HIGHLIGHTS

CIRCADIAN RHYTHMS

Pyramid of time

Oligonucleotide microarrays continue to have an impact on neuroscience research. Their latest incursion has taken place in the realm of circadian rhythms, a field that is repeatedly proclaimed as a beacon in the search for the genetic basis of behaviour. Rhythmicity depends on the circadian oscillation of several gene products that coordinate a cycling transcriptional programme. Several cycling genes have been identified, and significant advances in circadian biology have come from their study, particularly in *Drosophila*. But are there more genes that show rhythmic oscillations, or have we already exhausted the circadian mine? The results of a microarray analysis performed by McDonald and Rosbash indicate that many jewels are still left to be unearthed.

The authors used microarrays to compare gene expression in *Drosophila* heads at different time points, and identified more than 100 genes that showed circadian oscillations. Some of them corresponded to well-characterized circadian genes that form the core of the cycling transcriptional programme — *clock*, *period*, *timeless* — but many more were genes for which oscillations had not been detected before. The list included genes relevant to functions as varied as detoxification, olfaction, neuropeptide signalling, nutritional state and immunity.

If so many physiological processes show circadian rhythmicity, how are their cycles integrated? McDonald and Rosbash performed two experiments that have a bearing on this question. First, they repeated their microarray analysis using flies lacking the transcriptional activator *clock*, and discovered that no genes at all oscillated in these mutants. Second, they used a cell line in which *clock* expression could be induced, but only its primary targets were subsequently activated. They found that less than 10 genes were under the direct control of *clock*, some of which were also transcription factors. We can therefore imagine the circadian control of a range of physiological properties as a pyramid, in which *clock* sits at the top, interacting directly with only a handful of transcription factors and other gene products. These genes might subsequently orchestrate a transcriptional cascade that could spread to the wide variety of genes identified in this study.

Last, as the study of circadian rhythms in organs other than the brain has recently flourished, the finding that *clock* is at the top of the hierarchy, and might be the only circadian master regulator in *Drosophila*, should help us to integrate the analysis of rhythmicity across the whole organism in this and other species.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER McDonald, M. J. & Rosbash, M. Microarray analysis and organization of circadian gene expression in *Drosophila*. *Cell* 24 October 2001 (10.1016/S0092867401005451)

FURTHER READING Young, M. W. & Kay, S. A. Time zones: a comparative genetics of circadian clocks. *Nature Rev. Genet.* **2**, 702–715 (2001) | Mirnics, K. Microarrays in brain research: the good, the bad and the ugly. *Nature Rev. Neurosci.* **2**, 444–447 (2001)

ENCYCLOPEDIA OF LIFE SCIENCES circadian rhythms