Year of publication 2018


Histone deacetylation promotes transcriptional silencing at facultative heterochromatin

_Nucleic Acid Research_ Histone deacetylation promotes transcriptional silencing at facultative heterochromatin : [DOI : 10.1093/nar/gky232](https://doi.org/10.1093/nar/gky232)

**Summary**

It is important to accurately regulate the expression of genes involved in development and environmental response. In the fission yeast Schizosaccharomyces pombe, meiotic genes are tightly repressed during vegetative growth. Despite being embedded in heterochromatin these genes are transcribed and believed to be repressed primarily at the level of RNA. However, the mechanism of facultative heterochromatin formation and the interplay with transcription regulation is not understood. We show genome-wide that HDAC-dependent histone deacetylation is a major determinant in transcriptional silencing of facultative heterochromatin domains. Indeed, mutation of class I/II HDACs leads to increased transcription of meiotic genes and accumulation of their mRNAs. Mechanistic dissection of the pho1 gene where, in response to phosphate, transient facultative heterochromatin is established by overlapping IncRNA transcription shows that the Clr3 HDAC contributes to silencing independently of SHREC, but in an IncRNA-dependent manner. We propose that HDACs promote facultative heterochromatin by establishing alternative transcriptional silencing.


Diversification of human plasmacytoid predendritic cells in response to a single stimulus

_Nature Immunology_ : 19(1) : 63-75 : [DOI : 10.1038/s41590-017-0012-z](https://doi.org/10.1038/s41590-017-0012-z)

**Summary**

Innate immune cells adjust to microbial and inflammatory stimuli through a process termed environmental plasticity, which links a given individual stimulus to a unique activated state. Here, we report that activation of human plasmacytoid predendritic cells (pDCs) with a single microbial or cytokine stimulus triggers cell diversification into three stable subpopulations (P1-P3). P1-pDCs (PD-L1+CD80-) displayed a plasmacytoid morphology and specialization for type I interferon production. P3-pDCs (PD-L1-CD80+) adopted a dendritic morphology and adaptive immune functions. P2-pDCs (PD-L1+CD80+) displayed both innate and adaptive functions. Each subpopulation expressed a specific coding- and long-noncoding-RNA signature and was stable after secondary stimulation. P1-pDCs were detected in samples from patients with lupus or psoriasis. pDC diversification was independent of cell divisions or
preexisting heterogeneity within steady-state pDCs but was controlled by a TNF autocrine and/or paracrine communication loop. Our findings reveal a novel mechanism for diversity and division of labor in innate immune cells.

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**Native Elongating Transcript Sequencing reveals global anti-correlation between sense and antisense nascent transcription in fission yeast**

RNA : [DOI : 10.1261/rna.063446.117](https://doi.org/10.1261/rna.063446.117)

**Summary**

Antisense transcription can regulate sense gene expression. However, previous annotations of antisense transcription units have been based on detection of mature antisense long non-coding (aslnC)RNAs by RNA-Seq and/or micro-arrays, only giving a partial view of the antisense transcription landscape and incomplete molecular bases for antisense-mediated regulation. Here, we used Native Elongating Transcript sequencing to map genome-wide nascent antisense transcription in fission yeast. Strikingly, antisense transcription was detected for most protein-coding genes, correlating with low sense transcription, especially when overlapping the mRNA start site. RNA profiling revealed that the resulting aslncRNAs mainly correspond to cryptic Xrn1/Exo2-sensitive transcripts (XUTs). ChIP-Seq analyses showed that antisense (as)XUTs expression is associated with specific histone modifications patterns. Finally, we showed that asXUTs are controlled by the histone chaperone Spt6 and respond to meiosis induction, in both cases anti-correlating with levels of the paired-sense mRNAs, supporting physiological significance to antisense-mediated gene attenuation. Our work highlights that antisense transcription is much more extended than anticipated and might constitute an additional non-promoter determinant of gene regulation complexity.


**History, Discovery, and Classification of IncRNAs**


**Summary**

The RNA World Hypothesis suggests that prebiotic life revolved around RNA instead of DNA and proteins. Although modern cells have changed significantly in 4 billion years, RNA has maintained its central role in cell biology. Since the discovery of DNA at the end of the nineteenth century, RNA has been extensively studied. Many discoveries such as housekeeping RNAs (rRNA, tRNA, etc.) supported the messenger RNA model that is the pillar of the central dogma of molecular biology, which was first devised in the late 1950s. Thirty years later, the first regulatory non-coding RNAs (ncRNAs) were initially identified in bacteria.
and then in most eukaryotic organisms. A few long ncRNAs (IncRNAs) such as H19 and Xist were characterized in the pre-genomic era but remained exceptions until the early 2000s. Indeed, when the sequence of the human genome was published in 2001, studies showed that only about 1.2% encodes proteins, the rest being deemed “non-coding.” It was later shown that the genome is pervasively transcribed into many ncRNAs, but their functionality remained controversial. Since then, regulatory IncRNAs have been characterized in many species and were shown to be involved in processes such as development and pathologies, revealing a new layer of regulation in eukaryotic cells. This newly found focus on IncRNAs, together with the advent of high-throughput sequencing, was accompanied by the rapid discovery of many novel transcripts which were further characterized and classified according to specific transcript traits. In this review, we will discuss the many discoveries that led to the study of IncRNAs, from Friedrich Miescher’s “nuclein” in 1869 to the elucidation of the human genome and transcriptome in the early 2000s. We will then focus on the biological relevance during IncRNA evolution and describe their basic features as genes and transcripts. Finally, we will present a non-exhaustive catalogue of IncRNA classes, thus illustrating the vast complexity of eukaryotic transcriptomes.