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Telomere position effect epigenetic conversions and paused replication forks

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The transmission of epigenetic marks on histones and DNA is an integral part of eukaryotic DNA replication. This transmission culminates in the reconstitution of pre-existing chromatin structures or, alternatively, in an epigenetic conversion of the replicated locus. The subtelomeric genes of *S. cerevsiae* can be active or "silenced" and infrequently alternated between these two states. This phenomenon is referred to as Telomere Position Effect (TPE). The active or silenced states are determined by chromatin structures, which resemble euchromatin and heterochromatin in metazoans. We have a good understanding of the processes that establish and maintain these chromatin structures, but have very superficial understanding of the processes that lead to a conversion of the epigenetic state of these genes. Recently, we have developed an assay for the quantitative assessment of the frequency of epigenetic conversions at the telomeres of S. cerevisiae. We have documented that the destruction of Chromatin Assembly Factor-1 (CAF-1) or the helicase *RRM3* substantially reduce the frequency of conversions. CAF-I is a histone chaperone, which reassembles nucleosomes after the passage of the replication forks. RRM3 encodes a DNA helicase that helps the resumption of replication of paused replication forks. Of note, subtelomeric DNA contains multiple RRM3-dependent replication pausing sites. Current models suggest that both Rrm3p and CAF-1 are recruited to replication forks via an interaction with the Proliferating Cell Nuclear Antigen (PCNA, POL30) and that this interaction is regulated by the DBF4-Dependent Kinase, DDK. In this presentation, we propose to use TPE as model for replication-coupled epigenetic conversions. We will present our recent studies on the role of two kinases that phosphorylate (CDK and DDK) on the stability and activity of CAF-I.

Speaker Biography

Krassimir Yankulov has completed his PhD from the Imperial Cancer Research Fund, London, England in 1994 and also completed his Post-doc at the Amgen Institute, Toronto, Canada. Since 1998, he is a Professor at the Department of Molecular and Cellular Biology at the University of Guelph in Canada, Ontario. His main focus of research is on epigenetics in yeast. He has published over 40 publications that have been cited over 2000 times. He is serving as an Editorial Board Member of *Frontiers* in *Genetics* and of *PLoS One.*

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