The selfish pursuit of sex

SIR — No satisfactory explanation for the origin and evolution of sex in eukaryotes has been proposed that is based solely on the selective advantage (to organisms) derived from genetic shuffling, a primary consequence of meiosis[1]. Several theories do see genetic shuffling as a byproduct of some other selective advantage, and one, 'the molecular symbiont' hypothesis, would have it as a primary advantage, but an advantage accruing to genetic parasites, not organisms[1]. This idea, first proposed by Hickey[2] and by Rose[3], has the weakness that no gene that is an integral part of the eukaryotic sexual process has been shown to have been derived from a selfish mobile element[1,4]. In fact, a good example has been in the literature for some time, but its significance has never been recognized.

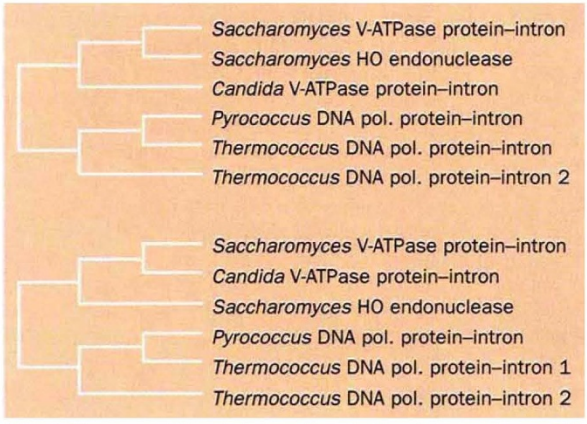

FIG. 1 Two possible phylogenetic relationships between HO endonuclease, fungal V-ATPase protein introns and archaebacterial DNA polymerase protein–introns. The upper tree was obtained by parsimony analysis (using PAUP 3.1 program), whereas the lower tree was generated by neighbour-joining of a protein-distance matrix (using PHYLIP 3.5 programs) and protein maximum likelihood (using MOLPHY 2.2 programs), all inferred from 57 clearly alignable amino-acid positions. The exact topology of the fungal sequences cannot be discerned, but all methods confirm with strong statistical support that HO and the two ATPase protein–introns are most closely related and diverged at about the same time.

Recently, a new class of selfish mobile element has been discovered, the protein–intron (intein). These elements are endonucleases that are also known to 'home', a particular type of mobility that uses double-stranded-break repair to invade uninfected alleles[5]. Interestingly, these mobile elements are also related to the endonuclease encoded by the homothallic switching (*HO*) gene in the yeast *Saccharomyces cerevisiae*, the factor responsible for initiating a mating-type switching cascade in this organism[6]. Closer examination reveals that HO is most closely related to the V-type ATPase protein–introns found in both *Saccharomyces* and the related *Candida tropicalis*. Phylogenetic analysis of these sequences, together with their next closest relatives, protein–introns found in archaebacterial DNA polymerase genes, indicates that HO endonuclease probably arose from a homing protein–intron at roughly the same time that *Saccharomyces* diverged from *Candida* (see figure), about 135 million years ago[7]. The alternative, that protein–introns are degenerate derivatives of HO endonuclease[5], is a far less parsimonious interpretation of the phylogeny.

Although there are cases of selfish elements directing the fusion of mitochondria to promote their own spread in eukaryotes[8], the relationship between HO endonuclease and protein–introns is the first strong evidence for a mobile element actually becoming integrated into the sexual cycle of the nucleus. To understand the significance of this relationship, one must appreciate the effect that frequent mating-type switching could have on the spread of a transposon. In a heterothallic population under certain conditions, such as a discontinuous or patchy population distribution with little mixing, subpopulations of essentially clonal lineages of one mating type may arise. Haploid individuals from a population bearing an element that increases the frequency of mating-type switching would more often find compatible mates under these conditions: within their original clonal lineage they would be able to mate with close relatives lacking the element, and when introduced into a new subpopulation they will be able to outcross regardless of the resident mating type. The immediate increase in accessible mates for this strain could thus facilitate the exposure of uninfected genomes to the element and favour its rapid spread throughout the population.

The mating-type switching system in contemporary *Saccharomyces* is a complex, highly regulated pathway in which HO has a single, central role. When HO arose, it may have become integrated into an already existing switching system that was less efficient, perhaps a passive system that relied only on gene conversion. The introduction of an endonuclease that cut the expressed mating-type locus in addition to its homing site could significantly increase the frequency of mating-type switching by forcing a gene conversion event to take place to repair the lesion.

It has been suggested that the primary selective advantage for the development of mating-type switching was to favour diploidy, a measure that improved the organism's ability to repair damaged DNA[6]. We suggest, however, that by assuming this role in mating-type switching, the mobile protein–intron may have improved its own chances of propagation. If this proposal is correct, the establishment of HO in the ancestral *Saccharomyces* population was not primarily the consequence of organism-level selection for more frequent mating-type switching[6], but rather may have been the result of a selfish transposon which had cleverly exploited a pre-existing mating-type switching process to speed its own spread.

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Neanderthal computer skulls

SIR — Fossil specimens can be restored, measured and replicated without physical contact using a combination of computerized tomography (CT), computer-assisted reconstruction and rapid prototyping. We have used this procedure to reconstruct and reinterpret fragments of a Neanderthal child's skull from Devil's Tower in Gibraltar (Fig. 1*a*,*b*). We have developed an interactive software package to generate accurate object surfaces from serial CT data which permits three-dimensional morphometry and computer-assisted reconstruction of fossils. Rapid prototyping of computer-generated reconstructions was achieved using stereolithography (layer-by-layer production of successive thin profiles by laser-induced polymerization of a photosensitive liquid).

The Devil's Tower specimen is represented by five individual fragments: incomplete mandible, right maxilla, right temporal, fused frontal bones and left parietal. Of these original fragments, only the last two articulate directly. All fragments were originally attributed to a single individual[1] with an estimated age at death of 3–4 years[2,3]; but it has also been suggested that the fragments came from two separate individuals of different ages[4].

Using a graphics workstation equipped with a stereo monitor (Onyx, Silicon Graphics; Mountain View, California), three-dimensional skull reconstruction was achieved in four stages (Fig. 1*a*). (1) The