domain of the EphA5 receptor, stimulates adhesion to fibronectin and laminin, with subsequent morphological changes. These effects are blocked by an antibody against β1-integrin. Experiments with inhibitors implicate mitogen-activated protein kinases and Src-family protein kinases in this response. Huai and Drescher have used a similar system to fish for molecules downstream of ephrin-A activation, and find a mysterious 120 kDa protein that becomes phosphorylated on a tyrosine residue before integrin-mediated adhesion occurs.

We're beginning to paint — albeit in broad brushstrokes — a picture of how ephrins and Eph receptors communicate their mixed messages, but now we must focus in on the fine detail. Are the adhesive effects of truncated Eph receptors due to 'reverse' signalling to *ephrin-A*-expressing cells? What's the order of events upon ephrin activation, and what's the identity of the 120 kDa stranger lurking in the shadows?

Cath Brooksbank

References and links

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So it seems that the transport of *ASH1* mRNA is pretty much solved. But how many other mRNAs might be localized in yeast, and should we expect similar chains of linkers for each of them?

Raluca Gagescu

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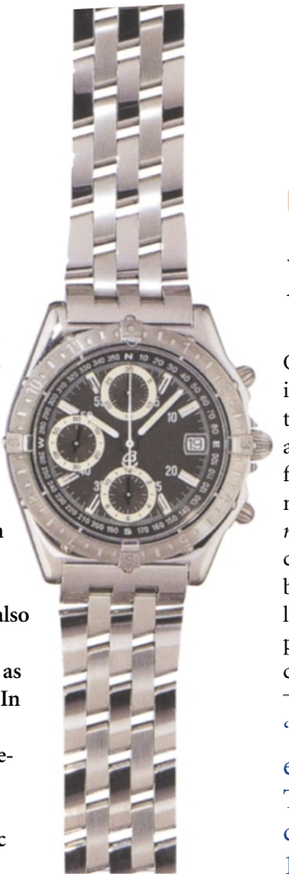
CIRCADIAN RHYTHMS

Working the night shift



Circadian clocks are regulated with the precision of a Swiss watch. They continue to tick without external cues, but they can also be reset (or 'entrained') by environmental signals such as light–dark cycles. But how? In December's *Nature Neuroscience*, Paolo Sassone-Corsi, David Allis and colleagues link light entrainment to the dynamic remodelling of chromatin.

In mammals, the nerve centre of the circadian clock is the hypothalamic suprachiasmatic nucleus (SCN). Animals kept in darkness and given a pulse of light during the 'subjective night' (the time of day corresponding to the dark period in a normal light–dark cycle) show a phase-shifting of normal rhythms, accompanied by the expression of various clock and immediate-early genes in the SCN. These changes in gene expression are thought to be responsible for the light entrainment.

What controls the dynamic regulation of these genes at the chromosomal level? To investigate, Sassone-Corsi and colleagues studied the effects of a night-time light pulse on phosphorylation of histone H3 — a central event in the remodelling of chromatin. They observed such light-induced phosphorylation in the SCN of mice, but not in other structures tested.

The authors next showed that a time course of H3 phosphorylation parallels the induction profile of an early-response gene — *c-fos* — in the same SCN neurons, indicating that the two events are linked. Moreover, when mice were given baclofen, a drug that inhibits light-induced phase-shifts during the subjective night, both phosphorylation of histone H3 and expression of *c-fos* were reduced. Again, the implication is that one pathway controls both events.

These results may indicate, conclude the authors, that "dynamic chromatin remodelling in the SCN occurs in response to a physiological stimulus *in vivo*". And the next step in unravelling this complex molecular clockwork will be to identify the light-induced kinase that is responsible.

Alison Mitchell

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DEVELOPMENT

Divide and rule

Cell-cycle control in eggs and early embryos has its own set of rules. In *Drosophila melanogaster*, the first mitosis is delayed until after fertilization, after which S phase and M phase are alternated for thirteen simplified cell cycles. Maternal mutations in three genes — *pan gu* (*png*), *plutonium* (*plu*) and *giant nuclei* (*gnu*) — disrupt this control, yielding eggs that replicate their DNA before fertilization, and embryos with fewer, larger nuclei; but how? A paper in *Development* provides the first mechanistic insights into this conundrum.

"In the beginning, the heavens and earth were still one and all was chaos. The universe was like a big black egg, carrying Pan Gu inside itself. After 18 thousand years Pan Gu woke from a long sleep. He felt suffocated, so he took up a broadax and wielded it with all his might to crack open the egg."

Ancient Chinese legend

Fenger and colleagues found that *png* encodes a serine/threonine protein kinase expressed in the early embryo. It binds PLU and the complex has kinase activity *in vitro*. How does this complex control the cell cycle? A clue came from examining *png* mutant embryos: these have lower levels of cyclins A and B, and lower CDC2 kinase activity, so they carry on synthesizing DNA but can't undergo mitosis. *png*, therefore, is needed to limit S phase and promote mitosis, which can be achieved by maintaining mitotic cyclin levels. However, no direct interaction between PNG–PLU and cyclins or CDC2 was found. Instead, the authors speculate, PNG–PLU might stabilize cyclins by blocking their access to the protein degradation machinery.

Many questions remain; for example, what are PNG's substrates? And does GNU interact with PNG–PLU? But one mystery has been solved: in vertebrates, the dual-function kinase Mos (see the Timeline by Yoshio Masui on page 228) prevents division of unfertilized eggs. Invertebrates don't have Mos, but we now know that PNG can carry out some of its functions in flies.

Cath Brooksbank

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