

Minireview

Where does fission yeast sit on the tree of life?

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Abstract

The budding yeast *Saccharomyces cerevisiae* and the fission yeast *Schizosaccharomyces pombe* are as different from each other as either is from animals: their ancestors separated about 420 to 330 million years ago. Now that *S. pombe* is poised to join the post-genome era, its evolutionary position should become much clearer.

Fission yeasts are a unique group of fungi that are characterized by features of ascomycetes (for example, fungal-type cell wall, closed mitosis, an ascus-type sporangium, and ascomycete-like mode of sex determination, and so on) but appear extremely divergent in terms of gene sequence. Yeasts are generally defined as unicellular (occasionally dimorphic) fungi without fruiting bodies, which propagate either by budding (like *Saccharomyces*) or by fission (like *Schizosaccharomyces*). This definition covers a wide variety of organisms (at least 500 species) of phylogenetically heterogeneous origin, among them ascomycetes and basidiomycetes. Genomic sequencing of the fission yeast *Schizosaccharomyces pombe* is due for completion this summer, and should illuminate the vexed issue of the fission yeasts' position in the tree of life. This minireview summarizes the facts and hypotheses about their evolution and phylogenesis that have been published during the pre-genome era.

The species *Schizosaccharomyces pombe* was the first fission yeast to be discovered and the one on which the 'fission yeast' genus *Schizosaccharomyces* was founded [1]. Most taxonomic systems accept as fission yeasts one four-spored species, *S. pombe*, and two eight-spored species, *S. japonicus* and *S. octosporus* (reviewed in [2]). The use of molecular methods to estimate genetic relatedness confirmed this classification [3]. Most laboratory strains used in genetics and molecular biology originate from the Swiss isolate, *S. liquefacies*, which Urs Leupold used for his genetic analysis in the early 1950s [4]. Since *S. liquefacies* turned

out to be conspecific with *S. pombe*, we classify these laboratory strains as *S. pombe*, where they belong to the variety *S. pombe* var. *pombe* (Figure 1).

S. pombe is very divergent

Because of the lack of useful phenotypic traits, the phylogenetic assessment of most microorganisms relies almost

Kingdom	Mycota
Phylum	Ascomycota
Subphylum	Archiascomycotina (<i>Taphrinomycotina</i>)
Class	Schizosaccharomycetes
Order	Schizosaccharomycetales
Family	Schizosaccharomycetaceae
Genus	Schizosaccharomyces
Species	<i>S. pombe</i>
	<i>S. pombe</i> var. <i>pombe</i>
	<i>S. pombe</i> var. <i>malidevorans</i>
	<i>S. japonicus</i> (<i>Hasegawaea japonica</i>)
	<i>S. japonicus</i> var. <i>japonicus</i>
	<i>S. japonicus</i> var. <i>longobardus</i>
	<i>S. japonicus</i> var. <i>versatilis</i>
	<i>S. octosporus</i> (<i>Octosporomyces octosporus</i>)

Figure 1
A taxonomy of fission yeasts (based on [19,20]).

exclusively on molecular techniques. The usual procedure is the collection of multiple related nucleotide or amino-acid sequences followed by sequence alignment and then the application of phylogeny inference techniques to derive estimates of evolutionary relationships from the patterns of shared and varied nucleotides or amino acids at homologous positions in the alignment [5]. The methods most commonly used are maximum parsimony, maximum likelihood, and distance methods most commonly analyzed by the neighbour-joining algorithm [5]. When rRNA sequences were used to generate phylogenetic trees, *S. pombe* was found to be very divergent - appearing as deep-rooting branches - although the location of the branching point on the suggested phylogenies was rather controversial. The divergence was so great that certain trees grouped *S. pombe* with metazoans rather than with yeasts or other fungi. In addition, many *S. pombe* proteins turned out to be more similar to their mammalian homologs than they are to their *Saccharomyces cerevisiae* counterparts (reviewed in [2]). These results inspired many molecular biologists to believe that *S. pombe* might be more closely related to higher eukaryotes, especially to animals, than is *Saccharomyces cerevisiae*.

In principle, the high degree of divergence can be interpreted as the indication of an early separation either from the fungal lineage or from the animal lineage after the fungal clade had already been separated from animals. Both possibilities have found support in different molecular phylogenies (reviewed in [2]). This apparent discrepancy might be due to the use of single genes for tree construction: phylogenies derived from comparisons of single genes are rarely consistent with each other, because genomes are composed of an amalgam of genes with complicated histories and variable rates of

evolution. If the origin of a lineage is investigated by looking at the history of molecules which are themselves changing at different rates, the phylogenies inferred are frequently incompatible. Phylogenetic analysis can also be confused by the fact that genomes are mosaics with a complex interspersion of conserved ancestral genome parts and novel sequences originating from duplications and horizontal gene transfer. In the completely sequenced *Saccharomyces cerevisiae* genome, 1,858 genes appear to have arisen by gene duplication [6]. Horizontal gene transfers, a major force for change during prokaryotic evolution [7], are thought to be less important in eukaryotic phylogenesis [6,8].

When speculating on the phylogenetic position and affiliation of *S. pombe*, one should bear in mind that it shares many features with ascomycete species - for example, it has a fungal-type cell wall, closed mitosis (no nuclear envelope breakdown), an ascus-type sporangium, an ascomycete-like mode of sex determination, and so on). Thus, we can be fairly confident that fission yeasts diverged from the ascomycete branch, not from the animal clade after the separation of the fungi.

Phylogenetic roots

Many rRNA phylogenies, and most protein-based phylogenies, suggest that the animal and fungal lineages share a more recent common ancestor than either does with the plant lineage (see, for example [9-12]). Some data indicate that their last common ancestor was a flagellated protist similar to extant choanoflagellates [10]. Because chytrids (*Chytridiomycetes*, a flagellated class of fungi) and choanoflagellates both have flattened mitochondrial cristae

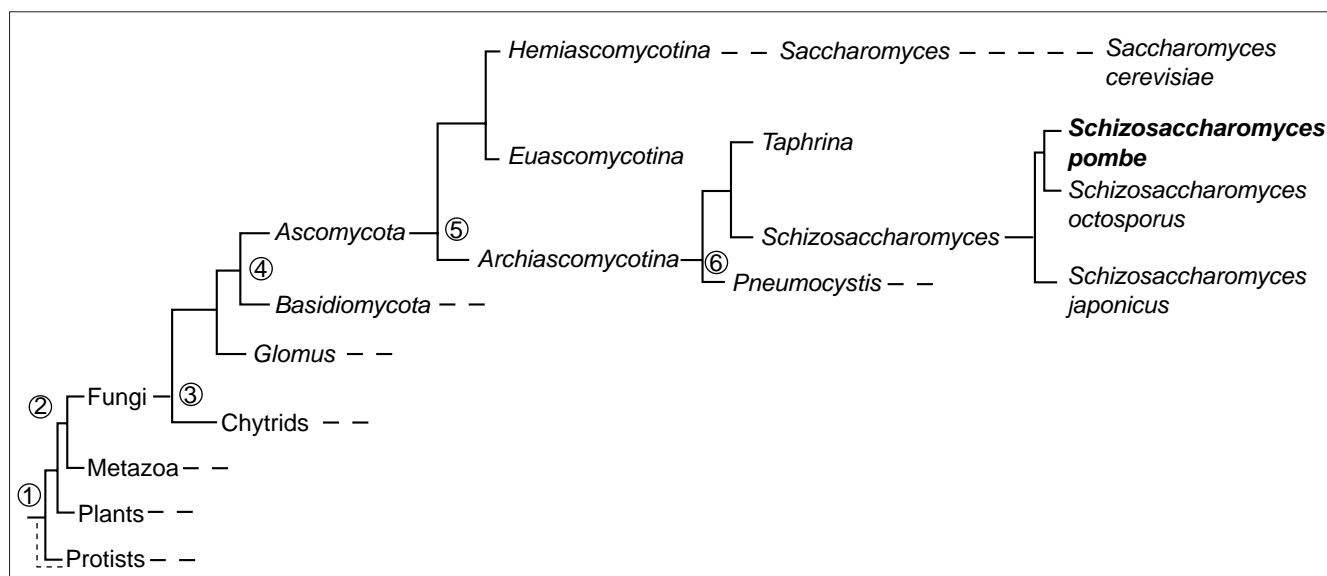


Figure 2

A consensus phylogeny of fission yeasts. Times are (1) 1,200 million years ago (Ma); (2) 1,100 to 1,000 Ma; (3) 600 to 500 Ma; (4) 400 Ma; (5) 420 to 330 Ma; (6) 250 Ma. (Modified from [2,9,12-15,20].)

and a single posterior flagellum, the most recent common ancestor to the animals and fungi might have been a unicellular protist with these characteristics [10]. But, on the basis of ribosomal protein peptide and nucleotide sequences, Plantae and Animalia appear to be sister clades, and Fungi form a more distant clade [13]. Thus, the early history of fungi remains an unresolved issue at present. Likewise, the estimated time of their divergence is also uncertain, varying from 1,000 million years ago [12] to 1,500-2,600 million years ago [13].

Berbee and Taylor [14] constructed a phylogeny based on 18S rRNA and a time scale (calibrated by fossil evidence) for the origin and radiation of the major lineages of the true fungi. They found that a branch (equivalent of *Archiascomycotina*) including the peach leaf curl fungus *Taphrina*, the mammal pathogen *Pneumocystis* and the fission yeast *S. pombe* separated very early, about 330 million years ago. A phylogenetic analysis of HMG-CoA reductase protein sequences suggested that the separation of fission yeasts from the lineage leading to *Saccharomyces cerevisiae* took place 420 million years ago [15]. A consensus phylogeny of fission yeasts, with a proposed time scale, is shown in Figure 2.

It is hypothesized that all present-day ascomycetous taxa evolved from filamentous ancestors, and that even the first true yeasts were filamentous [14]. The ability of *S. japonicus* to alternate between yeast and hyphal morphologies [16] indicates that fission yeasts might also originate from filamentous ancestors. It is tempting to suppose that *S. japonicus* had diverged from the lineage before the yeast morphology became dominating, whereas *S. octosporus* and *S. pombe* separated only after the transition had become irreversible.

Ancient or modern?

Because of their common root, one would expect a higher degree of sequence homology between the genes of *S. pombe* and *Saccharomyces cerevisiae* than between the homologous genes of *S. pombe* and extant animals, but this is not the case. A possible reason for this is that fungi evolve faster - with more changes in unit time - than either plants or animals [12]. It is most probably this higher rate of evolution that accounts for the enormous evolutionary gap between the two yeasts. Nevertheless, it cannot explain why *S. pombe* appears to be somewhat less distant from animals in certain features. To solve this controversy, one must suppose that the lineage of *Saccharomyces cerevisiae* has evolved faster and, thus, has become more different from the common ancestors of fungi and animals and also from the extant animal species. This hypothesis is consistent with the finding that, since the separation of the two lineages, the *Archiascomycotina* species have accumulated somewhat fewer substitutions (3.0%) in their 18S rRNA gene sequences than have yeasts in the lineage leading to *Saccharomyces* (3.1%) [14].

New data and new methods have recently revealed that most of the deep-branching species on all trees are in fact misplaced, because they are in general fast-evolving organisms [17]. Higher evolutionary rates tend to pull organisms closer to the base of the tree. In this light, *S. pombe* could represent a branch evolving faster than the budding yeast lineage, and its assignment to *Archiascomycotina* could be a tree-construction artifact. In this case, however, it has had more chance to drift and specialize than has *Saccharomyces cerevisiae*, and thus its sequences and molecular processes should be more divergent from the homologous sequences and functions of animal cells.

An accurate determination of the time of divergence of *S. pombe* can be expected from comparisons of complete genome sequences and from more sequence comparisons with other *Schizosaccharomyces* species: adding more related species to the sequence analysis usually results in a breakage of long (deep) branches and an improvement of the molecular phylogeny [18]. We can expect to place the fission yeasts on the tree of life with far more confidence once we know much more of their genome sequence.

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