グローバル COE 特別セミナー

分子細胞生物学研究所セミナー

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演題 **Mechanisms coordinating chromosome replication and transcription.**

日時 11 月 1 日（ 月） 15: 10~16: 10

場所 東京大学分子細胞生物学研究所　セイホクギャラリー

In response to replication stress, the integrity of replication forks is preserved by the ATM and ATR-dependent checkpoint responses and by specialized SUMO and Ubiquitin pathways. Under unperturbed conditions, fork progression must be also controlled to maintain the integrity of the replisome–fork complexes at pausing sites, to coordinate replicon fusion at termination of DNA synthesis and to deal with the collision between transcription and replication. DNA topoisomerases play crucial roles in facilitating fork progression during unperturbed DNA synthesis and in response to replication stress.

We used a combination of genetic, genomic and mechanistic studies in yeast to identify the factors involved in coordinating replication fork progression with the Mec1 and Rad53 (ATR and Chk2 respectively in humans)-mediated checkpoint response. We found that several proteins involved in mRNA biogenesis, mRNA export and gene gating play an important role in promoting fork reversal at stalled replication forks, specifically when the checkpoint response is defective. These and other data suggest that the checkpoint response controls the physical connections between replicating chromosomes and the nuclear envelope to facilitate fork progression across transcribed units and to prevent aberrant topological transitions at stalled forks.

1. Fachinetti D, Bermejo R, Cocito A, Minardi S, Katou Y, Kanoh Y, Shirahige K, Azvolinsky A, Zakian VA, Foiani M. Replication termination at eukaryotic chromosomes is mediated by Top2 and occurs at genomic loci containing pausing elements. Mol Cell. 2010 Aug 27;39(4):595-605.
2. Branzei D, Foiani M. Maintaining genome stability at the replication fork. Nat Rev Mol Cell Biol. 2010 Mar;11(3):208-19. Review.
3. Bermejo R, Capra T, Gonzalez-Huici V, Fachinetti D, Cocito A, Natoli G, Katou Y, Mori H, Kurokawa K, Shirahige K, Foiani M. Genome-organizing factors Top2 and Hmo1 prevent chromosome fragility at sites of S phase transcription. Cell. 2009 Sep 4;138(5):870-84.
4.

主催　東京大学分子細胞生物学研究所、グローバル COE