Gene regulation, Chromatin, Sirtuins, and Aging.

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Regulation of gene expression: transcriptional regulation and epigenetics.
How the gene expression is regulated is fundamental to most aspects of biology. Research in our laboratory focuses on understanding how gene expression is regulated at the transcription level, particularly studying the interactions between protein and DNA as they occur in vivo, in the chromatin.
Our experiments are mostly performed in the yeast *Saccharomyces cerevisiae*, and our attention is focused to the ribosomal DNA (rDNA) locus.
We are studying genes that regulate transcriptional silencing and genome stability (Sir2p, yeast sirtuins, DNA Topoisomerase1, histones). We use classical and modern molecular biology techniques. Moreover, a combination of genetic and biochemical methods are also employed.
The purpose of the studies of our lab is to discover more about the ways that cells regulate transcription. Our findings will increase our perception of how chromatin dynamics influence gene expression and maintain the genome integrity. Several factors we investigated on have homologues in human cells signifying that our discoveries may provide insight into mechanisms that regulate gene expression in higher eukaryotes.

In *Saccharomyces cerevisiae* the repeated units of the ribosomal locus, transcribed by RNA polymerase I (Pol I), are interrupted by nontranscribed spacers (NTSs). These NTS regions are transcribed by RNA polymerase III to synthesize 5S RNA and by RNA polymerase II (Pol II) to synthesize, at low levels, noncoding RNAs (ncRNAs). While transcription of both RNA polymerase I and III is highly characterized, at the ribosomal DNA (rDNA) locus only a few studies have been performed on Pol II, whose repression correlates with the SIR2-dependent silencing. The involvement of both chromatin organization and Pol I transcription has been proposed, and peculiar chromatin structures might justify "ribosomal" Pol II silencing. Reporter genes inserted within the rDNA units have been employed for these studies. We studied, in the natural context, yeast mutants differing in Pol I transcription in order to find whether correlations exist between Pol I transcription and Pol II ncRNA production. Here, we demonstrate that silencing at the rDNA locus represses ncRNAs with a strength inversely proportional to Pol I transcription. Moreover, localized regions of histone hyperacetylation appear in cryptic promoter elements when Pol II is active and in the coding region when Pol I is functional; in addition, DNA topoisomerase I site-specific activity follows RNA polymerase I transcription. The repression of ncRNAs at the rDNA locus, in response to RNA polymerase I transcription, could represent a physiological circuit control whose mechanism involves modification of histone acetylation.