BDR SEMINAR (Kobe & online hybrid)

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16:00-17:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom

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

※Non-BDR members: Please register from the following link.
https://krs2.riken.jp/m/bdrseminarregistration (Registration deadline: July 23)

The Mechanism of Mitotic Arrest-Dependent Telomere Deprotection

Summary

Telomeres, composed of repetitive DNA and the shelterin complex (including TRF1/TRF2), protect chromosome ends from activating the DNA damage response (DDR). TRF2 aids the formation of a T-loop by enabling the 3' telomere end to invade double-stranded telomeric DNA. Disruption of telomere function, through either telomere shortening or loss of shelterin function, leads to telomere deprotection. This activates DDR, causing cell cycle arrest, chromosome fusions, and/or cell death, which underlie replicative senescence or tumorigenesis depending on the cellular context. We discovered that during mitotic arrest, Aurora Kinase B (AURKB) causes mitotic arrest-dependent (MAD) telomere deprotection, the only known active telomere deprotection mechanism (Hayashi et al., Nat Struct Mol Biol, 19(4): 387-394, 2012). We proposed this is involved in the pharmacological effects of anti-tumor mitotic inhibitors and preventing cells from transformation during telomere crisis (Hayashi et al., Nature, 522: 492-496, 2015). However, the molecular mechanism of MAD telomere deprotection remained elusive.

Using interactomics, super-resolution imaging, and molecular biology techniques, we identified the Chromosome Passenger Complex (CPC) and the BLM-TOP3A-RMI1/2 (BTR) complex as key players in this process. AURKB phosphorylates TRF2 and TRF1: the phosphorylation of TRF2 basic domain attenuates its protective function on T-loop against BTR activity, while TRF1 phosphorylation paradoxically promotes deprotection through interaction with the CPC complex (Romero et al., Nat Commun, 16(1): 1-19, 2025). In this seminar, I will discuss our recent findings on MAD telomere deprotection and its potential role in mitosis and meiosis.