BDR SEMINAR in Kobe

"CDB SEMINAR" and "QBiC SEMINAR" have been renamed "BDR SEMINAR".

Andres Canela

National Cancer Institute, USA

Monday, July 9, 2018

16:00-17:00, Seminar Room A7F

Genome organization drives chromosome fragility

* This seminar is a part of the Epigenetics Seminar Series 2018-2019.

Summary

The folding and organization of DNA within the nucleus produces torsional stress resulting in DNA entanglements. Using a methodology to map in the genome DNA double strand breaks (DSBs) generated by the activity of Topoisomerase 2, we find that Topoisomerase 2B (TOP2B) releases torsional stress specifically at chromosome loop anchors, bound by CCCTC-binding factor (CTCF) and cohesin. We also observe that TOP2-induced DSBs occurred in the same DNA regions that typically undergo chromosomal translocations in cancer. Thus, TOP2B activity relieves torsional stress in the DNA during genome organization, but paradoxically makes chromatin loop anchors vulnerable target regions in oncogenic translocations. Additionally, these Top2B-mediated DSBs are largely transcription-, replication and cell-type-independent. Our studies demonstrate that polymorphisms between two different mice species that change CTCF, cohesin occupancy and loop formation also re-localize TOP2B-induced DSBs. In conclusion, loop anchors serve as fragile sites that generate DSBs and chromosomal rearrangements.

Canela A. et al. (2017) Genome Organization Drives Chromosome Fragility. Cell 170(3):507-521.

Canela A. et al. (2016) DNA Breaks and End Resection Measured Genome-wide by End Sequencing. Mol Cell 63(5):898-911.

Host: Ichiro Hiratani
Developmental Epigenetics, BDR
hiratani@cdb.riken.jp
Tel:078-306-3179(ext:95-3179)

RIKEN Center for Biosystems Dynamics Research (BDR)