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**Special seminar at Radiation Biology Center**

**Graduate School of Biostudies**

**Date: December 4th(Mon), 2023 4:00 pm-5:00 pm**

**Venue: Seminar room at RBC (放生研一階セミナー室)**

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**A network of mitotic kinases safeguards centromere integrity in human cells**

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Abstract

Centromeres require structural strength to withstand the spindle pulling forces, while enabling efficient resolution of DNA entanglements during mitosis. The latter is facilitated by the ultrafine DNA bridge (UFB)-binding complex, which comprises PICH DNA translocase, Polo-like kinase 1 (PLK1), BTRR dissolvasome and RIF1-PP1s. Unexpectedly, human centromeres suffer severe DNA breakages triggered by the UFB-binding complex when PLK1 is non-functional. Here, we identify multiple mitotic kinases that collaborate to strictly restrain the spatiotemporal activation of the UFB-binding complex during chromosome biorientation. Stable formation of the BTRR dissolvasome is crucial for PICH interaction but this can be disrupted by Aurora B and CDK1 at the centromere. Simultaneously, the MPS1-PLK1 axis also phosphorylates the BLM helicase, inhibiting unlawful centromeric DNA unwinding. Together, these measures prevent illegitimate activation of the complex, averting destruction of the kinetochore-associated chromatin, which otherwise causes centromere disintegration. Additionally, we find that RIF1-PP1s can antagonise the CDK1 inhibitory effect to promote premature assembly of the UFB-binding complex. Our study thus unveils a specific pathway to preserve human centromere chromatin during chromosome alignment.

オクスフォード大大学院在学中、Ultrafine bridgeを発見し、その後ポスドクを経て、現在サセックス大Genome Stability Centreでラボ主催者としてご活躍です。今回、分子生物学会に招聘されて来日されます。ゲノム安定性、染色体研究にご興味のある先生がたは、ぜひご来聴ください。

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