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IN BRIEF

O TRANSCRIPTION

Unidirectional human promoters

Many mammalian genes are transcribed not only in the forward but also the reverse orientation; yet it is unclear what genetic elements and chromatin features mediate the initiation of such 'divergent' transcription. By mapping genome-wide transcription initiation in HeLa cells using 5'-GRO-seq. Duttke et al. identified multiple divergent promoter pairs that were associated with genes in the forward direction and with non-annotated regions in the reverse direction, and separated by nucleosome free regions (NFRs) of ~200 bp. In vitro transcription experiments revealed unidirectional transcription from reverse-direction start sites, which was driven by core promoters similar to but not overlapping those driving forward transcription. Importantly, genomic data analyses suggested that about half of HeLa NFR-associated promoters are unidirectional, and thus that divergent transcription is not a ubiquitous feature of mammalian promoters.

ORIGINAL RESEARCH PAPER Duttke, S. H. C. et al. Human promoters are intrinsically directional. Mol. Cell 57, 1–11 (2015)

CHROMATIN

ZNF143 in the loop

Chromatin interactions (looping) between promoters and distal regulatory elements depend on DNA binding by transcription factors. Bailey et al. set out to identify chromatin-looping factors by comparing human genome-wide binding profiles of >70 transcription factors and found that zinc finger protein 143 (ZNF143) binds directly to RNA polymerase II-bound promoters and indirectly to CTCF- and cohesin complex-bound enhancers. Chromatin conformation capture data revealed that ZNF143 preferentially binds regions of chromatin interactions between promoters and distal elements, including those that are lineage- and cell type-specific. Depleting ZNF143 decreased the interactions between two examined genes and their distal elements, and resulted in reduced expression. Furthermore, allelic variations (SNPs) affecting ZNF143 binding were found to modify its chromatin interactions. Thus, ZNF143 binding at promoters is required for chromatin looping with distal regulatory elements.

ORIGINAL RESEARCH PAPER Bailey, S. D. et al. ZNF143 provides sequence specificity to secure chromatin interactions at gene promoters. Nature Commun. 6, 6186 (2015)

O GENE EXPRESSION

DYRK1A targets Pol II

Dual-specific tyrosine-regulated kinase 1A (DYRK1A) has key roles in developmental processes and tissue homeostasis, and its dysregulation has been associated with human pathologies. Although DYRK1A is present in the nucleus and cytoplasm, its role in the nuclear compartment was elusive. Now, Di Vona *et al.* show that DYRK1A is recruited to the promoters of growth-related genes that are actively transcribed by RNA polymerase II (Pol II). Promoter sequences bound by this kinase are characterized by a conserved palindromic motif. Moreover, DYRK1A interacted with and phosphorylated the Pol II carboxy-terminal domain (CTD) at Ser2 and Ser5, and its depletion decreased the association of Pol II with target promoters. Thus, DYRK1A regulates transcription by phosphorylating the CTD at residues necessary for transcriptional elongation.

ORIGINAL RESEARCH PAPER Di Vona, C. et al. Chromatin-wide profiling of DYRK1A reveals a role as a gene-specific RNA polymerase II CTD kinase. *Mol. Cell* <u>http://dx.doi.org/10.1016/j.molcel.2014.12.026</u> (2015)