

# Recent Trends in Eukaryotic Transcription: Crucial Role of Gene Architecture in Transcriptional Regulation

## Editorial

The Human Genome Project has identified more than 25,000 genes in our cells. Not all of these genes are expressed at the same time or in every cell of our body. A fundamental question in gene expression is how the coordinated expression of genes is achieved during growth, development and homeostasis. The expression of genetic information is regulated to a great extent at the level of transcription. In eukaryotes, RNA polymerase II is the main transcription enzyme, which transcribes protein coding genes and a number of non-coding RNAs. The transcription by RNA polymerase II is regulated by cis-acting DNA elements and trans-acting accessory protein factors. The enhancer, promoter and terminator are the most important DNA elements required for transcription by RNA polymerase II, while accessory protein factors include gene-specific transcription factors, the general transcription factors and termination factors. The generally accepted view is that the factors occupying the promoter region play a dedicated role in initiation of transcription and those operating at the terminator end are exclusively required for the termination step of transcription. The research in my and other laboratories has challenged this dogma.

Genomewide analysis has revealed that a number of general transcription factors and termination factors crosslink to both the 5' and the 3' ends of genes. We demonstrated that TFIIB, TFIIF and the coactivator Mediator complex, which are essential for initiation of transcription, do not merely localize at the 3' end of genes, but also play a role in termination of transcription [1-3]. Further research in other laboratories revealed that the function of TFIIB as a termination factor is evolutionarily conserved, occurring in yeast, mammalian systems and flies [4,5]. Similarly, the termination complexes have been found occupying both ends of genes in almost every eukaryotic system that has been investigated so far. The termination factors play a critical role in enhancing promoter directionality, which is favoring promoter-initiated transcription to proceed in the sense direction producing mRNA, while suppressing the transcription of non-coding uaRNA in the upstream anti-sense direction [6-9]. The importance of termination factors in conferring promoter directionality is now well established across eukaryotic taxa.

The next question is how the initiation and termination factors are recruited at both the ends of a gene. Research in my laboratory shows that the promoter and terminator regions of a gene are juxtaposed during transcription resulting in the formation of a gene loop [10,11]. Such gene loops are formed due to protein-protein interactions of the factors occupying the distal ends of a gene, and have been observed during transcription in yeast, humans, flies and plants [5,12-14]. The physical proximity of the promoter and terminator regions in the



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gene loop allows the initiation factors to contact the 3' end of the gene and affect termination, and termination factors to interact with the 5' end of the gene and affect promoter directionality. Gene loops also enhance transcription by coupling termination to reinitiation [8].

Apart from promoter-terminator gene loops that have been well characterized in yeast, higher eukaryotes exhibit another type of loop, the enhancer-promoter loop, which also plays a critical role in transcriptional regulation [15]. These observations unequivocally demonstrate that apart from DNA sequence elements and accessory protein factors, gene architecture also plays a vital role in transcriptional regulation in eukaryotes.

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