BDR SEMINAR (Kobe & online hybrid)

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Tuesday, December 5, 2023

14:30-15:30

2F Large Conference Room, DB Building A, Kobe / Zoom

Zoom meeting URL will be announced on the event day by e-mail.

※Non-BDR members: Please register from the following link.

https://krs1.riken.jp/m/bdrseminarregistration (Registration deadline: Dec 3)

Identification of a specific mitotic pathway safeguards centromere integrity in human cells

Summary

Centromeres are a specialised chromatin that needs to be maintained in a robust structure to withstand spindle pulling forces but accessible for sister DNAs disentanglement during mitosis. The latter resolution process is facilitated in anaphase by a multienzyme complex known as the ultrafine DNA bridge (UFB)-binding complex, which comprises PICH DNA translocase, BTRR dissolvasome, Polo-like kinase 1 and RIF1-PP1s. Unexpectedly, human centromeres suffer severe DNA breakages triggered by the UFB-binding complex when PLK1 is non-functional during chromosome alignment. How PLK1 exerts this non-canonical function in centromere protection is currently unknown. Here, we identify a group of mitotic kinases that collaboratively regulate the spatial and temporal activity of the UFB-binding complex for the protection of centromere structures. Stable formation of the BTRR dissolvasome promotes its interaction with PICH but this can be transiently disrupted by Aurora B and CDK1 at centromeres. Simultaneously, the MPS1-PLK1 axis phosphorylates the BLM helicase subunit, inhibiting unlawful DNA unwinding. This two-tier measure effectively averts the destruction of the kinetochore-associated chromatin by the complex, allowing stable maintenance of chromosome biorientation; otherwise, the centromere is severely disintegrated. Our study thus unveils an important regulatory mechanism of the UFB-binding complex during mitosis. I will discuss further how this specific pathway preserves the integrity of centromeres in human cells.

Host: Ichiro Hiratani

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