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NON-CODING RNAS

A new member of the family

Since their discovery, non-coding RNAs have been in the spotlight owing to their key roles in the regulation of gene expression. Now, Chen and colleagues identify a new member of the non-coding RNA family: long non-coding RNAs that are flanked by small nucleolar RNA sequences (sno-lncRNAs).

The authors identified a group of intron-derived lncRNAs, the ends of which corresponded to intronic snoRNAs (which have roles in rRNA modification and alternative splicing, among others). These sno-lncRNAs were expressed by many cell types, in particular pluripotent cells, and the most abundant sno-lncRNAs were those from chromosomal region 15q11–q13. The 15q11–q13 sno-lncRNAs had the characteristic snoRNA C/D boxes, which are known to facilitate association with proteins from snoRNP complexes. Consistent with this, C/D boxes of 15q11–q13 sno-lncRNAs co-immunoprecipitated with the snoRNP proteins fibrillarin and 15.5K. Importantly, deletion of the C/D boxes revealed that these motifs have crucial roles in processing and stabilization and are thus necessary for sno-lncRNA biogenesis. On the basis of their findings, Chen and colleagues propose that sno-lncRNAs arise when introns carrying snoRNAs on their ends are processed without removing their internal sequence. This could give rise to linear RNAs that are flanked by snoRNAs or to circular molecules that resemble snoRNP structures.

Next, the authors investigated the localization of sno-lncRNAs. Focusing on 15q11–q13 sno-lncRNAs, they found that these localized in the nucleus, but, unlike C/D box-containing snoRNAs, they did not accumulate in nucleoli or Cajal bodies. Instead, they associated with the genomic region from which they were transcribed; however, it is also possible that they localize in previously undescribed subnuclear structures.

So what is the function of sno-lncRNAs? Many lncRNAs regulate gene expression; however, knockdown of 15q11–q13 sno-lncRNAs had little effect on the expression of the 15q11–q13 locus *SNURF–SNRPN* and only affected a very small number of genes from other genomic regions. Instead, the authors observed that 15q11–q13 sno-lncRNAs associated directly with the alternative splicing regulator FOX2, and knockdown of sno-lncRNAs led to changes in FOX2-regulated splicing.

The authors hypothesize that these sno-lncRNAs sequester FOX2, which leads to small changes in FOX2-regulated splicing, similarly to other lncRNAs functioning as 'molecular sinks'. Interestingly, loss of snoRNAs from 15q11–q13 is linked to Prader–Willi syndrome, so understanding the function of sno-lncRNAs might offer insights into the pathogenesis of this disease.

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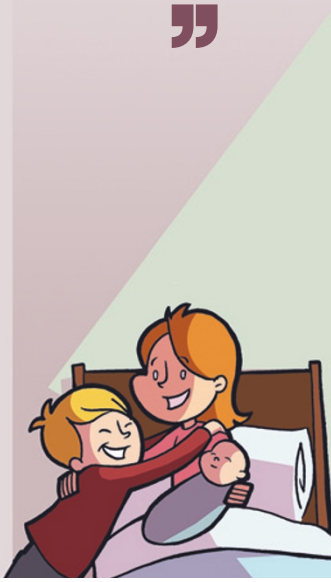
ORIGINAL RESEARCH PAPER Yin, Q.-F. *et al.* Long noncoding RNAs with snoRNA ends. *Mol. Cell* 5 Sep 2012 (doi:10.1016/j.molcel.2012.07.033)

> "knockdown of sno-lncRNAs led to changes in FOX2-regulated splicing"



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