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# Leading or lagging - it makes no difference

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DNA replication begins with DNA polymerase III creating a replication fork that divides the double-stranded DNA into leading and lagging strands. This fork can stall if the polymerase III holoenzyme encounters a physical obstruction such as DNA regulatory structures, another polymerase holoenzyme, or a mutation in one or both strands. Molecular sensors detect the stall and activate a second set of polymerases, causing the mutation to be bypassed and either corrected or incorporated into the daughter strands - potentially resulting in cancer or in neurodegenerative disease. Recent identification of many of the DNA polymerases involved in translesion synthesis (TLS) has helped shed new light on the molecular mechanisms of mutagenesis, and in the May 23 issue of Science, Vincent Pagés and Robert Fuchs at the Centre National de la Recherche Scientifique Cancérogenèse et Mutagenèse Moléculaire et Structurale further elucidate the mechanism of action of TLS polymerases (*Science*, **300:**1300-1303, May 23, 2003).

Pagés and Fuchs made plasmid constructs in which they forced a single mutation in one or other strand; and by artificially introducing strand heterology, they monitored the kinetics of synthesis of each strand. They discovered that the lesion in either strand did not affect the synthesis of the opposing strand, suggesting that the opening of the replication fork continues as a result of uncoupling of synthesis of leading and lagging strands. In either strand, TLS occurred after the same time delay of around 50 minutes and thereafter proceeded at the same rate.

"The strategy implemented here will be useful to unravel the complex biochemistry of various TLS pathways *in vivo*, thus providing a powerful complement to *in vitro* approaches," the authors conclude.

# References

1. Checking on the fork: the DNA-replication stress-response pathway

2. Polymorphism of genes encoding SOS polymerases in natural populations of *Escherichia coli*

3. *Science*, [http://www.sciencemag.org]

4. Centre National de la Recherche Scientifique Cancérogenèse et Mutagenèse Moléculaire et Structurale, [http://www.cnrs.fr/index.html]