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Abstract:

Although the functions of most of circular RNAs (circRNAs) are not characterized, they likely impact many biological processes. Indeed, in addition to generating a linear transcript many protein-coding genes produce circRNAs.

By applying original strategies on seven Total-RNA-seq datasets from testis sampled during the puberty, we detected 126 introns in 114 genes able to produce circRNAs and 5,236 exonic circRNAs produced by 2,516 genes. Comparing our RNA-seq datasets to datasets from the literature (embryonic cortex and postnatal muscle stages) revealed highly abundant intronic and exonic circRNAs in one sample each in pubertal testis and embryonic cortex, respectively. In pubertal testis with circRNAs in abundance, 24% of protein-coding genes produced linear and circular transcripts. This abundance was due to higher production of circRNA by the same genes in comparison to other testis samples, rather than the recruitment of new genes. By comparing the total-RNA-seq and mRNA-seq data, we found no global relationship between exonic circRNA and mRNA productions in pubertal testis. In the list of genes with significant expression of linear transcripts, we found 84% of genes identified as able to produce ExoCirc-RNAs. The genes able to produce circRNA + mRNA were significantly longer than the genes that only produced mRNAs. So, we showed that exonic circRNAs are typically produced by large genes that are also able to produce mRNAs

Among the 5,236 ExoCirc-RNAs, we noted the presence of 213 single-exon circRNAs and we showed that exons capable of constituting these single-exon circRNAs are significantly longer than those that can only be included in multi-exon circRNAs.

We chose to only retain multi-exon circRNAs (5,023) to study the proximal environment of each exon involved in a circular junction. We identified single exons involved in the circular junctions of multi-exon circRNAs that we named ‘extreme exons’. For each extreme exon, we identified the two proximal exons (internal and external) and the two proximal introns. The comparison of pairs [extreme exon - external exon] showed that extreme exons are significantly smaller than their external exon counterparts. The comparison of pairs [internal intron - external intron] showed that external introns are significantly longer than internal introns. Ragan et al. (2019) showed that these features probably create preconditions for circRNA production by promoting looping interactions between flanking introns.

Our data indicate that the production of circRNAs is mainly related to the structure of genes generating circRNAs.

Ragan C, et al. Insights into the biogenesis and potential functions of exonic circular RNA. Scientific reports 2019;9(1):2048.