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Salle de conférence Bâtiment 84, Ecole Polytechnique

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Functional interplay between the chromatin assembly factor 1 (hCAF-1) and the BLM helicase in mammalian cells

DNA replication and repair occurs in the context of DNA packaged into chromatin. Flaws in the DNA replication process, known as replication stress, result in inaccurate chromosome duplication and mitotic abnormalities, promoting genome and epi-genome instability contributing to tumorigenesis. Homologous recombination (HR), a DNA repair mechanism acting as a tumor suppressor pathway, plays a crucial role in the recovery of dysfunctional forks.

We show in human cells, that the anti-recombinase helicase BLM interaction with the large subunit of the hCAF-1 complex (CHAF1A) interaction is dependent on the BLM-SUMOylation and is mediated by the CHAF1A-SUMO interaction motif (SIM). Hallmarks of Bloom Syndrome patient derived cells (BS cells) includes increased sister chromatid exchange (SCE) and micronuclei. We established that BLM-SUMOylation is required to suppress micronuclei and that CHAF1A depletion reverts the micronuclei rate to that of BS-BLM-Wild type cells.

The contribution of the BLM:CHAF1A interaction to genome stability maintenance will be discussed.