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Genomic location and biogenesis of intronic microRNA

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The majority of microRNA (miRNA) loci are located within intronic regions and they are transcribed by RNA polymerase II as part of their hosting transcription units. The primary transcripts are cleaved by Drosha to release ~70 nt pre-miRNAs that are subsequently processed by Dicer to generate mature ~22 nt miRNAs. It is generally believed that intronic miRNAs are released by Drosha from spliced introns after the splicing reaction has occurred. However, our database searches and experiments indicate that intronic miRNAs are processed from unspliced intronic regions prior to splicing catalysis. Interestingly, cleavage of an intron by Drosha does not significantly affect the production of spliced mRNA, indicating that a continuous intron may not be required for splicing and that the exons may be tethered to each other by the splicing commitment complex. Hence, Drosha may cleave intronic miRNAs between the splicing commitment step and the splicing catalysis step, thereby ensuring both miRNA biogenesis and protein synthesis from a single primary transcript. Our study provides a novel example of eukaryotic gene organization and RNA processing control.