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EPIGENETIC CONTROL OF RNA POLYMERASE II TRANSCRIPTION AND DNA RECOMBINATION BY H4K16 ACETYLATION, AT rDNA OF *S. CEREVISIAE*

CESARINI E.*, D'ALFONSO A.*, CAMILLONI G.*,**

*) Dipartimento di Biologia e Biotecnologie, Università di Roma, La Sapienza, 00185 Roma (Italia)
**) Istituto di Biologia e Patologia Molecolari, CNR, Roma (Italia)

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In *S. cerevisiae* the ribosomal locus (rDNA) represents a region in which DNA replication, transcription and recombination meet both physically and functionally. The locus is a single gene cluster, consisting of approximately 150 repeated units. Each repeat contains the 35S and 5S genes, transcribed by RNA Polymerase I and III, and a non transcribed spacer (NTS). Despite its name, the latter sequence could be transcribed by RNA polymerase II to produce non coding RNAs (ncRNAs). In yeast, ribosomal ncRNAs transcription, may locally displace cohesins leading to rDNA copy number variation and extrachromosomal ribosomal circles (ERCs) production. These events are considered markers of genome instability and aging. Recently it has been shown that also the replication efficiency is essential for rDNA recombination rate. Each unit contains an ARS element (rARS) but only 20% of these origins are active in a single cell cycle. Once a rARS has fired, replication proceeds bidirectionally but the leftward-moving fork is blocked at the RFB (replication fork barrier) site. DSBs originating at the stalled forks may lead to ERCs formation and copy number variation. All this implies that the basic DNA transactions, DNA replication, Recombination and Pol I, II and III transcription, occurring at rDNA need to be finely controlled.

Interestingly, mutant strains of the NAD-dependent histone deacetylase Sir2p increase their replication efficiency, recombination rate and ncRNA production, suggesting that these processes are epigenetically linked. Considering the NAD-dependent histone deacetylase activity of Sir2p we want to investigate whether other sirtuins of *S. cerevisiae* (*HST*1-4) could affect recombination and/or RNA Pol II transcription and/or DNA replication, and to verify if the relationship is based on histone acetylation.