
[3] Karami, Yasaman, and Emmanuelle Bignon. "Cysteine hyperoxidation rewires communication pathways in the nucleosome and destabilizes the dyad." *bioRxiv* (2023): 2023-10.

Jeudi 29 février 14h30 - Salle de conférences