CIRCADIAN RHYTHMS

Timing with miRNAs

Circadian rhythms such as the locomotor activity rhythm are regulated by changes in gene transcription; however, little is known about the role of post-transcriptional mechanisms. Kadener *et al.* identify candidate microRNAs (miRNAs) that influence circadian rhythmicity and show that in *Drosophila melanogaster* the miRNA bantam regulates the translation of the core clock protein CLK.

miRNAs suppress protein translation by binding to the 3′ untranslated region (UTR) of target mRNAs and by forming a silencing complex with other factors including, in *D. melanogaster,* the protein AGO1. Immunoprecipitation experiments showed that several mRNAs, including that encoding the core clock component CLK, were bound to AGO1-containing complexes in *D. melanogaster* head extracts. In cultured S2 cells in which the luciferase gene was placed under the control of the 3′ UTR of *Clk*, luciferase levels were increased when RNA silencing was inhibited, suggesting that *Clk* mRNA translation is regulated by miRNAs.

Overexpression of one of the miRNAs identified as potential regulators of circadian rhythms, bantam, in circadian pacemaker cells lengthened the circadian cycle of flies. To test the importance of the three bantam-binding sites that the authors identified in the 3′ UTR of *Clk* for *in vivo* circadian rhythmicity, either wild-type *Clk* transgenes or *Clk* transgenes lacking the three bantam sites in the 3′ UTR were introduced into a *Clk*-deficient fly strain. Only the wild-type transgene was able to rescue the arrhythmic behaviour of the *Clk*-deficient flies. These results indicate that bantam regulates *Clk* mRNA translation and is required for normal circadian rhythmicity.

Here, the authors demonstrate a role for miRNAs in the regulation of circadian locomotion activity. As the bantam-binding sites in *Clk* are evolutionarily conserved, this study suggests that similar mechanisms might also act in other species.

Claudia Wiedemann

ORIGINAL RESEARCH PAPER Kadener, S. *et al.* A role for microRNAs in the *Drosophila* circadian clock. *Genes Dev.* 20 Aug 2009 (doi:10.1101/gad.1819509)