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## **LES SÉMINAIRES DE L'INMG**

*Epigenetic strategies : nucleosome remodeling, histone modifications and histone variants*

Par

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**Salle Guillermond**

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Chromatin impedes the binding of protein factors to the underlying DNA sequences. The cell uses three main “epigenetic tools” to overcome the chromatin barrier, namely, chromatin remodelers, histone variants and histone post-translational modifications. We will give specific examples of how either one of these “epigenetic tools” functions.

Chromatin remodelers are sophisticated nano-machines, which are able to alter histone-DNA interactions and to mobilize nucleosomes. Neither the mechanism of their action nor the conformation of the remodeled nucleosomes are, however, yet well understood. We have studied the mechanism of RSC-induced chromatin remodeling by using high resolution microscopy and state of the art biochemistry techniques. The data illustrates how RSC remodels the nucleosome *in vitro* and shed light on its *in vivo* function.

The crystal structure of the CENP-A nucleosome was recently solved. Intriguingly, in contrast to the canonical nucleosome (where 147 bp of DNA are wrapped around the histone octamer), only the central 121 bp were visible, suggesting flexible CENP-A nucleosomal ends. Why the CENP-A nucleosome exhibits flexible DNA ends is totally unknown. Our data show that the flexible DNA ends of the CENP-A nucleosome are required for mitotic fidelity.

The Aurora family of oncogenic kinase consists of two major members, Aurora A and Aurora B. Both kinases exhibit very high homology. They show, however, quite distinct localization and function. Histone H3 is specifically phosphorylated, presumably by the oncogenic kinase Aurora B, at serine 10 at the onset of mitosis. Here we will present data on the distinct function of the two Aurora kinases and the mechanism of phosphorylation of histone H3 by Aurora B.

### Selected publications (2010-2016)

1. Roulland, Y., Ourarhni, K., Bednar, J., Boopathi, R., Naidenov, M., Ramos, L., Papin, C., Papai, G., Skoufias, D., Schultz, P., Angelov, D., Hamiche, A. & **Dimitrov, S.** « The flexible ends of CENP-A nucleosome are required for mitotic fidelity », *Molecular Cell*, 2016 Aug 3. pii: S1097-2765(16)30281-7. doi: 10.1016/j.molcel.2016.06.023. [Epub ahead of print]
2. Latryck, C., Marek, M., Ourarhni, K., Papin, C., Obri, A., Stoll, Y., Ignatieva, M., **Dimitrov, S.**, Romier, C. & Hamiche, A. « YL1, H2A.Z-specific histone chaperone, required for ATP-dependent deposition of H2A.Z in chromatin », *Nature Struct & Mol. Biol.* 2016 Apr;23(4):309-16.
3. Obri, A., Ourarhni, K., Papin, C., Diebold, M.-L., Padmanabhan, K., Marek, M., Stoll, I., Roy, L., Relly, P., Mak, T.W., **Dimitrov\***, **S.**, Romier\*, C. & Hamiche\*, A. (2014) « ANP32E is a histone chaperone that removes H2A.Z from chromatin » *Nature* (full article), 505(7485):648-53.  
(\*corresponding authors)
4. Goutte-Gattat, D., Shuaib, M., Ourarhni, K., Gautier, T., Skoufias, D.A., Hamiche, A & **Dimitrov, S.** (2013) « The phosphorylation of the CENP-A NH<sub>2</sub>-terminus in mitotic centromeric chromatin is required for kinetochore function », *Procl. Natl. Acad. USA* 110, 8579-8584
5. Chantalat, S., Héry, P., Barral, S., Thuret, J.-Y., **Dimitrov, S.** & Gérard, M. (2011) « Histone H3 at lysine 36 is involved in the formation of constitutive and facultative heterochromatin », *Genome Research* **21(9):1426-37**
6. Syed, S. H., Goutte-Gatat, D., Becker, N., Meyer, S., Shukla, M., Hayes, J.J., Everarers, R., Angelov, D., Bednar, J. & **Dimitrov, S.** (2010) "Single base resolution mapping of H1-nucleosome interactions and 3D organization of the nucleosome", *Proc. Natl. Acad. Sci. USA* 107, 9620-9625
7. Shuaib, M., Ourarhni, K., **Dimitrov, S.** & Hamiche, A. (2010) "HJURP binds CENP-A via a highly conserved N-terminal domain and mediates its deposition to centromeres" *Proc. Natl. Acad. Sci. USA* 107(4):1349-54
8. Shukla, M., Syed, S., Montel, F., Fivre-Moskalenko, C., Bednar, J., Travers, A., Angelov D. & **Dimitrov, S.** (2010) "Remosomes: novel RSC generated non-mobilized particles with ~180 bp of DNA loosely associated with the histone octamer", *Proc. Natl. Acad. Sci. USA* 107(5):1936-41  
(ranked with score 12 at Faculty 1000)