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Chromosome-Length Polymorphism in Fungi†

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INTRODUCTION

Fungal cytogenetics began with Barbara McClintock (72), who, sitting on a bench under the eucalyptus trees at Stanford University, realized that she could solve the problem of seeing the small chromosomes of *Neurospora crassa* (48). Since then, numerous microscopists and geneticists have established a few fungi as important experimental systems for the study of meiotic chromosome behavior; e.g., see articles and reviews on *Neurospora crassa* (93, 104), *Coprinus cinereus* (64, 99), *Saccharomyces cerevisiae* (84, 105), *Schizosaccharomyces pombe* (55), and *Sordaria macrospora* (142). However, the small size of most fungal chromosomes has precluded the analysis of many of their features. Although translocations have been readily apparent (for example, see Pukkila and Lu [102]), the positions of centromeres or defining features in organisms with larger chromosomes (for example, the chromomeres and heterochromatic knobs characteristic of maize [13]) have not been determinable. In addition, many medically and agriculturally important fungi do not have known sexual stages, and mitotic material has not generally been suitable for the study of fungal chromosomes.

A new era in the analysis of fungal chromosomes began in the early 1980s, when David Schwartz constructed a new kind of electrophoresis system (116, 117). His invention of pulsed-field gradient gel electrophoresis (PFGE) and the subsequent modifications of this technique by others (reviewed in reference 56) have allowed a radically new approach to the study of fungal chromosomes. With this approach, the small size of fungal chromosomes was transformed from a drawback to a major asset, as many or all of the chromosomes of most fungi can be separated electrophoretically (Table 1) (17, 82, 120). With the development of PFGE, the mapping and cloning of fungal genes gained an important and powerful new tool. For fungi without known sexual cycles and when crosses cannot be made in the laboratory, the hybridization of gene probes to Southern blots of separated chromosomes has greatly augmented the more difficult parasexual analysis for the construction of linkage groups (115). Furthermore, the combination of PFGE and digestion by infrequently cutting restriction endonucleases has allowed physical mapping of previously relatively intractable fungi (16) (Table 1). The most useful electrophoretic karyotypes are those for which the separated chromosomes can be assigned to known genetic linkage groups, and this has been completely or partially achieved for several fungi (Table 1). In addition, complete physical maps have in some cases been developed (16, 28, 60). PFGE-separated chromosomes have been used to construct or define chromosome-specific libraries (10, 143), which have aided in gene cloning and chromosome mapping.

The ability to separate intact fungal chromosomes has led to the striking discovery that most species exhibit chromosome-length polymorphism (CLP) (Table 1 and Fig. 1). Polymorphism has been observed in both asexual and sexual fungi and most likely results from both mitotic and meiotic processes. The goals of this review are to summarize the general characteristics of fungal CLPs, with special attention to well-documented cases, and to discuss possible mitotic and meiotic mechanisms for the generation of fungal CLPs. I will focus on naturally occurring CLPs and will not cover changes caused by induced mutagenesis (e.g., ionizing radiation used for the induction of mutations). In addition, current methods for the electrophoretic analysis of fungal chromosomes are well covered elsewhere (5, 56, 82, 83, 120) and will not be emphasized here.

SEQUENCE CHANGES AND MECHANISMS WHICH LEAD TO FUNGAL CLPs

As a framework for thinking about the types and amount of CLPs observed in natural isolates of fungi, it is useful to think about possible types of chromosome sequence changes and known mechanisms for causing them. Therefore, this section will briefly review chromosomal rearrangements and the types of sequences known to be present in fungal genomes that can serve as substrates for these changes.

Figure 2 illustrates several of the types of chromosomal rearrangements that can lead to the generation of CLPs. Int-

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† This review is dedicated to my father, Louis Zolan, on the occasion of his eightieth birthday, and in appreciation of his consistent encouragement of my interest in science.

TABLE 1. Electrophoretic karyotypes of fungi[a]

Organism	Genome size (Mb)	Chromosome size range (Mb)	No. of chromosomes (haploid)	Confirmation	CLPs reported[b]	Reference(s)
Acremonium chrysogenum	33	2.6–6.4	8		No	135
Agaricus bisporus	34	1.2–4	13		No	49, 107
Aspergillus nidulans	31	0.4–4	10–15	Genetic map, cytology	Yes	9
Aspergillus niger	35.5–38.5	3.5–6.6	8	Genetic map	No	134
Aspergillus oryzae	35	2.8–7	8		No	54
Beauveria nivea	26–33	0.9–6.6	8–10[c]		Yes	125
Candida utilis	Not estimated	0.4–>3.5	≥8[c]		Yes	126
Candida albicans	16–17	0.66–4.3	8–9	Physical map	Yes	16
Cercospora kikuchii	28.4	2.0–5.5	8		No	39
Cladosporium fulvum	44	1.9–5.4	11		Yes	127
Cochliobolus heterostrophus	35	1.3–3.7	15 or 16	RFLP map	Yes	132
Colletotrichum gloeosporioides						
Type A	Not estimated	0.270–6	13–15		Yes	67, 70
Type B	Not estimated	0.330–>6	6–8		Yes	
Coprinus cinereus	37.5	1–5	13	Microscopy	Yes	101
Cryptococcus neoformans var. *neoformans*	21–24.5	0.770–3.9	12–13		Yes	98, 137
Fusarium oxysporum	41–51.5	0.8–6.7	11–14		Yes	81
Fusarium oxysporum f. sp. *cubense*	32.1–58.9	0.6–7.5	9–14		Yes	6
Fusarium solani	40	0.4–6	13		No	88
Histoplasma capsulatum	Not estimated	0.5–>5.7	≥7[c]		Yes	123
Leptosphaeria maculans	17.5–23	0.7–3.7	6–14		Yes	86, 97, 129
Magnaporthe grisea	40	3–10 and 0.47–2.2	7 + 1–4 minichromosomes	RFLP map	Yes	119
Mucor circinelloides	39	2.3–8.1	≥8		Yes	87
Nectria haematococca	8.5	<0.6–7	10–15		Yes	52, 80
Neurospora crassa	47	4–12.6	7	Microscopy, genetic maps	Yes	12, 91
Phanerochaete chrysosporium	15	1.8–5	7		Yes	20
Pneumocystis carinii	7–8	0.3–0.7	14–16		Yes	21
Pythium sylvaticum	37–38	1.9–5.1	≥13		Yes	69
Pythium ultimum	23.7–37.6	1.28–4.6	9–14		Yes	69a
Saccharomyces cerevisiae	13.5–14.5[d]	0.24–3	16	Physical map, microscopy, genetic map	Yes	89, 60
Schizophyllum commune	34–35	1.2–5.1	11	Microscopy	Yes	42
Schizosaccharomyces pombe	14	3.5–5.7	3	Physical map	No	28
Septoria nodorum	28–32	0.5–3.5	14–19		Yes	18
Septoria tritici	29.5–32.6	330–3.5	14–18		Yes	75
Tilletia caries, *Tilletia controversa*[e]	32.25–39.88	0.29–4.49	14–20		Yes	108
Tilletia indica	24	1–>3.3	≥11		Yes	131
Trichoderma longibrachiatum	33	2.8–6.9	7[c]		No	68
Ustilago hordei	18.4–25.9	0.170–3.15	16–21		Yes	74
Ustilago maydis	Not estimated	0.3–>2.0	20		Yes	50

[a] Values for genome size (haploid strains) and chromosome number are estimates made by the referenced authors.
[b] CLPs found in natural isolates; excludes mutagen- and transformation-induced CLPs.
[c] For these species, this number refers to bands on gels, not chromosome number.
[d] Using an estimate of 1 to 2 Mb for the size of the rDNA repeat (60).
[e] The two are considered one species, per reference 108.

rachromosomal events can include deletions caused by recombination between repeats of the same orientation (Fig. 2A) and unequal exchange within tandem repeats between sister chromatids or homologs (Fig. 2B). Chromosome breakage and healing (Fig. 2C) can lead to either a shortening of the chromosome and loss of material or translocations, which may be reciprocal or nonreciprocal.

Ectopic recombination between repeated sequences on nonhomologous chromosomes (heterochromosomal recombination) will lead to translocations (Fig. 2D), and recombination among subtelomeric regions can lead to chromosome end variability (Fig. 2E). In addition, recombination between homologs harboring two or more size polymorphisms can generate novel sizes of chromosomes (Fig. 2F). Finally (not illustrated), complete chromosome loss may occur if the sequences carried on that chromosome are not required for growth.

The genomes of fungi are known to contain sequences which can lead to CLPs by these processes. Transposable elements (Tns) or Tn-associated enzymes have been identified in *Cladosporium fulvum* (76, 77), *Fusarium oxysporum* (23, 24, 47), *Magnaporthe grisea* (25), *Neurospora crassa* (51), *Saccharomyces cerevisiae* (reviewed in reference 7), and *Schizosaccharomyces pombe* (57). All Tns can act passively in generating CLPs, as mobile sites of homology which can serve as substrates for ectopic recombination (139). Tns which transpose via DNA-mediated mechanisms, such as *hobo* of *Drosophila melanogaster* (58, 59, 65) and Ac and Ds of maize (30, 73), may also act as sites of chromosome breakage, which may induce ectopic recombination or translocations caused by the joining of nonhomologous sequences or chromosome shortening if the sequences distal to the Tn are not essential. The *Fot1* and *Impala* elements of *Fusarium oxysporum* may belong to this class of

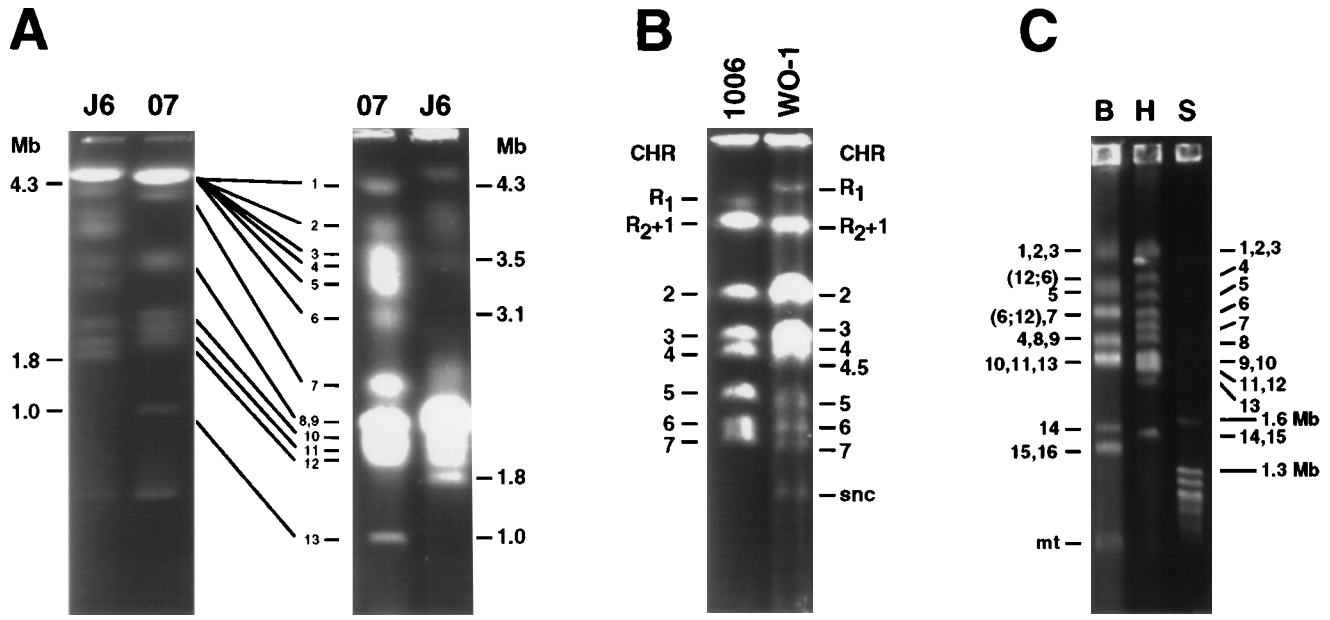

FIG. 1. Electrophoretic karyotypes of three fungi exhibiting extensive CLP. (A) *Coprinus cinereus* (reprinted from reference 143, with permission of the publisher). Lanes: J6, *C. cinereus* Java-6; O7, *C. cinereus* Okayama-7. Mb, megabases. Numbers to the left of the left panel and to the right of the right panel represent chromosome sizes. Numbers between the panels represent chromosome numbers in strain Okayama-7. (B) *Candida albicans* (reprinted from reference 16, with permission of the publisher). Lanes: 1006, nonswitching *C. albicans* 1006; WO-1, switching *C. albicans* WO-1; CHR, chromosome. R1 and R2 refer to rDNA-containing chromosomes. Other numbers refer to other chromosomes. snc, supernumerary chromosome, which is a translocation product (see text). (C) *Cochliobolus heterostrophus* (reprinted from reference 132, with permission of the publisher). Lanes: B, *C. heterostrophus* B30.A3.R.45; H, *C. heterostrophus* Hm540; S, *Saccharomyces cerevisiae*. On both the left and right sides of the panel, numbers followed by "Mb" refer to sizes, and other numbers refer to chromosomes, for strain B30.A3.R.45 on the left and strain Hm540 on the right. mt, mitochondrial DNA.

Tns (23, 24), although their involvement in CLPs has not been directly examined.

In addition to Tns, other dispersed repeats, although less common than in plants and vertebrates, are found in most fungi and may serve as sites of homology for ectopic recombination events, both intrachromosomally and heterochromosomally, and some fungi have mechanisms which may prevent the use of repeats in meiotic ectopic recombination. In *N. crassa*, the process of repeat-induced point mutation (RIP) causes premeiotic transition mutations and methylation of most repeated sequences, although the 5S rRNA genes, which are dispersed, are protected from RIP (118). One possible function for RIP is to change repeats enough so that they do not lead to ectopic recombination. In *Ascobolus immersus* (106) and *Coprinus cinereus* (33), repeated sequences are methylated but not mutated; it is possible that the methylation also serves to mark repeats so that they do not recombine ectopically.

If Tns and other repeated sequences are substrates for ectopic recombination, then increasing their number might be expected to increase the frequency of ectopic exchange within a population. The deliberate doubling of the number of *Ty1* elements (from about 25 to about 50) within a strain of *S. cerevisiae* did not lead to significantly decreased viability of spores in one meiotic generation, indicating that ectopic recombination was not increased (8). Therefore, either these elements are not efficient substrates for ectopic recombination or ectopic recombination among them is actively suppressed.

Changes in the copy number of tandem repeats are well known for fungi, in two ways. First, the tandem repeat containing the rRNA genes is apparently variable in length in all fungi and in some cases has been shown directly to be a source of CLPs (see below). Second, subtelomeric repeats have been shown in *S. cerevisiae* to be composed of a mosaic of repeat units (63), and recombination among subtelomeric repeats has been documented both for this organism and for *M. grisea* (29). These subtelomeric recombination events may be a source of CLP in fungi, as has been shown for the malarial parasite *Plasmodium falciparum* (19, 40), although direct measurements of the effect of subtelomeric recombination on CLP in fungi have not been made.

Finally, as discussed under Dispensable Chromosomes, portions of some fungal chromosomes are clearly dispensable. Therefore, it is likely that recombination between homologs of different sizes generates new chromosome sizes during meiosis (Fig. 2F). However, direct evidence for this process in fungi is so far lacking (this subject is discussed in full under Meiotic Changes).

OVERVIEW OF FUNGAL KARYOTYPES AND INTRASPECIFIC POLYMORPHISMS

Case Studies of Electrophoretic Karyotypes

In order to fully understand the nature and biological importance of fungal CLPs, a physical understanding of the arrangement of genes and nongenic sequences in strains exhibiting CLPs is needed. It is important to determine whether the CLPs result from changes involving rearrangements of linkage groups of genes or gains and losses of noncoding sequences. In fact, the available data suggest that within-species CLPs are a mixture of the two types of changes.

The most complete physical and genetic maps are available for laboratory strains of *S. cerevisiae*. In this organism, which has been mapped to 110-kb resolution physically and 15- to 20-kb resolution genetically (60), CLPs should in theory be attributable to known sequence rearrangements. In their direct comparison of six polymorphic chromosomes, Link and Olson

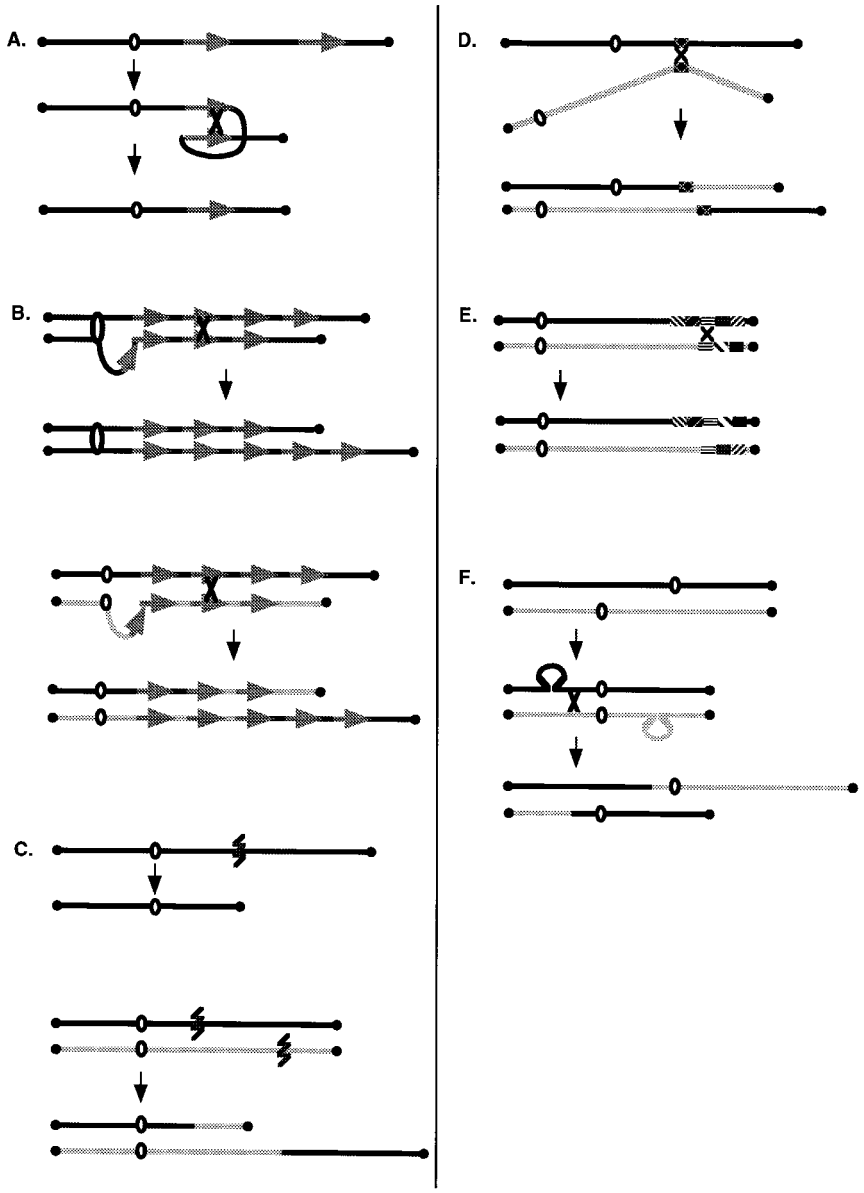

FIG. 2. Mechanisms by which CLPs may be generated. Each mechanism is described in the text. Symbols used: horizontal lines (solid or shaded), chromosomes; arrows along chromosomes, repeated sequences; ovals along chromosomes, centromeres; knobs at the ends of chromosomes, telomeres; X's, crossover points; jagged lines (C), breakpoints; hatched and lined boxes (E), subtelomeric repeats.

(60) found high conservation of *Sfi*I/*Not*I maps. In the case of chromosome VIII, which differed in the strains they examined by 30 kb, or about 5% of the size of the chromosome, they found most of the size difference in one *Sfi*I fragment which mapped to the central region of the chromosome, and part of the CLP reflected the absence of the subtelomeric Y sequences on the right arm of one of the chromosome VIII homologs compared.

Numerous CLPs are found in wild and industrial strains of *S. cerevisiae*. The types of CLPs observed include aneuploidy, changes in the occurrence and length of subtelomeric repeats, translocations, and uncharacterized CLPs for both baking strains (44a) and wine strains (2, 4). As expected, crosses between strains with pronounced CLPs, presumably including translocations, resulted in lowered spore viability. Translocations have also been documented and correlated with CLPs for laboratory strains of *S. cerevisiae* (116) and *N. crassa* (91).

The majority of studies of CLPs have been in fungi for which less genetic and physical data are available and for which the CLPs observed are often quite large. For example, Fig. 1A shows the electrophoretic separation of the chromosomes of two strains of the fungus *C. cinereus*. As is common for many filamentous fungi, there are two size groups of chromosomes, necessitating the use of different PFGE conditions to effect reasonable separation of most of the chromosomes. The two strains shown, Java-6 and Okayama-7, exhibit numerous CLPs, and it is not possible to identify homologs by inspection of the gel photograph alone. This electrophoretic karyotype has been partially correlated with the *C. cinereus* genetic map by the use of cloned gene probes and by genetic studies (101, 143). In

addition, the haploid chromosome number, 13, has been determined by numerous microscopic studies (41, 102). Although the two strains differ in the lengths of most or all of their chromosomes, they are interfertile, and new sizes of chromosomes appear after meiosis, indicating that recombination has probably occurred between homologs (143, 145). However, proof that the new chromosome sizes represent recombinants between presumptive homologs has not yet been obtained. The progeny of crosses between the two strains have a variety of karyotypes. Therefore, many of the length changes between these two strains likely represent gains and losses of nonessential sequences. However, genetic and molecular hybridization studies indicate that at least one translocation, which must be balanced, differentiates the genomes of Java-6 and Okayama-7. This translocation may involve chromosome 13, because some of the sequences isolated from a chromosome 13-specific library of Java-6 hybridize to chromosome 13 of Okayama-7, but others hybridize to a different, not identified, Okayama-7 chromosome (145).

Although the electrophoretic karyotype of *C. cinereus* is a useful tool for the assignment of genes to chromosomes and the construction of chromosome-specific libraries (143, 144), the physical basis for the CLPs cannot be determined without direct comparative physical mapping. In addition, although genetic markers are known for 10 of the 13 chromosomes (14), the lack of a more complete genetic map makes the interpretation of the genetic meaning of CLPs difficult.

A physical approach to the analysis of CLPs has been used to compare the complete electrophoretic karyotypes of two strains of *Candida albicans* (16), a pathogenic yeast which has no known sexual phase. In this study, *Sfi*I restriction maps were constructed and compared for strains 1006 and WO-1, which were chosen in part because their electrophoretic karyotypes are strikingly different (Fig. 1B). Strain WO-1 is a switching strain: it switches back and forth between growth in the normal yeast shape, producing white colonies, and an elongated, slipper-shaped form, producing opaque colonies (121). Switching is not accompanied by karyotypic changes, and except for the rDNA chromosome, the karyotype of both strains is stable under prolonged laboratory growth conditions.

The genome of strain 1006 consists of eight chromosome pairs, and the genome of WO-1 differs from it by three reciprocal translocations, so that six of its chromosome pairs have dimorphic homologs. Strikingly, the translocations have all taken place at or near *Sfi*I sites. Since the dispersed repeat RPS1 is known to contain four *Sfi*I sites (43), the data are consistent with a model in which the translocations have resulted from ectopic recombination between copies of RPS1. Sequencing of translocation breakpoints should provide information in support of or against this model.

In sexual fungi, a genetic approach to the examination of intraspecific CLPs may be taken. Tzeng et al. (132) constructed a restriction fragment length polymorphism (RFLP) map using a cross between two strains of *Cochliobolus heterostrophus*, Hm540 and B30.A3R.45, which differ by numerous CLPs (Fig. 1C). Three features of their data are particularly relevant to a consideration of CLPs. First, they documented a reciprocal translocation whose breakpoints map to the site of the virulence locus *Tox1*. This genetic translocation may explain the low viability reported for this cross and for other crosses between *tox1* and *TOX1* strains. Second, strain Hm540 contains 15 chromosomes, while strain B30.A3R.45, which is also haploid, has 16 chromosomes. Chromosome 16 of B30.A3R.45 is not an unusually small chromosome; it is 1.3 Mb, and several chromosomes of similar size are present in both parents. However, of the 91 random spore progeny analyzed in this study, two-thirds contained this extra chromosome. Of the one-third that did not, nine failed to hybridize with any of 15 markers specific to it. Thus, chromosome 16 in B30.A3R.45 most likely represents a B-like chromosome, similar to those found in numerous other organisms (46).

A third feature of the *C. heterostrophus* study was the documentation of several insertion and deletion events which contributed to the CLPs observed between the two strains. However, these documented events do not fully explain the extensive CLPs observed; the study was purposely done with probes depleted in repetitive sequences and is therefore necessarily incomplete in terms of the physical structures of the chromosomes. Therefore, numerous CLPs in these strains remain unexplained.

Extent of CLPs within Species

As the majority of chromosomes within fungal species are largely uncharacterized with respect to sequence content, it is difficult to define and quantify CLPs. In surveying karyotypic variation, certain basic issues come to mind. First, has adequate resolution of chromosomes been obtained? Inadequate resolution will lead to underestimates of the chromosome number. A useful solution to this problem has been described by Mills and coworkers (83). Bands from a gel containing unknown numbers of chromosomes can be cut out and digested with restriction enzymes. Then the separated fragments can be hybridized with a telomere-specific probe. Since each telomere-containing fragment will usually be of a unique size, individual telomeres can be identified and counted. A similar approach, using two-dimensional electrophoresis to produce chromosome-specific restriction profiles, was used to identify telomere bands in *Magnaporthe grisea* (29). An alternative method would be to sum the sizes of the bands generated by digestion with rare-cutting restriction enzymes; a single 2-Mb chromosome will generate only 2 Mb of fragments, and higher complexity will be readily apparent. However, this latter method decreases in usefulness as the size and number of comigrating chromosomes increase.

A more difficult issue to address is that of aneuploidy, which would lead to inaccurate estimates of chromosome number. With single-copy probes, sequence duplications can be discerned, but without complete genomic maps, it is difficult to determine whether a segment or an entire chromosome has been duplicated.

Beyond problems of resolution and ploidy determination, additional difficulties are endemic to the study of incompletely mapped genomes. First, if evidence of CLPs is obtained, it is important to determine whether the strains under comparison are really the same species. For example, the two yeasts *Kluyveromyces marxianus* and *Kluyveromyces lactis* are sometimes classified as the same species because individuals of the two species will mate. However, the hybrids between them produce offspring with no recombinant-sized chromosomes and no recombination of auxotrophic markers (124). Therefore, they are most likely different species, and as their karyotypes are strikingly different, their classification as the same species would overestimate the number and extent of CLPs from an intraspecific perspective. Second, when two presumptive homologs are compared, it is not always known whether they are truly homologous chromosomes, because some fungal genomes are so uncharacterized that designating homologs can be difficult. That is, it is often true that the sizes of true homologs correlate, but it is also clear from a number of studies that two chromosomes which comigrate are not necessarily homologous in sequence (for example, reference 16). In addition,

because translocations could be frequent, the use of a single or even a few single-copy probes is not sufficient to denote homologs and may also underestimate the amount of chromosomal rearrangement which has taken place (128).

Keeping these concerns in mind, it is evident that numerous CLPs, whatever their molecular basis, exist within populations of true species. CLPs are observed within both asexual and sexual populations. Kistler and Miao (53) proposed a meiotic maintenance hypothesis, stating that the amount and extent of CLPs will be found to be inversely correlated with the frequency of meiosis. It is certainly true that the fertility of crosses between strains with translocations will be lowered, so sexual populations and species are expected to exhibit fewer translocations that alter the linkage arrangements of essential genes. However, many CLPs are likely to involve changes that either do not affect the expression or dosage of genes or do so in a way that the organism tolerates. Therefore, although translocations per se are likely to be less abundant within sexual populations, CLPs in general do not necessarily have to be. For example, within a section (40 by 40 m) of a single wheat field, McDonald and Martinez (75) found that presumptive homologs varied in length by as much as 20% when strains of *Septoria tritici* (teleomorph *Mycosphaerella graminicola*) were compared. CLPs were also found to be abundant within three other sexual populations of *S. tritici*, and a similar study of *Stagonospora nodorum* also found numerous CLPs within sexual populations (74a). Fifteen spores from a single field-collected pseudoperithecium of *Leptosphaeria maculans* displayed 10 different karyotypes (97). A cross of two *M. grisea* strains used to generate an RFLP map revealed only one small translocation between the strains (119). In this cross, chromosome 4, which does not contain the *M. grisea* rRNA genes (rDNA), was significantly different between the two strains even though no changes in linkage arrangement of probe sequences was observed. Although insertion and deletion events were identified by 10 of the 97 RFLP markers used in this mapping study, markers for this chromosome were not well represented, and the nature of the CLP of chromosome 4 was not documented. A further report on this mapping cross (29) documented that the telomeric regions of all seven chromosomes were highly polymorphic, accounting for some of the CLPs observed.

Other studies have found a low number of CLPs in sexual populations. Geiser and coworkers (35) studied strains from different heterokaryon compatibility groups of *Aspergillus nidulans* and found a low amount of CLP when different groups were compared. However, low RFLP variation was also observed. Therefore, these data may be interpreted to mean either that meiosis has restricted the level of polymorphism or that the populations studied were of recent common ancestry and therefore were highly similar. Examination of electrophoretic karyotypes of *Gibberella fujikuroi* mating populations (anamorph *Fusarium moniliforme*) has also revealed a low amount of polymorphism within mating populations and greater polymorphism between them (140).

Asexual populations of *Fusarium oxysporum* f. sp. *cubense* showed more polymorphisms between than within vegetative compatibility groups (6). As would be expected, compatibility groups with the narrowest geographic distributions showed the least polymorphism, again arguing that recency of establishment may be critical to the extent of CLPs present in a population. Presumptively clonal populations of *M. grisea* were found to have variable karyotypes (128), although the authors did not demonstrate that this variability was in fact a barrier to mating and recombination among the strains examined. However, the extent of CLPs within baking strains of *S. cerevisiae* was found to correlate with reduced fertility in crosses among those strains (44a).

Thus, although it is logical that extensive translocations will be a block to the production of viable recombinant progeny and hence will be more prevalent between species than within them (26), the paucity of molecular data on the nature of CLPs makes it impossible to predict the extent of CLPs within sexual populations or the effect of the CLPs on fertility.

Dispensable Chromosomes

Dispensable chromosomes, or B chromosomes, have been observed for many species of plants and animals (46) but until recently were not known in fungi. They are defined as chromosomes with variable distribution within a species (present in only some individuals in some populations) which are completely dispensable to the individual in all tissues and are nonhomologous to the indispensable A set of chromosomes. They often display non-Mendelian patterns of inheritance, have a high frequency of mitotic nondisjunction, and exhibit various forms of meiotic drive (45). It is common for B chromosomes to have no detectable effect on the phenotype of the organisms, but this feature is variable.

In addition to entire dispensable chromosomes, dispensable regions of chromosomes are well known in some systems. Most notable are the heterochromatic knobs of maize (reviewed in references 13 and 46), which are supernumerary segments of otherwise nondispensable chromosomes.

Fungi appear to have both dispensable chromosomes and dispensable portions of chromosomes. Convincing evidence for a completely dispensable fungal chromosome in *Cochliobolis heterostrophus* has already been presented (132) (see Case Studies of Electrophoretic Karyotypes for details). Both a dispensable chromosome and dispensable portions of chromosomes are evident in *Nectria haematococca* mating population VI (79, 133). In this organism, *Pda* genes, necessary for the detoxification of the phytoalexin pisatin, are unexpectedly lost from some of the progeny in some crosses. This property seems to be inherent in all of the *Pda* genes so far characterized (78, 133), and in at least one case, the entire chromosome is apparently dispensable (79). The gene *Pda6* maps to a 1.6-Mb chromosome. In crosses between two strains carrying this chromosome, both of which are phenotypically Pda^+, some asci exhibited 4:4 segregation for the presence of the 1.6-Mb chromosome and for the Pda^+ phenotype. In some cases, a deletion derivative of this chromosome was present in Pda^- progeny, but in other Pda^- progeny, the chromosome seems to be completely missing. Although the only chromosome-specific probe hybridization reported was with the *Pda6* gene, use of the entire 1.6-Mb chromosome as a probe resulted in hybridization to a Pda^- progeny isolate with the deletion derivative chromosome but no reaction in a Pda^- progeny isolate which had no electrophoretically detectable remnant of the 1.6-Mb chromosome. As pointed out by Van Etten et al. (133) it may be appropriate to think of these pathogenicity genes as conditionally dispensable, i.e., necessary for growth in some contexts but not others, as is well established for the Ti plasmid of *Agrobacterium tumefaciens* or the sym plasmid of *Rhizobium* spp. Further understanding of the gene complement of the dispensable 1.6-Mb chromosome of *N. haematococca* may help to illuminate this issue.

Apparently dispensable chromosomes have also been found in *Colletotrichum gloeosporioides* (71). In Australia, there are two distinct pathotypes of *C. gloeosporioides*. The B biotype, race 3, contains a 1.2-Mb chromosome which is missing from non-race 3 type B strains. Ten clones specific to this chromo-

some fail to hybridize in the type B strains which are missing the 1.2-Mb chromosome, although other, repetitive sequences are present on both the 1.2-Mb chromosome and larger chromosomes. Therefore, the sequences represented by these clones are dispensable in the B biotype, and it will be interesting to determine, by analogy to the *N. haematococca* situation, whether they include genes necessary for race 3 pathogenicity.

Other studies have reported variable numbers of small chromosomes, sometimes termed minichromosomes, which exhibit polymorphism in size and number both between strains and in the progeny of crosses. The mere size differential between these chromosomes and the remainder of the karyotype is not sufficient to define them as dispensable; the dispensable chromosome of *C. heterostrophus* is the same size as a nondispensable chromosome, and in the case of uncharacterized small chromosomes, their derivation as translocation products of the larger chromosomes has not always been ruled out. However, in some cases the smallest chromosome of a strain does appear to have some of the properties of dispensable DNA sequences. For example, the smallest chromosome in strains of *Septoria nodorum*, which varies in size between 300 and 700 kb, is distinct in wheat-adapted and barley-adapted strains. Clones specific to this chromosome from one type of strain do not hybridize to chromosomes of the other, whereas clones derived from the larger chromosomes do cross-hybridize (14a).

A lack of Mendelian inheritance has been shown for the small chromosomes of *Bremia lactucae*, which are apparently composed primarily of repetitive DNA (32). In this case, although variable numbers of these chromosomes are seen in meiotic progeny, and although RFLP markers detected by probes specific to these chromosomes segregate aberrantly, all progeny contain at least one copy of these sequences. Thus, these chromosomes may not be completely dispensable, or else they may have an efficient mechanism of meiotic drive to maintain them in the population. Francis and Michelmore (32) also point out that in the absence of further information about the presence of centromeres and telomeres on the small chromosomes of *B. lactucae*, their status as true chromosomes or as linear, nuclear plasmids is unclear, and the same concern applies to the majority of the examples cited here.

DEVELOPMENTAL INSTABILITY OF THE KARYOTYPE

Mitotic Instability

With some notable exceptions (discussed below), mitotic stability of the karyotype is generally observed. Many researchers have reported that repeated preparations, often over a period of several years, yield the same electrophoretic karyotypes (*C. albicans* [16], other *Candida* spp. [85], *Colletotrichum gloeosporioides* [70], *Coprinus cinereus* [142a], *Fusarium oxysporum* f. sp. *cubense* [6], *Magnaporthe grisea* [128], *Septoria nodorum* [18], *Septoria tritici* [74a], and *Tilletia* spp. [108]). In many cases, deliberate subculturing for counted numbers of generations also did not change the karyotype. For example, 400 generations of growth of *Candida parapsilosis* did not result in any observable karyotypic changes (62). When 10 clones each of two different strains of *C. albicans* were grown for 100 generations, one strain did not show any variations, whereas for the other, karyotypic changes were reported for 3 of the 10 clones, and this strain is believed to be defective in some aspect of DNA metabolism (3).

An interesting study by Longo and Vezinhet (61) compared the mitotic stability of one haploid laboratory strain and one wild strain of *S. cerevisiae*. The karyotype of the haploid strain was stable for 412 generations. In contrast, the wild strain showed karyotypic changes, usually involving chromosome loss. Both the original and the derived wild strains would sporulate and make four-spored asci, but four viable spores were never obtained; thus, the true ploidy of the wild strain is unknown, and it is possible that all of the changes reported were chromosome losses, perhaps from a nominally diploid strain carrying some trisomies.

A different question about mitotic, or clonal, stability has been asked by investigators who grew organisms under nonlaboratory conditions. Karyotypic stability was found for strains of *S. cerevisiae* isolated before and after their use in wine fermentations (138). For *Fusarium oxysporum*, a strain reisolated every 4 weeks from artificially infested soil showed no karyotypic changes (81). Similarly, passage of two strains of *Ophiostoma ulmi* through the elm tree host did not result in any karyotypic changes except in the chromosome containing the rDNA (24a), and the karyotypes of *Colletotrichum gloeosporioides* type B pathogens are stable through repeated infections (70). The karyotype of the pathogen *Pneumocystis carinii* is stable within a colony of infected rats for at least 3 years (22). A recent study of *C. albicans* (27) illustrated the karyotypic stability of strains recurrently isolated from patients over the course of several months. All of these authors have pointed out that the stability of the karyotype under these conditions, combined with strain- and species-specific CLPs, makes electrophoretic karyotyping a useful tool in epidemiological and agricultural studies.

In contrast to these reports of karyotypic stability under nonlaboratory conditions, the karyotypes of two strains of *M. grisea* derived after numerous serial transfers in culture and passage through a rice cultivar were different from each other and from that of the original strain (128). The particular changes in these strains were not characterized, although the three strains were identical in their pattern of small chromosomes. At least some of the changes observed involved the rDNA chromosome, but some changes certainly did not. It cannot be ruled out that these CLPs resulted from physiological changes such as those described later for *C. albicans*, but it is possible that the high content of dispersed repeats in *M. grisea* (37, 119) contributes to an increased genomic plasticity in this fungus. Another significant finding from the work of Talbot et al. (128) was that the rearrangements found among different strains of *M. grisea* involve deletions, translocations, and more complex rearrangements. As stressed earlier (and as pointed out by the authors), it is clear that hybridization with single-copy probes may underestimate the complexity of chromosomal rearrangements detected in other studies.

Polymorphism in rDNA chromosome size. A prominent exception to the general mitotic stability of karyotypes is the chromosome(s) containing the long tract(s) of rDNA. Variability of the rDNA chromosome has been observed among different strains of many species, including *C. albicans* (44, 110, 113), *Coprinus cinereus* (103), *Cladosporium fulvum* (127), *Leptosphaeria maculans* (86), *Ophiostoma ulmi* (24a), *Pythium* spp. (69a), *S. cerevisiae* (89, 110), *Septoria nodorum* (18), and *Tilletia caries* (108). In a comparative study of 14 strains of *Ustilago hordei* (74), CLPs among 9 of 10 linkage groups studied averaged about 15% in size. The tenth linkage group, which contained the rDNA, was found to vary 86% in length. Variation in the rDNA chromosome has been observed after mitotic growth, after meiosis, after nutritional stress, and after transformation. Therefore, for this chromosome, much of the interstrain variation observed can be ascribed to developmental events which occur with regularity.

Where it has been directly examined, the number of rDNA

TABLE 2. rDNA tract variation[a]

Organism and strain	Interstrain variation			Developmental variation[b]		Reference
	Repeat size (kb)	rDNA tract length (kb)	Chromosome size (Mb)	rDNA tract length (kb)	Chromosome size (Mb)	
Candida albicans						110
3153A	11.6	291, 728[c]	2.52, 3.02	291, 728[c]	2.52, 3.02[d]	
WO-1	11.5, 12.5[d]	534, 2,200	2.20, 3.5			
Coprinus cinereus Ac18+				600, 1,100[e]	2.4, 3.0	103

[a] Data were selected to illustrate the range of sizes reported; additional measurements are presented in the primary references.
[b] This refers to events during mitotic or meiotic growth, including spontaneous mutagenesis and transformation. Induced mutagenesis is not included.
[c] The homolog assignment of different repeat tracts is unknown.
[d] *C. albicans* is a diploid; these are the sizes of the two homologs within the given strain.
[e] In this strain, two rDNA chromosomes were apparent, presumably because a mixed population of haploid cells was examined.

repeats in a tract has been found to be variable, and some studies have directly correlated CLPs in the rDNA chromosome with changes in the number of rDNA repeats in a tract (Table 2). The length of the rDNA tract is typically examined by digestion of chromosomes with a restriction enzyme which does not cut within the rDNA subunit. For example, in *Coprinus cinereus*, *Hin*dIII digestion of chromosomal plugs reveals two linked clusters of rDNA repeats (Fig. 3) (103). One of these, 100 kb in size, does not apparently vary in wild-type strains. The second, which is 1,100 kb in size in the control strain used by Pukkila and Skryzynia, has been shown to vary after transformation, during vegetative growth, and during premeiotic and meiotic divisions. Changes in the size of this band correlate directly with changes in the size of the chromosome containing the rDNA repeats (Table 2), and changes can be as large as 500 kb, or 17% of the initial length of the chromosome.

Similarly large, and correlated, changes in the size of the rDNA cluster and rDNA chromosomes were observed among clinical isolates and spontaneous mutants of *C. albicans* (Table 2) (110). In these mutants, which are also discussed below, numerous changes in electrophoretic karyotype were observed, but the rDNA chromosome varied about twice as often as other chromosomes. In 23 of 25 rDNA chromosomes from various origins examined, changes in the rDNA tract length were shown to be directly responsible for the chromosome size changes. The remaining two had undergone other chromosomal rearrangement events in addition to those involving rDNA.

Most strains of *S. cerevisiae* have one cluster of rDNA on chromosome XII, with reported rDNA cluster sizes ranging from 290 to 1,640 kb, which again correlate with changes in the size of this chromosome (Table 2) (15, 92, 110). A systematic study of clonal and meiotic variation with a diploid strain of *S. cerevisiae* (15) showed that the two rDNA-containing homologs varied to different extents. In one experiment, the larger homolog, initially 2.6 Mb, varied in 43% of 40 clonal isolates examined, while in the same isolates, only 13% of the smaller homologs (initially 1.5 Mb) were variable. In meiotic progeny of this diploid, the larger rDNA chromosome was stable, whereas the smaller homolog had increased in size in all 10 tetrads examined. In each case, the rDNA chromosome sizes segregated 2:2, meaning that the increase in size of the smaller homolog had taken place premeiotically.

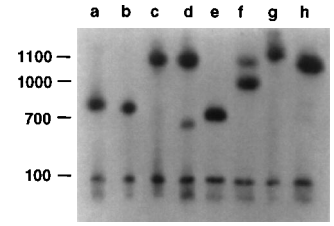

FIG. 3. Variability in the rDNA of *Coprinus cinereus* (reprinted from reference 103, with permission of the publisher). Fragment sizes are shown in kilobases. Lane h, *C. cinereus* 218; lanes a, b, c, d, and g, transformants of *C. cinereus* 218; lane e, oidial derivative of strain 218; lane f, oidial derivative of an oidial derivative (218-4) of strain 218.

In *N. crassa*, it has been shown that the number of copies of rDNA can vary and that strains with radically fewer or more rDNA copies were slow growing (109). Butler and Metzenberg (12) did not examine the size of the rDNA-containing chromosome but showed that the size of rDNA repeat tracts could vary nearly twofold and that the variation was most frequent during the postfertilization but prekaryogamy period. They also showed (11), by using a hybrid tract composed of two blocks of differentially marked repeats, that changes in the size of the tract were not confined to one region. A notable finding from their studies was that in the case of tracts at the normal position, which is near the terminus of linkage group V, and in the case of small interstitial tracts translocated to linkage group I, decreases in the number of rDNA repeats were found at a higher frequency than increases. For example, for the hybrid rDNA tract, which was initially measured as 1,450 kb, seven of eight random spore progeny examined had a change, and six of these were decreases. In contrast, in a cross between a strain with an unusually small rDNA tract, of 800 kb, and a strain with a tract of about 1,300 kb, nearly all of the progeny receiving the chromosome from the small-tract parent had an amplified rDNA tract. The rDNA amplification occurred both premeiotically and during meiosis.

Other studies have also shown growth-related amplification of rDNA sequences. In *Kluyveromyces lactis* (66), slow-growing strains have only 43 to 55% of the number of rDNA repeats found in fast-growing strains. When subjected to prolonged vegetative growth, slow-growing strains can increase their growth rate, and this increase correlates with an increase in the size of the rDNA cluster. Similarly, rapidly growing cultures of both *C. albicans* and *S. cerevisiae* have more copies of rDNA than slowly growing cultures (112). Thus, it seems that although a wide range of rDNA repeat numbers can be tolerated, under some conditions growth rate is tied to the number of rRNA genes, and fungi have mechanisms for ensuring that this number does not fall below a minimal size.

Cases of rapid karyotypic change. A striking feature of the literature on fungal karyotypes is the general conservation of the karyotype during mitotic growth. It is well known that normal diploid human cells have stable karyotypes in culture but that transformed cell lines have variable karyotypes and

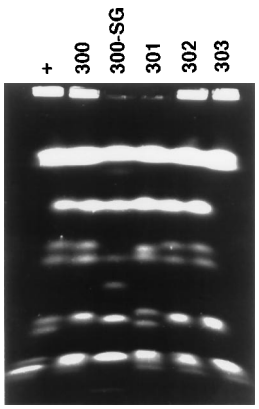

FIG. 4. Karyotypic variability in morphological mutants of *Candida albicans* (reprinted from reference 113, with permission of the publisher). Lanes: +, wild-type strain of *C. albicans*; 300, derivative of the wild-type strain; 300-SG, 301, 302, and 303, spontaneous nongerminative mutants derived from strain 300.

are prone to genomic alterations such as gene amplification (130). In fungi as well, controls during vegetative growth keep the frequency of karyotypic rearrangements low. For example, in *S. cerevisiae*, the frequency of mitotic ectopic recombination events, which can rearrange the karyotype, is only 0.1% of the rate during meiosis (95). As mentioned above, even though karyotypic changes are present when different strains are compared, growth of a given strain normally yields changes only in the rDNA chromosome.

A striking exception to mitotic stability of the karyotype has been seen in the work of Rustchenko and coworkers, who studied spontaneous mutants of *C. albicans* that displayed altered colony morphologies and which arose most frequently after prolonged culture in the cold (114). These cultures have many karyotypic changes, involving not only the rDNA chromosome but also other chromosomes (Fig. 4). Although the specific changes in the karyotypes in these mutants did not correlate with specific phenotypic changes, the work is important in that it showed a general loss of karyotypic maintenance control. Later studies (111) showed that strains incubated for long periods on medium with sorbose or arabinose as the only carbon source (neither is normally usable by the standard *C. albicans* strains) spontaneously yield mutants that are Sor^+ or Ara^+. In this case, specific karyotypic changes accompany the phenotypic changes, and although the breakpoints of the karyotypic rearrangements have not been mapped, they are predicted to be in the regions of the affected genes. Another study, in *Candida stellatoidea* (136), showed a similar phenomenon to the one documented in *C. albicans*; Suc^+ mutants arose after prolonged incubation of Suc^- cultures on medium with sucrose as the only carbon source, and each was reported to exhibit characteristic karyotypic changes. Similarly, Adams and coworkers (1) examined the electrophoretic karyotypes of strains of *S. cerevisiae* which had been grown for up to 1,000 generations under limiting organic phosphate at pH 6. Karyotypic changes in the cultures were observed, implying that karyotypic change is an adaptive mechanism under these conditions.

The mutants isolated by Rustchenko and others are strikingly similar to the adaptive mutants reported for *Escherichia coli* and *S. cerevisiae* (see reference 31 for a review). In all of these cases, mutants arise on selective medium long after standard replication of mutant cells has ceased. Although different interpretations hold for the origin of these mutants, one of the most interesting aspects of their generation is that they must arise by a mechanism operating in cells unable to undergo normal rounds of DNA synthesis. Instead, various levels and types of repair synthesis have been hypothesized (122), and the cells are said to enter a type of hypermutable state (36). In addition, it was recently shown that the appearance of such mutants in *E. coli* is dependent on *recA* and *recB* and that adaptive mutation in this organism therefore involves recombination (38). It seems logical that in the case of the *Candida* mutants, a similar hypermutable state is entered and that this state involves a release of the normally stringent control of the karyotype. It should be straightforward to test directly whether the appearance of adaptive mutants in fungi is accompanied by a loss of control of the karyotype. This loss could be viewed in two ways. First, it could be a loss of suppression of mitotic ectopic recombination. Second, and not mutually exclusively, it could be an induction of DNA repair processes which lead to an increased frequency of genomic rearrangements, presumably mediated by ectopic recombination. It will be particularly important to determine if this type of loss is unique to fungi without a sexual cycle and is exploited by the fungus as a means of enhancing variability, as suggested previously (114), or if this kind of karyotypic instability can be induced in organisms which do not have to rely on asexual variation. It is more likely that this hypermutational avenue is open to all fungi, since all can grow and propagate vegetatively; extreme rearrangements of the karyotype would produce barriers to the production of viable meiotic progeny.

It has also been reported that transformation can lead to dramatic changes in the karyotype of a fungus (3, 14a, 94, 103, 104a, 141). These changes can involve several chromosomes, including the rDNA chromosome, the chromosome into which the transforming DNA integrates, and other, unrelated chromosomes. Thus, the overall induction of repair processes in transformation may mimic their induction in resting-state mutants. It will be interesting to see if any mutants known to be defective in DNA metabolism (for example, references 34, 99, and 104) enhance or suppress this type of genomic rearrangement.

Meiotic Changes

Several studies have documented that strains with CLPs can undergo meiosis and produce viable spores. Two types of segregation of presumptive homologs have been observed in tetrad analysis from such crosses. In the case of homologous chromosomes which have one heterology, the CLPs segregate 2:2. An example of this in *Ustilago hordei* was reported by McCluskey et al. (74), who examined segregation of a chromosome carrying a telomere-linked deletion which included the gene *fill-1*. In a cross between a *fill-1* mutant strain and a closely related wild-type strain, the *fill-1* deletion chromosome segregated 2:2 with its wild-type homolog.

As pointed out by Ono and Ishino-Arao (90), if homologs have two or more heterologies, crossing-over between them can produce new chromosome sizes (Fig. 2). New chromosome sizes after meiosis have been reported for *Coprinus cinereus* (144, 145), *Ustilago maydis* (50) *S. cerevisiae* (90), *Pythium sylvaticum* (69), and *Leptosphaeria maculans* (97). In both *C. cinereus* and *L. maculans*, tetrads produced by crosses between strains with CLPs can contain apparently reciprocal recombinant products (96, 145). In *C. cinereus*, crosses between strains without CLPs do not lead to new chromosome sizes in the progeny (145), and the karyotype of *C. cinereus* strains is

known to be stable mitotically (except for the rDNA chromosome). Therefore, the new chromosome sizes observed in basidiospore progeny are dependent for formation on meiosis in a strain with CLPs. A logical conclusion from these studies is that these new chromosome sizes, which often are intermediate in size between the presumptive homologs of the parents (144, 145), do result from meiotic recombination between homologs containing more than one heterology (as diagrammed in Fig. 2). However, since it has not yet been demonstrated that the chromosomes of new sizes are in fact recombinants containing physical markers from the presumed homologs of the two parental strains, it is formally possible that intrachromosomal expansion or diminution may be taking place instead. If homologs of different sizes are undergoing recombination, it should be possible to demonstrate directly that new chromosomes are the products of reciprocal recombination between these homologs.

In random spore progeny and tetrads, the range of karyotypes observed after crosses between strains with many CLPs makes it likely that at least a portion of the CLPs are made up of dispensable sequences, which may be present, absent, or duplicated without phenotypic consequence. In the meiotic studies reported so far, the nature of the heterologies between homologs was not known except for the specific case of the *fill-1* deletion described above. Therefore, it is unknown whether the heterologies are clustered, either as changes in the lengths or composition of subtelomeric repeats or as interstitial heterologies akin to the heterochromatic knobs of maize (13), or whether they represent the sum of several differences across the lengths of the homologs. It is unlikely, however, that most CLPs represent changes in the linkage arrangements of coding sequences, since so many different karyotypes are viable. However, some CLPs are undoubtedly due to translocations, and the tetrads produced by crosses in which the two parents display many CLPs have lowered viability (44a, 100).

CONCLUSIONS

CLPs are widespread among fungal species and result both from genetic translocations and from gains and losses of what are probably nonessential sequences. Most CLPs are still uncharacterized with respect to their content and origin. However, it is clear that long tandem repeats, such as rDNA tracts, are frequently variable in length and that other chromosomal rearrangements are suppressed during normal mitotic growth. The mitotic stability of the karyotype and the interstrain variation represent an apparent paradox; if strains are so stable mitotically, why is there so much interstrain variation? For asexual organisms, the answer may be twofold. First, a low level of mitotic rearrangement does take place, and more divergent karyotypes likely represent strains which have been growing separately for the longest periods of time. Second, certain physiological states, such as starvation, may induce a relaxation of the tight mitotic control of the karyotype or induce DNA repair functions which lead to rearrangements. For sexual species, the mechanisms that apply to asexual fungi operate and, in addition, meiotic recombination increases the overall karyotypic variability in a population while suppressing genetic translocations. The range of karyotypes observed in fungi indicates that many karyotypic changes may be genetically neutral, at least under some conditions. In addition, new linkage combinations of genes may also be advantageous in allowing adaptation of fungi to new environments.

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REFERENCES

1. **Adams, J., S. Puskas-Rozsa, J. Simlar, and C. M. Wilke.** 1992. Adaptation and major chromosomal changes in populations of *Saccharomyces cerevisiae*. Curr. Genet. **22:**13–19.
2. **Bakalinsky, A. T., and R. Snow.** 1990. The chromosomal constitution of wine strains of *Saccharomyces cerevisiae*. Yeast **6:**367–382.
3. **Barton, R. C., and S. Scherer.** 1994. Induced chromosome rearrangements and morphologic variation in *Candida albicans*. J. Bacteriol. **176:**756–763.
4. **Bidenne, C., B. Blondin, S. Dequin, and F. Vezinhet.** 1992. Analysis of the chromosomal DNA polymorphism of wine strains of *Saccharomyces cerevisiae*. Curr. Genet. **22:**1–7.
5. **Birren, B., and E. Lai.** 1993. Pulsed field gel electrophoresis: a practical guide. Academic Press, Inc., San Diego.
6. **Boehm, E. W. A., R. C. Ploetz, and H. C. Kistler.** 1994. Statistical analysis of electrophoretic karyotype variation among vegetative compatibility groups of *Fusarium oxysporum* f. sp. *cubense*. Mol. Plant-Microbe Interact. **7:**196–207.
7. **Boeke, J. D.** 1989. Transposable elements in *Saccharomyces cerevisiae*, p. 335–374. *In* D. E. Berg and M. M. Howe (ed.), Mobile DNA. American Society for Microbiology, Washington, D.C.
8. **Boeke, J. D., D. J. Eichinger, and G. Natsoulis.** 1991. Doubling Ty1 element copy number in *Saccharomyces cerevisiae*: host genome stability and phenotypic effects. Genetics **129:**1043–1052.
9. **Brody, H., and J. Carbon.** 1989. Electrophoretic karyotype of *Aspergillus nidulans*. Proc. Natl. Acad. Sci. USA **86:**6260–6263.
10. **Brody, H., J. Griffith, A. J. Cuticchia, J. Arnold, and W. E. Timberlake.** 1991. Chromosome-specific recombinant DNA libraries from the fungus Aspergillus nidulans. Nucleic Acids Res. **19:**3105–3109.
11. **Butler, D. K., and R. L. Metzenberg.** 1990. Expansion and contraction of the nucleolus organizer region of Neurospora: changes originate in both proximal and distal segments. Genetics **126:**325–333.
12. **Butler, D. K., and R. L. Metzenberg.** 1989. Premeiotic change of nucleolus organizer size in *Neurospora*. Genetics **122:**783–791.
13. **Carlson, W. R.** 1977. The cytogenetics of corn, p. 225–304. *In* G. F. Sprague (ed.), Corn and corn improvement. American Society of Agronomy, Inc., Madison, Wis.
14. **Casselton, L. A.** 1995. Genetics of *Coprinus*, p. 35–48. *In* U. Kuck (ed.), The mycota II: genetics and biotechnology. Springer-Verlag, Berlin.

14a. **Caten, C.** Personal communication.

15. **Chindamporn, A., S.-I. Iwaguchi, Y. Nakagawa, M. Homma, and K. Tanaka.** 1993. Clonal size-variation of rDNA cluster region on chromosome XII of *Saccharomyces cerevisiae*. J. Gen. Microbiol. **139:**1409–1415.
16. **Chu, W., B. B. Magee, and P. T. Magee.** 1993. Construction of an *Sfi*I macrorestriction map of the *Candida albicans* genome. J. Bacteriol. **175:** 6637–6651.
17. **Cooley, R. N.** 1992. The use of RFLP analysis, electrophoretic karyotyping and PCR in studies of plant pathogenic fungi. *In* U. Stahl and P. Tudzynski (ed.), Molecular biology of filamentous fungi. UCH Publishers, Inc., New York.
18. **Cooley, R. N., and C. E. Caten.** 1991. Variation in electrophoretic karyotype between strains of *Septoria nodorum*. Mol. Gen. Genet. **228:**17–23.
19. **Corcoran, L. M., J. K. Thompson, D. Walliker, and D. J. Kemp.** 1988. Homologous recombination within subtelomeric repeat sequences generates chromosome size polymorphisms in P. falciparum. Cell **53:**807–813.
20. **Covert, S. F., J. Bolduc, and D. Cullen.** 1992. Genomic organization of a cellulase gene family in *Phanerochaete chrysosporium.* Curr. Genet. **22:**407–413.
21. **Cushion, M. T., M. Kaselis, S. L. Stringer, and J. R. Stringer.** 1993. Genetic stability and diversity of *Pneumocystis carinii* infecting rat colonies. Infect. Immun. **61:**4801–4813.
22. **Cushion, M. T., J. R. Stringer, and P. D. Walzer.** 1991. Cellular and molecular biology of *Pneumocystis carinii*. Int. Rev. Cytol. **131:**59–107.
23. **Daboussi, M. J., and T. Langin.** 1994. Transposable elements in the fungal plant pathogen *Fusarium oxysporum*. Genetica **93:**49–59.
24. **Daboussi, M. J., T. Langin, and Y. Brygoo.** 1992. *Fot1*, a new family of fungal transposable elements. Mol. Gen. Genet. **232:**12–16.

24a. **Dewar, K.** Personal communication.

25. **Dobinson, K. F., R. E. Harris, and J. E. Hamer.** 1993. Grasshopper, a long terminal repeat (LTR) retroelement in the phytopathogenic fungus *Magnaporthe grisea*. Mol. Plant-Microbe Interact. **6:**114–126.
26. **Dobzhansky, T.** 1976. Organismic and molecular aspects of species formation, p. 95–105. *In* F. J. Ayala (ed.), Molecular evolution. Sinauer Associates, Inc., Sunderland, Mass.
27. **Doi, M., I. Mizuguchi, M. Homma, and K. Tanaka.** 1994. Electrophoretic karyotypes of *Candida* yeasts recurrently isolated from single patients. Microbiol. Immunol. **38:**19–23.
28. **Fan, J.-B., Y. Chikashige, C. L. Smith, O. Niwa, M. Yanagida, and C. R. Cantor.** 1988. Construction of a Not I restriction map of the fission yeast *Schizosaccharomyces pombe* genome. Nucleic Acids Res. **17:**2801–2818.
29. **Farman, M. L., and S. A. Leong.** 1995. Genetic and physical mapping of telomeres in the rice blast fungus, *Magnaporthe grisea*. Genetics **140:**479–492.
30. **Fedoroff, N. V.** 1989. Maize transposable elements, p. 375–411. *In* D. E. Berg and M. M. Howe (ed.), Mobile DNA. American Society for Microbiology, Washington, D.C.
31. **Foster, P. L.** 1993. Adaptive mutation: the uses of adversity. Annu. Rev. Microbiol. **47:**467–504.
32. **Francis, D. M., and R. W. Michelmore.** 1993. Two classes of chromosome-sized molecules are present in *Bremia lactucae*. Exp. Mycol. **17:**284–300.
33. **Freedman, T., and P. J. Pukkila.** 1993. *De novo* methylation of repeated sequences in *Coprinus cinereus*. Genetics **135:**357–366.
34. **Game, J. C.** 1993. DNA double-strand breaks and the *RAD50-RAD57* genes in *Saccharomyces*. Semin. Cancer Biol. **4:**73–83.
35. **Geiser, D. M., M. L. Arnold, and W. E. Timberlake.** 1994. Sexual origins of British *Aspergillus nidulans* isolates. Proc. Natl. Acad. Sci. USA **91:**2349–2352.
36. **Hall, B. G.** 1991. Increased rates of advantageous mutations in response to environmental challenges. ASM News **57:**82–86.
37. **Hamer, J. E., L. Farrall, M. J. Orbach, B. Valent, and F. G. Chumley.** 1989. Host species-specific conservation of a family of repeated DNA sequences in the genome of a fungal plant pathogen. Proc. Natl. Acad. Sci. USA **86:**9981–9985.
38. **Harris, R. S., S. Longerich, and S. M. Rosenberg.** 1994. Recombination in adaptive mutation. Science **264:**258–260.
39. **Hightower, R. C., T. M. Callahan, and R. G. Upchurch.** 1995. Electrophoretic karyotype of *Cercospora kikuchii*. Curr. Genet. **27:**290–292.
40. **Hinterberg, K., D. Mattei, T. E. Wellems, and A. Scherf.** 1994. Interchromosomal exchange of a large subtelomeric segment in a *Plasmodium falciparum* cross. EMBO J. **13:**4174–4180.
41. **Holm, P. B., S. W. Rasmussen, D. Zickler, B. C. Lu, and J. Sage.** 1981. Chromosome pairing, recombination nodules and chiasma formation in the basidiomycete *Coprinus cinereus*. Carlsberg Res. Commun. **46:**305–346.
42. **Horton, J. S., and C. A. Raper.** 1991. Pulsed-field gel electrophoretic analysis of *Schizophyllum commune* chromosomal DNA. Curr. Genet. **19:**77–80.
43. **Iwaguchi, S., M. Homma, H. Chibana, and K. Tanaka.** 1992. Isolation and characterization of a repeated sequence (RPS1) of *Candida albicans*. J. Gen. Microbiol. **138:**1893–1900.
44. **Iwaguchi, S., M. Homma, and K. Tanaka.** 1992. Clonal variation of chromosome size derived from the rDNA cluster region in *Candida albicans*. J. Gen. Microbiol. **138:**1177–1184.

44a. **Jager, D.** Personal communication.

45. **Jones, R. N.** 1991. B-chromosome drive. Am. Nat. **137:**430–442.
46. **Jones, R. N., and H. Rees.** 1982. B chromosomes. Academic Press, New York.
47. **Julien, J., S. Poirier-Hamon, and Y. Brygoo.** 1992. *Foret1*, a reverse transcriptase-like sequence in the filamentous fungus *Fusarium oxysporum*. Nucleic Acids Res. **20:**3933–3937.
48. **Keller, E. F.** 1983. A feeling for the organism. W. H. Freeman and Company, New York.
49. **Kerrigan, R. W., J. C. Royer, L. M. Baller, Y. Kohli, P. A. Horgen, and J. B. Anderson.** 1993. Meiotic behavior and linkage relationships in the secondarily homothallic fungus *Agaricus bisporus*. Genetics **133:**225–236.
50. **Kinscherf, T. G., and S. A. Leong.** 1988. Molecular analysis of the karyotype of *Ustilago maydis*. Chromosoma **96:**427–433.
51. **Kinsey, J. A., and J. Helber.** 1989. Isolation of a transposable element from *Neurospora crassa*. Proc. Natl. Acad. Sci. USA **86:**1929–1933.
52. **Kistler, H. C., and U. Benny.** 1992. Autonomously replicating plasmids and chromosome rearrangement during transformation of *Nectria haematococca*. Gene **117:**81–89.
53. **Kistler, H. C., and V. P. W. Miao.** 1992. New modes of genetic change in filamentous fungi. Annu. Rev. Phytopathol. **30:**131–152.
54. **Kitamoto, K., K. Kimura, K. Gomi, and C. Kumagai.** 1994. Electrophoretic karyotype and gene assignment to chromosomes of *Aspergillus oryzae*. Biosci. Biotech. Biochem. **58:**1467–1470.
55. **Kohli, J.** 1994. Meiosis: telomeres lead chromosome movement. Curr. Biol. **4:**724–727.
56. **Lai, E., B. W. Birren, S. M. Clark, M. I. Simon, and L. Hood.** 1989. Pulsed field gel electrophoresis. BioTechniques **7:**34–42.
57. **Levin, H. L., D. C. Weaver, and J. D. Boeke.** 1990. Two related families of retrotransposons from *Schizosaccharomyces pombe*. Mol. Cell. Biol. **10:**6791–6798.
58. **Lim, J. K.** 1988. Intrachromosomal rearrangements mediated by hobo transposons in Drosophila melanogaster. Proc. Natl. Acad. Sci. USA **85:**9153–9157.
59. **Lim, J. K., and M. J. Simmons.** 1994. Gross chromosome rearrangements mediated by transposable elements in *Drosophila melanogaster*. BioEssays **16:**269–275.
60. **Link, A. J., and M. V. Olson.** 1991. Physical map of the *Saccharomyces cerevisiae* genome at 110-kilobase resolution. Genetics **127:**681–698.
61. **Longo, E., and F. Vezinhet.** 1993. Chromosomal rearrangements during vegetative growth of a wild strain of *Saccharomyces cerevisiae*. Appl. Environ. Microbiol. **59:**322–326.
62. **Lott, T. J., R. J. Kuykendall, S. F. Welbel, A. Pramanik, and B. A. Lasker.** 1993. Genomic heterogeneity in the yeast *Candida parapsilosis*. Curr. Genet. **23:**463–467.
63. **Louis, E. J., E. S. Naumova, A. Lee, G. Naumov, and J. E. Haber.** 1994. The chromosome end in yeast: its mosaic nature and influence on recombinational dynamics. Genetics **136:**789–802.
64. **Lu, B. C.** 1982. Replication of deoxyribonucleic acid and crossing over in *Coprinus*, p. 93–112. *In* K. Wells and E. K. Wells (ed.), Basidium and basidiocarp. Springer-Verlag, New York.
65. **Lyttle, T. W., and D. S. Haymer.** 1992. The role of the transposable element *hobo* in the origin of endemic inversions in wild populations of *Drosophila melanogaster. Genetica* **86:**113–126.
66. **Maleszka, R., and G. D. Clark-Walker.** 1990. Magnification of the rDNA cluster in *Kluyveromyces lactis*. Mol. Gen. Genet. **223:**342–344.
67. **Manners, J. M., A. Masel, K. S. Braithwaite, and J. A. G. Irwin.** 1992. Molecular analysis of *Colletotrichum gloeosporioides* pathogenic on the tropical pasture legume *Stylosanthes*, p. 250–268. *In* J. A. Bailey and M. J. Jeger (ed.), *Colletotrichum*: biology, pathology and control. C.A.B. International, Wallingford, United Kingdom.
68. **Mantyla, A. L., K. H. Rossi, S. A. Vanhanen, M. E. Penttilä, P. L. Suominen, and K. M. H. Nevalainen.** 1992. Electrophoretic karyotyping of wild-type and mutant *Trichoderma longibrachiatum* (*reesei*) strains. Curr. Genet. **21:**471–477.
69. **Martin, F.** 1995. Meiotic instability of *Pythium sylvaticum* as demonstrated by inheritance of nuclear markers and karyotype analysis. Genetics **139:**1233–1246.

69a. **Martin, F. N.** Personal communication.

70. **Masel, A., K. Braithwaite, J. Irwin, and J. Manners.** 1990. Highly variable molecular karyotypes in the plant pathogen *Colletotrichum gloeosporioides*. Curr. Genet. **18:**81–86.
71. **Masel, A. M., J. A. G. Irwin, and J. M. Manners.** 1993. Mini-chromosomes of *Colletotrichum* spp. infecting several host species in various countries. Mycol. Res. **97:**852–856.
72. **McClintock, B.** 1945. *Neurospora*. I. Preliminary observations of the chromosomes of *Neurospora crassa*. Am. J. Bot. **32:**671–678.
73. **McClintock, B.** 1984. The significance of responses of the genome to challenge. Science **226:**792–801.
74. **McCluskey, K., and D. Mills.** 1990. Identification and characterization of chromosome length polymorphisms among strains representing fourteen races of *Ustilago hordei*. Mol. Plant-Microbe Interact. **3:**366–373.

74a. **McDonald, B.** Personal communication.

75. **McDonald, B. A., and J. P. Martinez.** 1991. Chromosome length polymorphisms in a *Septoria tritici* population. Curr. Genet. **19:**265–271.
76. **McHale, M. T., I. N. Roberts, S. M. Noble, C. Beaumont, M. P. Whitehead, D. Seth, and R. P. Oliver.** 1992. *CfT-I*: an LTR-retrotransposon in *Cladosporium fulvum*, a fungal pathogen of tomato. Mol. Gen. Genet. **233:**337–347.
77. **McHale, M. T., I. N. Roberts, N. J. Talbot, and R. P. Oliver.** 1989. Expression of reverse transcriptase genes in *Fulvia fulva*. Mol. Plant-Microbe Interact. **2:**165–168.
78. **Miao, V., and H. Van Etten.** 1992. Three genes for maackiain metabolism in the plant pathogen *Nectria haematococca*: meiotic instability and relationship to a new gene for pisatin demethylase. Appl. Environ. Microbiol. **58:**801–808.
79. **Miao, V. P., S. F. Covert, and H. D. Van Etten.** 1991. A fungal gene for antibiotic resistance on a dispensable ("B") chromosome. Science **254:**1773–1776.
80. **Miao, V. P. W., D. E. Matthews, and H. D. Van Etten.** 1991. Identification and chromosomal locations of a family of cytochrome P-450 genes for pisatin detoxification in the fungus *Nectria haematococca*. Mol. Gen. Genet. **226:**214–223.
81. **Migheli, Q., T. Berio, and M. L. Gullino.** 1993. Electrophoretic karyotypes of *Fusarium* spp. Exp. Mycol. **17:**329–337.
82. **Mills, D., and K. McCluskey.** 1990. Electrophoretic karyotypes of fungi: the new cytology. Mol. Plant-Microbe Interact. **3:**351–357.
83. **Mills, D., K. McCluskey, B. W. Russell, and J. Agnan.** Electrophoretic karyotyping: method and applications. *In* R. P. Singh and U. S. Singh (ed.), Molecular methods in plant pathology, in press. Lewis Publishers, Inc., Chelsea.
84. **Moens, P. B.** 1994. Molecular perspectives of chromosome pairing at mei-

osis. Bioessays **16:**101–106.
85. **Monod, M., S. Porchet, F. Baudraz-Rosselet, and E. Frenk.** 1990. The identification of pathogenic yeast strains by electrophoretic analysis of their chromosomes. J. Med. Microbiol. **32:**123–129.
86. **Morales, V. M., G. Séguin-Swartz, and J. L. Taylor.** 1993. Chromosome size polymorphism in *Leptosphaeria maculans*. Phytopathology **83:**503–509.
87. **Nagy, A., C. Vagvolgyi, E. Balla, and L. Ferenczy.** 1994. Electrophoretic karyotype of *Mucor circinelloides*. Curr. Genet. **26:**45–48.
88. **Nazareth, S. A., and C. V. Bruschi.** 1994. Electrophoretic karyotype of *Fusarium solani*. Microbiology **140:**1373–1375.
89. **Olson, M. V.** 1991. Genome structure and organization in *Saccharomyces cerevisiae*, p. 1–39. *In* J. R. Broach, J. Pringle, and E. Jones (ed.), The molecular and cellular biology of the yeast *Saccharomyces*: genome dynamics, protein synthesis, and energetics, vol. 1. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.
90. **Ono, B., and Y. Ishino-Arao.** 1988. Inheritance of chromosome length polymorphisms in *Saccharomyces cerevisiae*. Curr. Genet. **14:**413–418.
91. **Orbach, M. J., D. Vollrath, R. W. Davis, and C. Yanofsky.** 1988. An electrophoretic karyotype of *Neurospora crassa*. Mol. Cell. Biol. **8:**1469–1473.
92. **Pasero, P., and M. Marilley.** 1993. Size variation of rDNA clusters in the yeasts *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*. Mol. Cell. Biol. **236:**448–452.
93. **Perkins, D. D., and E. G. Barry.** 1977. The cytogenetics of *Neurospora*. Adv. Genet. **19:**133–285.
94. **Perkins, D. D., J. A. Kinsey, D. K. Asch, and G. D. Frederick.** 1993. Chromosome rearrangements recovered following transformation of *Neurospora crassa*. Genetics **134:**729–736.
95. **Petes, T. D., and C. W. Hill.** 1988. Recombination between repeated genes in microorganisms. Annu. Rev. Genet. **22:**147–168.
96. **Plummer, K. M., and B. J. Howlett.** 1995. Inheritance of chromosomal length polymorphisms in the ascomycete *Leptosphaeria maculans*. Mol. Gen. Genet **247:**416–422.
97. **Plummer, K. M., and B. J. Howlett.** 1993. Major chromosomal length polymorphisms are evident after meiosis in the phytopathogenic fungus *Leptosphaeria maculans*. Curr. Genet. **24:**107–113.
98. **Polacheck, I., and G. A. Lebens.** 1989. Electrophoretic karyotype of the pathogenic yeast *Cryptococcus neoformans*. J. Gen. Microbiol. **135:**65–71.
99. **Pukkila, P. J.** 1994. Meiosis in mycelial fungi, p. 267–281. *In* J. G. H. Wessels and F. Meinhardt (ed.), The mycota I: growth, differentiation and sexuality. Springer-Verlag, Berlin.
100. **Pukkila, P. J.** 1992. Methods of genetic manipulation in *Coprinus cinereus*, p. 249–264. *In* S. T. Chang, J. A. Buswell, and P. G. Miles (ed.), Culture, collection, and breeding of edible mushrooms. Gordon & Breach, Philadelphia.
101. **Pukkila, P. J., and L. A. Casselton.** 1991. Molecular genetics of the agaric *Coprinus cinereus*, p. 126–150. *In* J. W. Bennett and L. L. Lasure (ed.), More gene manipulations in fungi. Academic Press, Inc., San Diego.
102. **Pukkila, P. J., and B. C. Lu.** 1985. Silver staining of meiotic chromosomes in the fungus *Coprinus cinereus*. Chromosoma **91:**108–112.
103. **Pukkila, P. J., and C. Skrzynia.** 1993. Frequent changes in the number of reiterated ribosomal RNA genes throughout the life cycle of the basidiomycete *Coprinus cinereus*. Genetics **133:**203–211.
104. **Raju, N. B.** 1992. Genetic control of the sexual cycle in *Neurospora*. Mycol. Res. **96:**241–262.
104a. **Ramesh, M., and M. E. Zolan.** Unpublished data.
105. **Roeder, G. S.** 1990. Chromosome synapsis and genetic recombination: their roles in meiotic chromosome segregation. Trends Genet. **6:**385–389.
106. **Rossignol, J.-L., and M. Picard.** 1991. *Ascobolus immersus* and *Posospora anserina*: sex, recombination, silencing, and death, p. 266–290. *In* J. W. Bennett and L. L. Lasure (ed.), More gene manipulations in fungi. Academic Press, Inc., San Diego.
107. **Royer, J. C., W. E. Hintz, R. W. Kerrigan, and P. A. Horgen.** 1992. Electrophoretic karyotype analysis of the button mushroom, *Agaricus bisporus*. Genome **35:**694–698.
108. **Russell, B. W., and D. Mills.** 1993. Electrophoretic karyotypes of *Tilletia caries*, *T. controversa*, and their F1 progeny: further evidence for conspecific status. Mol. Plant-Microbe Interact. **6:**66–74.
109. **Russell, P. J., and K. D. Rodland.** 1986. Magnification of rRNA gene number in a *Neurospora crassa* strain with a partial deletion of the nucleolus organizer. Chromosoma **93:**337–340.
110. **Rustchenko, E. P., T. M. Curran, and F. Sherman.** 1993. Variations in the number of ribosomal DNA units in morphological mutants and normal strains of *Candida albicans* and in normal strains of *Saccharomyces cerevisiae*. J. Bacteriol. **175:**7189–7199.
111. **Rustchenko, E. P., D. H. Howard, and F. Sherman.** 1994. Chromosomal alterations of *Candida albicans* are associated with the gain and loss of assimilating functions. J. Bacteriol. **176:**3231–3241.
112. **Rustchenko, E. P., and F. Sherman.** 1994. Physical constitution of ribosomal genes in common strains of *Saccharomyces cerevisiae.* Yeast **10:**1157–1171.
113. **Rustchenko-Bulgac, E. P., and D. H. Howard.** 1993. Multiple chromosomal and phenotypic changes in spontaneous mutants of *Candida albicans*. J. Gen. Microbiol. **139:**1195–1207.
114. **Rustchenko-Bulgac, E. P., F. Sherman, and J. B. Hicks.** 1990. Chromosomal rearrangements associated with morphological mutants provide a means for genetic variation of *Candida albicans.* J. Bacteriol. **172:**1276–1283.
115. **Scherer, S., and P. T. Magee.** 1990. Genetics of *Candida albicans*. Microbiol. Rev. **54:**226–241.
116. **Schwartz, D. C., and C. R. Cantor.** 1984. Separation of yeast chromosome-sized DNAs by pulsed field gradient gel electrophoresis. Cell **37:**67–75.
117. **Schwartz, D. C., W. Saffran, J. Welsh, R. Haas, M. Goldenberg, and C. R. Cantor.** 1982. New techniques for purifying large DNAs and studying their properties and packaging. Cold Spring Harbor Symp. Quant. Biol.**47:**189–195.
118. **Selker, E. U.** 1990. Premeiotic instability of repeated sequences in Neurospora crassa. Annu. Rev. Genet. **24:**579–613.
119. **Skinner, D. Z., A. D. Budde, M. L. Farman, J. R. Smith, H. Leung, and S. A. Leong.** 1993. Genome organization of *Magnaporthe grisea*: genetic map, electrophoretic karyotype, and occurrence of repeated DNAs. Theor. Appl. Genet. **87:**545–557.
120. **Skinner, D. Z., A. D. Budde, and S. A. Leong.** 1991. Molecular karyotype analysis of fungi, p. 86–103. *In* J. W. Bennett and L. L. Lasure (ed.), More gene manipulations in fungi. Academic Press, Inc., San Diego.
121. **Slutsky, B., M. Staeball, J. Anderson, L. Risen, M. Pfaller, and D. R. Soll.** 1987. "White-opaque transition": a second high-frequency switching system in *Candida albicans*. J. Bacteriol. **169:**189–197.
122. **Stahl, F. W.** 1988. A unicorn in the garden. Nature (London) **335:**112–113.
123. **Steele, P. E., G. F. Carle, G. S. Kobayashi, and G. Medoff.** 1989. Electrophoretic analysis of *Histoplasma capsulatum* chromosomal DNA. Mol. Cell. Biol. **9:**983–987.
124. **Steensma, H. Y., F. C. M. de Jongh, and M. Linnekamp.** 1988. The use of electrophoretic karyotypes in the classification of yeasts: *Kluyveromyces marxianus* and *K. lactis*. Curr. Genet. **14:**311–317.
125. **Stimberg, N., M. Walz, K. Schörgendorfer, and U. Kück.** 1992. Electrophoretic karyotyping from *Tolypocladium inflatum* and six related strains allows differentiation of morphologically similar species. Appl. Microbiol. Biotechnol. **37:**485–489.
126. **Stoltenburg, R., U. Klinner, P. Ritzerfeld, M. Zimmermann, and C. C. Emeis.** 1992. Genetic diversity of the yeast *Candida utilis*. Curr. Genet. **22:**441–446.
127. **Talbot, N. J., R. P. Oliver, and A. Coddington.** 1991. Pulsed field gel electrophoresis reveals chromosome length differences between strains of *Cladosporium fulvum* (syn. *Fulvia fulva*). Mol. Gen. Genet. **229:**267–272.
128. **Talbot, N. J., Y. P. Salch, M. Ma, and J. E. Hamer.** 1993. Karyotypic variation within clonal lineages of the rice blast fungus, *Magnaporthe grisea*. Appl. Environ. Microbiol. **59:**585–593.
129. **Taylor, J. L., I. Borgmann, and G. Séguin-Swartz.** 1991. Electrophoretic karyotyping of *Leptosphaeria maculans* differentiates highly virulent from weakly virulent isolates. Curr. Genet. **19:**273–277.
130. **Tlsty, T. D., A. White, and J. Sanchez.** 1992. Suppression of gene amplification in human cell hybrids. Science **255:**1425–1427.
131. **Tooley, P. W., M. M. Carras, R. Beck, G. Peterson, and M. R. Bonde.** 1995. Separation of *Tilletia indica* chromosomes using CHEF gel electrophoresis. Mycologia **87:**61–67.
132. **Tzeng, T., L. K. Lyngholm, C. F. Ford, and C. R. Bronson.** 1992. A restriction fragment length polymorphism map and electrophoretic karyotype of the fungal maize pathogen *Cochliobolus heterostrophus.* Genetics **130:**81–96.
133. **Van Etten, H., D. Funnell-Baerg, C. Wasmann, and K. McCluskey.** 1994. Location of pathogenicity genes on dispensable chromosomes in *Nectria haematococca* MPVI. Antonie van Leeuwenhoek J. Microbiol. Serol. **65:**263–267.
134. **Verdoes, J. C., M. R. Calil, P. J. Punt, F. Debets, K. Swart, A. H. Stouthamer, and C. A. M. J. J. Van den Hondel.** 1994. The complete karyotype of *Aspergillus niger*: the use of introduced electrophoretic mobility variation of chromosomes for gene assignment studies. Mol. Gen. Genet. **244:**75–80.
135. **Walz, M., and U. Kück.** 1991. Polymorphic karyotypes in related *Acremonium* strains. Curr. Genet. **19:**73–76.
136. **Wickes, B. L., J. E. Golin, and K. J. Kwon-Chung.** 1991. Chromosomal rearrangement in *Candida stellatoidea* results in a positive effect on phenotype. Infect. Immun. **59:**1762–1771.
137. **Wickes, B. L., T. D. E. Moore, and K. J. Kwon-Chung.** 1994. Comparison of the electrophoretic karyotypes and chromosomal location of ten genes in the two varieties of *Cryptococcus neoformans*. Microbiology **140:**543–550.
138. **Wightman, J. D., X. Xu, B. M. Yorgey, B. T. Watson, M. R. McDaniel, N. J. Michaels, and A. T. Bakalinsky.** 1992. Evaluation of genetically modified wine strains of *Saccharomyces cerevisiae*. Am. J. Enol. Vitic. **43:**283–289.
139. **Wilke, C. M., E. Maimer, and J. Adams.** 1992. The population biology and evolutionary significance of Ty elements in *Saccharomyces cerevisiae*. Genetica **86:**155–173.
140. **Xu, J.-R., K. Yan, M. B. Dickman, and J. F. Leslie.** 1995. Electrophoretic karyotypes distinguish the biological species of *Gibberella fujikuroi* (*Fusarium* section *Liseola*). Mol. Plant-Microbe Interact. **8:**74–84.
141. **Xuei, X., and P. L. Skatrud.** 1994. Molecular karyotype alterations induced by transformation in *Aspergillus nidulans* are mitotically stable. Curr. Genet. **26:**225–227.
142. **Zickler, D.** 1977. Development of the synaptonemal complex and the "re-

combination nodules'' during meiotic prophase in the seven bivalents of the fungus *Sordaria macrospora Auersw*. Chromosoma **61:**289–316.

142a. **Zolan, M. E.** Unpublished data.

143. **Zolan, M. E., J. R. Crittenden, N. K. Heyler, and L. C. Seitz.** 1992. Efficient isolation and mapping of *rad* genes of the fungus *Coprinus cinereus* using chromosome-specific libraries. Nucleic Acids Res. **20:**3993–3999.

144. **Zolan, M. E., N. K. Heyler, and M. A. Ramesh.** 1993. Gene mapping using marker chromosomes in *Coprinus cinereus*, p. 31–35. *In* R. H. Baltz, G. D. Hegeman, and P. L. Skatrud (ed.), Industrial microorganisms: basic and applied molecular genetics. American Society for Microbiology, Washington, D.C.

145. **Zolan, M. E., N. K. Heyler, and N. Yeager Stassen.** 1994. Inheritance of chromosome-length polymorphisms in *Coprinus cinereus*. Genetics **137:**87–94.