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TEMASEK LIFESCIENCES LABORATORY

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The Auditorium (Level 1)
Hosted by: Dr Toshiro Ito

A long inverted repeat transiently stalls DNA replication by forming hairpin structures on both leading- and lagging-strands

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Prof Hisaji Maki was born and grew up in Kyushu, the Southern part of Japan. The typical character of Kyushu people is open- and simple-minded. Prof Hisaji learned molecular genetics in Kyushu University and biochemistry in Stanford University. He has been interested in and studied on spontaneous mutagenesis and DNA replication for many years.

Long inverted repeats (LIRs), often found in eukaryotic genomes, are unstable in Escherichia coli where they are recognised by the SbcCD (Mre11/Rad50), an endonuclease/exonuclease capable of cleaving hairpin DNA. It has long been postulated that LIRs form hairpin structures exclusively on the lagging-strand template during DNA replication, and SbcCD cleaves these hairpin-containing lagging-strands to generate DNA double-strand breaks. Using a reconstituted oriC plasmid DNA replication system, we have examined how a replication fork behaves when it meets a LIR on DNA. We have shown that leading-strand synthesis stalls transiently within the upstream half of the LIR. Pausing of lagging-strand synthesis at the LIR was not clearly observed, but the pattern of priming sites for Okazaki fragment synthesis was altered within the downstream half of the LIR. We have found that the LIR on a replicating plasmid was cleaved by SbcCD with almost equal frequency on both the leading- and lagging-strand templates. These data strongly suggest that the LIR is readily converted to a cruciform DNA, before the arrival of the fork, creating SbcCD-sensitive hairpin structures on both leading- and lagging-strands. We propose a model for the replication-dependent extrusion of LIRs to form cruciform structures that transiently impede replication fork movement.

Recent Publications:

1. Chew Theng Lim, Pey Jiun Lai, David R. F. Leach, **Hisaji Maki**, and Asako Furukohri. A novel mode of nuclease action is revealed by the bacterial Mre11/Rad50 complex Nucl. Acids Res. first published online August 28, 2015
2. Kang Wei Tan, Tuan Minh Pham, Asako Furukohri, **Hisaji Maki**, and Masahiro Tatsumi Akiyama. Recombinase and translesion DNA polymerase decrease the speed of replication fork progression during the DNA damage response in Escherichia coli cells. Nucl. Acids Res. 43: 1714-1725, 2015
3. Mio Ikeda, Asako Furukohri, Gaelle Philippin, Edward Loechler, Masahiro Tatsumi Akiyama, Tsutomu Katayama, Robert P. Fuchs, and **Hisaji Maki.** DNA polymerase IV mediates efficient and quick recovery of replication forks stalled at N2-dG adducts. Nucl. Acids Res. 42: 8461-8472, 2014