分子細胞生物学研究所セミナー

演者 **Keiko Muraki, Ph.D.**
Postdoc at John P. Murnane laboratory, Department of Radiation Oncology, University of California, San Francisco

演題 **Mechanism of the sensitivity of subtelomeric regions to DNA double-strand breaks**

日時 **３月２４日（木）15：00 ～ 16：30**

場所 **東京大学分子細胞生物学研究所**
生命科学総合研究所Ｂ棟 ３階 301 会議室

主催 **東京大学分子細胞生物学研究所**
ゲノム情報解析研究分野（連絡先：20756）

Classical nonhomologous end-joining (C-NHEJ) is a major pathway for DNA Double-strand breaks (DSBs) repair. On the other hand, the caps on the ends of chromosomes, called telomeres, keep the ends of chromosomes from appearing as DNA double-strand breaks (DSBs) and prevent chromosome fusion. We have previously reported that I-SceI endonuclease-induced DSBs near telomeres in a human cancer cell line are much more likely to generate large deletions and gross chromosome rearrangements (GCRs) than interstitial DSBs. This repair deficiency at subtelomeres has been proposes as a mechanism by which oncogene-induced replication stress promotes telomere dysfunction, leading to chromosome instability in human cancer cells, or senescence in normal human cells.

Our current results show that inhibition of MRE11 nuclease activity with Mirin reduces the frequency of large deletions and GCRs, indicating that inappropriate processing of DSBs by MRE11 is involved in the formation of large deletions and GCRs. In contrast, MRE11 nuclease-independent C-NHEJ functions normally at subtelomeric DSBs. Combined, our results demonstrate that subtelomeric regions are proficient in C-NHEJ, but that subtelomeric DSBs are highly prone to inappropriate processing, which promotes large deletions and GCRs, involving Alternative NHEJ.