Nature Reviews Genetics | AOP, published online 22 January 2013; doi:10.1038/nrg3429

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The circadian clock is a molecular oscillator that regulates the transcription of genes within a 24-hour period to coordinate physiological processes. In a new paper, the authors identify a further level of regulation by the clock at the level of ribosome biogenesis and hence a mechanism by which global translation is regulated.

While studying rhythmic transcription patterns in mouse livers, Jouffe *et al.* observed rhythmic expression of many of the components required for translation initiation, such as eukaryotic translation initiation factor 4E (EIF4E) and EIF4E binding protein (EIF4EBP). Further investigation into the diurnal regulation of these proteins revealed oscillating phosphorylation patterns that result in conditions that are suitable for translation initiation peaking during the night, when rodents are active and consume food. The authors then showed that transcripts of components from the target of rapamycin (TOR) and ERK/MAPK (mitogen-activated protein kinase) cell signalling pathways, which regulate these phosphorylation patterns, are regulated by the circadian clock. That is, the regulated cell signalling activities mediate the diurnal changes in phosphorylation that regulate the activation of the translation initiation complex.

Because the activity of translation initiation factors was shown to be rhythmic, the authors then investigated whether translation itself was rhythmic. They found the relative amount of the purified polysomal RNA fraction (containing mostly actively translated mRNAs) was rhythmic. Comparing these polysomal mRNAs with the full cytosolic pool of mRNAs using microarrays showed that for ~2% of transcripts, rhythmic translation could not be explained by rhythmic alteration in mRNA levels. Most of these transcripts belonged to the 5′ terminal oligonucleotide tract family, which is involved in translation: many are ribosomal proteins or regulate translation elongation. The effects of this rhythmic translation on ribosome proteins was observable in the diurnal abundance of these proteins in the cytosolic fraction depleted of ribosomes. A limited diurnal expression of the ribosomal protein mRNAs was also observed.

Further investigation as to whether components of the ribosome in addition to the ribosomal proteins are rhythmically regulated revealed that the transcription of upstream binding factor (*Upf*), which regulates the expression of ribosomal RNAs, is under the control of the circadian clock. The dependence of the oscillation of ribosomal RNAs on the clock was confirmed in knockout mice for the circadian clock regulators *Cry1/Cry2* and *Bmal1* (also known as *Arntl*). This clock dependence was also confirmed in these mouse models for the oscillation of other mRNAs and proteins (such as the translation initiation factors) identified by the authors.

The authors' findings show that the circadian clock coordinates the regulation of the biogenesis of ribosomes at the level of transcription and translation, allowing this energy-consuming process to occur only during the dark, when feeding occurs. It will be interesting to see whether other fundamental cellular processes are directly coordinated by the circadian clock.

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ORIGINAL RESEARCH PAPER Jouffe, C. *et al.* The circadian clock coordinates ribosome biogenesis. *PLoS Biol.* **11**, e1001455 (2013)

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