

BEHAVIOURAL GENETICS

Beyond the body clock

Two recent papers reveal new roles for genetic components of the *Drosophila melanogaster* body clock, indicating that these genes have diverse biological functions.

period (*per*) is crucial for regulating circadian rhythms in flies, and its expression requires CREB (cAMP-responsive element-binding protein), a transcription factor that is also essential for long-term memory (LTM). But does *per* also function downstream of CREB in LTM?

Sakai *et al.* addressed this question using a courtship assay to analyse the roles of *per* and *CREB*. A virgin male fly will try to copulate with a female who has already mated, but his advances will be rejected. After a while, he learns to court her less, and if the exposure time is long enough, LTM will be established.

The authors first showed that *CREB* is required for LTM in this assay. A form of *CREB* that has a repressive rather than an activating effect blocked the ability of the male to establish LTM. Mutation of *per* had a similar effect, whereas its overexpression enhanced LTM by reducing the exposure period needed.

As expected, *per* was found to act downstream of *CREB* in LTM, as overexpressing the repressive form of *CREB* had no effect on the enhanced LTM produced by *per* overexpression. Interestingly, the role of *per* in LTM seems to be independent of its function in generating circadian rhythms, as mutations in other key circadian genes had no effect on LTM.

In a second paper, Tsai and colleagues used a collection of *P*-element

insertion lines to identify genes that are involved in cocaine responsiveness. One line with increased sensitivity contained an insertion in *Lmo*, a member of a family of genes with roles in neuronal development. The authors showed that one site of *Lmo* expression is in the ventral lateral neurons (LN_vs) — pacemaker cells that are essential for circadian rhythmicity in flies. Moreover, ectopic expression of wild-type *Lmo* in these cells was sufficient to rescue normal cocaine responsiveness in *Lmo* mutants.

So, is *Lmo* required for circadian activity and is this connected to the response to cocaine? The answer to the first question is 'yes', as circadian locomotor rhythms were disrupted in *Lmo* mutants. However, this was found to be independent of the role of *Lmo* in the cocaine response, which remains unaltered throughout the circadian cycle.

These studies reveal pleiotropic effects for genes that are involved in circadian rhythms, and this might well extend to other species. Unravelling the different molecular pathways that are involved in the distinct functions of these genes should prove an exciting direction for future work.

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References and links

ORIGINAL RESEARCH PAPERS

Sakai, T. *et al.* A clock gene, *period*, plays a key role in long-term memory formation in *Drosophila*. *Proc. Natl Acad. Sci. USA* **101**, 16058–16063 (2004) | Tsai, L. T.-Y. *et al.* *Lmo* mutants reveal a novel role for circadian pacemaker neurons in cocaine-induced behaviors. *PLoS Biol.* 23 November 2004 (doi:10.1371/journal.pbio.0020408)

WEB SITE

Ulrike Heberlein's laboratory:
<http://www.egc.org/pis/heberlein-c.htm>

IN BRIEF

GENOME BIOLOGY

A transcriptomic analysis of the phylum Nematoda.

Parkinson, J. *et al.* *Nature Genet.* **36**, 1259–1267 (2004)

Although an incredible amount of information is available for *Caenorhabditis elegans*, little is known about the other members of the diverse phylum to which this worm belongs. Parkinson and colleagues have now created >250,000 ESTs and used them to type the transcriptional diversity of 30 nematode species, including many parasites. More than half the >90,000 genes studied were found only in nematodes, and the authors identified tens of thousands of potential targets for drug and vaccine development.

EVOLUTION

Ciliary photoreceptors with a vertebrate-type opsin in an invertebrate brain.

Arendt, D. *et al.* *Science* **306**, 869–871 (2004)

Invertebrates predominantly use rhabdomeric photoreceptors (PRs) for vision, whereas vertebrates use ciliary receptors. The marine ragworm *Platynereis dumerilii* has rhabdomeric cells in its eyes but, as this work has found, has ciliary PRs in the brain. These 'deep brain' ciliary PRs express an opsin photopigment that is orthologous to vertebrate ciliary opsins. The authors suggest that deep brain PRs are involved in the control of photoperiodicity, and they reevaluate the evolution of PR cells since the last common ancestor of vertebrates and invertebrates.

GENOME BIOLOGY

Global identification of human transcribed sequences with genome tiling arrays.

Bertone, P. *et al.* *Science* 11 November 2004 (doi:10.1126/science.1103388)

The large size of the mammalian genome presents a special obstacle to a comprehensive investigation of coding sequences, but Bertone *et al.* have now produced a draft expression map for the entire human genome using high-density microarrays that contain more than 51 million oligonucleotide probes and representing ~1.5 Gb of non-repetitive genomic DNA. The authors identified more than 10,000 novel transcribed regions, revealing a more extensive and diverse set of expressed sequences than previously annotated, and were able to confirm that many of the genes predicted by sequencing projects are indeed transcribed.

GENE MAPPING

A single nucleotide polymorphism tagging set for human drug metabolism and transport.

Ahmadi, K. R. *et al.* *Nature Genet.* 19 December 2004 (doi:10.1038/ng1488)

David Goldstein and colleagues have genotyped 750 SNPs in European and Japanese populations to identify sets of SNPs — 'tagging' SNPs (tSNPs) — that are associated with variation in the metabolism and transport of medicines. The researchers have also used their dataset to investigate the use of tSNPs in linkage disequilibrium mapping studies, such as how many tSNPs are needed for sets to work in more than one population.

