by natural selection, which maintains a high overall arginine content but tolerates the gain and loss of arginine residues in different positions?

Perhaps, but which of these competing theories do the data best support? A key part of Wyckoff and colleagues' argument[3] is the supposition that altered protamines affect sperm morphology. Protamines are necessary for male fertility — infertile men often have abnormal ratios of protamines P1 and P2, and men with no protamine P2 are sterile[11]. But these are examples of quantitative differences in the levels of protamine expression, rather than the qualitative changes in protamine sequences.

There is too little variation among human protamine genes to see any difference in fertility associated with an altered protamine sequence. But we can turn the question around and ask whether there are any unusual features in the protamines of men whose sperm have abnormal morphology. Only some cases of round-headed sperm syndrome are associated with abnormal protamine levels[12], suggesting at best a weak causal link. More generally, the degree of condensation of chromosomes in sperm does not seem to be associated with rates of fertilization, implantation or pregnancy[13].

Perhaps the most definitive way to test the function of a gene is to insert the gene *de novo* into an organism and look for effects. When Stewart *et al.*[14] expressed the human protamine gene cluster in mice they found normal testis-specific expression, sperm morphology and fertility. Likewise, when an avian protamine called galline was expressed in the mouse[15] there was abnormal chromatin condensation, yet many of the resulting spermatozoa were functionally normal and most of the mice had normal fertility. These transgenic experiments are not definitive proof of functional equivalence, but they also do not support the idea that the rapid sequence divergence is caused by selection for functional divergence. Instead, they indicate that the main feature that is important to the function of protamines is their ability to bind DNA and compact chromatin.

If the only attribute driving the evolution of protamines was their ability to bind DNA, would we expect to see the observed significant excess of amino-acid changes and rapid evolution[3,9]? We have done a simulation of a protein sequence with natural selection, maintaining an optimum arginine content of 50% but ignoring the positions of those arginines, and find excess amino-acid substitution. So, although the statistics reported by Wyckoff *et al.* clearly show that the changes in protamines are not simply random, they do not help to resolve the two contrasting explanations.

It seems that the only way out of this impasse is to make reciprocal transgenic animals and test the function of the resulting sperm. Ideally these experiments would be done by gene replacement, and careful controls would be needed to assure that appropriate expression levels were achieved. In any case, rigorous analysis of the cause of evolutionary changes in human genes may often run into a brick wall because we cannot do the definitive experiment. Barring this, analytical approaches like that of Wyckoff *et al.*[3] may provide key insights to the evolutionary forces at play on human genes. ■

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erratum

Figure 1 of Victoria Lundblad's News and Views article "Telomeres: A tale of ends" (*Nature* **403,** 149; 2000) was printed incorrectly in some editions. The correct version is shown below.

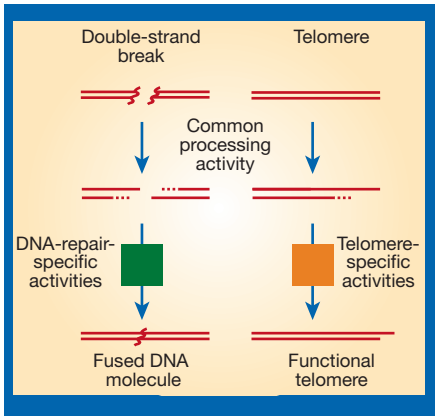

Figure 1 **Proposed set of common events at DNA double-strand breaks and telomeres. Evidence is growing for the idea that these two pathways are partially linked. Ahmed and Hodgkin[1] show that the *mortal germline-2* (*mrt-2*) gene, which is required for telomere replication, is also involved in monitoring DNA for double-strand breaks. The idea is that processing to resect one strand of a telomere or double-strand break could be resolved by activities that are specific for telomere maintenance (such as telomerase) or DNA repair (such as a DNA ligase).**

1. Ahmed, S. & Hodgkin, J. *Nature* **403,** 159–164 (2000).

Daedalus

States of non-mind

Why are we conscious? Evolution has been blamed. For some unexplained reason, conscious creatures were fitter than ones which behaved the same way but without consciousness; and Darwin did the rest.

If so, says Daedalus, then consciousness must be represented somewhere on the genome. Creatures which are conscious should have a set of genes absent in those which are not conscious. And consciousness is remarkably unitary. It can be abolished by many simple molecules (anaesthetics), leaving other bodily systems untouched. So it is probably coded for by one, or just a few, genes. How to identify them?

Daedalus recalls the strange syndrome of alcoholic 'palimpsest'. The alcoholic has absolutely no memory of some past episode, even though at the time he did not appear drunk. Actors have given brilliant performances, surgeons have conducted delicate operations that they would never later recall, in alcoholic palimpsest. Daedalus reckons that palimpsest is not a failure of memory, but of consciousness. Alcohol, itself a considerable anaesthetic, erases the consciousness of its victim. It leaves him as a perfectly functional human robot, seemingly normal and responsive, but in fact with no internal awareness.

So DREADCO biochemists are conducting delicate tests on advanced alcoholics, looking for hormones and neurotransmitters whose concentration correlates with the state of palimpsest. They hope to work out where these compounds come from, on what brain sites they bind or inhibit binding, and what proteins underlie their synthesis. Standard genetic detective work should then reveal the crucial genes of consciousness.

A major biological conundrum will thus be resolved. By seeking these genes in other creatures, the DREADCO team will discover which of them is conscious. Caring experimental biologists will rush to learn the results. Are experiments on mice, or frogs, or fish, or beetles, cruel? Or are these creatures merely unconscious chemical mechanisms? Genetics will give the answer. Daedalus even hopes to grant awareness to lower species by implanting the crucial genes in them, or deprive higher ones of it by deleting them. But how to tell if the operation has worked? Daedalus will induce alcoholism in the test creatures, and look for episodes of palimpsest. David Jones