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URLs

IN BRIEF

DRUG DISCOVERY

A small-molecule screen in *C. elegans* yields a new calcium channel antagonist.

Kwok, T. C. Y. & Ricker, N. *et al. Nature* **441**, 91–95 (2006)

Caenorhabditis elegans can be used to rapidly identify new small-molecule inhibitors and their targets, both of which are powerful tools for biological analysis and drug discovery. In a screen of 14,100 small molecules, 308 compounds induced a range of phenotypes. Nemadipine A, which is similar to a class of anti-hypertension drugs that antagonize a particular type of calcium channel, caused abnormal morphology and egg-laying defects. A suppressor screen identified *egl-19*, which encodes the correct type of calcium channel, as a nemadipine A target. Nemadipine A was then used to reveal calcium-channel redundancy in the egg-laying circuitry.

EPIGENETICS

Circadian regulator CLOCK is a histone acetyltransferase.

Doi, M. *et al. Cell* **125**, 497–508 (2006)

These authors show that CLOCK — a key component of the circadian pacemaker — has intrinsic histone acetyltransferase (HAT) activity. CLOCK proteins in which an acetyl-coenzyme A binding motif (which is similar at the sequence level to other well-characterized HAT proteins) has been mutated have reduced HAT activity. Their overexpression cannot rescue circadian gene rythmicity in cells in which the endogenous *Clock* gene has been mutated, demonstrating the importance of chromatin remodelling in circadian gene expression.

NEUROGENETICS

The molecular diversity of *Dscam* is functionally required for neuronal wiring specificity in *Drosophila*.

Chen, B. E. *et al. Cell* **125**, 607–620 (2006)

Dscam, the gene that encodes the Down syndrome cell-adhesion molecule, can potentially produce up to 38,016 different protein isoforms by alternative splicing. The authors showed that *Dscam* is essential for proper axonal branching in the fly, that alleles that could produce 22,176 isoforms did not fully rescue the phenotype, and that expression of individual isoforms has distinct partial-rescue phenotypic effects. This implies that much of the potential isoform diversity that is encoded by this gene is necessary for the differentiation of neurons.

EPIGENETICS

Intra- and inter-individual epigenetic variation in human germ cells.

Flanagan, J. *et al. Am. J. Hum. Genet.* 29 March 2006 [Epub ahead of print]

This study examines the amount of epigenetic variation in the human male germ line. By analysing cytosine methylation in specific genes, and a microarray analysis of CpG islands, the authors show that methylation patterns vary considerably between individuals and between sperm within an individual. Promoter CpG islands and pericentromeric satellites had the most variation, and some variation was age- and allele-dependent. The inter-individual epigenetic variation was much greater than the genetic variation, although it is unclear how much of it is inherited.