Intriguingly, seven out of the eight components of dREAM were found to be related to the *Caenorhabditis elegans* synMuv class-B gene products, which are important for the development of the worm's male and female reproductive systems. Brehm, Dyson and colleagues propose that synMuv class-B proteins form a complex that, like dREAM, represses sex-related gene targets and so controls the worm's sexual development. So, the evolutionary conservation of pRb-specific repressor complexes is extensive and the authors predict that 'dREAM-like' complexes might also exist in mammals.

Arianne Heinrichs

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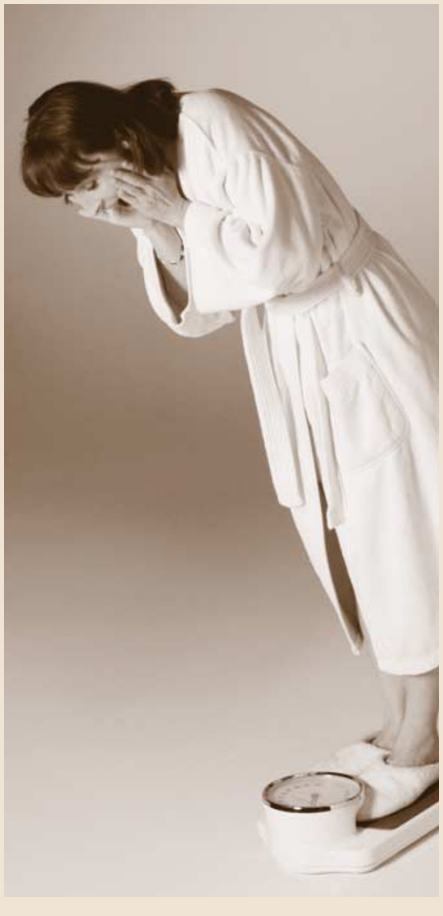


MICRORNA

Big secrets of a small world

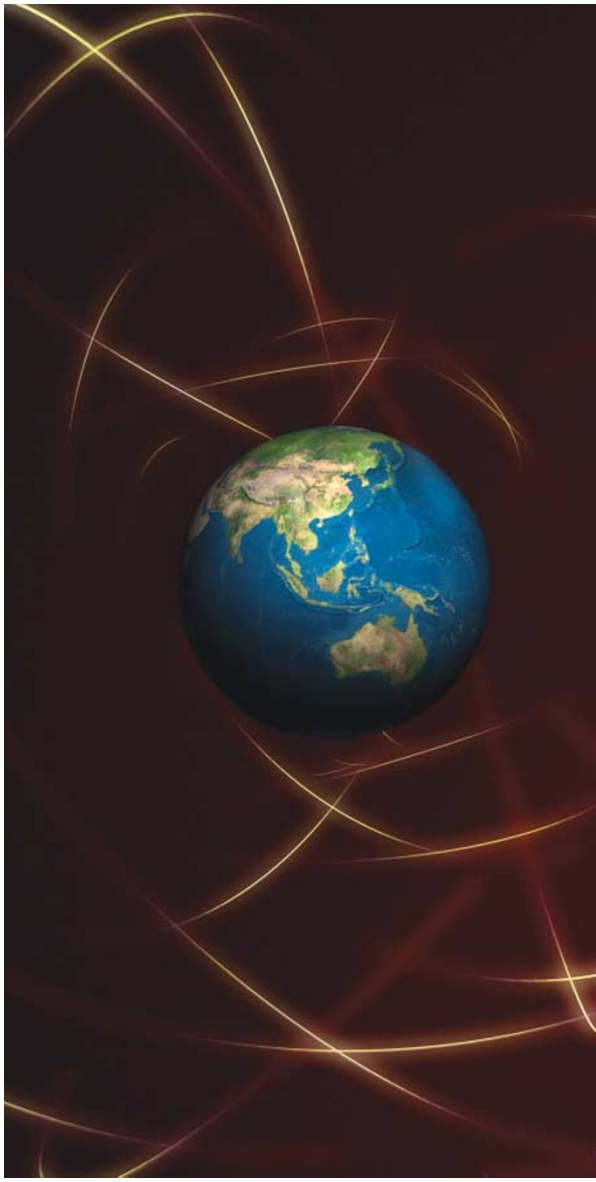
Micro (mi)RNAs are ~22-nt RNA molecules that inhibit the translation or induce the degradation of protein-coding mRNAs in plants and animals. Over the past decade, it has become clear that these small RNAs have important regulatory roles in fundamental cellular processes but, so far, it has been unclear how the expression of miRNA genes is controlled and which polymerase enzyme is responsible for transcribing these genes. Now, reporting in *The EMBO Journal*, V. Narry Kim and colleagues provide evidence that the miRNA genes are transcribed by RNA polymerase II (Pol II).

To find out more about miRNA transcription, the authors asked whether the primary transcripts of the miRNAs (pri-miRNAs) had 5′ methylguanosine caps and poly(A) tails — modifications that are trademarks of Pol-II transcription. First, they affinity purified cap-containing RNA from HeLa cells using glutathione *S*-transferase (GST)-immobilized cap-binding protein eIF4E and analysed the bound RNA by PCR after reverse transcription of RNA (RT-PCR). Of each tested pri-miRNA, 5–50% was bound by the GST–eIF4E column, indicating the presence of a cap modification. Similarly, oligo-dT cellulose beads were used to bind to RNA from HeLa cells that contained poly(A) tails, and the bound RNA was extracted and analysed by RT-PCR. Once again, all of the pri-miRNAs were represented in the polyadenylated-RNA fraction. So, primary transcripts of miRNAs are 'topped' and 'tailed' like their pre-mRNA counterparts, which indicates that they are transcribed by Pol II.

Another characteristic of Pol-II transcription is its inhibition by low doses of α-amantin and, when HeLa cells were treated with this peptide, the level of all the pri-miRNAs was reduced.

V. Narry Kim and co-workers then used a range of molecular techniques to define the promoter, the transcription-initiation site and the polyadenylation signal of an miRNA gene, *miR-23a~27a~24-2* (*miR-23a*). Furthermore, a reporter construct comprising the putative *miR-23a* promoter fused to a luciferase gene was transfected into a human cell line. This fusion construct was transcriptionally active and, importantly, luciferase activity was inhibited by α-amantin, which indicated that transcription of the *miR-23a* promoter was Pol-II dependent. Finally, chromatin immunoprecipitation, using antibodies that were directed against Pol II, confirmed that the enzyme did indeed bind to the promoter of an endogenous *miR-23a* gene.

This study presents evidence that miRNAs are transcribed by Pol II. But the affinity-purification



experiments revealed that a large proportion of a given pri-miRNA does not contain a 5′ cap or a poly(A) tail. Also, a detailed analysis of the promoter of the *miRNA-23a* gene did not detect the DNA elements that are common to most Pol-II promoters — such as the TATA box or the TFIIB recognition elements. So, further analysis of other miRNA genes will be necessary to understand miRNA promoters and their mechanisms of transcription. It seems as if the world of small RNAs still has many secrets to reveal.

Shannon Amoils

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WEB SITE

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