

NON-CODING RNA

Circular RNAs promote transcription

Exon-derived circular RNAs (circRNAs) are abundant in animal cells; the cell-specific expression of many of them suggests that they have regulatory roles, but these roles are largely unknown. Li *et al.* have now identified circRNAs that contain introns and that regulate gene transcription in *cis* by forming specific interactions with the U1 small nuclear ribonucleoprotein RNA (snRNA).

To examine whether circRNAs are involved in transcription regulation, the authors isolated non-coding RNAs from human cells that were crosslinked to and immunoprecipitated with RNA polymerase II (Pol II). Out of 111 Pol II-interacting circRNAs, 15 were further validated to be circular and to contain introns between the circularized exons; they were therefore named exon–intron circRNAs (EiCiRNAs). Two circRNAs,

EiCiEIF3J and EiCiPAIP2, were investigated in detail; depleting them decreased the transcription levels of the corresponding *EIF3J* or *PAIP2* genes. Furthermore, RNA–DNA double fluorescence *in situ* hybridization (FISH) revealed that EiCiEIF3J and EiCiPAIP2 colocalize with *EIF3J* and *PAIP2*, respectively, but not with flanking genes, suggesting that they regulate the transcription of their parental genes in *cis* (although they might also affect other loci in *trans*).

Next, the authors found that EiCiEIF3J and EiCiPAIP2 co-precipitated with the U1 snRNA and proteins (U1 snRNPs; a pre-mRNA maturation complex), and with the promoters of the parental genes. Moreover, EiCiEIF3J and EiCiPAIP2 each have one potential U1 snRNA-binding site at their retained introns, and sterically blocking them with

antisense molecules decreased the interactions of the EiCiRNAs with U1 snRNA and Pol II, the binding of these factors to the *EIF3J* and *PAIP2* promoters, and the transcription of the parental genes.

In summary, the interactions between U1 snRNA and the U1-binding sites of EiCiEIF3J and EiCiPAIP2 promote the transcription of *EIF3J* and *PAIP2*, respectively. There is evidence that generating circRNAs might compete with pre-mRNA maturation, but once produced, EiCiRNAs could establish positive feedback loops for their own expression as well as for that of their parental genes.

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Exon–intron circular RNAs regulate transcription in the nucleus. *Nature Struct. Mol. Biol.* <http://dx.doi.org/10.1038/nsmb.2959> (2015)

“the interactions between U1 snRNA and ... EiCiEIF3J and EiCiPAIP2 promote the transcription of *EIF3J* and *PAIP2*”

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