NEUROGENETICS

Mutant mice abhor a vacuum

A genetic study of a family of transcription factors has thrown up a surprising link between circadian genes and epilepsy, thanks to some knockout transgenic mice and the fortuitous involvement of a vacuum cleaner.

The PAR bZip protein family consists of three transcription factors — DBP, HLF and TEF — that fluctuate in expression according to a daily rhythm. To assign a physiological role to this small protein family in mice, Ueli Schibler and colleagues knocked out the three corresponding genes one at a time and in combination. Single, double and triple knockout animals were normal and fertile, although the triple knockout animals died prematurely. The reasons for the low survival rates were unclear until the researchers noticed that more animals died on Mondays and Thursdays — the two days on which the animal facility was routinely cleaned out. The vacuum cleaners used in this process provoked strong and often lethal epileptic seizures specifically in the triple knockout animals. Continuous electroencephalography (EEG) recordings confirmed what was seen when the noisy cleaner was switched on — that triple knockouts had abnormal EEG activity that developed into epileptic seizures.

The causal link between the PAR bZIP family and epilepsy might be explained by the involvement of pyridoxal kinase (*Pdxk*), which is normally regulated by the PAR bZIP proteins and, the authors found, is expressed at very low levels in the brains of the triple knockout animals. The PDXK enzyme is involved in converting vitamin B6 into a form that is required as a cofactor in the metabolism of several neurotransmitters. The connection between *Pdxk* misregulation and epilepsy is interesting for two reasons. First, vitamin B6 deficiency can cause epilepsy in humans and laboratory rodents. Second, the human *PDXK* gene lies close to cystatin B (*CSTB*), a gene that is involved in Myoclonic epilepsy of Unverricht and Lundborg, a hereditary form of epilepsy.

The PAR bZIP family has come along way since Schibler's group first discovered it 15 years ago. The remarkable sequence conservation of these proteins between mice and humans (92–98%) makes them appealing targets for understanding their common physiological functions. The authors suspect that the triple knockout mice have a low survival rate for reasons that are unrelated to epilepsy but, for the moment, this story is being kept tightly under wraps.

Tanita Casci

References and links

ORIGINAL RESEARCH PAPER Gachon, F. *et al.* The loss of circadian PAR bZIP transcription factors results in epilepsy. *Genes Dev.* **18**, 1397–1412 (2004)

FURTHER READING Steinlein, O. K. Genetic mechanisms that underlie epilepsy. *Nature Rev. Neurosci.* **5**, 400–408 (2004)

WEB SITE

Ueli Schibler's laboratory: http://www.molbio.unige.ch/schibler/index.php

IN BRIEF

CHROMOSOME BIOLOGY

Regulation of murine telomere length by *Rtel*: an essential gene encoding a helicase-like protein.

Ding, H. & Scherter, M. *et al. Cell* **17**, 873–886 (2004)

Telomere lengths vary between species, although little is known about how this process is controlled. The authors identified and cloned a candidate regulator, which they call regulator of telomere length (*Rtel*). They show that *Rtel*, which encodes a highly conserved protein with characteristic helicase motifs, is essential for mouse survival beyond 11.5 days of embryonic development and is required for telomere integrity and elongation, as well as chromosome stability.

BIOINFORMATICS

Gene finding in novel genomes.

Korf, I. *BMC Bioinformatics* 14 May 2004 (doi:10.1186/1471-2105-5-59)

As genomes are being sequenced at an ever-increasing rate, the pressure for fast and accurate gene prediction is growing. Most of the current *ab initio* gene-prediction programs require training, which is genome-specific and slow. Korf has devised a new *ab initio* gene-finding program called SNAP, which is easily adaptable to different genomes (Korf demonstrates it using genomes that range from plants to flies), can be optimized using a bootstrapping procedure and is freely available.

PLANT GENETICS

Stomatal development and pattern controlled by a MAPKK kinase.

Bergmann, D. C. *et al. Science* **304**, 1494–1497 (2004)

Plant leaves are peppered with thousands of evenly shaped pores, or stomata, that allow gases to be exchanged with the environment. By using mutant and gain-of-function analyses in *Arabidopsis thaliana*, Bergmann and colleagues show that YODA, a putative MAPKK kinase, regulates the number of cells that become stomata and their distribution by affecting the asymmetric division of stomatal precursor cells. The authors also used *yoda*-mutant plants in microarray experiments to identify genes, such as *FAMA*, that might interact with *YODA*.

NEUROGENETICS

Notch signaling in *Drosophila* long-term memory formation.

Ge, X. *et al. Proc. Natl Acad. Sci. USA* **101**, 10172–10176 (2004)

Many of us are familiar with the conserved function of Notch signalling in vertebrate and invertebrate development, but less so with its function in the adult brain. Ge and colleagues have used flies to investigate the effect of Notch on memory after Pavlovian training. Reducing *Notch* activity by using a temperature-sensitive or a dominant–negative allele specifically disrupted long-term memory (LTM), whereas overexpressing *Notch* facilitated LTM formation.