Transcription bodies regulate transcription by sequestering transcription machinery

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Transcription does not occur diffusely in the nucleus but is highly organized in sub-nuclear structures called transcription bodies[1]. While intensely studied, it is unclear whether such bodies have a function in transcription regulation.

In conventional models, hundreds of such transcription bodies form. These are difficult to observe and practically impossible to perturb for functional study[2]. During zebrafish Zygotic Genome Activation (ZGA), on the other side, two prominent transcription bodies emerge from one of the most expressed genomic loci, namely the *mir430* locus[3,4]. Importantly, by deleting this locus, we can specifically disrupt the formation of these bodies. This provides us with an excellent system to study the function of transcription bodies.

We found that the specific disruption of transcription bodies results in downregulation of hundreds of genes, providing experimental support for a model in which transcription bodies increase the efficiency of transcription. However, even more genes were found to be upregulated, counter to the suggested stimulatory effect of transcription bodies.

These upregulated genes have accessible chromatin and are poised to be transcribed in the presence of the two transcription bodies, but they do not go into elongation. Live-cell imaging showed that the disruption of the two large transcription bodies enables these poised genes to be transcribed in ectopic transcription bodies, suggesting that the large transcription bodies sequester a pause release factor.

A prediction of this model is that the overexpression of such a sequestered factor would phenocopy the removal of the two large transcription bodies. Indeed, the overexpression of CDK9 – which is enriched in the two large transcription bodies – in wild type embryos led to an increased number of ectopic transcription bodies in wild type nuclei.

Taken together, our results show that transcription bodies regulate transcription genome-wide: the sequestration of transcriptional machinery creates a favourable environment for transcription locally, while depriving genes elsewhere in the nucleus from the same machinery.

References

1. Sutherland, H. & Bickmore, W. A. Transcription factories: Gene expression in unions? *Nat. Rev. Genet.* **10**, 457–466 (2009).
2. Cisse, I. I. *et al.* Real-time dynamics of RNA polymerase II clustering in live human cells. *Science* **341**, 664–667 (2013).
3. Chan, S. H. *et al.* Brd4 and P300 Confer Transcriptional Competency during Zygotic Genome Activation. *Dev. Cell* **49**, 867–881 (2019).
4. Hadzhiev, Y. *et al.* A cell cycle-coordinated Polymerase II transcription compartment encompasses gene expression before global genome activation. *Nat. Commun.* **10**, 691 (2019).