Supplementary information S1. Roles of non-coding RNAs in regulating transcription and chromatin function.

The mounting evidence that nascent pre-mRNA interacts with many of the same chromatin regulators as long non-coding RNAs (lncRNAs) or enhancer RNAs (eRNAs)\(^1\)\(^-\)\(^6\) is beginning to blur the distinction between the roles these different RNA species have in the cell. However, the functionality of individual pre-mRNAs is limited by their relative low abundance and transitory nature. By contrast, ncRNAs can be retained in the nucleus and thus are more likely to have evolved specialised functions in the regulation of transcription and chromatin function:

- The high copy number of mature ncRNAs in the nucleus allows them to sequester proteins, for example the binding of positive transcription elongation factor b (P-TEFb) by the small nuclear RNA 7SK\(^7\)\(^,\)\(^8\), or to scaffold the formation of nuclear bodies such as paraspeckles around the lncRNA nuclear enriched abundant transcript 1 (NEAT1) (REF. 9).

- ncRNAs can remain stably tethered to chromatin, either in their nascent form — attached to stalled RNA polymerase II (Pol II) — or in their mature form through proteins such as heterogeneous nuclear ribonucleoprotein U (HNRNPU)\(^10\)\(^-\)\(^13\). Tethering could allow closer, more stable and more specialized regulatory functions on chromatin. ncRNAs may also become tethered to other nuclear structures, for example the interaction of the lncRNA X inactive specific transcript (Xist) with the lamin B receptor at the nuclear lamina\(^14\).

- Specialised sequences and structures have evolved in ncRNAs that enable interactions with specific proteins, for example the A repeat region in Xist, which binds SMART/HDAC1-associated repressor protein (SHARP)\(^15\)\(^,\)\(^16\), and the repeating RNA domain of the lncRNA functional intergenic repeating RNA element (Firre), which binds HNRNPU\(^11\).

- The shorter lengths of some ncRNAs may facilitate more rapid transcription than that of protein-coding genes. For example, transcription of eRNAs is induced before that
of their neighboring protein-coding genes\textsuperscript{17-19}, which may allow eRNAs to serve as the initial factor that recruits or antagonizes regulatory proteins.

References:


SUPPLEMENTARY INFORMATION

In format provided by Skalska, L. \textit{et al.} (doi:10.1038/nrm.2017.12)