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Posttranscriptional Regulation of miRNAs Harboring Conserved Terminal Loops

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SUMMARY

We recently found that hnRNP A1, a protein implicated in many aspects of RNA processing, acts as an auxiliary factor for the Drosha-mediated processing of a microRNA precursor, pri-miR-18a. Here, we provide the mechanism by which hnRNP A1 regulates this event. We show that hnRNP A1 binds to the loop of pri-miR-18a and induces a relaxation at the stem, creating a more favorable cleavage site for Drosha. We found that approximately 14% of all pri-miRNAs have highly conserved loops, which we predict act as landing pads for *trans*-acting factors influencing miRNA processing. In agreement, we show that 2'-O-methyl oligonucleotides targeting conserved loops (LooptomiRs) abolish miRNA processing *in vitro*. Furthermore, we present evidence to support an essential role of conserved loops for pri-miRNA processing. Altogether, these data suggest the existence of auxiliary factors for the processing of specific miRNAs, revealing an additional level of complexity for the regulation of miRNA biogenesis.

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