MICRORNA

Microprocessor measures up

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URLs
Drosha
http://ca.expasy.org/uniprot/Q9NRR4

DGCR8
http://ca.expasy.org/uniprot/Q8WYQ5

The biogenesis of microRNAs (miRNAs) involves the cropping of primary miRNA (pri-miRNAs) transcripts to produce precursor miRNAs (pre-miRNAs), which are subsequently cleaved to generate the mature miRNA. The cropping step requires the Drosha–DGCR8 complex, which is also known as Microprocessor. Kim and colleagues now shed light on some of the structural features of pri-miRNAs that ensure that Microprocessor releases the correct pre-miRNAs.

To obtain insights into the common structural features of pri-miRNAs, Kim and co-workers analysed the thermodynamic stability of each nucleotide in human and fly pri-miRNAs. They concluded that pri-miRNAs consist of an imperfect stem structure of ~3 helical turns with unstable segments at both ends. The overall structure comprises a terminal loop, upper stem, lower stem and flanking basal segments.

Kim and colleagues then carried out a systematic mutagenesis analysis to examine the significance of each of these structural parts. Whereas the terminal loop was not important for cleavage-site selection, the basal segments, specifically the distance from the single-stranded RNA (ssRNA) basal segments to the cleavage site in the double-stranded RNA (dsRNA) stem, were crucial.

The authors hypothesized that Microprocessor recognizes the single-stranded basal segments, and can therefore measure the distance from the ssRNA–dsRNA junction to the cleavage site. Biochemical approaches indeed showed that the DGCR8 subunit interacts specifically with pri-miRNAs, and that the basal segments are crucial for DGCR8 binding.

They then confirmed these findings using artificial pri-miRNA substrates that consisted of a simple 'ssRNA-tail–3-helical-turns–ssRNA-tail' structure that had no sequence homology to any known pri-miRNAs. Cleavage by Microprocessor occurred ~11 base pairs from the ssRNA–dsRNA cleavage junction, as occurs for natural pri-miRNAs, and artificial substrates that lacked the ssRNA tails did not bind to DGCR8.

Kim and co-workers therefore propose that DGCR8 functions as a molecular anchor that allows the distance from the ssRNA–dsRNA junction to be measured, and ensures accurate pri-miRNA cleavage by Microprocessor.

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ORIGINAL RESEARCH PAPER Han, J. *et al.* Molecular basis for the recognition of primary microRNAs by the Drosha–DGCR8 complex. *Cell* **125**, 887–901 (2006)
FURTHER READING Kim, V. N. MicroRNA biogenesis: coordinated cropping and dicing. *Nature Rev. Mol. Cell Biol.* **6**, 376–385 (2005)