Abstract

Identification of histone residues of relevance in transcription-replication conflicts

Iván Núñez-Martín[1], Belén Gómez-González[1], Andrés Aguilera[1]

[1]Centro Andaluz de Biología Molecular y Medicina Regenerativa (CABIMER), Universidad de Sevilla-CSIC-Universidad Pablo de Olavide, Seville, Spain

DNA replication deals with different obstacles while the replication fork advances through the genome, including DNA damage, topological stress or tightly bound proteins. Transcription is a major contributor to genome instability due to its capability to hinder fork progression. Transcription-replication conflicts (TRCs) may occur either in a head-on or in a codirectional orientation, being head-on conflicts more harmful than the codirectional ones. Given that transcription and replication occur in the context of a chromatinized DNA template, it is feasible that nucleosome positioning and histone modifications contribute to TRCs and their consequent impact on genome integrity. To study the contribution of chromatin to TRCs and genome instability, we took advantage of different plasmid-borne recombination systems that rely on strong head-on or codirectional conflicts. Thus, we did an automated screening using *Saccharomyces cerevisiae* collections to identify viable histone H3 and H4 mutants that increase TRC-mediated genome instability, assayed by hyper-recombination. Here, we present the different stages of the screening up to final candidates and following experiments that validate their genome instability phenotypes. These mutants are currently being characterized to reveal the molecular mechanism by which specific histone mutations impact on TRC origin and resolution and how chromatin protects genome integrity.