RÉSUMÉ

Birth and HIV

J. J. GOEDERT and colleagues (*The Lancet* **338,** 1471–1475; 1991) looked at data on 100 sets of twins born to women infected with HIV, and found that birth order and type of delivery had a considerable effect on which twin, if any, had become infected. In the cases that could be evaluated, 50 per cent and 38 per cent of first-born twins, delivered vaginally and by caesarian respectively, had been infected, against 19 per cent of second-born twins delivered by either route. The data support the idea that mother–infant transmission of HIV occurs not only during gestation but in labour; and the authors propose that they can be explained by the greater exposure of first-born twins (in caesarian deliveries, usually the one lying lower in the uterus) to infectious cervical and vaginal blood and mucus. They conclude that some form of cleansing the birth canal might well prove effective in reducing the incidence of mother–infant infection.

Two into nothing

PUT two oscillators with exactly the same natural frequency side by side, and you would expect to find perfect resonance. But not so. The resonant frequency of the pair is split into two components, one increased and the other decreased by a small amount that depends on the strength of coupling between the oscillators. F. Bernardot *et al.* (*Europhys. Lett.* **17,** 33–38; 1992) use as their resonators a collection of sodium atoms (as few as three) and an evacuated cylindrical cavity of superconducting niobium, each of which can absorb microwaves at a frequency of 68 gigahertz. As expected not only does the resonant frequency split into two (the Rabi splitting) as the atoms enter the cavity, but the splitting increases as more atoms are introduced. Similar experiments have been conducted at CalTech using just a pair of atoms in a Fabry–Perot resonator, and the test with a single atom is not far off.

Seeing red

IN 1986 Hogness and his colleagues identified three genes for the pigments of colour vision. Two of these were on the X chromosome and were assigned as the green and red cone pigments on the grounds that red–green colour blindness is X-linked. Now D. D. Oprian *et al.* (*Biochemistry* **30,** 11367–11372; 1991) have expressed and isolated all three proteins, which, when combined with their common chomophore, 11-*cis*-retinal, generate coloured products with absorption maxima at exactly the wavelengths found in single cones by microspectrophotometry. The spectroscopic mechanism by which the proteins induce such large and varied perturbations of the retinal spectrum is now open to study.

interpretation of the result would be that the postsynaptic response is increased.

So unless data arise that cannot be explained by present hypotheses on the mechanism of transmission in the central nervous system, an increase in the amplitude of miniature currents would, I believe, be interpreted most simply and by most workers in the field as a change in responsiveness of the postsynaptic membrane. Such a change has been seen by Manabe *et al.* As the authors observe, although the change in miniature amplitude would be sufficient to explain the potentiation of evoked currents, additional presynaptic effects can certainly not be ruled out.

The Long Term Problem[5] may not be completely solved. But this new study at least clarifies the point that an increase in postsynaptic response to release of a vesicle from the presynaptic terminal occurs on induction of LTP. □

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MOLECULAR BIOLOGY

Extinction by indirect means

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FUSE two different types of somatic cell, and in the resulting hybrid the specialized gene products of one of the parent cells will often be extinguished. This phenomenon, known as tissue-specific extinction, is intriguing in itself, but study of it has also held out the promise of netting a very big fish indeed — an understanding of the direct negative-control mechanisms operating during the differentiation of mammalian cells.

Two groups, led respectively by G. Schütz (Boshart *et al.*[1]) and R. E. K. Fournier (Jones *et al.*[2]), have now identified the molecular mechanism at play in one case of tissue-specific extinction. The first step on the way was made in 1984, when, using microcell fibroblast–hepatoma hybrids, Killary and Fournier[3] described the chromosomal localization of the gene for TSE1 (tissue-specific extinguisher 1). They found that if chromosome 11 of the mouse (or its human homologue 17) from a fibroblast was introduced into a rat hepatoma cell genome, it caused extinction of expression of the liver-specific hormone-inducible enzyme tyrosine aminotransferase (TAT). Loss of this chromosome led to the re-expression of TAT. It was concluded that the chromosome carries a locus coding for a diffusible factor having a negative effect on expression of the TAT gene, from which it follows that the locus must be active in fibroblasts but not in hepatoma cells.

In subsequent work, Fournier and co-workers determined that TSE1 has several liver-specific target genes[4], all of them inducible by glucocorticoids and cyclic AMP. A second important clue came from the observation that TSE1 action is fully alleviated by hormone action[5]. Boshart *et al.* found that the *cis*-acting sequences through which TSE1 action is mediated is a cAMP response element, located in the enhancer 3.6 kilobases upstream of the TAT gene. This deduction stemmed not only from transfection assays involving the relevant sequences, but also from footprints *in vivo*[6], and led Schütz's group to speculate that the TSE1 product changes the phosphorylation state of a protein important for functioning of the cAMP response element of the TAT gene (for example, by way of a specific phosphatase activity).

At this point it is helpful to recall the outline of the cAMP induction pathway. In the absence of hormonal stimulation, the enzyme protein kinase A is inactive because of the association of regulatory subunits with catalytic subunits. Cyclic AMP binds to the regulatory subunits to liberate the catalytic subunits. The catalytic subunits of protein kinase A can then phosphorylate a protein which binds to the cAMP response element, resulting in the activation of transcription. TSE1 could act directly or indirectly at any one of these steps.

The Schütz and Fournier laboratories achieved the molecular cloning of TSE1 in different ways. Both groups made use of microcell fibroblast – hepatoma hybrids containing only fragments of human chromosome 17 (ref. 7). These provide pairs of nearly isogenic clones where only a fragment of fibroblast chromosome 17q (marked by the *neo* gene) is retained, either including TSE1 or not. Boshart *et al.*[1] pursued their hypothesis that TSE1 prevents protein binding at the cAMP response element of the TAT gene. A first series of experiments revealed a sevenfold reduction in the activity of protein kinase A in $TSE1^+$ compared to $TSE1^-$ hybrids, but only in the absence of cAMP. This implied that catalytic subunit expression is similar in the two cell lines. So Boshart *et al.* turned their attention to the regulatory subunits, thinking that perhaps one of them is up-regulated by TSE1. The answer was simpler than expected — Southern blot analysis revealed that regulatory subunit R1α is localized to