phase shift and a 180° phase reversal, attributable to selection rules.

Thus Koonin's idea may have a practical importance which transcends the massive-neutrino controversy. That is, BEFS can also be used as a probe of local atomic structure, yielding both interatomic distances and coordination numbers. The great advantage of EXAFS-type probes, compared with techniques like X-ray diffraction, is that crystalline samples are not needed. Moreover BEFS does not require a synchrotron X-ray source, although long count times may be needed to obtain an adequate signal-to-noise ratio. Koonin gives several potential applications, together with approximate calculations of the size of the effect. For example, with tritium as a β-emitter, one could map the locations of hydrogen in solids, a feat which is difficult with other techniques, because hydrogen is a weak scatterer. Interestingly, the calculations of BEFS were all made using scattering amplitudes and phase shifts from Koonin and Meredith's computational recipes[4].

As for the heavy neutrino, the earliest evidence of this came from the β-decay of tritium implanted in germanium[5] which gave a spectrum with small departures from that predicted at the high-energy tail. Koonin also cites evidence from frozen molecular tritium experiments. In each case, the BEFS effect would have a magnitude comparable to the observed effect, although Koonin does not believe it gives the whole explanation. And experiments with sulphur and germanium isotopes, in which the β-decay energy is much greater, would not be affected by the BEFS effect, according to Koonin. □

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MOLECULAR BIOLOGY

Signal recognition revisited

Sean Munro

DISCONCERTING but true — deletion of the budding-yeast homologue of a gene encoding a protein involved in some seemingly crucial cellular process does not necessarily result in the death of the yeast cell. A further surprising example of this phenomenon is described by Hann and Walter in *Cell*[1]. They find that budding yeast, *Saccharomyces cerevisiae*, contains a 'signal recognition particle' but that the particle is not essential for the organism's viability.

The signal recognition particle (SRP) helps proteins destined for export from the cell, or incorporation into membranous compartments, either to cross or to become incorporated into a lipid bilayer. In eukaryotic cells this involves insertion of the protein into the membrane of the endoplasmic reticulum[2,3]. The proteins are made with a hydrophobic signal sequence which can be removed once translocation has begun. The signal sequence is recognized by SRP, the binding of which inhibits further translation by the ribosome until the resulting complex docks onto a protein (the SRP receptor) in the membrane of the endoplasmic reticulum. At this stage, SRP is released and the nascent chain is passed to a translocation complex, or 'translocon', and translation resumes with the polypeptide cotranslationally passing through the membrane of the endoplasmic reticulum.

Thus SRP provides an elegant way of ensuring that proteins destined for the secretory pathway are not translated prematurely in the cytoplasm. It is assumed that this is desirable because such proteins might either fold too tightly to be subsequently threaded through the translocon or would fold abnormally and so aggregate.

The SRP is a complex of a short RNA molecule (7SL) and six proteins, the best characterized of these being SRP54 which binds to the signal sequence as well as to 7SL RNA[2,3]. Well-conserved homologues of the components of SRP have been found in a range of eukaryotic organisms[3], and two groups independently isolated a gene encoding an SRP54 homologue from *S. cerevisiae* and concluded that the gene was essential for viability[4,5]. All of this seemed consistent with SRP's central part in the secretory pathway.

Other reports were, however, at odds with this simple story. Studies *in vitro* showed that some small yeast proteins, notably prepro-alpha-factor, could cross the membrane of the endoplasmic reticulum post-translationally[6,7]. And biochemical and genetic studies in yeast demonstrated a requirement for members of the 70K heat-shock protein (hsp70) family for efficient translocation of particular proteins, including prepro-alpha-factor, into the endoplasmic reticulum[8,9]. These results could be explained by arguing that some small fraction of proteins are able to use hsp70 and other factors to get into the endo-

RÉSUMÉ

Off the shelf

MAKING monoclonal antibodies without the use of animals is a practical reality, report J. D. Marks *et al.* (*J. molec. Biol.* **222**, 581–597; 1991). They show how antigen-specific antibody fragments can be selected from a library of recombinant immunoglobulin genes, which were cloned from an unimmunized human donor and expressed on the surface of bacteriophage. The library was the key to success — with some 2 $\times$ 10^7 members it is similar in size to the B-cell repertoire of the mouse. Avoiding immunization *in vivo* obviates the problems associated with immunizing humans to order, and allows antibodies for many different antigens to be isolated from a single library. Immunizing animals does however provoke the selection of high-affinity antibodies that have undergone somatic mutation, and mimicking that process is the next challenge.

G whizz

RESULTS from the deep northeast Pacific pour cold water on the notion that there is a mysterious 'fifth force' (M. A. Zumberge *et al. Phys. Rev. Lett.* **67**, 3051–3054; 1991). Discrepancies in gravity measurements from a mineshaft, and others revealed in Eötvös's legendary laboratory determinations of big *G*, Newton's gravitational constant, hinted that all was not well with Newton's inverse-square law of gravity. The fifth force was intended to resolve the differences. In measuring the gravitational acceleration down to depths of 5 km under water, the new tests resemble the mineshaft experiments (conducted to 1-km depth) but avoid the dangers from unseen variations in density in the surrounding material. The measured value of big *G*, with a resolution of 2‰, agrees to within 1‰ with laboratory measurements, so removing any requirement for a fifth-force correction.

Injury and Alzheimer's

THE report of a new mouse model for Alzheimer's disease (see pages 432 and 476 of this issue) follows hard upon a paper in last week's *Lancet* in which G. W. Roberts *et al.* describe an association between severe head injury and the deposition of the β/A4 amyloid plaques characteristic of the disease. Following up their own hypothesis, Roberts and colleagues looked at the brains of 16 people who had died after suffering trauma to the head. They found abnormally large deposits of plaque had developed in the brief (6–18-day) interval between injury and death in six of the 16, and say that the study lends support to the view that head injury can result in the pathological β/A4 response also deeply implicated in Alzheimer's disease.