plasmic reticulum post-translationally and so would not require SRP to ensure cotranslational translocation. However a startling discovery was made following the cloning of a candidate for the *S. cerevisiae* homologue of 7SL[10]. This RNA molecule, scR1, does not have a size and sequence typical of a 7SL but its abundance and intracellular localization are consistent with such a role; yet scR1 is not an essential gene. So either it is not part of the SRP or the SRP is not actually essential in *S. cerevisiae*.

This issue has now been resolved by Hann and Walter[1]. They initially used antibodies against *S. cerevisiae* SRP54 to demonstrate that it was in a complex with scR1 and showed that deleting the scR1 gene prevented SRP54 assembling into a large particle, confirming that scR1 is the *S. cerevisiae* 7SL homologue. They then went back to their yeast without the SRP54 gene and discovered that they were not in fact dead, but rather were growing at a considerably reduced rate. Furthermore, deleting the genes for both scR1 and SRP54 resulted in the same slow growth rate as either deletion alone.

From this and the failure of low-stringency probing to reveal any genes related to SRP54 and scR1, Hann and Walter conclude that there are no structural homologues which can substitute in the deletion strains. This is a reasonable assumption and leads to the remarkable conclusion that in *S. cerevisiae* every protein that needs to get into the endoplasmic reticulum can do so without the help of SRP. Analysis of five such proteins in the SRP54-deficient strain revealed that all do indeed get into the endoplasmic reticulum, but with very different efficiencies. For some, more than half the protein made remained in the cytoplasm, whereas others were translocated as efficiently as in wild-type cells. Interestingly, when SRP54 was removed from cells by placing the gene under the control of a regulated promoter and then switching it off, translocation into the endoplasmic reticulum was initially more severely impaired than in the strains growing without the gene at all. This suggests the induction of other proteins to facilitate long-term growth without SRP.

The survival of yeast without SRP does not mean that it is an unimportant part of the secretory pathway; the yeast without it grow extremely slowly and in the fission yeast, *Schizosaccharomyces pombe*, 7SL does seem to be truly essential. What it does mean is that there must be a way for proteins to translocate into the endoplasmic reticulum without SRP to ensure that it is cotranslational. One possibility is that signal peptides on nascent chains can dock directly into the translocon so long as translation has not proceeded to a point where folding obscures the signal or prevents translocation. Alternatively the hsp70-dependent post-translational mechanisms may come into play, with hsp70 or other chaperones not only keeping the proteins in a soluble state but also stabilizing partially folded intermediates which would have the ability to unfold for translocation. Indeed, the level of heat-shock proteins is elevated in the SRP54-deficient yeast, although this may just be in response to the presence of abnormal proteins in the cytoplasm.

This now raises the question of how much these post-translational mechanisms using general chaperones contribute to protein translocation in normal cells. In the prokaryote *Escherichia coli*, many proteins are exported across the inner membrane post-translationally with the aid of the Sec B chaperone protein[11]. Although Sec B is not essential in this process, viability without it requires activation of the heat-shock response[12]. *Escherichia coli* also has an SRP-like particle, but given the considerable amount of post-translational translocation it may have only a minor involvement in protein export[13].

It may be that all organisms have several systems for cotranslational or post-translational translocation of proteins, all of which converge on a common translocon in the relevant membrane. During the course of evolution different proteins may have become more or less optimized to use of a particular system, with the result that the relative ratio by which these systems are used varies between different proteins in the same organisms and at a bulk level between organisms. However that may be, the study of protein translocation is likely to have much scope for debate as well as much to tell us about general mechanisms for protein folding and assembly. □

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DAEDALUS

Original gravity

MOTION sickness makes no biological sense. What possible evolutionary advantage can primitive man have gained from the disabling nausea and vomiting brought on by violent movement?

Daedalus comments that motion sickness is a product of sensory conflict. It arises when our eyes and limbs, judging our position and acceleration, find themselves contradicted by the balancing organs of the inner ear. In this connection he recalls that both strong alcohol and heavy water can bring on dizziness and vomiting when swallowed. They enter the bloodstream, diffuse into the canals of the inner ear, and — because they differ in density from the fluids inside — set up strange and dizzying convection currents.

Primitive man is unlikely to have encountered heavy water. But he may have come across strong alcohol. Most modern brewery yeasts produce a weak solution containing only 6–7 per cent alcohol. But suppose some enterprising yeast of the distant past, flourishing on honey, fruit and other sugar-rich sources, produced a juice containing (say) 50 per cent alcohol? Our ancestors might well have rushed to consume the product, to their ultimate regret and downfall. Helplessly drunk, the old man of the tribe could easily have been deposed by his younger rivals; nursing a throbbing hangover the morning after, he would have been easy prey for sabre-toothed tigers and similar predators. Female palaeo-alcoholics would have had fewer and less successful children. Hence, says Daedalus, the strong evolutionary advantage of the vomiting reflex. By ejecting the stomach contents whenever the inner ear gave strange, discordant signals, it saved our ancestors from the Demon Drink.

This elegant theory also explains the evolution of our other defence against alcohol — a liver which can destroy it at a staggering 10 grams an hour, far in excess of any known natural requirement. Our love-hate relationship with alcohol must go back a long, long way.

So Daedalus proposes an expedition to the African jungles in which our kind evolved, to search for that wild primeval yeast that gave us alcoholism and motion sickness. Once identified and cultivated, it could generate a range of new and ferocious fermented drinks, as potent as distillates like vodka. Brewers will rejoice — and so will astronauts. In microgravity their inner ears are, of course, free of all convection currents. Once acclimatized to this unique state, they should, according to Daedalus's theory, be able to enjoy the delights of the strongest alcohol, or even heavy water, with no queasiness at all. David Jones