THE CYTOGENETICS OF *Neurospora*

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I. Introduction

*Neurospora* was chosen by Beadle and Tatum (1941) for obtaining the first nutritional mutants, thus opening a new era of biochemical genetics and molecular biology. Since then, 5000 papers concerned with *Neurospora* have been published, and several fundamental genetic contributions have been made using *Neurospora*, for example, the first proof of gene conversion (Mitchell, 1955), the first demonstration of complementation between alleles (Fincham and Pateman, 1957; Giles *et al.*, 1957), and the discovery of genes that regulate recombination precisely in specific chromosome regions (Jessup and Catcheside, 1965).

Despite this activity, and despite *Neurospora*’s proved advantages for genetic research, cytogenetic knowledge has until recently progressed rather slowly. *Neurospora* is still far behind *Drosophila* (see Lindsley and Grell, 1968) and maize (Rhoades, 1950, 1955; Neuffer and Coe, 1974) in this respect, and is perhaps more nearly comparable to tomato (Rick and Butler, 1956; Rick, 1971, 1974), the mouse (Miller and Miller, 1975), or barley (Nilan, 1974). The slow progress in *Neurospora* cytogenetics is partly because of the small size of the chromosomes. The DNA content per haploid genome is only one-third that in *Drosophila* and less than 1/115 that in maize. Reliable, detailed observations of meiotic chromosome structure and behavior can be made using conventional light microscopy, as was first shown by Barbara McClintock (1945), but the process is necessarily slower and more difficult than with maize pachytene chromosomes or *Drosophila* salivaries.
However, *Neurospora* cytogenetics entered a new phase when it was realized that chromosome rearrangements could be identified and partially characterized simply by inspecting the ascospores that are shot out of fruiting bodies in groups that represent individual meiotic tetrads (Perkins, 1966a, 1967). At about the same time, simplified mapping methods were developed that have made it easier to locate point mutants and aberration break points. Since then, progress has been rapid. Over 160 rearrangements have been identified and mapped, and the number of known gene loci has been brought to over 400. Many of the rearrangements produce viable duplications covering specific chromosome segments, and these are being used extensively for cytogenetic experiments.

*Scope.* This review concerns genetically significant aspects of *Neurospora* cytology, and the relation between genes and chromosomes, with special emphasis on chromosome rearrangements. In addition to reviewing the published literature, numerous results are presented that have not been published previously. Many of these are cytological, appearing under various headings; one section concerns the morphology and identification of individual chromosomes. New genetic results mainly concern chromosome rearrangements; general characteristics of aberrations are given in the text, and a brief description of each known rearrangement is given in the Appendix. If not otherwise identified, cytological contributions are by Barry; genetic contributions are primarily by Perkins. The *Neurospora* results are related briefly to findings in other organisms. Some sections devoted to accessory topics are set in smaller print. These are not essential for understanding the sections that follow them.

Some topics are omitted because of space limitations. No attempt is made to deal with crossing over and interference (see Emerson, 1963, 1966, 1969; Perkins, 1962a,b; Bole-Gowda et al., 1962; Fincham and Day, 1971), intragenic recombination (see Emerson, 1969; Fincham and Day, 1971; Stadler, 1973), fine-structure mapping (see Catcheside, 1966; Fincham, 1974), molecular models of recombination (see Holliday, 1974; Hotchkiss, 1974; Sobell, 1974; Meselson and Radding, 1975; Wildenberg and Meselson, 1975; Wagner and Radman, 1975), or genetic aspects of DNA degradation, repair and synthesis (see Schroeder, 1975; Worthy and Epler, 1972, 1973). Other topics are dealt with only very briefly, such as the genetic control of recombination, and the cytoplasmic genome.

Literature citations do not include publications that appeared after December 1975, when this review was completed.

*Advantages of Neurospora for Cytogenetics.* *Neurospora* possesses several favorable features compared to the more conventional organisms that are used in cytogenetic research, and these in part compensate for the small size of its chromosomes. (1) All four products of individual
meioses survive. (2) Viable meiotic products are black-pigmented spores, allowing white inviable deficiency spores to be seen in stark contrast. A chromosome rearrangement is signaled by the presence of white spores in characteristic frequencies and patterns. Major rearrangement types can be distinguished simply from a visual inspection of the numbers of white spores in individual asci. (3) Progeny can be obtained either as random meiotic products, as unordered tetrads, or as ordered tetrads whose linear spore arrangement reflects the events of meiosis. The spores show high viability and germination. (4) The vegetative (somatic) part of the life cycle is haploid. (5) Duplications are more readily identified as partial diplods against a haploid background than as partial triploids against a diploid background. (6) Somatic variants can be obtained in pure culture. Any somatic cell can serve as a germ cell. (7) The multinucleate nature of vegetative stages and the absence of cross walls in the ascus allow internuclear interaction and complementation to be studied. Intraneural interactions can be studied in duplications. (8) The life cycle is short. Precise environmental control is possible. (9) Stocks can be maintained indefinitely in suspended animation. (10) Culture requirements and growth habit are such that stable mutants are readily obtained. Selective enrichment is often possible.

Smallness of the genome may itself be a potential advantage for molecular cytogenetics (see Petes et al., 1973).

*Neurospora* also shares advantageous features with the organisms more conventionally used in cytogenetic research, such as a low chromosome number, meiosis that is amenable to cytological examination, and distinctive chromomere patterns that enable individual chromosomes to be identified at pachynema.

Finally, a vast store of information already exists on *Neurospora*, the exchange of research information is well organized, and stocks are readily available for research. A stock center (FGSC) maintains about 3000 *Neurospora* cultures, including most of the described mutant genes, rearrangements, wild strains, special-purpose stocks, and cytoplasmic variants (Fungal Genetics Stock Center, California State University, Humboldt, Arcata, California 95521; founded 1960 under R. W. Barratt and W. M. Ogata). Research methods are well developed (Davis and de Serres, 1970; Ryan, 1950; Emerson, 1955; Stanford Neurospora Methods, 1963; Perkins et al., 1969; Perkins, 1972b,c, 1975). A newsletter publishes research notes, stock lists, bibliographies, a directory of *Neurospora* workers listing their special interests, and summaries of the biennial Neurospora Research Conferences (*Neurospora Newsletter*, founded 1962 and edited by B. J. Bachmann). Bibliographies list all research publications on *Neurospora* (Bachmann and Strickland, 1965; Bachmann, 1970, 1971–1976).
The genus Neurospora. Neurospora is a filamentous ascomycete belonging to the Class Pyrenomycetes and the Order Sphaeriales. This order includes other fungi well known to geneticists—Bombardia, Gelasinospora, Podospora, Sordaria, Ophiostoma, Glomerella, and Venturia. The genus was described by Shear and Dodge (1927) soon after the sexual stages were first recognized. Several conidiating Neurospora species are known, of which three are heterothallic with 8-spored asci (N. crassa, N. sitophila, and N. intermedia), and at least one is pseudohomothallic with 4-spored asci (N. tetrasperma). Crosses between species are sufficiently fertile that genes can be transferred from one species to another (see, for example, Finchem, 1951; Howe and Haysman, 1966; Metzenberg and Ahlgren, 1973). In addition, five true-homothallic species have been described—N. terricola, N. africana, N. dodgii, N. galapagosensis, and N. lineolata; these are all 8-spored and without conidia. For a conventional key to Neurospora species, based largely on morphology, see Frederick et al. (1969). An unconventional key, based on behavior in crosses with species-reference strains, is given by Perkins et al. (1976).

The most used species has been Neurospora crassa. This resulted largely from its choice for genetic work by C. C. Lindegren in the 1930s and by Beadle and Tatum in 1940. (B. O. Dodge, who did the first genetic work on Neurospora, favored the species N. sitophila and N. tetrasperma in his own research.) If statements in this review do not name another species, they refer to N. crassa.

Early History. Details of most investigations before the 1950s will not be covered in this review. Only highlights are sketched in the following paragraphs. Informal accounts of the early Neurospora work, by Lindegren (1973), Catcheside (1973), Horowitz (1973), and others, will be found in Neurospora Newsletter 20.

Shear and Dodge (1927) showed the mating-type system to be bipolar, with 4:4 segregation of the two mating-type alleles among unordered asci that were shot from the perithegium. Wilcox (1928) examined ascus development cytologically in N. sitophila, and showed that spindles do not overlap and that the linear array of ascospores reflects the events of meiosis. Wilcox (1928) and Dodge (1929) dissected out ascospores of N. sitophila in linear order, and showed that the mating-type alleles segregated either at first division (prereduction) or at second division (postreduction). Dodge (1931) also described the segregation of spontaneously arising morphological differences in N. sitophila. The cytological basis of pseudohomothallism in N. tetrasperma was shown by Dodge (1927) and Colson (1934) to involve overlapping spindles in the ascus and inclusion of two nonsister nuclei in one spore.

Lindegren studied the segregation in asci of mating type and of some morphological traits. He proposed that postreduction frequencies, as
reflected in ascospore order, measured the frequency of crossing over in the segment between a gene locus and its centromere. He discovered linked genes and showed (1933) that crossing over in *Neurospora* occurred reciprocally between chromatids at a 4-strand stage, just as in *Drosophila*. Lindegren (1936a,b) and Lindegren and Lindegren (1937, 1939, 1942) went on to construct the first linkage maps (eight genes in two linkage groups) and to study interference.

The mutants obtained by Beadle, Tatum, and their associates, beginning in 1940, provided a basis for constructing more complete maps. By 1949 six linkage groups had been established (Houlahan et al., 1949; Barratt and Garnjobst, 1949), and the seventh group was soon added (see Barratt et al., 1954).

McClintock (1945) first showed that chromosome morphology and behavior in the *Neurospora* ascus are similar to those in higher organisms, and that they can be studied by methods used in plant cytogenetics. She and Singleton (1948, 1953) described normal chromosome morphology and behavior in the ascus, identified and numbered the seven chromosomes, and noted that meiosis was similar in its main features to that in higher eukaryotes, though it differed in some details of chromosome contraction, pairing, and coiling.

The presence of chromosome rearrangements was suggested as an explanation for aborted ascospores ("partial sterility") in crosses involving an irradiated parent (Lindgren and Lindegren, 1941; Sansome et al., 1945). The first genetic evidence of chromosome rearrangements, pseudo-linkage, was obtained in the 1940s and reported by Houlahan et al. (1949). Several translocations were confirmed cytologically and aspects of their meiotic behavior were described by McClintock (1945, 1947, 1955), Singleton (1948), and St. Lawrence (1953).

**II. The Life Cycle, Incompatibility, and Ploidy**

*The Life Cycle*

Figure 1 shows the life cycle of a heterothallic species. The stages are described in some detail in the figure legend. For other diagrams and descriptions of the life cycle and of events in the ascus, see Fincham and Day (1971), Beadle (1945), and Emerson (1955, 1963, 1966).

There are two major phases—vegetative and sexual. The latter begins with fertilization and concludes with ascospore differentiation; it coincides with perithecial development and occurs within the perithecium. The vegetative phase begins with ascospore germination. Under ordinary laboratory conditions, generation time is 3–4 weeks.
N. tetrasperma is pseudohomothallic (secondarily homothallic) and differs from the heterothallic species in producing asci with four large ascospores, each of which contains nuclei representing two of the meiotic products—usually A and a. On germination, single ascospores thus give rise to heterokaryotic strains capable of self-fertilization (see Dodge et al., 1950; Fincham and Day, 1971).

Mating Type

Sexual compatibility is governed by two alleles, A (earlier called A or +) and a (earlier called B or −). Extensive attempts to produce a new mating-type allele by recombination in N. crassa have failed (Newmeyer et al., 1973), nor has any different mating-type allele been found among a large number of isolates collected from nature (Perkins et al., 1976). Mating-type alleles in the three heterothallic species and in the pseudohomothallic species N. tetrasperma are all indistinguishable from A and a of N. crassa. This has been shown by interspecific matings and by introgression.

There have been reports in the Sphaerialae of complete asci being produced in a normally heterothallic species by a single mating type. Lewis (1969) observed that ascospores from a cross between two Sordaria species were predominantly unpigmented. Rare asci that contained all black ascospores apparently originated by fusion between nuclei of only one of the parental types. In Neurospora crassa, a preliminary observation of Vigfussen and Cano (1974) is potentially important. They report that crude protein extracts of fertilized cultures induced the sexual phase in single-mating-type cultures, producing complete asci from which all eight progeny are of the original mating type.

Heterokaryosis and Vegetative (Heterokaryon) Incompatibility

The pseudohomothallic species N. tetrasperma is normally a heterokaryon containing two genetically different nuclei in the same cytoplasm. Heterokaryons may be produced also in heterothallic species by fusion of somatic cells, by breakdown of rare disomics, or by mutation. Formation of stable heterokaryons in N. crassa requires that the participating nuclei be genetically identical at all of the numerous heterokaryon-incompatibility (het) loci. At least ten different het loci have been identified (Mylyk, 1975).

The presence of different alleles at even one of the het loci precludes formation of stable heterokaryons (Garnjobst, 1953, 1955; Holloway, 1953, 1955). Anastomosis occurs but is followed by a vegetative incompatibility reaction that kills any cell in which unlike alleles are present (Garnjobst and Wilson, 1956). In some combinations the reaction is
Fig. 1. Life cycle of *Neurospora crassa*, a heterothallic species (adapted from Fincham and Day, 1971). Stages 1 to 4, from ascospore germination to fertilization, constitute the vegetative phase, and stages 4 to 8, from fertilization through ascospore maturation, the sexual phase. Nuclear fusion and meiotic prophase occur 4–5 days after fertilization at 25°C, and ascospores are shot from the perithecium from the ninth day. 1. The black ascospores, approximately 17 × 26 μm, can be isolated manually from an agar surface without use of micromanipulation apparatus. Ascospore dormancy is broken by heat or chemicals. The diagram shows a germinating ascospore, with hyphae growing from both ends. 2. The mycelium consists of branched, threadlike hyphae, made up of multinucleate cells separated by perforate cross-walls through which nuclei and cytoplasm can readily pass. Vegetative growth is loose and rapidly spreading (over 5 mm per hour at 37°C). 3. Vegetative spores are of two types: powdery airborne orange macroconidia (6–8 μm in diameter, mostly multinucleate) and smaller uninucleate microconidia. 4. Protoperithecia are formed by coiling of hyphae around the ascogonial cells. Specialized hyphae, the trichogyne, pick up nuclei of opposite mating type and transport them to the ascogonium within the protoperitheium. Fertilizing nuclei may originate from macroconidia, microconidia, or mycelium. Usually only one fertilizing nuclear type contributes to the
milder, and incompatible nuclei are eliminated without killing the cells (Pittenger and Brawner, 1961). A similar but nonlethal vegetative incompatibility reaction also occurs when unlike het alleles are present in heterozygous condition in the same nucleus. This behavior has been used extensively in studying duplications.

In *Neurospora crassa* the mating-type genes function not only in determining sexual compatibility, but also vegetatively as unlike het alleles (Beadle and Coonradt, 1944; Sansome, 1946; Gross, 1952; see Newmeyer et al., 1973). That is, both mt\(^A\) and mt\(^a\) (A and a) must be present to make functional perithecia in the sexual phase, but if they are brought together in the vegetative phase they result in an incompatibility reaction similar to that shown by other het genes, both in heterokaryons (Garnjobst and Wilson, 1956) and in heterozygous duplications (Newmeyer, 1965; Newmeyer and Taylor, 1967; Perkins, 1972a, 1975). The vegetative incompatibility function has never been separated from the mating-type locus in extensive tests (Newmeyer et al., 1973).

In *N. sitophila* (Mishra, 1971) and in *N. tetrasperma*, opposite mating types do not show any heterokaryon-incompatibility reaction. However, Metzenberg and Ahlgren (1973) have shown that when the mating-type alleles of *N. tetrasperma* are introgressed into *N. crassa* they are vegetatively incompatible with each other and with the opposite mating types of *N. crassa*. The same is true for the *N. sitophila* mating-type genes introgressed into *N. crassa* (Perkins, 1976). It therefore appears that contents of a perithecium, but exceptions are revealed when the fertilizing parent is heterokaryotic (see, for example, Nakamura and Egashira, 1961). Selective fertilization has also been detected when a heterokaryon is used as male parent (Egashira and Nakamura, 1972). 5. Upon fertilization, the haploid A and a nuclei do not fuse, but proliferate within the perithecium, forming heterokaryotic asogenous hyphae. Emerson (1966) estimates that seven to ten divisions occur before nuclear fusion. 6. The final, conjugate division before ascus formation occurs in a binucleate hook-shaped structure, the crozier. A and a fuse, and the diploid zygote nucleus immediately enters meiosis. Although the fusion nucleus is the only diploid nucleus in the life cycle, the entire sexual phase until ascospore formation is functionally similar to a diploid, in that the two gametic parental genomes are present in a 1:1 ratio in a common cytoplasm. 7. Meiosis is described in Section III, A. For details of meiosis and ascus development, see drawings in Fincham and Day (1971, Fig. 1) and photographs in Barry (1969) and Singleton (1953). Asci do not develop synchronously; numerous asci are initiated successively from the same asogenous hypha. Mature, 8-spored ascus measure about 20 × 200 μm. 8. The perithecial wall is maternal in origin. Derivation of perithecial tissues has been analyzed using genetic mosaics obtained when maternal cultures are heterokaryotic for a maternally expressed gene per, governing perithecial color (Johnson, 1975a,b). Mature perithecia (400–600 μm in diameter) develop a beak terminating in an ostiole through which ascospores are forcibly extruded in groups of eight, each comprising the contents of an ascus.
the mating-type alleles of *N. tetrasperma* and *N. sitophila* possess an innate vegetative incompatibility similar to *N. crassa*, but that this is suppressed in their normal genetic background. An unlinked gene, *tcl* (tolerant), has been found in *N. crassa* that suppresses the vegetative incompatibility of the *crassa* mating-type alleles without affecting crossing behavior (Newmeyer, 1970).

The vegetative incompatibility associated with mating type or with other *het* genes disappears completely during the sexual stages, from fertilization through ascospore maturation. For a review of heterokaryosis and its genetic control see Davis (1966). More recent references will be found in Perkins (1975) and in Section V, E, 6, b.

**Diploidy and Numerical Aneuploids in Normal Sequence.** Numerous attempts have been made to obtain stable diploids in *Neurospora*, but without success (e.g., by Smith, 1974; Sansome, 1956; Jean M. Foley, personal communication 1963). Case and Giles (1962) tested the possibility that somatic fusion of haploid nuclei would occur in a heterokaryon, followed by chromosome reassortment, and they showed that it did not occur.

However, "pseudowild-type" progeny (from crosses with closely linked complementing markers in repulsion phase) originate as rare disomic ascospores which break down rapidly to form heterokaryons made up of haploid nuclei (first described by Mitchell *et al.*, 1952). Multiply disomic ascospores and presumably completely diploid ascospores are readily produced meiotically in crosses of appropriate genotype, for example those involving meiotic mutants (see Section III, C, 1 and Smith, 1975), but the disomic or diploid condition is rapidly reduced to haploid. Haploidization is frequently accompanied by mitotic recombination (Coyle and Pittenger, 1965; Threlkeld and Stoltz, 1970; Smith, 1974). Unstable disomics also originate in *Neurospora* by 3:1 segregation from heterozygous translocations (Section V, C, 1, e).

Disomics are known in other fungi that are relatively much more stable (see, for example, Käfer and Upshall, 1973; Shaffer *et al.*, 1971). Stable diploids can be obtained readily in *Aspergillus* (Roper, 1952), and they are a normal feature of the life cycle in *Saccharomyces cerevisiae*.

III. Meiosis and Mitosis

**A. Description of Normal Meiosis and Mitosis in the Ascus**

Encouraging progress has been made in the cytological study of meiosis in fungi since the subject was reviewed by Olive (1965). Electron
microscopy has been used with increasing effectiveness (e.g., by Westergaard and von Wettstein, 1966; Lu, 1967a; Zickler, 1970; Schrantz, 1970; Gillies, 1972; Byers and Goetsch, 1975), effective variations of staining techniques have been applied in light microscopy (e.g., Lu, 1967b; Zickler, 1967; Lu and Raju, 1970), quantitative spectrophotometry has been used to study DNA replication (Rossen and Westergaard, 1966), and meiotic mutants have been examined (e.g., Simonet and Zickler, 1972). However, the basic description of Neurospora meiosis by McClintock (1945) and Singleton (1953) still stands as a model for filamentous fungi, though it has been augmented.

1. N. crassa and Other Heterothallic Neurospora Species

Four nuclear divisions occur in the ascus—two meiotic, followed by two mitotic. The latter are sometimes referred to as the third and fourth divisions in the ascus. All the divisions are conventional, although there are interesting minor differences from higher organisms. The sequence of events in the ascus was first described by McClintock (1945) for N. crassa, then in greater detail with photographic documentation by Singleton (1948, 1953). A further description of meiotic prophase relating to diplonema was added by Barry (1969). Gillies (1972) found synaptonemal complexes at pachynema, and described their characteristics. Meiosis in other ascomycetes has been studied with the light and electron microscopes, and the contributions of Rossen and Westergaard (1966) on Neottiella, and Zickler (1970, 1973) on species of Ascobolus, Podospora, and Sordaria are of particular interest in interpreting similar or contrasting features in Neurospora. A detailed study by Lu (1967b) of the very closely related fungus Gelasinospora calospora shows that events in the ascus are very similar to those in Neurospora.

A summary description of divisions in the ascus will be given here. Chromosome structure and morphology will be described in Section IV, A.

a. Stages through Pachynema. In Neurospora crassa the ascus is generated from the penultimate cell of a crozier. The two haploid nuclei, derived from a conjugate nuclear division in the crozier, fuse in the young budding ascus. Then the two nucleoli fuse as the chromosomes condense into very short univalents, which begin to pair. Meiosis in Neurospora and other ascomycetes differs from that in higher organisms in this respect (see McClintock, 1945; Westergaard, 1964): the chromosomes begin to pair when they are very short, but as pairing continues the chromosomes elongate through pachynema and into a diffuse diplonema, rather than contracting from leptotene to diplonema as in higher eukaryotes, such as maize and lily. At pachynema in Neurospora the paired homologous chromosomes lie parallel to one another 2000–5000 Å apart and show
little relational coiling (see Fig. 4). The varied spacing may be an artifact of fixation and staining because the characteristic "railroad track" appearance varies according to the fixative used. Alternatively, it could be due to actual changes as pachynema progresses, with the widest separation at late pachynema.

Pachytene chromosomes appear to be much more closely paired in maize than in Neurospora, yet the synapsed chromosomes are separated by roughly comparable distances in each. Synaptonemal complexes are the same width in both organisms. Probably the distance seems to be greater in Neurospora because the amount of chromatin is so much smaller relative to the width of the synaptonemal complex.

b. Synaptonemal Complex. From serial sections of pachytene nuclei of N. crassa, Gillies (1972) was able to reconstruct the entire set of seven complexes, determining their size and other characteristics. Each complex of a bivalent is attached to the nuclear envelope at each end, except for the nucleolus organizer end of chromosome 2, which is free. Width of the complex is 2000 Å, including the 1200 Å central region plus two 400 Å lateral elements. The lateral elements are banded, which seems characteristic of the ascomycetes (Westergaard and von Wettstein, 1972).

The synaptonemal complexes are one-third shorter than pachytene chromosomes prepared with acetic–lactic–ethanol fixative (Table 1 of Gillies, 1972). They may differ in length because the complexes were measured before the chromosomes had extended to the full length characteristic of late pachynema, when the chromosome measurements were made. Alternatively, if the measurements were from cells of comparable stages, differences in processing must have resulted in shrinking or stretching (Gillies, 1972).

Gillies observed thickenings of the central component ("nodes") in varying numbers in the complexes in most nuclei. Schrantz (1970), Zickler (1973), and Radu et al. (1974) have found similar structures in other fungi. These apparently correspond to the "recombination nodules" observed by Carpenter (1975b) in female Drosophila.

c. Postpachytene Stages. After pachynema the chromosomes become indistinct during a diffuse diplonema (Barry, 1969). The stage recognized as conventional diplonema follows, but it is rarely observed, indicating that it must be of very brief duration. Chiasmata are visible then and in the following stage, diakinesis (see Singleton, 1953, Figs. 34, 35). Singleton (1953) made general chiasma counts at diakinesis, observing that most bivalents usually have two chiasmata, with sometimes three in the longer chromosomes or only one in the shorter. This would indicate that the total genetic map should be more than 700 units, which agrees with other estimates of its minimum length (Section IV, B, 2, c).
The chromosomes are very short at metaphase I; the longest does not exceed 2 µm. Anaphase is asynchronous so that often some dyad chromosomes reach the poles before other bivalents separate on the metaphase plate (see Fig. 2). The anaphase-I (and II) chromosomes are rounded rather than linear (V or J shaped). The spindle is intranuclear. The nuclear membrane is present throughout the division, disintegrating only near the spindle equator, and closing by constriction and new synthesis around the daughter nuclei at telophase (Wells, 1970; Westergaard and von Wettstein, 1970; Zickler, 1970; Mu’Azu, 1973). Divisions at all other stages are intranuclear, both in the ascus and in vegetative cells.

After the first telophase the chromosomes become extended again during a brief interphase, when a small nucleolus is formed. Soon the chromosomes contract to enter the second meiotic division, which is conventional in appearance. During both meiotic divisions the spindle is usually parallel or slightly oblique to the long axis of the ascus. At the second division the spindles are tandem to one another without overlapping.

The two meiotic divisions are followed by a mitotic division. No cross walls in the ascus separate any of the daughter nuclei. The nuclei retain their sequential placement in the ascus such that the top and bottom four nuclei are the separate products of the first meiotic division, and the top and bottom two nuclei in each half of the ascus are the products of

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**Fig. 2.** Anaphase I in *Neurospora crassa*. The division is asynchronous, with five chromosomes near each pole while two bivalents are still disjoining in the center. Note the generally spherical shape of the anaphase chromosomes. (Orcin staining, ×3000.)
the second division. Adjacent nuclei by pairs (1–2, 3–4, 5–6, 7–8) are identical sister nuclei.

An ascospore wall is then formed around each of the eight nuclei, including adjacent cytoplasm. A second mitotic division occurs in each immature ascospore. In both mitotic divisions in the ascus, the aggregation of chromosomes on a metaphase plate and subsequent disjunction of chromatids to the poles on a spindle is very clear. These divisions are typical mitoses. At late anaphase and telophase of the mitotic division, a ring of chromosomes is formed (Weijer and McDonald, 1965) which is suggestive of the appearance of some division figures seen in somatic nuclei.

The centrosomes become progressively more conspicuous at the second and third divisions. [The centrosome is also called centriole, centrosomal plaque, spindle-pole body, polar organelle, and other names (see Lu, 1967b; Zickler, 1970; Wells, 1970; Mu’Azu, 1973). Centrosome is used here, for brevity.] Zickler (1970) observed variations in centrosome shape, structure, and degree of attachment to the nuclear membrane in species of *Ascobolus* and *Podospora*. The centrosome may not be primarily involved in delimiting the ascospore (see Zickler, 1970), contrary to earlier interpretations (Singleton, 1953), but it is the site to which the spindle fibers (microtubules) converge, and it seems also to be involved in the spacing and orientation of the nuclei within the ascus.

**d. The DNA Cycle.** Meiosis and mitosis in the ascus of *Neottiella rutilans* are similar to those in *Neurospora*. Rossen and Westergaard (1966) have measured the comparative DNA content of *Neottiella* nuclei spectrophotometrically, using Feulgen staining. They found that the amounts of DNA indeed correspond to what might be expected for each division stage: nuclei of vegetative hyphae, paraphyses, and asco-genous hyphae have the haploid amount of DNA; nuclei in the croziers before the conjugate division have up to the diploid amount; conjugating nuclei just prior to fusion in the ascus each have the diploid amount; the fusion nucleus has a tetraploid level; each nucleus of the tetrad at the completion of meiosis has the haploid amount. There is a round of DNA replication preceding each of the third and fourth divisions in the ascus. The critical finding is that replication of the bulk of the DNA for the meiotic divisions has been completed before the haploid gametic nuclei fuse in *Neottiella*. This observation precludes a direct relation between crossing over and total DNA replication.

A similar study has not been made in *Neurospora* because of inability to obtain Feulgen staining or to label chromosomal DNA specifically with a radioisotope (Baer and St. Lawrence, 1964; Fink and Fink, 1962a,b). It is reasonable to assume, however, that a similar pattern of DNA
replication would be found, with the bulk of premeiotic DNA replication completed prior to karyogamy.

Meiosis and ascus development in the other heterothallic Neurospora species N. sitophila and N. intermedia follow the pattern of N. crassa (E. G. Barry, unpublished; Wilcox, 1928, on N. sitophila).

2. Ascus Development in Homothallic Species

N. B. Raju (1976) has examined meiosis and related stages in the five homothallic Neurospora species. Two nuclei fuse in the crozier, just as in the heterothallic and pseudohomothallic species, and subsequent stages are essentially similar to those described for N. crassa.

3. Ascus Development in Pseudohomothallic Species

The 4-spored species N. tetrasperma exhibits a precise genetic control of cellular events coordinated with meiosis. The divisions in the ascus are similar to those in N. crassa (Colson, 1934; Cutter, 1946). However, spindles overlap at the second nuclear division in the ascus, and ascospore walls are formed in such a way that each of the four spores contains daughter nuclei derived from two different first-division products. The mating-type locus is close to centromere, and alleles A and a usually segregate at division I, so that 98% of ascospores are heterokaryotic A+a, and each resulting culture is thus capable of entering the sexual cycle and forming perithecia without fertilization from an external source. The rare asci where crossing over has occurred in the short interval between mt and centromere produce homokaryotic A+A and a+a spores (see Dodge, 1927; Sansome, 1946; Howe, 1963, 1964; Hung, 1972).

The tetrasperma system undoubtedly evolved from ancestors that were heterothallic with 8-spored asci. Reversion from the 4-spored to the 8-spored condition can be accomplished by a single dominant mutant gene E (Dodge et al., 1950). The opposite change from 8- to 4-spored asci is not readily accomplished in a normally 8-spored species, as might be expected. Pateman (1959) selected over several generations for large spores in N. crassa and obtained strains that produced occasional 4-spored asci, but the basis of this condition was multigenic and recessive, and many of the asci had defective spores.

Pseudohomothallic species having asci with four heterokaryotic spores are known in other genera. In some (for example Gelasinospora tetrasperma—Dodge, 1937) heterokaryosis for the mating-type alleles is achieved as in N. tetrasperma. In Podospora anserina, however, the same end result is achieved in a completely different way. The mating-type locus is far from the centromere, and a nearly invariable exchange occurs so that the mating-type alleles segregate at the second division in 98% of asci (Rizet and Engelmann, 1949). Spindles are aligned and
ascospore walls are delimited so that each of the four spores includes daughter nuclei derived from two different second-division products (for diagrams and references, see Fincham and Day, 1971, p. 302). Pseudohomothallism must therefore have evolved independently in different ascomycetes.

B. SOMATIC DIVISIONS

Mitosis in the Hyphae. Coordinated studies with both light and electron microscopes now show the somatic nuclear divisions in fungi to be mitotic in nature, complete with spindles, separate anaphase chromosomes, and centrosomes. The clearest demonstration of the mitotic divisions in ascomycetes, both in somatic hyphae and in the ascus, is by Zickler (1970, 1971). There has been a long history of controversy (see Robinow and Bakerspigel, 1965), some investigators interpreting the somatic nuclear divisions as classical mitoses, others maintaining that they were not because spindles and chromosomes could not be resolved at metaphase and anaphase in the tiny nuclei.

Zickler employed both light-microscope and phase-contrast observations of living material as well as of hematoxylin-stained material, and electron microscopy of double-stained preparations. She found that the divisions are extremely rapid, taking only 6–7 minutes, with the spindle and metaphase-anaphase stages visible for only 2–3 minutes, whereas interphase lasts 3–4 hours. Her observations were made with numerous species of Ascocholus, Sordaria, and Podospora. These are so closely related that there is no hesitation in extrapolating the results to Neurospora, but it would be gratifying, even so, to have electron-microscope studies showing the fine specific detail of somatic mitosis in Neurospora, which has been at the center of the controversy.

C. GENETIC VARIANTS AFFECTING MEIOSIS OR RELATED STAGES

1. Meiotic Mutants

Several mutant genes have been identified in Neurospora crassa that block the normal course of development during the sexual phase, between fertilization and ascospore maturation. Of special interest are those that affect meiosis itself, or the stages immediately before meiosis. Mutants of this type have also been used for the genetic dissection of meiosis in higher organisms (e.g., Sandler et al., 1968; Rhoades and Dempsey, 1966; Gottschalk, 1973) and in other fungi (Bresch et al., 1968; Esposito et al., 1970; Simonet and Zickler, 1972; Wheeler and Driver, 1953; Heslot, 1958; Esser and Straub, 1958; El Ani and Olive, 1962).

Of the genes that affect chromosome pairing and disjunction in Neurospora, the recessive mei-1 was the first to be thoroughly studied (Smith,
1975). mei-1 apparently originated from a wild-collected strain, and was long known as the Abbott factor, responsible for ascospore abortion. There is little or no crossing over in mei-1 × mei-1, nondisjunction is high, and the ascospores are mostly white and inviable. The few viable ascospores are always heterozygous for markers in one or more linkage groups, and they probably originate as unstable diploids.

Cytological observations of mei-1 have been made by B. C. Lu and D. R. Galeazzi (personal communication). In homozygous condition, mei-1 results in failure of chromosome pairing during prophase I. Chromosomes may be associated occasionally at points or regions. The components of the synaptonemal complex are present, but normal complexes are formed only rarely. Daughter chromosomes fail to separate cleanly at the second and third divisions, and may then be enclosed in the same nuclear envelope. When the centrosomes divide, they may form an abnormal spindle with four poles. Thus, when the division is completed some centrosomes may have no associated chromosomes, or else a subnormal number.

The recessive gene mei-3 (Newmeyer and Galeazzi, 1974) completely blocks early stages of meiotic development, so that perithecia are barren. Karyogamy occurs, but chromosomes fail to pair normally. Few asci are seen at later stages; these are abnormal with few or no spores (N. B. Raju, unpublished). mei-3 also causes loss of duplicated chromosome segments (see Section V, E, 4).

Another recessive gene, mei-4, varies in its expression from highly barren to almost normally fertile, depending on the genetic background (Newmeyer and Galeazzi, 1974). In the moderately barren crosses studied by B. C. Lu and D. Galeazzi (personal communication), the first meiotic division is normal, but in the second and third divisions daughter chromosomes fall to separate cleanly in some asci, much as in crosses homozygous for mei-1. Consequently, irregular disjunctions occur. Some centrosomes appear to separate from the nucleus at the third division. Abnormal spores are delimited that may lack nuclei, or they may already possess two nuclei before the fourth division.

The dominant Mei-2 results in extensive nondisjunction (Smith, 1975). The defect is at zygonema when chromosome pairing fails, although some segments may show partial pairing. At metaphase I some bivalents are found, but most chromosomes are univalent; disjunction is abnormal. Thereafter the divisions are normal (B. C. Lu, unpublished). Several other strains have been tentatively identified as dominant meiotic mutants; characteristically most of the ascospores from heterozygous crosses that involve them are white and inviable.

Except for mei-3, the meiotic mutants described so far have all been
recognized initially by their effects on fertility or on ascospore viability, resulting from defects of pairing, disjunction, or spore formation. Several radiation-sensitive mutants are also homozygous-barren, with development blocked usually but not always before karyogamy (uvs-3, -5, and -6; Schroeder, 1970; N. B. Raju, unpublished). More subtle effects are characteristic of the rec and cog genes which regulate meiotic recombination in specific local regions (see D. G. Catcheside, 1974, 1975, and Section IV, B, 3).

Mutant genes acting at stages of the sexual cycle other than meiosis may be of no less interest for other aspects of cytology and development, but they can hardly be called meiotic mutants. This category includes mutants with altered ascospore morphology (Barry et al., 1972; Novak and Srb, 1973; Srb et al., 1973, 1974), notably the dominant gene R: Round spore (Mitchell, 1966); mutants with abnormal ascus shape such as pk: peak (= bis:biscuit) (see Srb et al., 1974); and female-sterile mutants which are unable to form perithecia (see Myllyk and Threlkeld, 1974).

Mutant strains have been described by Vigfusson et al. (1971) and Weijer and Vigfusson (1972) that are male-sterile and female-fertile.

2. Effects of Aneuploidy

Most or all of the segmental duplications known in Neurospora result in barren perithecia when they are crossed to either euploid or duplication strains of the opposite mating type. The block in perithecial development varies, but is most commonly at the crozier stage (N. B. Raju, unpublished). Further details are given in Section V, E, 3. Numerical aneuploids such as disomics are apparently too unstable to have recognizable effects on perithecial development or fertility.

3. Spore Killers

Three factors are known in Neurospora that resemble Segregation Distorter (SD) in Drosophila (for SD, see Hartl and Hiraizumi, 1976; Peacock and Miklos, 1973). The Neurospora factors, called Spore Killer (SK), were first recognized because ascI from SK/ SK⁺ contained exclusively four black and four shrunkn white spores. No chromosome rearrangement would be expected to have such a result; instead, the observation suggested an ascospore-color mutant that was expressed autonomously in each spore. However, the surviving, black ascospores proved to be those carrying the factor responsible for spore death, SK, rather than its sensitive allele, SK⁺. Ascospores that did not contain SK deteriorated, a behavior exactly opposite that expected of an autonomously expressed ascospore-color gene, where the wild type survives.
Moreover, all the ascospores from $SK-1 \times SK-1$ were viable and black. $SK-1$ was discovered in crosses between $N. sitophila$ strains from Nigeria and Virginia, U.S.A. (B. C. Turner, unpublished). Nigeria $\times$ Nigeria and Virginia $\times$ Virginia crosses resulted in a majority of black ascospores and 8B:0W asci, whereas asci from reciprocal crosses between strains from the two sources were all 4B:4W (with 95% first-division segregation). Progeny from the viable, black spores were almost all (>95%) of the Virginia type. Similar crosses with $N. sitophila$ isolates from many other localities showed that each of them was either one type or the other—$SK-1$ (Virginia) or $SK-1^*$ (Nigeria).

A different Spore Killer, $SK-2$, was found in stocks that had been derived from a Borneo strain of $N. intermedia$ by recurrent backcrosses to $N. crassa$ (Blakely and Srb, 1962). In further crosses of these strains to $N. crassa$ we noticed that the asci were exclusively 4B:4W, and almost all progeny from the viable, black spores repeated this behavior. $SK-2$ is located at or near the centromere of linkage group III, and it segregates independently of markers in the other six linkage groups. $SK-2$ makes many inviable spores when it is homozygous in the $N. crassa$ background, but when $SK-2$ strains of $N. intermedia$ are used, derived directly from the original Borneo strain, homozygous crosses produce mostly viable ascospores and 8B:0W asci.

N. B. Raju (personal communication) has examined heterozygous crosses cytologically. Both $SK-1$ and $SK-2$ behave similarly. Meiosis and ascus development are normal, so far as can be seen with the light microscope. This is true of chromosome pairing, behavior of centrosomes, ascospore delimitation, and the fourth nuclear division in the spores. The nuclei in all eight ascospores look normal and identical for some time after the ascospore walls have formed. Then while four of the spores continue to enlarge and mature normally, the other four remain small and their nuclei shrink or slowly degenerate.

A third Spore Killer has been found in $N. intermedia$ strains collected in New Guinea. $SK-3$ from Rona is similar to $SK-1$ and $SK-2$ in its behavior, with the added feature that some naturally occurring strains that do not themselves show the $SK-3$ killer effect are nevertheless resistant to killing by $SK-3$.

4. Bubble Asci

In many crosses with $N. crassa$ laboratory stocks, numerous small sacs are found in the perithecia that contain chains of eight tiny round refractile bodies with a diameter about one-fourth the length of a normal mature ascospore. N. B. Raju (unpublished) has shown that these bubble asci originate by degeneration of asci that develop normally until the
third division is completed and spores have been delimited. All the asco-
spores in an affected ascus begin to degenerate and shrink at that time. The
frequency of bubble asci varies from less than 10% to over 80% in
different crosses, but is constant for the same combination of parents. A
high frequency of bubble asci is partially correlated with inbreeding
(D. Newmeyer and N. B. Raju, unpublished observations). Several widely
used standard wild types show a high frequency. The abnormal asci re-
ported by McNelly-Ingle and Frost (1965) probably include bubble asci
as well as other abnormalities.

The degenerated spores in bubble asci are apparently produced non-
selectively and do not interfere with genetic analyses. They also do not
interfere in the diagnosis of our typical identified rearrangements, because
deficiency ascospores from heterozygous aberrations are usually much
larger than bubble ascospores. Bubble asci are probably never ejected
from the perithecium, and the tiny bubble spores are readily overlooked
when perithecia are opened.

IV. The Wild-Type Genome

A. THE CHROMOSOMES

1. Chromosome Size

The meiotic chromosomes of Neurospora are small, but within the range
of study with the light microscope. Lengths of the seven chromosomes at
pachynema range from 7 to 19 μm (Singleton, 1953). This is immense
compared to somatic chromosomes, where the entire nucleus in the hyphae
is only about 2 μm in diameter. However, it is small compared to maize,
where the ten chromosomes range from 37 to 82 μm in pachytene length
(Rhoades, 1950). At metaphase I, the Neurospora bivalents contract to
lengths of 1.7 to less than 1 μm. The enormous differences in chromosome
size between meiotic and somatic cells, and between stages of the cell
cycle, are presumably not due to changes in DNA content [see Rossen
and Westergaard (1966) for quantitative data from another ascomycete,
Neottiella, where similar size differences are found].

2. Chromosome Composition

a. DNA Content. Horowitz and Macleod (1960) showed by chemical
analysis that haploid nuclei from microconidia of N. crassa contain
4.63 × 10^{-14} gm of DNA (2.8 × 10^{10} daltons or 4.5 × 10^7 nucleotide
pairs). Other methods gave comparable amounts: 2.2 × 10^{10} daltons by
DNA:DNA reassociation kinetics (Ray and Dutta, 1972), and 2.8 × 10^{10}
daltons by sucrose density gradient centrifugation (Brooks and Huang, 1972). Other fungi have similar amounts of DNA.

*Neurospora* is about midway between *E. coli* and *Drosophila* in DNA content, and much closer to *coli* (10 ×) than to higher plants or vertebrates. In fact, the DNA content of a small chromosome in *Neurospora* is probably less than that of the *E. coli* chromosome. It is reduced even more in some rearrangement strains of *Neurospora* (for example, \( T(IV;VI) \alpha 45502 \) and \( T[II \rightarrow (IV;V)] \alpha 179 \)), where the smallest translocation chromosome is much smaller than any in the wild type. The DNA content per haploid genome for representative organisms can be seen in Table 1.

**b. Repetitive and Unique-Sequence DNA.** Brooks and Huang (1972) report that about 20% of *Neurospora crassa* DNA is repetitive or redundant. Their experiments indicate that little of the repetitive DNA comes from the mitochondria, which according to Luck and Reich (1964) contribute less than 1% of the total DNA of the cell. [The mitochondrial DNA also contains repeated sequences (Wood and Luck, 1969).] However, Dutta (1973) reports that 10–12% of the DNA consists of repeated sequences, while about 90% behaves in reassociation kinetics as though it were composed of unique copies; and Dutta and Chaudhuri (1975) conclude that 3–4% of the total comes from the mitochondria.

**i. DNA specifying tRNA and rRNA.** The experiments of Brooks and Huang (1972) indicate that 2.3% of the repetitive DNA hybridizes with ribosomal RNA (rRNA) and 1.2% hybridizes with transfer RNA (tRNA). When their hybridization experiments were conducted with the total DNA of the cell, 1% hybridized with rRNA and 0.3% with tRNA. They calculate the complexity of the redundant DNA to be \( 2 \times 10^8 \) daltons, and they suggest an average repeat frequency of about 60 copies per genome for all repeated genes. The 1% of the total DNA attributed to rRNA cistrons corresponds to 100–200 rRNA genes by their estimates, while the 0.3% tRNA cistrons corresponds to 3000 total copies.

Chattopadhyay et al. (1972) calculate that about 100 copies of the rRNA genes exist in each nucleus, and that individual copies have essentially identical DNA sequences. When the tRNA genes were isolated by shearing DNA into fragments of \( 1.2 \times 10^6 \) daltons and hybridizing with tRNA, Ray and Dutta (1972; Dutta and Ray, 1973) found 0.3% of the total *Neurospora* DNA to be composed of tRNA cistrons, in agreement with the report by Brooks and Huang (1972). Ray and Dutta (1972) calculate that if there are 60 different species of tRNA each may be represented an average of 44 times in the genome, giving a grand total of 2640 tRNA cistrons.

**ii. DNA specifying mRNA.** Dutta (1973) reports that 35% of the
TABLE 1
Comparative Genome Size of Representative Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Haploid chromosome number</th>
<th>Total pachytene chromosome length (µm)*</th>
<th>Haploid DNA content (daltons × 10⁹)</th>
<th>Total genetic map length* (centi-morgans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>1</td>
<td>28b</td>
<td>9.2c</td>
<td>2600d</td>
</tr>
<tr>
<td>Saccharomyces cerevisiae</td>
<td>17</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Neurospora crassa</td>
<td>7</td>
<td>76e</td>
<td>28p</td>
<td>&gt;1000f</td>
</tr>
<tr>
<td>Drosophila melanogaster</td>
<td>4</td>
<td>50–90de</td>
<td>110k</td>
<td>287h</td>
</tr>
<tr>
<td>X-chromosome only</td>
<td>—</td>
<td>11–20dzi</td>
<td>—</td>
<td>70a</td>
</tr>
<tr>
<td>Zea mays</td>
<td>10</td>
<td>552f</td>
<td>330n</td>
<td>1119e</td>
</tr>
<tr>
<td>Lycopersicon esculentum</td>
<td>12</td>
<td>387p</td>
<td>1200n</td>
<td>969e</td>
</tr>
<tr>
<td>Mus musculus</td>
<td>20</td>
<td>229r</td>
<td>1500t</td>
<td>1200–</td>
</tr>
<tr>
<td>Homo sapiens</td>
<td>23</td>
<td>234q</td>
<td>1800t</td>
<td>2530q</td>
</tr>
</tbody>
</table>

* The values in columns 3 to 6 are, in some cases, approximations, or they may be based on incomplete information. Other values may be found in the literature. These are presented only for the purpose of making a general comparison with Neurospora.  
LM: Measurement with the light microscope of conventionally fixed and stained material. EM: Measurement with the electron microscope of synaptosomal complexes.  
† Based on 1100 µm double-stranded DNA, measured with the electron microscope.  
P Tentative because of high variability in crossing over. For calculations, see Section IV, B, 2, c.  
§ Salivary gland polytene chromosome lengths are 2219 µm (entire complement) and 414 µm (X-chromosome) (Lindsay and Grell, 1968).  
# Euchromatic regions only, except for X-chromosome, which is to nucleolus organizer. The SC shortens as meiosis progresses.  
¶ The autosomes only.

References:  
^Cairns (1963).  
^Byers and Goetsch (1975).  
^Mortimer and Hawthorne (1975).  
^Singleton (1953).  
^Gillies (1972).  
^Horowitz and Maceo (1960).  
^Lindsay and Grell (1968).  
^Carpenter (1975a).  
^Laird (1971).  
^Rasch et al. (1971).  
^Rhoades (1950).  
^Gillies (1973).  
^Evans and Rees (1971).  
^Barton (1950).  
^Khush and Rick (1968).  
^M. J. Moses (personal communication).  
^Miller and Miller (1975).  
^Hultén and Lindsten (1973).  
^A. T. C. Carpenter (personal communication).

unique sequence DNA hybridizes with RNA which has been transcribed during log phase mycelial growth.

Bhagwat and Mahadevan (1973) have labeled RNA at 8, 16 and 24 hours after the beginning of germination and growth of conidia. Identifying the mRNA (messenger RNA) component extracted from the hyphae, they find that the mRNA transcribed at different times after the beginning of conidial germination and growth is different both by amount
of the total DNA to which it hybridizes and by the amount with which it overlaps the mRNA transcribed at the other times, thus indicating differential activity of genes in the maturing culture.

c. Histones. Neurospora crassa appears to have very little histone protein associated with the chromosomes. Dwivedi et al. (1969) and Leighton et al. (1971) were unable to isolate and identify any histones, but Hsiang and Cole (1973) have isolated two "slightly lysine-rich" histones from Neurospora chromatin. Hsiang and Cole find that there is only 25% as much histone protein as in higher eukaryotes; and they believe that the earlier failures may have been due to the small quantity of histones, proteolytic degradation, and other isolation procedures that gave low yields of chromatin and histones. Other basic proteins may be present in Neurospora chromosomes, since there is a requirement for putrescine, which is a precursor of spermidine and other polyamines (Davis et al., 1970; Deters et al., 1974).

3. Techniques for Chromosome Cytology

Conventional techniques developed for eukaryotic plants and animals are not usually successful in fixing and staining Neurospora chromosomes. However, variations have been developed that stain chromosomes effectively during meiotic and mitotic divisions in the asci. McClintock (1945), Singleton (1948, 1953), St. Lawrence (1950, 1953), Barry (1966), Phillips (1967), and Pincheira and Srb (1969) have obtained good results with orcein or carmine, and B. C. Lu (personal communication) and Raju (1976) have used hematoxylin effectively in Neurospora. Hematoxylin and carmine stain the nucleolus and centrosome intensely, while orcein stains the nucleolus only lightly and the centrosome not at all. Good staining of chromosomes in the asci of numerous other ascomycete genera has also been obtained using Giemsa (Rogers, 1965, and later publications).

The procedures we now follow and recommend for Neurospora are described by Barry (1966) for acetoorcein and by Raju (1976) for hematoxylin. Most of the observations reported in the following sections have employed ethanol-acetic acid-lactic acid fixation followed by staining with acetoorcein.

A technique for producing giant conidia promises to make vegetative nuclei of Neurospora more accessible to observation. When conidia are suspended in medium containing 3.2 M ethylene glycol, they form spheres that grow without cell division (Bates and Wilson, 1974). N. B. Raju (unpublished observations) has examined these cytologically using hematoxylin. Nuclei divide, and chromosomes can be observed at different mitotic stages. Some giant nuclei become polyploid.
Particular genotypes also promise to be technically useful in cytology. For example, N. B. Raju (unpublished) has found that a dominant mutant discovered by Newmeyer has as one of its effects the induction of waves of synchronized mitoses in ascogenous hyphae. Thus, large numbers of nuclei in precisely the same stage of division may be observed together, and different stages are characteristic of different groups of hyphae.

Attempts to stain Neurospora meiotic chromosomes with Feulgen have apparently not been successful. Weijer and McDonald (1965) have used a modified Feulgen reaction to obtain chromosome staining in the two mitotic divisions in the ascus. The Feulgen reaction has been used successfully for staining somatic nuclei (Horowitz and Macleod, 1960; Somers et al., 1960; Weijer, 1965), but other stains are probably preferred.

In Gillies' (1972) studies of the synaptonemal complex, he reports difficulty in staining chromosomes and obtaining contrast between chromosomes and nucleoplasm for electron microscope observations of meiosis.

4. Chromosome Identification and Morphology

a. Chromosome Number. McClintock (1945) showed the haploid number to be 7 in N. crassa, and all later observations of chromosomes in the ascus have been in agreement. [However, Somers et al. (1960) reported a minute eighth chromosome in somatic nuclei.]

The same number has since been found in all the other Neurospora species: N. sitophila (Fincham, 1949; Dodge et al., 1950; Perkins et al., 1976), N. tetrasperma (McClintock and Weaver, reported by McClintock, 1945; Dodge et al., 1950), N. intermedia (Perkins et al., 1976), and the five homothallic species N. terricola (Nelson and Backus, 1968), N. africana, N. dodgei, N. lineolata, and N. toroi (Raju, 1976). [Early counts of $n = 6$ for N. tetrasperma by Colson (1934) and Cutter (1946) were probably incorrect.]

b. Chromosome Morphology at Pachynema

i. Idiograms. McClintock (1945) drew up karyotypes numbering the seven chromosomes from longest to shortest and showing relative lengths of the chromosomes measured at pachynema and at mitotic metaphase stages in the ascus. She tentatively determined the probable centromere position of each chromosome by measurement at mitotic metaphase in the third division when the chromosomes show a sharp bend at the centromere. The centromere is not visible in the meiotic stages, although McClintock supposed it to be correlated with the position of the heaviest chromomere of each pachytene chromosome. Singleton (1948, 1953) subsequently published more detailed idiograms showing the identifying morphological features of each chromosome. Each chromosome was
distinguished by its chromomere pattern and length at pachynema, and by its centromere position and length at mitotic metaphases in the ascus. Singleton's chromosome maps were assembled from observations of about 20 pachytene figures where most or all of the chromosomes could be identified. He regarded the maps as tentative. They are reproduced in the upper part of Fig. 3.

Fig. 3. Pachytene chromosome morphology of *Neurospora crassa*. Above: The chromomere pattern as drawn by Singleton (1953). a and b identify the largest chromomeres of each chromosome. Below: The patterns that we now regard as most characteristic of each chromosome. Not all chromomeres are included in the diagram (compare with Fig. 4). In many nuclei the chromomeres identified here are not seen and chromosome identification depends on length, or will be in doubt. Even though the patterns of chromosomes 3, 4, and 5 appear to be very distinct, these chromosomes may be easily confused if the conspicuous chromomere does not stain or show clearly. The heteromorphic, double chromomere in 1 is visible in about 50% of nuclei. This may be due to stretching when the chromosome is spread out. The achromatic gap in 2 is not always observed. Singleton's chromosome 7 is our chromosome 6.
The pachytene maps which we feel are more typical of the usual chromomere patterns and configurations are shown in the lower part of Fig. 3. These revised maps are also tentative working maps for our present studies. Probably one may expect to find other typical patterns, depending on the combinations of strains used. Most of our observations are now made on strains from the Oak Ridge wild-type (74-OR23-1A and 74-OR8-1a) background.

ii. Variability of chromomere patterns. It has been our experience that each chromosome is not always identifiable, and that the chromomere patterns are not distinctive for all the chromosomes, at least throughout the pachytene stage when aberrations are analyzed and their breakpoints are located most effectively. There are two difficulties that contribute to the problem of correct chromosome identification. The first is that the chromosomes undergo change during pachynema, which is a stage of long duration, and the chromomere patterns shift as the stage progresses. Some chromosomes may also elongate faster than others. The second difficulty is that different strains probably differ slightly in their chromomere patterns. The strains now used as standards are apparently somewhat different in this respect from the combinations used by Singleton and McClintock.

Probably for these reasons, Singleton may have omitted or confused some of the chromomere positions in his idiograms. For example, chromosome 1 has a conspicuous, central, heavy chromomere (the \( a \)-chromomere) surrounded by a heavily stained region in Singleton’s diagram. This largest chromomere is almost exactly in the middle of the chromosome, and there is a second, less-marked chromomere (\( b \)) about halfway between the \( a \)-chromomere and one end of the chromosome. In most of our figures, and in some of Singleton's diagrams reconstructing the figures he photographed (his Figs. 22–23A, 27A and 30A), the \( a \) and \( b \) chromomeres are about equally intense, and they divide the chromosome into approximate thirds (see Fig. 3).

iii. Heterochromatin. Large and numerous chromomeres are a conspicuous feature of the pachytene chromosomes, with the largest and darkest blocks of chromomeres usually appearing in two sets in the mid-region of chromosome 1. McClintock (1945) and Singleton (1953) recognized chromosome regions at second telophase which they called heterochromatic. However, our convention has been simply to refer to the more darkly and intensely stained regions as “heavy” chromomeres. The chromomeres are observed during pachynema and other prophase stages, but variable chromatic regions are not observed at metaphase of meiosis and mitosis in the ascus. Detecting heterochromatin by a possible differential time of onset of DNA synthesis by chromosome or chromosome region has not been feasible for technical reasons, mostly because of the inability to
obtain specific radioisotope labeling of DNA (Fink and Fink, 1962a,b; Baer and St. Lawrence, 1964), but also because the continuous formation of new waves of asci in the perithecium in asynchronous development prevents recognition of specific early or late synthesis by chromosome segments in any one ascus.

None of the chromosome ends are marked by knobs of great contrasting size, except the satellite of the nucleolus chromosome. Variations in the size of the terminal chromomeres are seen among nonhomologous chromosomes, however. Nor have any striking heteromorphic chromosomes or chromomeres yet appeared among *N. crassa* stocks of different background, excepting the satellite and chromosome aberrations. Crosses between wild strains of *N. intermedia*, and interspecies crosses of *N. crassa* by *N. intermedia* have shown some differences in chromomere patterns (Perkins et al., 1976). *N. intermedia* chromosomes are much less well marked by heavy chromomeres than are *N. crassa* chromosomes, in the asci of both intraspecific and interspecific crosses.

iv. Spear ends. At pachynema, McClintock, Singleton, and St. Lawrence recognized “spear ends” of chromosomes 1 and 6—paired homologs appeared to be touching at the tips while elsewhere the pairs were separated and lying parallel. In our preparations, this seems not to be a consistent feature of any chromosome pair. Any apparent spear ends can equally well be attributed to a partial twist of the bivalent. In studies of the synaptonemal complexes of *Neurospora*, Gillies (1972) found that all homologous ends of pachytene chromosomes are separated at their sites of attachment to the nuclear membrane.

v. Appearance of univalent chromosomes. Sometimes unpaired chromosomes (univalents) or portions of unpaired chromosomes can be clearly recognized. At other times their identification is uncertain. The difficulty lies essentially with the small diameter of *Neurospora* chromosomes. If two paired homologs are closely associated or twisted about one another at pachynema, it may be impossible to resolve their double nature. Furthermore, unpaired and paired chromosomes differ in their morphology. The chromatids of an unpaired chromosome are unraveled, and appear to separate somewhat from one another, thus making a fuzzy doubleness and a width sufficient to suggest the diameter and other characteristics of an indistinct bivalent. For a synapsed pair, the chromatids of each chromosome are not visible with the light microscope, and each chromosome appears to be a single strand. Unpaired regions or chromosomes thus often mimic a normal paired region or chromosome. In paired regions, the chromomere patterns are usually distinct and sharp at midpachynema, but unpaired sections often show no such crisp pattern and may be darkly staining yet indistinct in fine detail.

vi. Description of individual pachytene chromosomes. Chromosome 1
can be identified with a high degree of certainty. It is the longest chromosome of the complement by a significant margin (one half again the length of chromosome 2). There are numerous distinctive chromomeres. Confusion regarding the actual position of the heavy a and b chromomeres, discussed above, does not interfere in practice with the identification. The pachytene morphology of an inverted chromosome 1 can be seen in Fig. 4.

Chromosome 2 is usually easy to identify because it bears the nucleolus organizer region, and at pachynema the nucleolus is a very conspicuous body in the nucleus. The region of chromosome 2 near the organizer in a typical nucleus is well marked by large chromomeres displaying a characteristic pattern. In some nuclei, chromosome 2 may be shorter than 3.

Some strains of Neospora crassa (the St. Lawrence and Oak Ridge wild types and their derivatives) have a small satellite at the end of the nucleolus organizer region which may be identified in well stained, con-

Fig. 4. Pachynema in Neospora crassa. The photograph is of one focal level of the nucleus, and the accompanying drawing shows the entire nuclear complement of seven chromosomes. (Chromosome 5 has been shifted to the right in the drawing to avoid a confusing overlap with parts of 2 and 4. The overlap in the actual nucleus was not a problem because the arms were in different focal planes.) Chromomere detail is shown in the drawing, and each chromosome is identified; only 6 is not clear. Chromosome 1 is homozygous for inversion H4250. One parent contained the original inversion, but in the second parent the inversion sequence was derived by mei-3-induced somatic breakdown from an H4250 duplication (see Section V, E, 4, b). (Orcein staining, ×4000. Stocks obtained from D. Newmeyer.)
trasting figures. At pachynema when the nucleolus is at its greatest size, the satellites are seen on the surface of the nucleolus, usually in the hemisphere opposite the organizers. Photographs showing the organizers and satellites can be found in Barry and Perkins (1969); see also Fig. 4. Many stocks, both mutant and wild-type, lack the satellite.

Chromosomes 3, 4, and 5 are all about the same size, and in the usual orcein-stained nucleus they do not develop constant and distinctive patterns. In some figures, our comparisons by chromomere patterns match rather well with the McClintock–Singleton diagrams. In others they do not, and our identifications are then very tentative. Since the chromosomes are rarely flattened into two dimensions in our preparations, measurements of true length are not accurate enough to distinguish among the members of the 3-4-5 group.

Chromosomes 6 and 7 are about equal in size, and usually they are clearly smaller than the intermediate chromosomes 3, 4, and 5. In darkly stained nuclei they are generally not in doubt because the chromomere patterns are distinctive, but in lightly stained nuclei we have found these two chromosomes to be more similar than the McClintock–Singleton descriptions would suggest. Each has a large, shifting, median or submedian chromomere, the a chromomere. Singleton’s (1953) chromosome 7, which other workers (McCIntock, St. Lawrence, Barry) call 6, has several additional large chromomeres arranged in a distinctive pattern. Singleton’s chromosome 6 (7 for McCIntock, St. Lawrence, and Barry) is less well marked, by comparison with 7. However, in Singleton’s maps of chromosomes 6 and 7, the overall pattern is much the same, with the a and b chromomeres spaced along the chromosome at about the same ratios from the ends, and with chromomeres at the tips of each chromosome, although the tip chromomeres differ in size.

c. Recognition of Chromosomes at Condensed Stages. Phillips (1967) was able to recognize interchanges involving chromosome 2 at diakinesis and metaphase I by the rings and chains that indicate aberration pairing in translocation heterozygotes. Our experience has been that the small chromosome size at metaphase I, the possibility of overlapping bivalents, and the unsynchronized anaphase-I disjunction make identification unreliable at this stage, except for chromosome 2 if the nucleolus is still attached.

d. Chromosome Morphology at Later Stages in the Ascus. The number, size, centromere position, and arm ratios of the mitotic chromosome complement have been diagrammed tentatively by McClintock (1945) and Singleton (1953). The mitotic karyotype is obtained at metaphase of the third nuclear division in the ascus, when the chromosomes may be seen clearly in polar view on the metaphase plate. Each chromosome
has a V or J shape, with the bend presumably located at the centromere. The following fourth division, after the ascospores have been delimited, is also useful for observing chromosome morphology except that the chromosomes are smaller and more crowded inside the nucleus.

B. Marker Distribution and Genetic Mapping

1. The Markers

Over 400 gene loci have been mapped to the seven linkage groups of *Neurospora crassa*. The broad categories of phenotypes are listed in Table 2.

**TABLE 2**

Numbers of Nonallelic Genes of Various Types That Have Been Mapped to Linkage Groups in *Neurospora crassa*

<table>
<thead>
<tr>
<th>Type of mutant</th>
<th>Linkage group</th>
<th>Total mapped</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>Nutritional</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>Other biochemically defined</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Morphology</td>
<td>31</td>
<td>13</td>
</tr>
<tr>
<td>Resistance to toxic agents</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Irreparable temperature-sensitive</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Suppressor</td>
<td>8</td>
<td>—</td>
</tr>
<tr>
<td>Radiation-sensitive</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Recombination</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Meiotic</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Vegetative incompatibility</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Carotenoid</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>Melanin</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Modifier</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rhythm</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Lethal</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Sterility</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Growth rate</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Mating type</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Total genes</td>
<td>124</td>
<td>43</td>
</tr>
</tbody>
</table>

(29%) (10%) (9%) (16%) (16%) (8%) (12%)

* A mutant is listed under only one category, even though it might equally well fall under several categories. Uptake and permeability mutants are not listed separately, but are included under another heading, such as resistance, other biochemically defined, or irreparable temperature-sensitive.
Several types of mutants have not been found, or are rare. There are few autonomous ascospore color mutants compared to Sordaria, Ascochlorella or Podospora. This may be because white spores are usually inviable, or because they fail to survive the high temperature routinely used to break dormancy. White ascospores of one mutant type have been shown to germinate spontaneously (Johnson, 1975a). Several other categories of mutants are as yet underrepresented in Neurospora compared to other fungi—for example, radiation-sensitive, super-suppressor, meiotic, and inositol-requiring genes.

2. Genetic Maps and Marker Distribution

All the genes in Table 2 have been assigned to linkage groups, but by no means all are mapped accurately within groups. Useful maps have been published by Fincham and Day (1971), Davis and de Serres (1970), and Radford (1972). Uncertainties of map location are shown by Radford (1972), who has also listed known loci with brief descriptions of phenotypes, including known enzyme phenotypes (Radford, 1976).

The maps presented in Fig. 5 have been prepared specifically to show the genes that are referred to in this review and its Appendix. These maps are not complete. Numerous useful, well mapped markers are not included because they do not happen to have been employed in the studies reported here. For special reasons, the positions of a few rearrangement breakpoints are shown, mainly those that mark linkage-group ends.

Gene symbols are identified in the legend to Fig. 5. Neurospora genetic nomenclature follows Drosophila usage more closely than that of maize, yeast, Aspergillus, or bacteria (Barratt and Perkins, 1965; Barratt, 1989). Different genes having the same basic symbol (“mimic genes”) are distinguished by numbers (e.g., arg-1, arg-2) as in Drosophila, rather than by capital letters as in bacteria. This usage predates the introduction of the bacterial system and is more suited to an organism having mating types designated A and a. (The only exception in Neurospora is ad-3A ad-3B, retained because of long-standing use.) Neurospora suppressors are also symbolized as in Drosophila, with su for the mutant suppressor, su* for its wild-type allele. The three-letter gene symbols of bacterial genetics are used for some classes of genes such as amino-acid auxotrophs (Perkins and Barratt, 1973). No scale is shown in Fig. 5, because uncontrolled variability of recombination is so great in Neurospora. Linkage group I is estimated to be about 200 map units (centimorgans) in length. Interval lengths in published maps may be based on recombination values from crosses with either high or low crossing over, or they may represent pooled values, or values felt to be most representative. Whatever their basis, their predictive value for distances is limited to within perhaps one order of magnitude for any strains that are not highly homogeneous. The gene orders, of course, should be invariant.

a. Distribution of Genes and Rearrangements. The distribution of mapped loci and rearrangements among the seven linkage groups is shown in Table 3. Both the number of genes in each group and the involvements
Fig. 5. Genetic map of *Neurospora crassa* showing only loci named in this review. Parentheses indicate that order is uncertain relative to outside markers; where vertical lines do not intersect the map, order within parentheses is uncertain. Distances are only roughly to scale; interval lengths can vary as much as 10-fold in crosses of different parentage. Because of the large number of loci, linkage group IV and the left half of I are both expanded to about 1.5 × the scale of the other groups. The second line is a continuation of linkage group I.

The following genes are not shown, though they are referred to: Linkage group I: ser-3 is near cys-5 and cys-11; cyt-1 is between ser-3 and leu-3; sn is near centromere, probably left; rg is near his-2; het-5 is right of thi-1; tre and mig are between ad-9 and al-2; us-6 is near and left of al-2. Linkage group II: pi is probably an allele of col-10; pcon is an allele of nuc-2; cpt is between arg-5 and pe. Linkage group III: us-4 is near ad-4; het-7 is right of trp-1. Linkage group IV: rib-2 is right of T(S4342); tol is near trp-4. Linkage group V: al-3, trp-5, and Mei-2 are near int; erg-1 and erg-2 are in VR. Linkage group VI: het-9 is in VIR; lys-5 is allelic with asco. Linkage group VII: thr-1 is near met-7; het-10 is right of for; the centromere position is uncertain relative to qa and met-7.


For full symbols of the translocations and inversions, see the Appendix.
TABLE 3
Comparison of Cytological Lengths of the Seven Neurospora Chromosomes with the Numbers of Genes and Rearrangements Mapped in Each

<table>
<thead>
<tr>
<th>Linkage group</th>
<th>I</th>
<th>V</th>
<th>III</th>
<th>IV</th>
<th>VI</th>
<th>II</th>
<th>VII</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corresponding chromosome No.</td>
<td>1</td>
<td>2</td>
<td>(3)</td>
<td>(4)</td>
<td>(5)</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Mapped genes ($N = 426$)</td>
<td>29%</td>
<td>16%</td>
<td>9%</td>
<td>16%</td>
<td>8%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Number of rearrangements in which involved ($N = 336$)</td>
<td>27%</td>
<td>12%</td>
<td>11%</td>
<td>17%</td>
<td>12%</td>
<td>12%</td>
<td>9%</td>
</tr>
<tr>
<td>Genes plus rearrangements ($N = 762$)</td>
<td>28%</td>
<td>15%</td>
<td>10%</td>
<td>16%</td>
<td>10%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Measured length of synaptonemal complex (total = 45.5 μm)</td>
<td>22%</td>
<td>16%</td>
<td>15%</td>
<td>13%</td>
<td>12%</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

---

*See Section IV, C and Table 4 for basis of linkage group—chromosome assignments. Chromosomes were numbered in the order of cytological length (McClintock, 1945; Singleton, 1953).

*Includes all genes that have been mapped to linkage groups and that are thought to be nonallelic. See Table 2 for the distribution of genes by phenotype category and linkage group.

*Based on the 167 rearrangements summarized in Table 5 and described in the Appendix. Values are not based on number of breakpoints; e.g., inversions are counted only once, and an insertion-translocation is counted once for donor chromosome and once for recipient.

*Gillies (1972). Average for three nuclei reconstructed from thin sections.

in gross rearrangements are approximately proportional to the cytological length of the corresponding chromosome at pachynema. (The slight excess in I might be expected because this linkage group contains the mating-type alleles and other markers favorable for detecting linkage.) There is no obvious concentration of any phenotypic category of mutant in a particular linkage group.

Rearrangement breakpoints do not appear to be distributed randomly within individual linkage groups. Centromere regions and chromosome tips seem more likely to be involved, and there is a suggestion of excess breaks in IVR.

The distribution of genes within linkage groups can be seen from the genetic maps. Identified loci are the most crowded in a portion of I that includes mating type and the centromere, and in the proximal half of IVR. There is an unexplained lack of markers in the left arms of III and V. Cytological observations indicate that the centromere is not near the end of III, and the genetic map would thus be expected to have two arms. Nothing is known about recombination in III, but crossing over is known not to be suppressed in VI, where 35% recombination occurs between a centromere marker, *lys-1*, and the terminal cytological marker
sat, satelliteless (Barry and Perkins, 1969). There is thus no reason to suspect that the arm is genetically inert. VL bears the nucleolus organizer near its tip. There is no evidence of chromosome breakage from entanglement of a terminalized chiasma in the nucleolus. (In Neurospora, the nucleolus is usually detached from the chromosomes before anaphase I.)

Rick (1971) summarized information on silent regions in the chromosomes of several organisms and noted that when the two arms of the nucleolus organizer chromosome are compared, mapped genes are preferentially more abundant in the arm opposite the nucleolus, in both tomato and maize. Neurospora apparently conforms to the same pattern.

b. Clustering of Functionally Related Mutations. When nutritional markers originally became available in Neurospora, one of the first questions to be asked was whether functionally related genes would be linked or clustered. The answer was clearly no clustering, for one biosynthetic pathway after another (see Horowitz, 1965). However, there are several exceptions. Some of these appear to be single genes with multiple functions, others clearly involve separate genes. Where the products have been studied, enzyme aggregates or multifunctional enzymes are usually found.

Histidine biosynthesis is specified by nine genes in the histidine operon of Salmonella. In Neurospora, the corresponding genes are scattered through four linkage groups. However, three of the enzyme activities are specified by a single region (his-3) in Neurospora, and an enzyme or aggregate has been purified that possesses all three activities (see Ahmed et al., 1964; Ahmed, 1968; Catcheside, 1965; Catcheside and Angel, 1974; Webber, 1965; Minson and Creaser, 1969). Two distinct activities are both specified by the pyr-3 locus (Davis and Woodward, 1962; Williams and Davis, 1968). Multiple enzymic functions are also specified by trp-3 (see Crawford, 1975) and trp-1 (DeMoss et al., 1967).

The mutants mac and met-6 behave recombinationally as though they were at different sites within a single gene locus (Murray, 1969). However, they differ in response when adenine as well as methionine is added, they complement one another (Murray, 1969), and they differ in the activity of two different enzymes related to folyl polyglutamate biosynthesis (Ritari et al., 1973).

Other examples in Neurospora involve clustered genes that govern related functions. The aro cluster consists of five genes governing steps in the aromatic synthetic pathway (Gross and Fein, 1960; Giles et al., 1967; Rines et al., 1969). The aro genes are transcribed together and their products form an aggregate. The qa (quinate) cluster consists of one regulatory and three structural genes governing the aromatic catabolic pathway (Chaleff, 1974a,b; Case and Giles, 1975). The products are not aggregated.
met-7 and met-9 appear to be adjacent genes (Murray, 1970). They specify different enzymes (Kerr and Flavin, 1970), yet mutant sites in the two loci are so close that they undergo coconversion. The *Neurospora* maps also reveal several other apparently adjacent pairs of genes with functionally related phenotypes—*cys-1, cys-2* (Murray, 1965); *thr-2, -3* (Perkins et al., 1962; Emerson, 1950); *ibv-1, -2* (Kiritani, 1962); *arg-10, -11* (Newmeyer, 1957); *cys-5, -11* (Murray, 1965, 1968b); *erg-1, -2* (Grindle, 1974); *tre, mig* (Sussman et al., 1971); *pcon, preg* (Littlewood et al., 1975); and *pyr-3, arg-2* (Reissig, 1960, 1963). Other related gene pairs are close but not contiguous—*ad-3A, ad-3B* (de Serres, 1969) and *al-1, al-2* (Hungate, 1945; Subden and Threlkeld, 1970; Perkins, 1971b).

It is not known whether there is any functional relation between the two distinct roles of the mating-type alleles—in sexual crossing and in vegetative incompatibility (Section II). A functional relation has been suggested between mating type and the closely linked locus *un-3*, which is known to affect membranes (Kappy and Metzenberg, 1967).

For a general review of genetic clustering of biochemically related functions in fungi, see Fink (1971).

c. Estimates of Total Map Length. Because crossover frequencies are extremely variable in *Neurospora* (Section IV, B, 3), any estimate of overall genetic map length will be unreliable within wide limits. Nevertheless, rough estimates can be based either on cytological chiasma counts or on genetic recombination frequencies.

An average of at least two chiasmata are observed per bivalent (Singleton, 1953; E. G. Barry, unpublished observations), indicating that the total map length is at least 700 units.

Maps compiled from genetic data by Fincham and Day (1971) total about 750 units. Several linkage groups have since been extended by means of newly discovered genes or rearrangement breakpoints, bringing the total length to perhaps 900 units. This is in reasonable agreement with an independent estimate based on exchange frequencies in a long segment of IR which was multiply marked so that all exchanges could be detected (Perkins, 1962a). On this basis, the longest linkage group is estimated to be 200 units, and it (chromosome 1) represents 22–25% of the total genome, based on cytological measurement of synaptonemal complexes and pachytene chromosomes (see Gillies, 1972). Thus the total length in *Neurospora* is probably at least 1000 genetic map units. How this value compares with genetic maps in other organisms can be seen in Table 1.

3. Crossing-over Variability and Its Basis

Recombination between the same two markers may vary 2-fold, 4-fold, or even 10-fold in crosses of different parentage (see, for example, Stadler,
1956; Nakamura, 1966; Landner, 1971; Catcheside and Corcoran, 1973). Yet recombination values are reproducible within close limits in repeated crosses between the same two strains. It is not known whether an increase in crossing over in one region is accompanied by a compensating decrease elsewhere in the genome, except that chiasma interference is positive (see, for example, Perkins, 1962a).

Structural heterozygosity and genic regulation have both been considered as possible causes of the variability of recombination. Abnormal crossing over and changed linkage relations have several times led to the recognition that chromosome rearrangements were present in heterozygous condition in particular crosses (for example, by Houlnahan et al., 1949; de Serres, 1971). It may also be that paracentric inversions are present in some stocks and have gone undetected. (The problem of "silent" paracentrics will be discussed in Section V, C, 3.) However, most cases of crossing-over variability appear to be due to genic control.

Recombination (rec) genes have been shown to regulate both intragenic and intergenic recombination in specific regions located at a distance from the controlling gene (Jessup and Catcheside, 1965). Three rec systems have been described in studies by D. G. Catcheside and his associates B. R. Smith, K. K. Jha, D. E. A. Catcheside, D. R. Smyth, P. L. Thomas, T. Angel, B. Austin, and D. Corcoran. The experimental results and interpretations have been reviewed by D. G. Catcheside (1974); see also Catcheside and Corcoran (1973) and D. E. A. Catcheside (1974). Differences at all three rec loci are present among commonly used laboratory wild-type stocks (Catcheside, 1975). More than one region may be under control by the same rec gene. High recombination is recessive to low for all the rec genes studied. One example is known of a different class of element, cog (recognition), which is closely linked to his-3. The dominant cog* allele must be present in order for high recombination to occur in or near his-3 when the appropriate rec gene is homozygous recessive. The existence is inferred of a third class of genes with local effects on recombination.

Other approaches have also been used in attempts to clarify the genetic basis of crossing-over variability (Frost, 1961; Lavigne and Frost, 1964; Towe, 1958; Stadler and Towe, 1962; Nakamura, 1966; Landner, 1971, 1974; de Serres, 1971). These include selection and inbreeding. It was shown by Towe (1958), Stadler and Towe (1962), and Cameron et al. (1966) that inbreeding tends to increase crossing over. Other experiments showed that reciprocal recombination between the closely linked genes ad-3A and ad-3B was greater when markers originated in different genetic backgrounds than when they arose in the same background (de Serres, 1971). These results must now be evaluated in light of the findings on
regulation of recombination. If high recombination requires that recessive \textit{rec} genes be homozygous, inbreeding may be expected sometimes but not always to increase recombination, depending on what regions are being monitored, what \textit{rec} alleles are initially present, and which of them are retained during inbreeding.

4. Mapping Methodology

Genetic mapping consists of three phases—detection of linkage, determination of gene order, and estimation of interval length. In choosing methods to solve a practical mapping problem at any of these stages, it is important not to confuse the objectives of mapping with investigations into the mechanism of recombination.

\textit{a. Linkage Detection.} In terms of labor, random isolates are more efficient than tetrads for detecting linkage (Perkins, 1953), and unordered tetrads are more efficient than ordered tetrads. Effort can be minimized by using multiply marked tester strains such as \textit{alcoy} (Perkins et al., 1969), \textit{multicent} (Perkins, 1972c) and related follow-up testers (Perkins, 1972b, 1973). Markers in these strains have been selected for ease and reliability of scoring. The \textit{multicent} tester contains proximal markers for all seven linkage groups, in normal sequence: \textit{mt, bal, acr-2, pdz, at, ylo-1, wc}. \textit{alcoy} contains three independent reciprocal translocations, each associated with a marker: \textit{al-1 (I;II), cot-1 (IV;V), ylo-1 (III;VI)}. Other less complete multiple-group testers are also available from FGSC.

If tetrad data are available, gene-to-gene linkage is indicated by an excess of Parental Ditype over Nonparental Ditype tetrads (Perkins, 1953).

\textit{b. Determining Gene Order.} The method of preference is to use random isolates from 3-point crosses, where gene order is established not from absolute recombination frequencies, but from the relative frequencies of single- and double-crossover classes. Chiasma interference is positive in \textit{Neurospora} (see, e.g., Perkins, 1962a), and this increases the efficiency of determining gene order by reducing double crossovers relative to singles. Because crossing over is so highly variable, map sequences are likely to be incorrect if gene order is determined solely by combining the recombination values of single intervals from different crosses. Many errors have resulted from using 2-point data in this way. Maps with completely reliable sequences can be built up by basing gene order on a series of overlapping 3-point crosses that have intervals in common.

In special situations, gene order can be resolved most easily by testing for duplication-coverage (Perkins et al., 1969). That is, a right–left test is made, using the breakpoint of a chromosome rearrangement as a reference point. Duplication-generating rearrangements such as insertional
translocations are employed. If rearrangements with appropriate breakpoints are available, determining the order of closely linked genes by duplication coverage can be far quicker and easier than by conventional 3-point tests.

Centromere mapping is a special case. Location of the centromere is already known with varying degrees of certainty for each of the seven linkage groups. Historically, the centromere positions were based on critical crossovers in ordered tetrads. Only rarely now does the need arise to determine a gene-centromere sequence, and that occurs when a gene is found to map between the most proximal loci that are reliably positioned in opposite arms. When this occurs, the gene-centromere order can be established in any of three ways—by ordered tetrads, by unordered tetrads, or by random ascospores where an appropriate chromosome rearrangement makes mapping possible by duplication coverage. The use of ordered tetrads has been familiar since Lindegren's work in the 1930s. Unordered tetrads are the usual method of centromere mapping in organisms such as yeast and *Chlamydomonas*, and they might well be used to advantage for this purpose in *Neurospora*, where the presence in a cross of gene markers at two or more known centromeres would enable ejected groups of eight ascospores to be treated as though they had been isolated in order. See Mortimer and Hawthorne (1975) for this and other aspects of mapping with unordered tetrads.

The ability to determine centromere location by duplication-coverage of nearby genes depends upon availability of a duplication-generating rearrangement with one breakpoint near the centromere in question. Since centromere regions seem prone to be involved in rearrangements, a number of such strains are available (Fig. 19). (Combinations of overlapping reciprocal translocations can also be used, where one breakpoint adjoins the centromere.) The method is best illustrated in linkage group I, where the centromere has been shown to lie between the left-arm duplication 39311 and the right-arm duplication *AR173*, hence between *mei-3* (covered by 39311) which must be in the left arm, and *un-2* (covered by *AR173*) which must be in the right arm. This method is far less laborious than isolating and scoring the large number of ordered asci that would be required for conventional mapping.

i. **Appropriate uses of tetrad analysis.** Tetrad analysis have unquestionably played an important role in research on the mechanism of recombination, providing basic information on gene conversion, crossing over, and interference. Fungal tetrads have contributed in an essential way to molecular models of eukaryote recombination. Ascus analysis has also been very useful for distinguishing whether a variant was cytoplasmic or chromosomal, for constructing double-mutant stocks involving mimic genes or suppressors, and for identifying and characterizing chromosome rearrangements.
The most familiar use of ordered tetrads has been to determine gene-centromere distances from second-division segregation frequencies. This was a novel and fascinating feature in the early years of Neurospora genetics, enabling a direct determination of what could be arrived at only indirectly in higher organisms. Consequently, ordered-ascus analysis seems to have become associated with Neurospora as though it were a fundamental cornerstone of all genetic analysis with the organism. (This is the impression given by many textbooks.) Ordered asci have been a mixed blessing, however, because they have often been used unnecessarily where the needed information could have been obtained by a less laborious method, as has been shown for routine mapping. Tetrads analysis is certainly not the best or most economical method for gene-gene mapping, and gene-centromere mapping that would require tetrads is rarely necessary any longer.

ii. **Estimation of interval length.** Recombination frequencies are highly variable in different genetic backgrounds in Neurospora (Section IV, B, 3), and the marker genes used for mapping are of mixed ancestry. Thus there is usually little point to refining the statistical analyses of mapping data, or to applying corrections for undetected multiples, or to enlarging the data beyond a modest level, because the uncontrolled background variability of recombination is so large. The idea of a genetic map of Neurospora with standard interval lengths is illusory.

For organisms or strains in which markers are all in the same background, so that recombination frequencies are more nearly constant, cumulative map lengths would ideally be built up using recombination frequencies in marked intervals short enough to preclude the occurrence of double crossovers (probably 10 or 15 units). In an organism like Neurospora, this would be most economically and reliably accomplished using random isolates in sufficient numbers to minimize statistical error (Fig. 8 of Barratt et al., 1954, can be adapted for this purpose). The eight spores of an ascus yield far less information than eight ascospores isolated at random (Mather and Beale, 1942).

If tetrads data are already available for use, the best estimate of the map length of an interval between two genes is given by the formula \( \text{map distance} = 50 \times (T + 6NPD)/(PD + NPD + T) \), where \( PD, NPD, \) and \( T \) are frequencies of Parental Ditype, Nonparental Ditype, and Tetratype asci (Perkins, 1949). This corrects for undetected 2-strand and 3-strand double exchanges on the basis of 4-strand doubles, which are manifested as Nonparental Ditypes. The validity of this formula across long distances has been shown in experiments where closely spaced intermediate markers enabled all multiple exchanges to be detected between the distant markers to which it was applied (Perkins, 1962a).

C. **LINKAGE GROUP–CHROMOSOME CORRELATIONS**

Chromosomal assignment of particular linkage groups was first attempted by Singleton (1948) and by St. Lawrence (1953), at a time when the genetic maps were still rudimentary and the number of chromosome structural variants was small. Now, 28 years later, assignment of the seven linkage groups to specific chromosomes is for all practical pur-
poses complete. Only a beginning has been made, however, toward locating genes within individual chromosomes. The present status of linkage group–chromosome correlations is shown in Table 4. Linkage groups are designated with Roman numerals, and chromosomes with Arabic numbers.

**General Methodology.** The assignment of linkage groups to chromosomes has depended on chromosome aberrations, which can be recognized and localized both genetically and cytologically. An aberration is mapped genetically to a linkage group (or groups) and the aberrant chromosome

<table>
<thead>
<tr>
<th>Linkage group&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Chromosome association&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Aberration&lt;sup&gt;c&lt;/sup&gt;</th>
<th>References&lt;sup&gt;d&lt;/sup&gt;</th>
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<tr>
<td>I 1</td>
<td>R55, 4637</td>
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<td>St. Lawrence (1953)</td>
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<td></td>
<td>4637</td>
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<td>McClintock (1955)</td>
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<td>Singleton (1948)</td>
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<td>4637, S1007, 17084, H4250</td>
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<td>Barry (1967)</td>
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<td>AR190, S1325, 36703</td>
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<td>Barry and Perkins (1969)</td>
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<td>Barry (1972); Perkins</td>
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<td></td>
<td>NM149, 39311</td>
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<td>E. G. Barry (unpublished; 1972)</td>
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<td>III (3)</td>
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<td>IV (4)</td>
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<td>E. G. Barry (unpublished)</td>
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<tr>
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<td>NM149, AR190, S1325, 36703, sat</td>
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<td>Barry and Perkins (1969)</td>
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<td></td>
<td>46802</td>
<td></td>
<td>E. G. Barry (unpublished)</td>
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<tr>
<td>VI (5)</td>
<td>45502, 46802</td>
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<td>E. G. Barry (unpublished)</td>
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<tr>
<td>VII 7</td>
<td>S1229</td>
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<td>S1007, 17084</td>
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<sup>a</sup> Linkage group numbers (Roman) were assigned in chronological order of discovery (see Barratt et al., 1954).

<sup>b</sup> Chromosome numbers (Arabic) were assigned in descending order of length (McClintock, 1945). Parentheses indicate that the association is probably correct but is subject to some uncertainty.

<sup>c</sup> Or heteromorphic satellite (*sat*).

<sup>d</sup> References are omitted to studies that do not support the assignments made in this table; all contrary findings are discussed in the text, however.
(or chromosomes) is identified cytologically. Two rearrangements are examined cytologically which have one genetic linkage group in common and a second linkage group that is not in common. The chromosome altered in both strains must be the counterpart of the shared linkage group. Examples of this type of analysis will be given below.

Aberrations are also the best means of determining the location of specific genes within a chromosome. This is because rearrangement breakpoints can be placed precisely on linkage maps by genetic analysis (see Section V, A, 3). However, attempts to use rearrangements for intrachromosomal correlations have not been very productive so far. There is often uncertainty in recognizing chromomere patterns of the aberrant chromosomes. Sometimes there may be mispairing in the region of the breakpoints or even "slippage" where the paired regions are nonhomologous. Consequently, only tentative intrachromosomal correlations have been possible using the usual structural rearrangements.

One unambiguous intrachromosomal localization has been made, however, and this employed a heteromorphic chromosome deficient in the small satellite that lies distal to the nucleolus organizer in chromosome 2. The satellite is clearly located at the left end of linkage group V (Barry and Perkins, 1969).

*Steps in Establishing the Linkage Group-Chromosome Correlations.* Singleton (1948) made a brief attempt to associate linkage groups and chromosomes using four chromosome aberrations that had been only partially mapped genetically. He very tentatively suggested that chromosome 2, the nucleolus-organizer chromosome, is linkage group I. In view of his limited observations, it is not surprising that his suggested correlation proved to be wrong.

The first detailed effort to correlate linkage groups with chromosomes was made by St. Lawrence (1953). She concluded from cytogenetic studies that chromosome I is linkage group II, 2 is IV, and 6 is I. (These are not quite right, as will be seen.) St. Lawrence's correlations were based on examination of a complex aberration, R55, which had major rearrangements in three chromosomes (1, 2, 6) for which she located breakpoints in three linkage groups (I, II, IV). Her determination that I was 6 was based on the argument that the R55 breakpoints found in chromosome 6 and linkage group I were both far out in their respective arms, while the breakpoints of chromosomes 1 and 2 and linkage groups II and IV were all near their respective centromeres. Observations on two other translocations supported and extended this conclusion. Her correlation of linkage group IV with chromosome 2 was based on an analysis of T(IV;VI)45502. This translocation is linked in groups IV and VI (Houlahan et al., 1949). B. McClintock (personal communication to St. Lawrence) identified an exchange between chromosome 2 and another, smaller chromosome, possibly 4. Since 45502 and R55 both involved only chromosome 2 and linkage group IV in common (R55 was shown not to be linked to ad-1 in VI), St. Lawrence concluded that linkage group IV equals chromosome 2.

Study of T(U;II)4637 completed St. Lawrence's analysis. This translocation has breakpoints in IR (Houlahan et al., 1949) and IIR (St. Lawrence, 1953; Hagerty, 1952). B. McClintock (personal communication to St. Lawrence) determined that
the translocation was between chromosomes 1 and 6. Since translocations R55 and 4637 both showed involvement of chromosomes 1 and 6 and linkage groups I and II, and since chromosome 6 by other evidence seemed to be linkage group I, St. Lawrence concluded that chromosome 1 should be linkage group II.

Barry (1962, 1967), however, proposed that the St. Lawrence correlations of I = 6 and II = 1 should be reversed with I = 1 and II = 6. This amendment was based on studies of translocations T(I;VII)17084 thi-1 and T(I;VII)S1007 which both involve linkage groups I and VII. Neither translocation has an abnormality of chromosome 6, whereas chromosome VII is involved in both. Also, inversion strain In(II → IK)H4250 involves both group I (Newmeyer and Taylor, 1967) and chromosome 1. Further confirmation that chromosome 1 is linkage group I was found in other studies (Barry and Perkins, 1969; Barry, 1973).

Barry (1960a) proposed that VII = 7. A complex chromosome rearrangement in S1229 is linked in I, II, IV, and VII, and it appeared to involve chromosomes 1, 2, 6, and 7. The involvement of a chromosome (7) and a linkage group (VII), in addition to those detected by St. Lawrence in R55, indicated that VII = 7. Supporting observations were reported by Barry (1967) on T(I;VII)S1007 and T(I;VII)17084 thi-1.

Phillips (1967) examined four translocations that showed interchanges involving chromosome 2. The translocations (36703, R2355, 46502, and C-1670) all involved linkage group V, but only one of them involved IV. He therefore proposed that chromosome 2 corresponds to V rather than to IV. This was confirmed (Barry and Perkins, 1969) by using other translocations and mapping the satellite of chromosome 2 to linkage group V.

The earlier errors can now be explained as follows. St. Lawrence did not test R55 for V linkage, presumably because she had already located a linkage group involvement for each of the chromosomes known to be aberrant. McClintock's determination that translocation 45502 involved chromosome 2 was probably in error because of stock problems. The aberration is separable from a closely linked pyr-3 mutant which was present in the stock with the original aberration, but this may not have been realized at first, and derived stocks with the mutant may have been thought to contain the aberration also. McClintock made several observations of supposed 45502 stocks. In 1945 she reported that the translocation "involved a very unequal exchange of segments of two nonhomologous chromosomes. The breaks appear to have occurred close to the end of the long arm of chromosome 1 and close to the centromere in the long arm of one of the chromosomes with a subterminal centromere, possibly 4." In 1952, McClintock's observations were as described by St. Lawrence (1953). In 1955 she again examined stocks derived from the original 45502, but found no gross structural rearrangements. It now seems probable that different aberration stocks, or suspected aberrations, were examined in the three studies. (It is not unusual for more than one rearrangement to be found in the same strain following mutagenesis, or for a second aberration to occur spontaneously. Examples of both are documented in the Appendix.) Singleton (1948) also examined a 45502 strain and interpreted it as a reciprocal translocation between chromosomes 1 and 6. E. G. Barry (unpublished) has examined available strains of 45502 known genetically to involve IV and VI, and believes them to contain a translocation between chromosomes 4 and 5. Barry's (1960a) initial analysis of S1229, which appeared to support the St. Lawrence correlation of 2 with IV, was rechecked, and the conclusion that 2 = IV was withdrawn (Barry and Perkins, 1969).
This completes the chromosome assignments for four linkage groups—
I, II, V and VII. These are considered to be firmly established.

The remaining three linkage groups, III, IV and VI, are clearly asso-
ciated with the three middle-sized chromosomes, 3, 4, and 5. The tentative
assignments shown in Table 4 are probably correct, although an error
may possibly have occurred because the three chromosomes are similar
in size and appearance, and their chromomere patterns tend to be incon-
sistent. It is doubtful if such an error would ever be of any practical
consequence, because the experimental usefulness of the three is severely
limited because of their similarity. It is proposed to designate the chro-
mosome numbers permanently as shown in Table 4. Number 3 is the chro-
mosome bearing linkage group III, 4 carries IV, and 5 carries VI. If
further refinement of techniques makes morphological distinctions prac-
tical, it is proposed that these numbers be retained, even if the chromo-
some lengths prove to be out of order.

In order for all linkage groups to correspond exactly with chromosome
numbers, three changes would now be required (II, V, and VII). How-
ever, the present linkage group numbers are so firmly established in
general use that we do not propose to make any changes. To do so would
only introduce confusion.

*Basis of the Tentative III, IV, VI Assignments.* From our cytological analysis of
T(IV;VI)45502, one breakpoint is probably near centromere in the long arm of
chromosome 4, and the other is probably near the tip of 5. The resulting exchange
has produced one very long chromosome (most of 5 plus three-fourths of 4), which
is about the length of chromosome 1, and one very short chromosome (the centro-
mere and short arm of 4, and the tip of 5). In the genetic map, the positions of
45502 breakpoints are close to centromere in IVR and far distal in VIR. It can be
concluded that IV = 4 and VI = 5 from the position of genetic and cytological
breakpoints. This conclusion is based on the assumption that cytologically and
genetically determined distances correspond.

If IV = 4 and VI = 5, then chromosome 3 and linkage group III are associated
by default, being the last chromosome and linkage group not otherwise designated.
However, Griffiths, et al. (1974) tentatively proposed a correlation of chromosome
3 with linkage group IV. Their evidence is based on a cytogenetic study of
T(I \(\leftrightarrow\) IV)Y112M15 ad-3, which involves I and IV. They state that in one nucleus
one of the chromosomes involved corresponds cytologically to McClintock's descrip-
tion of 3.

In no other fungus or eukaryotic microorganism has there been a well
established correlation between a linkage group and a specific cyto-
logically recognizable chromosome. However, Mu'Azu (1973) has tenta-
tively suggested four correlations of chromosomes and linkage groups of
*Sordaria brevicollis,* based on cytogenetic analyses of six translocations.
D. Cytoplasmic Genes

Mutant strains of *Neurospora* are known whose differences from wild type are transmitted independently of the nuclear chromosomes, as first shown by Mitchell and Mitchell (1952) and Mitchell *et al.* (1953). The mutants show slow or abnormal growth, abnormal cytochromes, and respiratory defects. No drug-resistant cytoplasmic mutants have been reported. With one exception (Srb, 1963) transmission of the cytoplasmic determinant is strictly maternal, i.e., through the protoperithecial parent. The cytoplasmic factor carried by the paternal (fertilizing) parent is excluded or eliminated. Abnormal cytoplasm has been transmitted by microinjection, using techniques developed by Wilson (1961). The cellular locus of the cytoplasmic genes is probably, but not certainly, the mitochondria (Diakumakos *et al.*, 1965). Measurements of individual molecules by electron microscopy (Agsteribbe *et al.*, 1972) or by reassociation kinetics (Wood and Luck, 1969) show that the mitochondrial DNA of *Neurospora* is long enough to contain at least 50 genes. No evidence has been obtained of recombination between different cytoplasmic determinants.

For a review and critique of cytoplasmic inheritance in *Neurospora* and other fungi, see Sager (1972, Chapter 5).

V. Chromosome Rearrangements

Structural rearrangements occur frequently in *Neurospora*, are readily recognized, and can be used quite effectively. This is fortunate because the possibility of cytogenetic manipulation by means of numerical variants is extremely limited in *Neurospora*, as disomics and diploids are highly unstable and only one useful heteromorph chromosome variant is known. Most cytogenetic experiments must depend therefore on chromosome aberrations.

Each of the 167 rearrangements that have been characterized in *Neurospora crassa* is described in the Appendix. A sizable number of these rearrangements can be used to produce nontandem duplications—aneu- ploids of recombinational origin equivalent to partial diploids. These are valuable research tools, resembling the tertiary or telo-trisosomics of plant cytogenetics in some of their applications.

Appendix Table 1 gives a complete list of the reciprocal translocations, arranged according to linkage groups. All possible combinations of the linkage groups are represented among the 123 interchanges. Two mutual
insertions are also listed. Appendix Table 2 lists the identified duplication-producing rearrangements, 42 in all. These fall into three categories—insertions, quasiterminal rearrangements, and those still uncertain whether interstitial or terminal. The two Appendix tables are intended to serve as indexes, in which a rearrangement having desired specifications can be identified by isolation number. Information on it can then be found in the main part of the Appendix, where the aberrations are all arranged in a single sequence according to isolation numbers, without regard to aberration type. The main Appendix entry summarizes information on each rearrangement, describing its type, map relations, phenotype, fertility, genetic behavior, cytology, and origin. Rearrangements discovered and analyzed by other workers are included. Secondarily derived rearrangements (such as the duplications generated by meiotic recombination from each of the known duplication-generating aberrations) are not listed as separate entries in the Appendix or the Appendix tables.

A. Methods of Identifying and Mapping Rearrangements

1. Detection

Almost all the Neurospora rearrangements were detected initially by noting that defective, white ascospores were produced in crosses heterozygous for the rearrangement, a situation exactly comparable to pollen abortion in flowering plants (Belling, 1914). Pollen abortion that originates from heterozygous rearrangements is termed semi-sterility or partial-sterility in plant cytogenetics. These terms are best avoided in Neurospora because they would be confused with sterility of other types, such as barrenness of perithecia. Only a handful of the known Neurospora rearrangements were discovered because of altered linkage (e.g., T(I;VII) 17084 th-1), and only one translocation was first recognized cytologically, by abnormal meiotic pairing (T(V → VII)EB4).

Standard methods for identifying and analyzing rearrangements have been described by Perkins (1974). The procedure will be summarized here.

About 90 or 95% of ascospores from structurally homozygous crosses are viable and develop normal black pigment. In contrast, heterozygous reciprocal translocations usually produce 50% defective, inviable spores, due to deficiencies, while insertional translocations and other aberration types that generate viable duplications typically produce 25% defective ascospores. The deficiency ascospores remain unpigmented or pale; for simplicity they will be called white. (Point mutants that result in white ascospores are rare in Neurospora, compared to rearrangements.) In
searching for new rearrangements, each strain to be tested is crossed to a normal-sequence tester strain on agar medium in a small (12 × 75 mm) tube. Ten days later, when ascospores have matured and been shot from the perithecia, the glass wall of each tube is examined, and the proportion of black and white spores is estimated. Strains producing less than 90% black spores are saved for further testing.

Putative rearrangement strains are then subjected to a second step of analysis that employs unordered asci, which can be obtained in large numbers by the method of Strickland (1960). Each strain to be tested is crossed on a petri dish to the same normal-sequence tester as before. After 10 days, unordered asci are collected as spontaneously shot groups of eight ascospores on an agar slab under the inverted cross plate. The collecting slab is exposed for a period ranging from a few seconds to several minutes, depending on the rate of shooting, and is then scanned, classifying each well separated group according to number of black and white spores. The major classes are 8:0, 6:2, 4:4, 2:6, 0:8 (Black: White).

2. Diagnosis

Frequencies of the unordered ascus classes in crosses of Normal × Rearrangement immediately enable us to classify most rearrangements into two main categories, according to whether they do or do not generate viable duplication progeny. The frequencies also provide information on the positions of break points relative to centromeres.

Frequencies of the unordered ascus types from structurally homozygous crosses are shown in Fig. 6. In contrast, Fig. 7 shows the frequencies for heterozygous translocations. The top row is typical of translocations that do not produce viable duplications. Two examples are given, with breakpoints far from centromere (A), and close to centromere (B). Examples in the bottom row are typical of duplication-producing translocations whose breakpoints are far from centromere (C) and close to centromere (D).

The ascus frequencies from translocations that do not produce viable duplications are typically symmetrical around 4B:4W, with 8:0 = 0:8. The ascus frequencies from duplication-producing translocations are usually symmetrical around 6B:2W, with 8:0 = 4:4. The occurrence of 6B:2W asci in significant numbers usually indicates that viable duplications are being formed. The meiotic basis for these distributions will be described later for each specific type of rearrangement. Frequencies of unordered tetrad types which correspond to the histograms in Fig. 7 are given as part of the description of each aberration in the main part of the Appendix.
Fig. 6. Results of structurally homozygous crosses, when the parents are both wild types (left), and when they both contain the same reciprocal translocation (right). In this and succeeding figures, histograms show the frequencies of unordered ascii having various members of black (viable) and white (inviable) ascospores. There are five major classes, ranging from all black (leftmost histogram) through 6B:2W, 4B:4W, 2B:6W, to all white (rightmost). N is the observed number of ascii. Rare ascii with odd numbers of defective spores (5:3, 7:1, etc.) are not shown. Reproduced from Perkins (1974).

The rearrangements that do not produce viable duplications are predominantly reciprocal translocations. The rearrangements that are capable of making viable duplications are predominantly insertional and quasiterminal translocations. Other tests in addition to the ascus patterns are required in order to distinguish one type of duplication-producing rearrangement from another.

Advantages and Limitations of Unordered Tetrads for Diagnosing Rearrangements. The examples given in Fig. 7 conform well to theoretical expectations. The arrays of ascus types are distributed symmetrically around the 4B:4W or the 6B:2W class. From such a result it can be confidently inferred that a strain is a rearrangement, and the type of rearrangement can be predicted with reasonable confidence.

Because the contents of unripe ascii are usually not ejected, the problem of distinguishing true 0:8 ascii from unripe ascii of other types is avoided when the analysis is based on unordered ascii that have been shot out of the peritheciun. If a similar analysis is made by opeaining perithecia, unripe as well as ripe ascii are seen and may not readily be distinguished from one another, leading to an excess of ascii in the 0B:8W class.
In some situations, errors of diagnosis may occur when unordered tetrads are used. Nonblack ascospores may result from mutant ascospore-color genes rather than deficiencies. Conversely, lethal deficiencies from some rearrangements do not prevent the ascospores that contain them from becoming black. Ascii of the 0:8 type may be underrepresented because they disintegrate. Most of these exceptions are rarely encountered. The most common departure from ideal expectations occurs when one of the inviable duplication-deficiency classes from a nonterminal reciprocal translocation becomes pigmented. The resulting ascus array, and the patterns of black and white ascospores in individual ascii, misleadingly resemble those of an insertional or quasiterminal translocation. Fifteen of the 123 identified nonterminal reciprocal translocations are clearly of this type (see $T(III;V)AR177$ as an example).

Unordered tetrads are so informative in analyzing aberrations that ordered tetrads are not required even to determine centromere positions. A few special applications
where ordered asci are necessary or useful have been listed by Perkins (1974, p. 485). Anomalies that can lead to misdiagnosis are discussed and examples given by Perkins (1974, pp. 474-477). It is clear that the preliminary diagnosis based on ascus types should be confirmed by other methods.

3. Genetic Verification and Mapping

Following such a preliminary diagnosis based on abortion patterns in the asci, each rearrangement is then verified and analyzed genetically, using appropriately marked tester strains. First the aberration breakpoints are mapped to linkage groups. For this purpose a normal-sequence tester such as multicent is preferable to alcoy, which itself contains translocations (Section IV, B, 4, a). In mapping a rearrangement, segregants are scored for Rearrangement vs. Normal by the incidence of white spores in test crosses. The breakpoint of a translocation is treated as though it were a mutant allele with the phenotype “50% black spores in test cross.” The “allelic” normal sequence has the contrasting phenotype “90% black spores in test cross.”

If few or no ascospores are produced, the test cross is classed as barren. Usually the necks of barren perithecia are rudimentary or absent. It is characteristic of most or all duplications in Neurospora that crosses involving them are barren.

In this way, the rearrangement is confirmed, linkage groups are identified, breakpoints are located, and if duplications are produced they are verified. For details of the identification and verification procedures, see Perkins (1974).

4. Cytological Verification

Genetic analysis has usually been complemented by cytological examination only when a rearrangement is of special interest. Each type of chromosome rearrangement is recognized cytologically by its heterozygous meiotic pairing with standard-sequence chromosomes, or by the production of bridges and acentric fragments. Identification of Neurospora aberrations is very similar to the meiotic analyses developed in maize, with allowances for the smaller chromosome size. Pachynema is the most favorable stage for diagnosing Neurospora aberrations.

5. Simulation of Synthetic Lethal Genes by Rearrangement Breakpoints

The breakpoints in simple (nonterminal) reciprocal translocations and inversions are in fact formally equivalent to synthetic lethal genes (Dobzhansky, 1946) in normal sequence. Most Neurospora rearrangements clearly cannot be attributed to synthetic lethals. Either they are known to generate viable duplications, or they have been confirmed cytologically, or markers show new linkage relations in homozygous aberration sequence. Where none of these tests has been made, there remains a remote possibility that a pair of synthetic lethal genes could be responsible for the properties attributed to a rearrangement. It might be especially difficult to dis-
tistinguish short mutual insertions from synthetic-lethal point-mutants. However, this is no problem for the two Neurospora aberrations believed to be mutual insertional translocations—\( T(I \leftrightarrow V)Str325 \) and \( T(I \leftrightarrow IV)Y112M15 \ ad-3A \). Genetic and cytological evidence shows that they are both chromosome rearrangements.

6. The Need for Quantitative Data on Induced Rearrangements

A committee of the Environmental Mutagenesis Society has listed quantitative studies of chromosome aberrations in microbial eukaryotes among major recommendations for future research: “Cytogenetic tests are now feasible only with the higher eukaryotes. It would be of great significance for determining comparative rates for point versus chromosomal mutation to possess a system capable of detecting chromosomal aberrations in a microbial eukaryote” (Drake, 1975).

Among eukaryotes with small genomes, Neurospora seems the most likely practical source for both types of information. Point mutations can already be measured and characterized very precisely (see, for example, de Serres and Malling, 1971; Malling and de Serres, 1973). If Neurospora is to be considered as a test organism for chromosome aberrations, methods must now be developed for obtaining reliable quantitative measures of new rearrangements. Availability of such methods would also enable rearrangement frequencies to be compared in genotypes suspected of affecting chromosome stability and DNA repair.

The rationale behind the quoted recommendation is as follows: When organisms in a phylogenetic series are examined, their sensitivity to radiation-induced forward mutation per rad per locus is directly proportional to DNA content per haploid genome (Abrahamson et al., 1973). Likewise cellular radiosensitivity is proportional to chromosome volume and nucleotide content (see Sparrow et al., 1967; Underbrink et al., 1968). This correspondence between sensitivity and DNA content allows extrapolations to be made with increased confidence from experimental organisms to man. It is still not known whether a similar relation holds for induced chromosome rearrangements. Such information is needed in order to evaluate whether point mutations or chromosome rearrangements are the more hazardous in relation to environmental mutagens.

B. THE IDENTIFIED REARRANGEMENTS: TYPES, FREQUENCIES, ORIGINS, AND PHENOTYPES

1. Types

The numbers of rearrangements of various types that have been identified are summarized in Table 5. Reciprocal translocations are the most frequent, followed by insertional translocations and quasiterminal (tip) translocations. There are no paracentric inversions and only three pericentric inversions, all of which involve a chromosome tip.

The 167 rearrangements are probably a representative sample of those newly arisen aberrations that result in ascospore abortion. Some bias doubtless exists against aberrations that have very drastic effects on ascospore abortion; these may have been rejected as too complex for analysis. At the other extreme, a bias must exist against aberrations with slight or borderline effects. These may not have been recognized in the
TABLE 5
Identified Rearrangements in *Neurospora crassa*, Summarized
According to Type of Aberration

<table>
<thead>
<tr>
<th>Type</th>
<th>Number*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Rearrangements that do not generate viable duplications by meiotic recombination in crosses by Normal</strong></td>
<td></td>
</tr>
<tr>
<td>Reciprocal translocations</td>
<td>123</td>
</tr>
<tr>
<td>Mutual insertions</td>
<td>2</td>
</tr>
<tr>
<td>Inversions</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>125</strong></td>
</tr>
<tr>
<td></td>
<td><em>(75%)</em></td>
</tr>
<tr>
<td><strong>II. Rearrangements that regularly generate viable duplications by meiotic recombination in crosses by Normal</strong></td>
<td></td>
</tr>
<tr>
<td>Insertional translocations</td>
<td>19(^b)</td>
</tr>
<tr>
<td>Intrachromosomal transpositions</td>
<td>1</td>
</tr>
<tr>
<td>Quasiterminal translocations</td>
<td>12</td>
</tr>
<tr>
<td>Quasiterminal pericentric inversions</td>
<td>3</td>
</tr>
<tr>
<td>Type uncertain</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total rearrangements</strong></td>
<td><strong>42</strong></td>
</tr>
<tr>
<td></td>
<td><em>(25%)</em></td>
</tr>
</tbody>
</table>

* Similar rearrangements from the same experiment, that could have had a common origin, are counted only once. Duplications or other secondarily derived aberrations are not included.

\(^b\) Including some that are complex.

first place, or they may have been abandoned because of scoring difficulties. Short intrachromosomal transpositions with small displacements would not be detected by our methods, nor would short inversions. Tandem or nontandem duplications that arose directly as deviants from wild type would escape detection. Deficiencies would be lethal in a haploid organism unless sheltered, and would not be transmitted. Deficiencies of considerable length have, in fact, been obtained somatically by de Serres (1969) using techniques that allowed them to be rescued in heterokaryotic condition.

The properties of each of the rearrangement types will be described and discussed in separate sections to follow. The basis for recognition and diagnosis of each type will be shown, and a possible explanation will be suggested for the absence of paracentric inversions.

2. Origin and Frequency

The aberrations have come from a variety of sources. Some were encountered as newly arisen variants in routine crosses. Others were recognized as present in various laboratory stocks. A majority were obtained by screening the survivors of experiments primarily designed to recover
point mutants. Most of these experiments involved mild UV-irradiation followed by a procedure to enrich for particular mutant types. Less commonly, X-rays or chemical mutagens were used.

The frequency of recovered rearrangements has not been determined as a function of treatment. It is our impression, based on several UV experiments where both point mutants and rearrangements have been sought, that the frequency of recovery is in the same order of magnitude for new gross rearrangements as for gene mutations. With UV doses giving 10 to 50\% survival of treated conidia, from 5 to 20\% of survivors have been found to contain new gross rearrangements. For representative recovery frequencies see Table 4 in Perkins (1974). Tector and Käfer (1962) have found new rearrangements in a high proportion of Aspergillus nuclei following commonly used radiation dosages.

Neurospora strains have been collected from nature in such a way as to sample local populations from many geographical regions (Perkins et al., 1976). These were examined for structural differences within populations, and only two rearrangements have been found and confirmed. Both of them were reciprocal translocations, recovered as single isolates.

3. Fertility and Vegetative Phenotype

A vast majority of the 167 rearrangements are homozygous fertile and have no obvious mutant phenotype. In Aspergillus also, most balanced rearrangements are morphologically wild type (Käfer, 1965; Ngà, 1968).

Eight of the rearrangements are barren in crosses where the rearrangement is homozygous—i.e., perithecia are formed that produce no ascospores, or few. Ascospore production is somewhat reduced in an additional five cases when rearrangement sequence is homozygous. Fourteen rearrangements have not been tested as homozygotes because of female-sterility (nine) or for lack of a recombinant with mating type (five).

Twelve rearrangements acquired at their origin a mutant phenotype that is allelic with a known gene locus and inseparable by recombination from the arrangement: HK53 cut, K79 me-7, Y112M4i ad-3B, Y112M15 ad-3A, C161 aro, TM429 his-3, S1325 nic-2, C-1670 pk-1 (bis), 4540 nic-2, 4637 al-1, 17084 thi-1, and 46702 inl. Several other rearrangements are inseparable from a mutant phenotype that is not known to be allelic with a previously recognized gene locus—NM139 bs, S1229 arg, and T51M156 un are examples. To this list should be added 17 other rearrangements classified as morphologically mutant and nine as near-wild. These have not been tested for allelism with known morphological mutants. They include eight of the nine female-sterile rearrangements.

At least 18 rearrangements arose simultaneously with a linked but separable point mutation: T54M94 (un-18), NM136 (arg-3), NM160 (phe-1), AR174 (per), NM177 (mo), AR216 (al-1 or -2), AR221 (ilv),
Y234M419 (ad-1), D304 (morph), A420 (trp-5), H4250 (arg-1), S4342 (pt), 5936 (leu-3), Y16329 (phe-2), 36703 (arg-1), 39311 (suc), 45502 (pyr-3), 47711 (ilv). Also, five examples are known where two linked but separable rearrangements appear to have arisen simultaneously: T54M140b originated with another still unanalyzed rearrangement, Y112M4i originated with Y112M4r, AR180b with AR180r, B362ı with B362r, and STL384b with STL384r.

4. Position Effect

No observations in Neurospora suggest a variegated-type position effect, but the growth habit might make a variegated phenotype difficult to detect. Rearrangements that originated simultaneously with mutant phenotypes have either been separable by recombination, or can be explained in terms of a breakpoint within a gene or within a single transcriptional unit. Several closely linked genes are simultaneously inactivated in T(II;III)C161 aro (Gross and Fein, 1960). However, this is the result expected of a breakpoint within a cluster of genes that are coordinately transcribed (see Section IV, B, 2, b). All three functions specified by his-3 are missing in T(I;VII)TM429 his-3, which has one break in the locus and no detectable deletion (Catchridge and Angel, 1974).

Position effects might be anticipated when closely linked genes with coordinate functions are separated from each other by rearrangement. al-1 is separated from al-2 by Tp(IR → IR)T54M94 and arg-2 is separated from pyr-3 in two translocations, S1229 and S4342. The relevant phenotypes are not noticeably altered in any of the three rearrangements, however.

A translocation in Aspergillus (VIII → III) is characterized by a variegated morphological phenotype which is allelic with a known gene located at or near one of the breakpoints (Clutterbuck, 1970). Evidence suggests but does not prove that the wild-type allele can be recovered from the rearrangement by crossing over; if so, it would be the first example of a variegated-type position effect in fungi.

C. REARRANGEMENTS THAT DO NOT MAKE VIABLE DUPLICATIONS

Within this category, no duplication progeny survive from crosses of Rearrangement × Normal, because whenever aneuploid segregants are duplicated for one chromosome segment they are deficient for another. Most of the Neurospora rearrangements that behave in this way are reciprocal translocations. Two are probably mutual insertions. Inversions behaving in this way would also be expected, but none has been found.
1. Reciprocal Translocations

Simple reciprocal translocations are the most readily identified and the most commonly occurring rearrangements in *Neurospora* (Table 5). Appendix Table 1 lists the 123 mapped reciprocals according to linkage groups, and they are described individually in the Appendix.

a. Ascus Effects and Their Meiotic Basis. Unordered asci from crosses heterozygous for typical reciprocal translocations show a distinctive distribution of the frequencies of ascus types (Fig. 7A, B). The meiotic origin of these ascus types is shown in Fig. 8. Normal disjunction of the centromeres of the two chromosomes involved in an interchange should produce 8:0 and 0:8 asci with equal frequencies when there is no crossing over in the interstitial centromere-breakpoint intervals (top half of Fig. 8). Occurrence of interstitial crossing over is expected to result in 4:4 asci (bottom half). 4:4 asci will thus be rare if interchange points are both close to their respective centromeres, but frequent if one or both interchange points are far out in a chromosome arm. The breakpoints of many translocations have been mapped genetically, and they conform generally to these expectations. The examples in Fig. 7 were selected to show the two extremes—*T*(I;V)36703, with breakpoints far out from centromere, and *T*(I;IV)NM137, with breakpoints close in to centromere. For additional examples showing intermediate amounts of interstitial crossing over, see Fig. 3 in Perkins (1974).

b. Cytology of Reciprocal Translocations. Pachynema is by far the most reliable and informative stage for verifying and diagnosing interchanges. Completely paired heterozygotes show a typical cross-shaped arrangement of the four bivalent arms (for photographs, see Barry, 1967, Figs. 2, 5, 7; Barry and Perkins, 1969, Fig. 1; Fincham and Day, 1971, Fig. 26). Pachytene associations have been used to confirm the genetic analysis of numerous translocations and to relate linkage groups to specific chromosomes (Section IV, C).

In theory, the contracted stages following pachynema should be useful for verifying and diagnosing interchanges, which should appear as rings or chains of four chromosomes. In practice in *Neurospora*, however, diakinesis and metaphase I are very limited in their usefulness. The chromosomes are so small that recognition of a quadrivalent may be uncertain, and overlying bivalents can easily be mistaken for an interchange complex (see, for example, Fig. 4 in Barry, 1967). In spite of these difficulties, contracted stages have been used successfully to study interchanges that involve the easily recognized nucleolus organizer chromosome (Section IV, A, 4, c).

McClintock and Singleton (Singleton, 1948) attempted to analyze
Fig. 8. The origin and constitution of asci containing various numbers of deficient spores, from crosses of Reciprocal Translocation (black centromeres) × Normal (white centromeres). Segments originally in one of the Normal chromosomes are shown as solid lines, those in the other Normal chromosome as dotted lines. The consequences of segregation without crossing over are shown in the two top diagrams. Crossing over between either breakpoint and centromere is expected to produce 4:4 asci, as shown in the bottom two diagrams. Other linear orders of black and white spore-pairs are possible, depending on which chromatids were involved in crossing over; the resulting unordered tetrad is classed as 4:4 regardless of its original order. The defective spores are of two types, representing complementary duplication-deficiency classes. These may or may not be recognizably different, depending on the particular translocation. If adjacent-2 segregations occurred (where homologous centromeres failed to disjoin), 0:8 asci would result, with all spores deficient (not shown in the figure). Reproduced from Perkins (1974).

Translocations by determining changes in chromosome lengths and arm ratios at metaphase of the third division in the ascus. In our experience this stage is of doubtful practical value because of small chromosome
size and possible inaccuracies of measurement if a chromosome is tilted in the polar plane.

c. Some Research Applications of Reciprocal Translocations

i. Mapping genes to linkage group. The efficiency of assigning unmapped point mutants has been greatly increased by a tester strain (acronym alcoy) containing three independent translocations tagged by markers which can be scored visually (Section IV, B, 4, a). A majority of new point mutants readily show linkage to one of the markers, and linkage group assignment is then completed with a single follow-up cross (Perkins et al., 1969; Perkins, 1972b).

ii. Production of duplications. Intercrosses between translocations that involve the same arms of the same two linkage groups can produce viable duplications (Section V, D, 3). Such duplications can be used for mapping centromeres (Section IV, B, 4, b).

iii. Balancer stocks. Because suitable inversions are not available, there are no balancers in Neurospora similar to ClB, BasC, and FM1 of Drosophila, which would prevent crossover products from surviving and therefore enable specific chromosomes to be transmitted as intact units. However, Burnham (1968) has devised another method for constructing balancer stocks by combining translocations that involve opposite arms of the same two chromosomes. These eliminate crossovers in either of the interstitial regions. Two-chromosome double-interchange stocks of this type are being constructed in both maize and Neurospora (Kowles, 1972, 1973). Attempts are also being made to create stocks of maize and Neurospora that would involve several or all the chromosomes in a single Oenothera-like multiple-interchange complex (Burnham, 1946, 1973; Phillips and Magill, 1969).

iv. Interference. 4B:4W asci from reciprocal translocations are equivalent to tetratype segregations for two unlinked genes. When there is no chiasma interference between interstitial exchanges, the upper limit for 4B:4W frequencies is two-thirds. Higher values would require that chiasma interference be positive. The highest observed frequencies in Neurospora are 67 or 68%, for translocations AR92, NM163, and 36703. Interference is known to be positive from other criteria, and eventually translocations should be found where 4:4 asci exceed two-thirds.

v. Centromere behavior and disjunction

(a) Alternate and adjacent segregation. Measures of alternate versus adjacent segregation of centromeres in translocation heterozygotes are of interest because of the possibility of genetic control of centromere disjunction, as in Oenothera. Information can be obtained from unordered asci in two ways, comparing 8B:0W with 0:8 asci, and comparing crossovers with noncrossovers among 4B:4W asci.

8:0 and 0:8 asci. With no interstitial crossing over, 8B:0W asci result when alternate centromeres go to the same pole at anaphase I. 0B:8W's result when adjacent centromeres go together. This could happen in either of two ways, with homologous centromeres disjoining (called adjacent-1) or failing to disjoin (called adjacent-2) (Fig. 8 shows the first two types, but does not show adjacent-2). Adjacent-2 segregation is found in maize when interchange points are close to the centromeres, but not when they are far enough out for interstitial crossing over to occur regularly (Burnham, 1949, 1950). Apparently adjacent-2 occurs in either situation in the mouse (Searle et al., 1971).
McClintock (1945) opened perithecia and observed four ascus classes from *Neurospora* translocation $T(IV;VI) 45502$, including one class with eight tiny, degenerate spores. These she attributed to adjacent-2 segregation. They may well have been bubble asci instead, as described in Section III, C, 4.

With most *Neurospora* translocations, the frequencies of 8:0 and 0:8 ascis are about the same. This 1:1 ratio is consistent with either of two hypotheses: (1) alternate equals adjacent-1, with no adjacent-2 segregation occurring; or (2) alternate segregations equal the sum of adjacent-1 plus adjacent-2. Endrizzi (1974) has shown cytologically that the second is true for two translocations in cotton, and that there are actually two subtypes, alternate-1 and alternate-2, corresponding to the two adjacent types.

4:4 ascis. A different population of meioses is represented by the 4B:4W's. These result from interstitial crossing over (Fig. 8, bottom half). Among the 4:4 ascis, only parental combinations of markers survive following alternate segregation, and only crossover combinations survive following adjacent-1 segregation. Adjacent-2 segregation results in 0:8's, and cannot produce 4:4 ascis, even if crossing over has occurred interstitially.

If *Neurospora* resembles cotton in having two equally frequent types of alternate segregation, and if $alt-1 + alt-2 = adj-1 + adj-2$, then an excess of the 4:4 class having parental marker combinations might be observed. The magnitude of the excess would depend on the frequencies of type-1 and type-2. If $alt-1 = alt-2 = adj-1 = adj-2$, the expected ratio would be 2:1 for parental:recombinant 4:4 ascis. Such an observation would be inconsistent with the traditional view that $alt = adj-1$, for which the predicted ratio of parental:recombinant 4:4 ascis is 1:1.

(b) 3:1 segregation. Sometimes three chromosomes of an interchange complex are included in one daughter nucleus, and only one is included in the other nucleus. The disomics arising from translocations in this way, by 3:1 segregation, are called tertiary disomics. They resemble normal-sequence (primary) disomics in their instability (Section II). A few aneuploid progeny are commonly found in crosses of Translocation × Normal in *Neurospora*. These have been attributed to occasional 3:1 segregations. With some translocations, 3:1 segregations are apparently frequent. Actual frequencies are difficult to determine accurately because the extra chromosome is so rapidly lost, producing balanced fertile haploid nuclei that cannot be distinguished from one or the other parental type when they are test crossed.

Disomics that originate from 3:1 segregation can be recognized, however, by the presence of translocation-linked markers in heterozygous or heterokaryotic condition. In this respect they resemble the segmental duplications from duplication-generating rearrangements such as insertional translocations, to be discussed in sections that follow. Indeed, conventional reciprocal translocations can at first be mistaken for insertional or quasiterminal translocations if 3:1 segregations occur in significant numbers. Examples where some confusion has existed can be found in the Appendix (see translocations T51M158, T54M140b, NM129, AL876, D305).

The following criteria may be useful in distinguishing tertiary disomics from segmental duplications: (a) Heterozygosity is not limited to a single region in the products of 3:1 segregation, as it is in the segmental duplications from insertional or quasiterminal translocations. Markers anywhere in the two interchanged chromosomes may be heterozygous in one or another disomic progeny. (b) There is no a priori expectation for a fixed frequency of aneuploids from 3:1's, as there is from insertional or quasiterminal translocations, where one-third of viable progeny are segmental duplications. With 3:1's, the frequency of disomy for markers in a given
segment is usually well below one-third. (e) Disomics are somatically less stable than all or most segmental duplications. (d) Most aneuploids from 3:1 segregation are not barren in backcrosses. (Occasionally an exception is aneuploid is barren and highly stable in a cross known to undergo 3:1 segregation. This might result if different chromosomes were lost in separate nuclei of the disomic, and the two nuclei, each with a deficiency but complemented by the other, then displaced the original disomic type to form a stable balanced heterokaryon.)

3:1 segregation in other organisms. Disomics in Aspergillus nidulans are relatively stable and can be recognized by characteristic morphologies (Käfer and Upshall, 1973). Single heterozygous translocations increase the frequency of disomics 50- to 100-fold for the two chromosomes involved (Upshall and Käfer, 1974). A comparable increase may well occur in Neurospora. Trisomics from interchange heterozygotes are well known in plants (see Burnham, 1962). They have been put to practical use in agriculture (Wiebe and Ramage, 1971). Over 50 cases of 47- or 45-chromosome offspring have been reported in man, that apparently originated by 3:1 segregation from translocation heterozygotes (Lindenbaum and Bobrow, 1975).

2. Mutual Insertions

Two Neurospora rearrangements appear to be of this type—\( T(I \Leftrightarrow V)S1325 \) nic-2 and \( T(I \Leftrightarrow IV)Y112M15 \) ad-3A. Both are inverted insertional translocations that differ from typical insertionals in producing no viable duplication progeny. With both rearrangements, the long inserted IR segments should be viable as duplications, because even longer IR duplications are known to be viable, that include the same intervals. Absence of duplications could be explained in both rearrangements if an unmarked, short interstitial segment of \( V \) (or IV, respectively) had been inserted into I, simultaneously with excision of the long I segment and its insertion into V (or IV). This explanation is inferential and is unproved for both strains, although observations on chromosome pairing at pachynema suggest the presence in \( S1325 \) of a short \( V \rightarrow I \) insertion (see Appendix for details and references). It should be noted that these strains resemble paracentric inversions in many respects, and both were diagnosed as inversions before a second linkage group was known to be involved.

3. Inversions

a. Paracentric Inversions. There are no paracentric inversions among the 167 rearrangements that have been identified in Neurospora, nor are there any reliably established cases in other fungi. In a critique of all published reports of supposed inversions in Neurospora and other fungi, it was concluded that the evidence either favors another type of rearrangement, or is inadequate to prove unequivocally that a paracentric is actually involved (Perkins, 1974).

A possible rationale has been offered for the failure to find paracentric
inversions (Perkins, 1974). It is suggested that dicentric bridges abort the entire ascus in which they occur. This would prevent the detection of paracentricies by the spore-pattern method, because they would have no or little visible effect on the appearance of surviving asci.

Evidence supporting this explanation comes from the study of inverted insertional translocations. These are detected by the spore-pattern method, despite the loss of asci with dicentric bridges, because they also produce white spores by centromere segregation without crossing over. There is both genetic and cytological evidence from inverted insertionals suggesting that bridge formation usually results in loss of the entire ascus [Section V, D, 1, a, (iii)]. If so, cryptic paracentric inversions may in fact be present in apparently normal Neurospora strains where their presence is unsuspected.

Some parallels are suggested by the behavior of paracentric inversions in the mouse. Although numerous translocations had been identified, no inversions were known in mice until they were deliberately sought by looking for bridges at anaphase I of meiosis (Roderick, 1971; Roderick and Hawes, 1974). Fertility is not reduced in either male or female mice by heterozygous paracentric inversions, suggesting, as one hypothesis, that genetically unbalanced gametes are eliminated because of bridge formation.

A cytological approach may now be the most feasible way to identify a paracentric inversion in Neurospora, since other methods have failed. A paracentric inversion should be distinguishable from an inverted insertional translocation because dicentric bridges that resulted from crossing over in the paracentric inversion would be mostly limited to the first division, whereas bridges from inverted insertional translocations occur regularly also at the 2nd, 3rd, and 4th divisions [described in Section V, D, 1, a, (iii)]. A possible complication would result if a breakage-fusion-bridge cycle was initiated in the paracentric inversion by breakage of the anaphase-I bridge. This could result in bridges at the 3rd and 4th divisions, but not at the 2nd division.

A second possible complication is an unexplained background of “spontaneous” anaphase-II bridges in some Neurospora crosses thought not to contain an aberration of any type, as well as in crosses with aberrations which should not make bridges. In standard wild-type crosses, telophase-II bridges may be found in as many as 10% of the divisions. No acentric fragments accompany this bridge formation. If the asci containing them survive, such bridges might account for some part of the 5–10% of white spores found in wild-type crosses.

b. Pericentric Inversions. We have not succeeded in identifying a single nonterminal pericentric inversion. There is no obvious reason for
this failure. The rationale for failing to find paracentric inversions does not apply to pericentrics, because no diecentric bridges are produced when the centromere is located inside the inversion. Heterozygous pericentric inversions would be expected to produce complementarily duplication-deficiency products by crossing over, and should thus be recognizable visually by inspection of ascospores or asci. Single-crossover asci should be 4B:4W. The frequency of aborted spores would depend on length of the inversion, effectiveness of pairing, and frequency of crossing over.

It is known that inversions can occur and survive in Neurospora. Three pericentric inversions have in fact been found and mapped, all of them quasiterminal—In(IL → IR)H4250, In(IL → IR)NM176, and In(IL → IR)AR16. (Because one breakpoint is at a chromosome tip, each of these produces viable duplications by meiotic crossing over. They will therefore be described in Section V, D, 2, b.) It can be calculated from the behavior of these long-terminal pericentrics that a nonterminal pericentric inversion only half their length should still produce enough white ascospores to be readily detected as an aberration.

D. REARRANGEMENTS THAT GENERATE Viable NONTANDEM DUPLICATIONS VIA MEIOTIC RECOMBINATION

About one-fourth of the rearrangements known in Neurospora fall under this heading (Table 5). The 42 that have been mapped are listed in Appendix Table 2 and are described individually in the Appendix.

Nontandem duplications are regularly produced by meiotic recombination in three types of crosses, each with two subtypes according to whether two chromosomes are involved, or a single chromosome:

Type 1: Normal × Insertional rearrangement (Fig. 9), with subtype (a), insertional translocations, and subtype (b), transpositions within one chromosome.

Type 2: Normal × Quasiterminal rearrangement (Fig. 10), with subtype (a), quasiterminal reciprocal translocations, and subtype (b), quasiterminal pericentric inversions.

Type 3: Rearrangement × Partially overlapping rearrangement (Fig. 11), with subtype (a), partially overlapping reciprocal translocations, and subtype (b), partially overlapping inversions.

Duplication progeny from crosses of the first and third type are pure, in the sense that nothing is missing. Duplication progeny from crosses of the second type are presumably deficient for one chromosome tip; in order for them to survive, that tip must contain no essential gene. With translocations (subtypes a), duplication progeny result from independent segregation and ideally constitute one-third of the surviving progeny.
a. Insertional translocations between chromosomes

Origin:

(normal sequence)  
\[
\begin{array}{c}
1 \ 2 \ 3 \\
\end{array}
\]

\[\rightarrow\]

(insertional)  
\[
\begin{array}{c}
\quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

(or 3 2 1)

Meiotic pairing, normal x translocation:

\[
\begin{array}{c}
1 \ 2 \ 3 \\
\quad \quad \quad \quad \\
\quad \quad \quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

\[\rightarrow\]

\[
\begin{array}{c}
1 \ 2 \ 3 \\
\quad \quad \quad \quad \\
\quad \quad \quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

segregation
can
give

b. Transpositions within one chromosome

Origin:

(normal sequence)  
\[
\begin{array}{c}
1 \ 2 \ 3 \\
\end{array}
\]

\[\rightarrow\]

(transposed)  
\[
\begin{array}{c}
1 \ 2 \ 3 \\
\quad \quad \quad \quad \\
\quad \quad \quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

(or 3 2 1)

Meiotic pairing, normal x transposed:

\[
\begin{array}{c}
1 \ 2 \ 3 \\
\quad \quad \quad \quad \\
\quad \quad \quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

\[\rightarrow\]

\[
\begin{array}{c}
1 \ 2 \ 3 \\
\quad \quad \quad \quad \\
\quad \quad \quad \quad \\
1 \ 2 \ 3 \\
\end{array}
\]

crossing over
can
give

Fig. 9. The origin of duplication progeny from crosses involving insertional rearrangements. a. Above: Genesis of an insertional translocation by rearrangement of the normal sequence. Below: Meiotic production of a duplication by independent segregation in Insertional Translocation \(\times\) Normal. b. Above: Genesis of an intrachromosomal transposition by rearrangement of the normal sequence. Below: Meiotic production of a duplication by crossing over in Transposition \(\times\) Normal.
a. Tip-nontip reciprocal translocations

Origin:

Meiotic pairing, normal x translocation:

b. Tip-nontip pericentric inversions

Origin:

Meiotic pairing, inversion x normal:

crossing over can give

Fig. 10. The origin of duplication progeny from crosses involving quasiterminal rearrangements. a. Above: Genesis of a quasiterminal reciprocal translocation by rearrangement of the normal sequence. Below: Meiotic production of a duplication by independent segregation in Translocation x Normal. b. Above: Genesis of a quasiterminal pericentric inversion by rearrangement of the normal sequence. Below: Meiotic production of a duplication by crossing over in Inversion x Normal.
Fig. 11. The origin of duplication progeny from intercrosses between overlapping rearrangements having breakpoints suitably placed in the same two chromosome arms. a. Above: Genesis of two partially overlapping reciprocal translocations, by two independently occurring rearrangements of the normal sequence. Below: Meiotic production of a compound duplication by independent segregation in the intercross. b. Above: Genesis of partially overlapping inversions, by two independently occurring rearrangements of the wild type. (The inversions could both be paracentric and in the same arm.) Below: Meiotic production of a compound duplication by crossing over in the intercross.
With intrachromosomal transpositions or inversions (subtypes $b$), duplication progeny result from crossing over, and their frequency depends upon the distance between breakpoints.

All these types and subtypes have been observed in *Neurospora*, and they will be considered in sequence below. It is characteristic of them all to produce unordered asci of the $6B:2W$ type, which is diagnostic of duplication-producing rearrangements.

In symbols for rearrangements that produce viable duplication progeny, an arrow is placed between the two linkage groups (or arms). The linkage group (or arm) preceding the arrow is the source (donor) of the duplicated segment. For example, in the insertional translocation $T(I \rightarrow II)39311$, a segment of $I$ has been inserted into $II$, and duplication progeny will possess the group-$I$ segment in two doses. Duplications from a particular rearrangement always contain the same loci.

1. Insertions

   a. Insertional Translocations. At least 20 insertional translocations have been identified. The properties of one insertional, $T(I \rightarrow II)39311$, have been studied in especial detail, both genetically and cytologically (Perkins, 1972a; Barry, 1972).

   i. Ascus effects and their meiotic basis. Frequencies of the ascus types characteristic of insertions are shown in Fig. 7C and D. Additional examples can be found in Fig. 5 of Perkins (1974). The meiotic basis for these proportions is shown in Fig. 12. When there is no crossing over, normal centromere disjunction results in $8:0$ and $4:4$ asci with equal probability (top half). Asci of the $6:2$ type are produced by interstitial crossing over. They will be rare if the proximal breakpoints are both close to their respective centromeres, and frequent if one or both of the interstitial regions are long. The breakpoints of the examples in Fig. 7C,D have been mapped genetically and their locations are consistent with the frequencies of $6:2$ asci.

   The translocated inserted segment and its homolog are shown as unpaired loops in Figs. 9, 12, and 13. Alternatively, they might pair with each other, with consequences described below.

   ii. Cytology at prophase I. (a) Insertion not paired. The situation is simplest at pachynema when pairing does not occur between the translocated segment and its normal homologous segment. The deleted or the inserted segment bulges or loops out as a univalent strand from a bivalent with paired ends (just as diagrammed in Figs. 9 or 12). Figure 13 shows the appearance of one such loop (see also photographs in Barry, 1972). This loop-pairing pattern is frequently seen when short insertional translocations are examined, and it can be used to identify the specific chromo-
Fig. 12. The origin and constitution of asci containing various numbers of deficient spores from crosses of an Insertional Translocation (black centromeres) × Normal (white centromeres.) The consequences of segregation without crossing over are shown in the two top diagrams. Crossing over between either breakpoint and centromere is expected to produce 6:2 asci, as shown in the bottom two diagrams. The order of black and white spore-pairs is not necessarily as shown. The defective spores are all identical, containing the same deficiency and no duplication. Pairing and crossing over between the translocated segment and its normal homolog are not shown in the diagram. Reproduced from Perkins (1974).

somes involved in the exchange when the chromosome lengths are measurable and the chromomere patterns are clear.

(b) Insertion paired. The situation at pachynema is more complex when the interstitial translocated segment pairs with its normal homolog.
Complexes of four chromosomes are seen sometimes during prophase and at metaphase I. The looped part of the complex at pachynema should distinguish an insertional translocation from a reciprocal translocation and indicate the position and size of the translocated segment. Long insertions are known from both genetic and cytological evidence usually to be paired. Yet such paired chromosome complexes are rarely clear and interpretable cytologically. The paired loops are difficult to trace through three-dimensional angles with their abrupt changes in pairing partner at the break points, just as is true for inversions (Section V, D, 3, b). Insertional translocations have the further complication that a second chromosome pair is involved.

iii. Effects of crossing over in the inserted segment. When the translocated insertion pairs with its normal homolog, the genetic and cytological consequences of crossing over are critically different, depending on whether the translocated segment is inverted or noninverted with respect to its new centromere. (These orientations have been called dyscentric and eucentric. The simple terms inverted and noninverted will be used in this sense.)

When crossing over occurs between the inserted segment and its normal homolog, dicentric bridges and fragments are produced if the insertion is inverted, but not if it is in its original orientation. Diagnosis of an insertion as inverted can thus be accomplished cytologically, by noting a heightened frequency of bridges and fragments. This is straightforward
with long insertionals, but a reliable cytological determination is difficult when the insertion is short, because the background frequency of bridges and fragments is high, even in control crosses that are supposed to be structurally homozygous, and this makes any small increase difficult to recognize. It is more difficult to be certain that an insertion is not inverted, because failure to detect increased bridge formation could be due to short genetic length or to absence of pairing rather than to a noninverted orientation. Orientation can be determined genetically in $T \times T$ crosses if two gene markers are present within the insertion (see Perkins, 1972a, for an example). Introducing markers by crossing over is practical only with long insertions, however.

Despite these difficulties, at least five of the 20 insertionals listed in Appendix Table 2 have been diagnosed as inverted. Not all the rest have been examined cytologically. Among those that have, a low frequency of bridges and fragments suggests that some are noninverted, but there is no positive evidence.

_Crossing over in noninverted insertions._ With noninverted insertions, crossing over could result in viable duplications having chromosome segments interchanged that were distal to the insertion—a new rearrangement would result having the properties of both a duplication and a reciprocal translocation. Patau (1963) and Lejeune and Berger (1965) have pointed out how crossing over of this type could account for otherwise unexplained cases of human anomalies attributed to aneuploidy. Study of such crossover-duplications in _Neurospora_ must await positive identification of a suitable long uninverted insertional.

D. Newmeyer (unpublished) has calculated that single exchanges within a paired noninverted insertion should produce only 4B:4W and 0:8 asci in a ratio of 3:1. Thus, ascus frequencies for a long insertional of this type might be quite different from those shown in Fig. 7C. Only one-third of the 4:4 asci from this source would contain viable Duplications, in contrast to 4:4’s from unpaired insertionals, which theoretically consist entirely of Duplications.

_Crossing over in inverted insertions: Dicentric bridges._ With inverted insertional translocations, crossing over between the inverted inserted segment and its normally placed homolog produces dicentric anaphase bridges and acentric fragments (S1325 and 39311 are examples). This resembles the behavior of paraacentric inversions, but with one important difference. Single crossovers in a heterozygous paraacentric inversion should result in bridges at anaphase I, except that where a second exchange of 3-strand type occurred proximal to the inversion bridge formation would be deferred to anaphase II. In contrast, with an inverted insertional translocation as many as 50% of the bridges resulting from
single crossovers may occur at anaphase II or later divisions in the ascus. This is a result of perfectly normal chromosome segregation and is expected if there is an equal probability that nonhomologous centromeres joined by a chromatid tie will go either to opposite poles (bridge) or to the same pole (no bridge) at each division (Fig. 14). (After the second division, twisting of homologs around one another would nullify this expectation, but there is little relational coiling of chromosomes in Neurospora.) Bridges are in fact observed frequently in the second and later ascus divisions with $T(I \rightarrow II)39311$ (Barry, 1972) and with other inverted insertional translocations.

It is unnecessary to invoke breakage–fusion–bridge cycles to explain this behavior, which is expected as a simple consequence if centromeres

![Diagram](image)

**Fig. 14.** Pairing of an inverted inserted segment with its normal homolog, followed by crossing over and segregation such as to result in a dicentric chromatid and an acentric fragment. Because centromeres shown solid are not homologous with centromeres shown open, the joined centromeres may segregate to the same (lower left) or to opposite (lower right) poles with equal probability at anaphase I. In the former case the dicentric does not form a bridge, but may do so at a later division.
joined by the chromatid tie fail to disjoin at anaphase I but do so later. However, if a breakage–fusion–bridge cycle does occur in *Neurospora*, then the bridges observed at mitotic divisions in the ascus could be a consequence either of the cycle, or of the earlier formed but previously unbridged dicentric.

*The fate of asci with dicentric bridges.* There is evidence suggesting that bridge formation usually results in loss of the entire ascus in which it occurs. In crosses with the long inverted insertional $T(I \rightarrow II)39311$, many asci contain anaphase-I bridges, and these asci should contain four black and four white spores if they survived. But no excess asci of the 4:4 type were found above those expected from other causes (Perkins, 1972a). Consistent with this, the number of asci observed to contain bridges and fragments in the later divisions is less than expected from the frequency of anaphase-I bridges, suggesting differential ascus mortality (E. G. Barry, unpublished).

*Acentric fragments.* Inverted insertional translocations produce a fragment only at the first division, though it may not appear in the cytoplasm until the second division. The locus content of the fragment is constant and unique for each translocation. It comprises the inserted segment plus both distal segments, including the chromosome tips. The fragment from a specific rearrangement may possess a strikingly distinctive morphology, which is cytologically recognizable (J. R. Singleton, unpublished observations of translocation $S1325$).

With $T(I \rightarrow V)S1325$, the acentric fragments were seen not to be degraded, but to persist in the cytoplasm in a micronucleus (J. R. Singleton, unpublished). Fragments from $T(I \rightarrow V)S1325$, $T(I \rightarrow II)39311$, and some other insertionals replicate and divide synchronously with the centric chromosomes of the regular nuclei of the ascus (Barry, 1972, 1973). Four micronuclei containing identical acentric fragments may thus be present in a single ascus following the fourth division, when two mitotic cycles have been completed. This is best documented for $T(I \rightarrow II)39311$. Fragments from some other insertionals do not persist and replicate, but become pycnotic.

*b. Intrachromosomal Transpositions.* One transposition has been identified in *Neurospora*, $Tp(IR \rightarrow IR)T54M94$. Viable duplications from Transposition $\times$ Normal have flanking markers always recombined in the direction that would be expected of an inverted insertion (B. C. Turner, personal communication). (A noninverted transposition could pair so as to form a double loop and give rise to duplications of two types, in the second of which the interstitial segment is duplicated and the flanking markers are in the complementary coupling phase.) See the Appendix for further details on $T(IR \rightarrow IR)T54M94$. 
c. Research Applications of Insertional Rearrangements

i. Production of duplications. Insertional translocations have been an important source of nontandem duplications for experimental use (Section V, E).

ii. Simulation of paracentric inversions. In the absence of any identified paracentric in Neurospora, inverted insertions provide an alternative opportunity for obtaining acentric fragments and dicentric bridges, and for reversing polarity. We are attempting to find out what portion of the genome is responsible for the difference between acentric fragments that survive and replicate, and those that cannot, and to determine whether viable acentric fragments can be transmitted through the cytoplasm. Inverted insertions might be used to see whether a breakage-fusion-bridge cycle (McClintock, 1938, 1939) can be initiated in Neurospora following anaphase rupture of a dicentric chromosome, and if so, whether broken ends are capable of healing. Inverted insertions might also serve as a source of tandem reverse-repeats (Wallace and Kass, 1974) and possibly of controlling elements (McClintock, 1950, 1951).

iii. Polarity in recombination. An inverted insertion, S1825, was used by Murray (1968a) to demonstrate that polarity in intragenic recombination is an intrinsic property of the marked chromosome segment and does not depend on orientation of the segment with respect to the centromere.

iv. Chromosome twisting and deferred bridging. The relative frequencies with which dicentric bridges occur in successive divisions in the ascus depend on the amount of chromosome twisting in the segment between the two nonhomologous centromeres. Differences in observed bridge frequencies might provide a sensitive measure of rigidly, twisting or coiling—properties of the chromosomes likely to be under genetic control and to be significant for such phenomena as chiasma interference.

v. Uses of insertional rearrangements in other organisms and reasons for their neglect. Few or no insertional have been identified in other organisms, with the striking exception of Drosophila, where identification of insertions has been facilitated by the salivary chromosomes. The first translocation ever found was in fact an insertional—Pale in Drosophila (discovered by C. B. Bridges in 1923, but shown to be an insertion only 12 years later). Over 70 Drosophila insertional are now listed by Lindsley and Grell (1968), and they have been put to many uses, such as to study position effect, dosage compensation, synapsis, recombination, chromosome replication, genetic fine structure, effects of hyper- and hypoploidy, and the functioning of sperm. In contrast to Drosophila, only one insertional translocation has been reported in maize (used to show the relation of crossing over to homologous pairing—Rhoades, 1968), and one in the mouse (used to study controlling elements and chromosome inactivation—review by Cattanach, 1975). For references on insertional and their applications, see Muller (1967) and Perkins (1972a). In medical genetics, balanced insertional translocations have been implicated several times in the origin of birth defects associated with partial trisomy (see, for example, Rethoré et al., 1972; Therkelsen et al., 1973; Grace et al., 1973).

It now appears from Neurospora that insertional translocations are common in their occurrence, though somewhat less frequent than reciprocals. Why then have these important and useful rearrangements not been recognized more readily in other organisms, and why are they not even mentioned in most textbooks? The neglect is probably because both genetic and cytological detection are more difficult than for reciprocal interchanges, the consequences of segregation and recombination are more complex, and stocks may fail to be established or may be lost because aneu-
ploid rather than euploid progeny are inadvertently retained. Further studies of insertionals should be rewarding, especially in haploid organisms, where they are relatively easy to recognize, manipulate, and preserve.

2. Quasiterminal Rearrangements

a. Translocations. At least 12 rearrangements have been identified where the breakpoints are at the tip of one chromosome and in a non-terminal region of a second chromosome (Appendix Table 2). Frequencies of the ascus types characteristic of a quasiterminal translocation are shown in Fig. 15A. (Additional examples can be found in Fig. 7 of Perkins, 1974.)

The ascus frequencies for quasiterminal translocations resemble those for insertionals, and they result from similar events in meiosis, as diagrammed in Fig. 16. When there is no crossing over, normal centromere disjunction results in 8:0 and 4:4 asci with equal probability (two top diagrams). Asci of the 6:2 type are produced by interstitial crossing over, and their frequency reflects the combined lengths of the two interstitial intervals. Since one of the breaks is necessarily at a chromosome tip, and since even the shortest chromosome arms are known to be of substantial length, 6:2 frequencies should never be very low with this type of rearrangement.

It is assumed without direct evidence that the tip breakpoint is subterminal rather than strictly terminal, and that the tip is translocated. Our diagrams and terminology

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Fig. 15. Frequencies of unordered ascus types in crosses of (A) Quasiterminal Translocation × Normal (left), and (B) Quasiterminal Pericentric Inversion × Normal (right). The translocation has one breakpoint at centromere, the other at the tip of VL, which is a moderately short arm; this is reflected in an intermediate frequency of 6B:2W asci. The inversion produces 6B:2W's from single exchanges and 4B:4W's from 4-strand doubles; symmetry is not expected. The inversion data are from Turner et al. (1969). Reproduced from Perkins (1974).
Fig. 16. The origin and constitution of asci containing various numbers of inviable spores, from crosses between Normal and a Reciprocal Translocation in which one breakpoint is effectively terminal. Because one of the duplication-deficiency classes is viable, the asci resemble those from an insertional translocation (Fig. 7C,D; Fig. 12) rather than from an ordinary reciprocal translocation (Fig. 7A,B; Fig. 8). The order of black and white spore-pairs is not necessarily as shown in the diagram. Reproduced from Perkins (1974).

conform with the impressive evidence in Drosophila, summarized by Muller and Herskowitz (1954), that breaks do not heal to form new stable ends, but must be capped by a preexisting telomere. [See also Cavalier-Smith (1974) on the origin and molecular structure of telomeres, and Roberts (1974, 1975) for recent observations in Drosophila.] Other models are not excluded, however. Healing to form new, stable chromosome ends has been reported by McClintock (1939, 1941) following a breakage-fusion-bridge cycle in maize, and by T. C. Hsu (1963) following breakage by radiation or chemicals in the hamster.
Some apparently terminal rearrangements could instead be noninverted insertions beyond the farthest known gene marker but short of the tip, so that the distal segment included essential loci. When there are no distal markers in either the donor or the recipient chromosome arm, the distinction between interstitial and terminal becomes difficult. Even then the two alternatives might be distinguished if there were appropriate markers within the transposed segment, because single crossovers there should be fully viable for a quasiterminal interchange, but one or both single crossover products might be inviable for an interstitial insertion. Where the two alternatives cannot be distinguished, it is simplest to assume that duplication-generating rearrangements are quasiterminal (two breaks required for origin) rather than insertional (three breaks).

Especially clear cytological evidence indicates that $T(IR \rightarrow VL)AR190$ is effectively terminal. The longest arm in the complement, IR, is translocated in its entirety (except for one known proximal gene) to the left tip of chromosome 2, distal to the nucleolus organizer (Barry and Perkins, 1969). Only a minute terminal satellite occupies this position in the normal sequence, and some fully viable strains even lack the satellite. No cytologically detectable nucleolus organizer activity has been removed to the IR break point in $T(IR \rightarrow VL)AR190$.

b. Quasiterminal Pericentric Inversions. The three known inversions are of this type, and they all involve linkage group I, where a substantial segment of the left arm has been transferred to the right tip. Frequencies of ascus types are shown in Fig. 15B.

The consequences of meiotic crossing over are diagrammed in Fig. 17. All ascus types other than 8:0's originate from crossing over within the long inverted segment. 6:2 asci come mainly from single crossovers and 3-strand doubles, 4:4's from 4-strand doubles, and 8:0's from noncrossovers and 2-strand doubles. Thus the frequencies of 8:0, 6:2 and 4:4 ascii are not expected to be symmetrical around the 6:2 class. For data and a fuller discussion of inversions of this type, see Newmeyer and Taylor (1967) and Turner et al. (1969).

Cytology of pericentrics. Only by making a loop can an inverted chromosome pair in complete register with its Normal homolog. We have observed such loops at pachynema with two Neurospora inversions, $In(IL \rightarrow IR)H4250$ and $In(IL \rightarrow IR)NM178$. Workable figures of this type are infrequent, however, because the pachytene nuclei are not flattened. The chromosomes tend to be oriented at approximate right angles in three dimensions at the breakpoint, making the inversion switches very difficult to trace, just as is true for paired insertions [Section V, D, 1, a, ii (b)]. The most convincing observations have been of nuclei where pairing was incomplete, with one or the other uninvited segment unpaired, as in Fig. 12 of Barry (1967) and the bottom left diagram in Fig. 10. These inversions do not form dicentric bridges or fragments. It should be possible to see altered arm ratios in chromosome 1 at metaphase of the third and fourth divisions in the ascus, but this has not been examined.
c. Research Applications of Quasiterminal Rearrangements

1. Production of duplications. (Section V, E describes the characteristics and uses of duplications.)

2. Duplication instability. Many duplications in Neurospora are unstable to varying degrees. The mechanism of breakdown and factors affecting it are most easily studied by means of the terminal duplications obtained as segregants from crosses of Normal with various quasiterminal rearrangements. Studies of this kind are described in Section V, E, 4.

3. Mapping chromosome ends. Appropriate quasiterminal translocations can be used as testers in a search for genes near unmarked chromosome tips. Distal interchange points of the known quasiterminal rearrangements are shown in Fig. 5. They serve to mark five of the 14 chromosome ends.

The most distal known gene markers are not necessarily located terminally in the physical chromosomes. Recombination between such a marker and the interchange...
point of a quasiterminal rearrangement may indicate that a long distal region remains unmarked. For example, uvs-2 shows 10% recombination with interchanges involving the IVR tip. It can thus be anticipated that gene loci remain to be discovered in the IVR segment distal to uvs-2. T(IR → VL)AR190 carrying nic-2 has been used (so far unsuccessfully) in searching for genes near the nucleolus organizer at the left end of V.

iv. Chromosomes with altered morphology. Some rearrangement strains contain altered chromosomes that are very short or very long, chromosomes that are acrocentrics, and at least one where the nucleolus organizer is no longer terminal. Base-tip translocations such as ALS159, AR190, AR300 alter chromosome size drastically. Further alterations can be produced by combining rearrangements. Altered chromosomes can be used to study pairing, recombination, or disjunction.

d. Quasiterminal Rearrangements in Other Organisms. Translocations of this type were among the first to be described in maize (Brink and Cooper, 1932). Rearrange-
ment breakpoints are commonly located near chromosome tips in Drosophila (Muller and Herskowitz, 1954), and this may also be true in man (Francke, 1972; Jacobs et al., 1974). Translocations that involve the terminal satellite are known in maize (Burnham, 1950) and barley (Hagberg and Hagberg, 1971); these resemble T(I → V)AR190 in Neurospora. Application of quasiterminal translocations to linkage detection has been illustrated in maize (Phillips et al., 1971).

For further examples of quasiterminal rearrangements in various organisms, see Muller and Herskowitz (1954), White (1973), Burnham (1962), and Clutterbuck (1970). For representative recent reports of quasiterminal translocations and inversions in man, and their role in the origin of partial trisomy, see Francke (1972), Dutrillaux et al. (1973), de la Chapelle and Schroeder (1973), Dallapiccola et al. (1974), and Rethore et al. (1974).

3. Partially Overlapping Rearrangements

a. Reciprocal Translocations. Viable nontandem duplications can also be obtained from crosses between two reciprocal translocations whose breakpoints involve the same two chromosome arms, as first proposed by Muller (1930). A condition for the production of viable duplications is that the translocations must overlap so that each has one breakpoint distal and one proximal, relative to the other, or they may have one breakpoint in common and their other breakpoints in a shared chromosome arm. If either of these conditions obtains, synapsis in the intercross between the two translocations resembles that of Insertional Transloca-
tion × Normal, as was seen in Fig. 11. One-third of the viable progeny from such a cross are duplicated for the segments between breakpoints. As with insertional translocations, the duplication progeny from partially overlapping reciprocals contain no deficiencies, and ascospores containing such duplications are viable and black (Perkins, 1971a, 1974).

Frequencies of ascus types are shown in Fig. 18C for a cross between two partially overlapping reciprocal translocations. (Two other examples are given in Fig. 11 of Perkins, 1974.) The distribution resembles that of an insertional translocation × Normal.
Fig. 13. Frequencies of unordered ascus types in a cross between reciprocal translocations that have overlapping breakpoints in the same two chromosome arms, as in Fig. 11. When each parent translocation is crossed to the normal-sequence tester, it produces unordered asci that are typical of a simple reciprocal translocation (diagrams A and B). Intercrosses between the two translocations result in the frequency distributions shown in C, which are typical of duplication-producing combinations.

Many reciprocal translocations in *Neurospora* have been intercrossed with other reciprocals whose breakpoints are known to fall in the same two chromosome arms or might do so, and over 30 different pairs of reciprocals have been shown to produce viable duplication progeny, indicating that they are partially overlapping. Evidence for this conclusion is of two types, consisting for each intercross of (1) frequencies of ascus types similar to Fig. 18C, and (2) identification of f₁ progeny as duplications (see Section, V, E, 3 and 4 for characteristics of duplications). Pairs of translocations whose breakpoints do not overlap properly give negative tests (examples in Table 1 of Perkins, 1974).

Intercrosses can be used in this way to determine the relative positions of breakpoints of pairs of reciprocal translocations, and if a particular pair overlaps so as to produce duplications, the breakpoints can be mapped precisely provided that suitable markers can be introduced so as to test for coverage.

b. Partially Overlapping Inversions. Similar considerations apply to intercrosses between overlapping inversions. Crossing over produces viable progeny that are duplicated for the two segments between the left breakpoints and between the right breakpoints. This has been tested in *Neurospora* by intercrossing the IL → IR inversions *H₄₂₅₀* and *NM₁₇₆*, which share a common breakpoint at the IR tip. Ascus frequencies were 18% 8:0, 64% 6:2, 16% 4:4, 1% 2:6, 0% 0:8 (*N* = 207), and viable duplications were recovered, as expected.

c. Successive Rearrangements. If two successive rearrangements
occurred at different times in the same cell lineage, resulting in an overlapping double rearrangement, and this was crossed to the normal sequence, pairing and segregation would resemble that of an intercross between the two corresponding single rearrangements.

\textit{d. Applications in Other Organisms}. Overlapping rearrangements have been widely used, and for many purposes. They were employed in \textit{Drosophila} by Muller and Prokofyeva (1935), Sturtevant and Beadle (1936), Kelstein (1938), Patterson \textit{et al.} (1940), Lindsley \textit{et al.} (1972), Rawls and Lucchesi (1974), and Steward and Merriam (1974); in \textit{Datura} by Blakeslee \textit{et al.} (1936); in maize by Gopinath and Burnham (1956) and Phillips and Springer (1972); and in barley by Hagberg (1962). For further examples, see Burnham (1962).

Translocations that involve the \textit{Drosophila} \textit{Y} chromosome offer special advantages for the production of duplication gametes (Lindsley \textit{et al.}, 1972). Because the \textit{Y} is largely inert, most breakpoints in it behave as though they were identical, and essentially all translocations between the \textit{Y} and a given autosome arm produce viable duplications when they are intercrossed. A series of such intercrosses can produce a precisely contiguous set of nonoverlapping duplications. Translocations between an inert \textit{B} chromosome and a chromosome of the normal complement might be used similarly in other organisms. [For \textit{B}-chromosome translocations in maize, see Roman (1947) and Beckett (1972).]

Käfer (1975b, 1977) has obtained interstitial duplications in \textit{Aspergillus} by a more complicated method which involves intercrossing translocations that have only one chromosome arm in common.

\section*{E. Nontandem Duplications and Their Characteristics}

\textit{Neurospora} has proved to be nearly ideal material for identifying and investigating the rearrangements that recurrently generate nontandem duplications. Such aberrations are recognized visually by the production of asci with unique patterns of black and white spores, as described in Section V, A, 2. The methods of detecting duplication-generating rearrangements are just as effective for short duplications as for long. Theoretically, it should be possible to recognize a rearrangement where only a single essential locus was translocated or inserted. At the other extreme, long duplications are quite viable in \textit{Neurospora}.

\subsection*{1. Mapped Duplications and Their Extent}

Duplications are produced by each of the 41 extant rearrangements listed in Appendix Table 2. Information on each duplication will be found in the Appendix following the description of the rearrangement that produces it. The segments covered by these duplications collectively cover at least half the genetic map (Fig. 19).

Duplication strains that cover any of the desired intervals shown in Fig. 19 can be obtained from a cross with the appropriate rearrangement, usually as one-third of the progeny. Since markers can be introduced from the normal-sequence parent, it is possible to obtain duplications that are
Fig. 19. Intervals covered by duplications from various duplication-generating aberrations. A broken line under the donor linkage group indicates the segment that is involved in the duplications produced by crossing each rearrangement by normal sequence. For clarity, short intervals have been greatly expanded. Interval lengths are thus grossly distorted. Dashed lines, ————, indicate the extent of duplications as determined directly by marker coverage. Dotted lines, . . . . , indicate segments not tested for coverage, but where duplication is inferred from other evidence. Dotted lines within parentheses, (. . . .), indicate segments not tested for coverage. Rearrangements are designated by isolation numbers at the right end of each duplicated segment. For the new location of each segment in rearranged sequence, and for other details, see Appendix. Duplications from overlapping rearrangements are not included in the figure. Since this paper was completed, new data show that ALS182 duplications include met-6, ALS176 duplications include un-15, Y16329 duplications include un-4, and AR33 duplications involve a terminal segment of VL that includes the nucleolus organizer. D305 duplications do not include ro-2, and NM152 duplications do not include arg-2.
heterozygous for known genes, to test for coverage of markers located in the donor chromosome, or to vary the genetic background as desired, all while working with duplications of exactly the same segment.

2. Source and Mode of Origin

All the identified Neurospora duplications are nontandem, and they were obtained exclusively as segregant progeny from crosses heterozygous for duplication-producing rearrangements.

Probably new duplications are also being produced directly as variants of the normal chromosome sequence, and are present among the survivors of mutant hunts when we examine them for new rearrangements. A stable new duplication would not be expected to produce the white, deficiency ascospores on which our recognition method depends for other rearrangement types. However, it would usually be expected to produce barren perithecia in a test cross. It is not clear how such an isolate could be tested routinely to prove that barrenness was due to a duplication rather than to a dominant gene mutation that affected fertility.

New variant strains that make barren perithecia have indeed been found with a low frequency in some of our mutant hunts. Mutants of this type were obtained by Schroeder (1970) as spontaneous somatic variants in the ultraviolet-sensitive strains uvF-3. Because their barrenness resembled that of known duplications under similar conditions, she suggested that they might be new duplications. Similar strains, barren both as male and female, were found among sterility mutants obtained by Weijer and Vigfusson (1972). These were attributed to gene mutation.

With duplications of recombinational origin there is usually no problem of recognition, because an entire new class of Duplication progeny is present rather than a single unique isolate. In the case of duplication-generating translocations, the new class makes up one third of the viable progeny (Section V, D). The Duplication class is typically barren in test crosses. Appropriate genes can be used to confer a distinctive marker genotype on the Duplications. Morphology of the Duplications may be grossly abnormal if vegetative incompatibility genes are heterozygous. Occasionally the Duplication class is intrinsically distinct in its vegetative morphology.

Do nontandem duplications generally originate de novo, or by recombination? Most textbooks assume that duplications usually arise directly from the normal chromosome complement, much as do other aberrations such as translocations. The probability of their arising indirectly by recombination is usually neglected. Yet simple considerations show that a recombinational origin is probably the more likely, because a new balanced duplication-generating rearrangement is at least as likely to occur originally as is the corresponding duplication, and once such a rearrangement is present, it is capable of producing a large number of identical duplications by meiotic recombination.
This is best seen when an aberration occurs in the somatic nucleus of a haploid organism. Figure 20 shows the origin of an insertional duplication and of the corresponding balanced insertional translocation. Similar considerations would apply to terminal duplications and translocations. The rearrangement is shown to occur between chromatids in the G2 period, following chromosome replication. The haploid nucleus is temporarily heterozygous for an insertional translocation, and this is resolved at the following mitosis in either of two equally likely ways, depending on centromere orientation. One outcome yields a duplication, the other a balanced insertional translocation.

If a similar aberration occurs in the G1 period, before replication, only one outcome is possible—an insertional translocation. No duplication can arise at that stage in a haploid nucleus. Thus the balanced translocation is at least as likely to occur as the duplication, and probably more likely, depending on what proportion of aberrations originate in G1.

We suggest that this result is not trivial. A single newly arisen duplication probably has little expectation of survival in nature, whereas the chances are considerable that a balanced translocation will survive and be transmitted for at least a few generations, because fitness of the

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**Fig. 20.** Suggested origin of (1) a nontandem interstitial duplication and (2) the corresponding insertional translocation, in *Neurospora*. It is seen that the outcome depends solely on orientation of centromeres at the division following occurrence of the rearrangement, and that each outcome is equally probable when the rearrangement occurs between chromatids at a stage following chromosome replication. Before replication in a haploid nucleus, an insertional translocation could be produced, but not a duplication.
balanced individuals is independent of the fitness of the Duplications that will constitute one-third of their viable progeny. For these reasons, balanced duplication-producing rearrangements appear to deserve fully as much attention as do the duplications themselves whenever the origin of nontandem duplications is considered, either in experimental situations or in nature.

3. Vegetative Phenotype of Duplications; Fertility

In general, Neurospora duplications deviate remarkably little from wild-type morphology and growth rate. However, the duplications from a few rearrangements are recognizably abnormal, and that abnormality cannot be attributed to heterozygosity for genes in the duplicated segment. (This is true, for example, of $Dp(II \rightarrow III)AR18$.) No general trend is evident relating normal or abnormal phenotypes to length of the duplication or to specific regions of the complement.

The phenotype of any duplication culture can, however, be grossly abnormal if it is heterozygous for alleles of a vegetative (heterokaryon) incompatibility gene (Newmeyer and Taylor, 1967; Perkins, 1975; Mylyk, 1975). This is a result of the genic content rather than an expression of the duplicated condition; when het genes are homozygous in the same duplication, the phenotype is typically normal or nearly so.

Fertility. When a duplication strain is crossed with a nonduplication strain of opposite mating type, perithecia are formed that are barren and produce few or no asci or ascospores [first observed by St. Lawrence (1953, and unpublished) with $R55\ and\ 4540$]. Typically the perithecial necks are rudimentary or short. This is true of nearly all the duplications known in Neurospora and does not depend upon whether the duplication strain is used as protoperithecial or as fertilizing parent. There is no obvious relationship between the degree of infertility and the length of the duplication or the specific segment involved. Crosses of Duplication $\times$ Duplication are also barren.

We do not understand why Neurospora duplications result in barrenness. Duplications in Aspergillus are apparently fully fertile. Duplications in many plants are transmitted through the female but not the male because of pollen-tube competition. But there is no evidence of competition in laboratory fertilizations of Neurospora. Initiation of perithecial development is not delayed after fertilization with a Duplication, in crosses destined to be barren, and both reciprocal crosses are equally barren when one of the parents is a Duplication.

The critical stage appears to be just when the conjugate nuclei fuse in the crozier, or are about to do so. In crosses with a series of duplications, N. B. Raju (unpublished) finds that karyogamy may or may not occur,
depending on the duplication. With some duplications, meiosis may be initiated but not completed. Rarely an ascus may be produced, with ripe ascospores.

A few duplications are sufficiently stable and fertile so that both segments of the duplication are retained through meiosis and delivered together intact in the f₁ ascospores. This occurs regularly with interstitial duplication $Dp(IV \rightarrow VII)S1229$ (Barry, 1960a) and occasionally with terminal duplication $Dp(IL \rightarrow IR)NM176$ (Turner et al., 1969; D. D. Perkins, unpublished). The crosses in which this occurs are nevertheless highly unproductive, and are clearly classified as barren. In crosses with some duplications, no ascospores whatever are produced. With other duplications a small number of spores are regularly produced—perhaps ten to a few hundred in each small cross tube, where many thousands would be present in fertile euploid crosses. These crosses can readily be distinguished as nonfertile if scoring is properly timed. They are classified as barren. Usually when ascospores appear in substantial numbers in the test cross of a duplication, this is because the duplication is unstable and has broken down, and it does not mean that the unchanged duplication is fertile.

4. Instability of Duplications

The previous section concerns strains that are still intact duplications and have not undergone changes in constitution. Most duplications are not completely stable and may change spontaneously either somatically or in the perithegium. The degree and kind of instability depend both on the specific duplication and on the genetic background (Section d, below).

Instability has been examined most carefully with terminal duplications, where a single event could result in euploid or homozygosis. These seem to be less stable than insertional duplications, where interstitial deletion or double mitotic crossing over would be required.

a. Somatic Instability. A few duplications are highly unstable even under nonselective conditions. Duplications from $T(IR \rightarrow VIR)NM103$ (Turner, 1975, 1976) and $T(IR \rightarrow VL)AR190$ (D. D. Perkins, unpublished) are the best-studied examples. Vegetative cultures accumulate nuclei that have completely lost one of the duplicate segments, becoming euploid by all available criteria. When appropriate markers are present, instability may result in visible recessive patches in vegetative cultures, but heterokaryosis may prevent the results of instability from becoming visible. The euploid nuclei can best be detected by the appearance of recessive phenotypes among the isolates from conidial plating. Crosses of such conidial isolates are fully fertile, and segregation is as expected of a euploid cross.
Most duplications are sufficiently stable that little variation is observed vegetatively under nonselective conditions. Somatic variants can be obtained, however, if the original duplication is placed at a selective disadvantage. This happens automatically whenever a duplication is heterozygous for alleles at a heterokaryon (vegetative) incompatibility locus (het locus). Such heterozygotes have very abnormal “inhibited” growth. Under these conditions fast-growing somatic variants are found that have lost one of the het alleles, either by deletion or by recombination resulting in homozygosis. Most studies of somatic instability and factors affecting it have employed het genes (Newmeyer, 1965; Newmeyer and Taylor, 1967; Schroeder, 1970, 1975; Mylyk, 1972; Newmeyer and Galeazzi, 1974, 1976a,b). A similar selection can be achieved by using cycloheximide when duplications are heterozygous for a recessive gene that confers resistance (Turner, 1975, 1976).

Some of the fast-growing somatic variants obtained by these selective systems are fertile in test crosses and therefore appear to be euploid, but most of them remain barren. The latter could be due to incomplete deletion of a duplicate segment or to a mitotic crossover that led to homozygosis for the selective marker. These alternatives are difficult to distinguish because the infertility interferes with progeny-testing. In one system it has been shown that most of the barren variants express recessive markers throughout the duplicated region, indicating either mitotic crossing over or extremely long but incomplete deletion (Newmeyer and Galeazzi, 1976a).

b. Instability after Fertilization. Perithecia from a Duplication parent are typically barren as a result of being aneuploid. When fertile perithecia appear in such crosses, they are found to contain nuclear types that have lost the duplicated segment. Segmental loss can occur either before or after fertilization. Distinction between the two is usually clear, and it depends on the time and pattern of appearance of the fertile perithecia. Perithecia whose fertility is restored by postfertilization loss are recognized because they are initially barren and become fertile only after a significant lag. In contrast, perithecia from prefertilization loss are immediately fertile with no lag in the appearance of necks or ascospores. However, the distinction is difficult with very unstable duplications.

The sexual phase automatically acts as a selective system enabling the results of postfertilization instability to be recognized by changes of individual perithecia from barren to fertile. Barrenness apparently results from the duplicated condition itself. Therefore, selective markers are irrelevant, and fertility cannot be restored by homozygosis, but only by loss of duplicated material.

Chromosome losses that change the peritheciun from barren to fertile
are usually such as to restore precisely the euploid condition, as though the parental chromosome tip has either been restored or is unnecessary. This is true within the limits of both genetic and cytological resolution for \( Dp(\text{IL} \rightarrow \text{IR})H4250 \), where fertile derivatives have been examined genetically (Newmeyer and Galeazzi, 1976a,b), and in one instance cytologically. Pachytene pairing of a euploid derivative of \( Dp(\text{IL} \rightarrow \text{IR})H4250 \) that arose by \( \text{mei-3} \)-mediated breakdown so as to restore the inversion sequence is shown in Fig. 4.

c. Nonrandomness of Spontaneous Breakdown. With \( Dp(I \rightarrow VI)NM108 \), the loss occurs with about equal probability either at the interchange point in translocation sequence so that normal sequence remains, or at the interchange point in normal sequence so that translocation sequence remains (Turner, 1975, 1976). Such an equally likely loss of either duplicated segment is not generally found, however, among the seven other duplications that have been tested adequately. For example, \( Dp(I \rightarrow V)AR190 \) reverts to euploid only by losing the duplicated segment from the translocated position, and it has never been observed to lose the segment from the normal position (Fig. 21). Several other duplications are known to resemble \( AR190 \) in this respect (for example, \( AR209, ALS176 \)). Other duplications usually resemble \( AR190 \), but not always; these occasionally break down by losing the other segment from the normal position (\( H4250 \) and \( NM176 \) are examples). No duplication is known where all or most of the losses are such as to restore the rearrangement sequence.

![Diagram](image)

**Fig. 21.** Alternate modes by which Duplication \( Dp(\text{IR} \rightarrow \text{VL})AR190 \) could lose a duplicated segment so as to restore the euploid condition.
The foregoing examples are all quasiterminal duplications. Breakdown products from insertional duplication $Dp(IIR \rightarrow IL)NM177$ have been examined by Metzenberg et al. (1974). When somatic variants occur, material is apparently lost from the inserted location. The loss is not complete, because the somatic variants are still barren, resembling in this respect many of the variants that originate vegetatively by spontaneous escape from het-incompatibility with the terminal duplications $H4250$ (Newmeyer and Galeazzi, 1976a) and $NM149$, and the interstitial duplication $39311$ (D. D. Perkins, unpublished).

Duplications from overlapping reciprocal translocations present a special problem which is still unsolved. When the perithecia change from barren to fertile, a simple deletion would be expected to restore the sequence of one or the other parental translocation. Unexpectedly, fertile perithecia from this source often produce 95% black ascospores, as though the normal sequence had been restored (D. D. Perkins, unpublished).

d. Genes Affecting the Stability of Duplications. Five genes affecting radiation sensitivity have been tested with $Dp(IL \rightarrow IR)H4250$ or $Dp(IL \rightarrow II R)39311$. Escape from inhibition due to $A/a$ heterozygosity was timed. $uvr-2$, -4 and -5 were without effect, but escape was speeded by $uvr-3$ and $uvr-6$ (Schroeder, 1970, 1974, 1975), indicating that they increase either mitotic crossing over or deletion. For a summary of the properties of these genes, see Schroeder (1975).

A gene linked to $Dp(II \rightarrow V)NM149$ affects the speed of escape from inhibition due to het-$C$/het-$c$ heterozygosity (Mylyk, 1972). $mei-3$, a gene in IL which somewhat resembles $uvr-3$ and -6 (Section III, C, 1), markedly speeded the restoration of fertility in barren duplications from at least four different rearrangements, and it also speeded vegetative escape from inhibition due to het incompatibility (Newmeyer and Galeazzi, 1974, 1976b). Other factors, not mapped, each affect vegetative or sexual-phase instability in characteristic ways (Newmeyer and Galeazzi, 1976a).

5. Nontandem Duplications in Aspergillus and Higher Organisms

J. A. Roper and his colleagues (B. W. Bainbridge, B. H. Nga, and J. L. Azevedo) have studied the vegetative instability of duplications in $A. nidulans$, using one duplication that originated as a unique spontaneous variant, and others obtained as progeny of duplication-producing rearrangements. The results have been reviewed by Roper (1973a,b). Several resemblances to Neurospora duplications are apparent: All duplications are essentially unstable. Duplicated material is lost by one or more steps to give effectively haploid derivatives. Loss can be from either position, but with at least one duplication it is predominantly from the translocated position. Instability is increased by caffeine, trypan blue, and by a $uvr$ mutant. A recessive factor reduces instability (Azevedo, 1975).
Some differences exist between Aspergillus and Neurospora. The Aspergillus duplications apparently do not affect fertility, and are readily transmitted through the sexual cycle. They are distinct from the wild type in morphology and growth rate. Because of its growth habit, uninucleate conidia, autonomously expressed color markers, and stability of vegetative diploids, Aspergillus is very favorable material for studying somatic instability, and the observations of Roper and his associates on vegetative changes go beyond those in Neurospora in several respects. It has been shown, for instance, that the duplication itself provokes instability, limited largely to the duplicated segment. Not only losses but also gains of material are found, in "deteriorated" sectors. On the other hand, meiotic mapping and analysis are accomplished more readily with Neurospora, and a larger number of genetically characterized duplication-producing rearrangements are available for comparison. Also, studies of duplication instability are not limited to somatic stages, but can readily be extended to the sexual phase.

In many higher plants, duplications are readily transmitted through the female but not the male, because pollen tubes bearing a duplication are unable to compete in growth down the style (see Burnham, 1962). In Drosophila, extensive hyperploidy usually results in decreased survival and abnormal morphology (Lindsay et al., 1972). Duplication in man (partial trisomy—aneupomie de recombinaison) characteristically results in developmental and neurological defects (see references cited following the sections on insertional and quasi-terminail rearrangements).

Segmental loss of duplicated chromosome material has been reported in barley, where deletion from a balanced tertiary trisomic reduces the extra chromosome to about one-third size. This has been called the "chopper" effect (Wiebe et al., 1974). The reduction increases plant vigor and increases transmittal of the chromosome through the pollen, compared to the original trisomic.

Segmental loss is one manifestation of the Ds-Ac controlling-element system in maize (McClintock, 1950). Conceivably a similar mechanism might be responsible for deleting duplicated segments in Neurospora.

6. Other Research Applications of Duplications

a. Mapping by Duplication Coverage. Nontandem duplications produced by any of the methods described above provide a quick and easy way of mapping closely linked genes by a right-left test (comparable to deletion mapping in bacteriophages) (Section IV, B, 4, b; Perkins et al., 1969). The same technique can be used for centromere mapping.

b. Vegetative Incompatibility. Genes affecting the ability of somatic hyphae to form stable heterokaryons (het-genes) are difficult to study genetically if scoring depends on heterokaryon tests, because a difference at any one of many het loci results in a similar incompatibility phenotype, and commonly used marker stocks differ at several het loci. This difficulty is avoided by using for the analysis duplications that are short enough to include only one het locus. Duplications heterozygous for het alleles have characteristic abnormal phenotypes (Newmeyer and Taylor, 1967; Perkins, 1975; Mylyk, 1975). A series of duplications have been used in this way to identify previously undetected het loci (Mylyk, 1975), and to show that natural populations of N. crassa are highly polymorphic for het genes (Mylyk, 1976).

c. Regulation. The ability to produce duplications of desired allele content allows the same gene combinations to be compared within the same nucleus in a heterozygous duplication, and in separate nuclei in a heterokaryon. This type of comparison has been made by Metzenberg et al. (1974) in studies of the regulation of alkaline phosphatase synthesis, using duplications from T(11→1)NM177.
d. Mitotic Recombination. The nontandem duplications now available are far more stable than the diploids or disomics described in Section II, and it should be possible to use duplications to study intra- and intergenic mitotic recombination in Neurospora, much as diploids are used in Aspergillus, yeast, or Ustilago. Such a system is being developed.

A test system where only a small part of the genome is diploid should be of special value in searching for and scoring recessive genes that affect recombination. Heterozygous duplications have been used for this purpose in Aspergillus (Parag and Parag, 1975). Disomics provide similar test systems in yeast (Roth and Fogel, 1971; Rodarte-Ramón and Mortimer, 1972).

e. Tests of Dominance. Duplications provide a more reliable test of dominance than do heterokaryons, because a 1:1 allele ratio is assured. (Very often duplications are also more convenient because heterokaryon incompatibility genes can be ignored in most of the genome.) An example is provided by cyh-1, where resistance is clearly recessive in duplications from T(I → VI)/NM103 (Turner, 1976). The resistant cyh-1 allele had originally been found dominant in heterokaryons, in carefully conducted tests with forcing markers (K. S. Hsu, 1963). Skewed nuclear ratios in the heterokaryons probably affected the tests, however.

A similar error could result with a duplication if it were so unstable that the dominant sensitive allele was usually lost during testing, and the resistance then expressed was mistakenly attributed to dominance rather than loss. In practice, instability has not interfered with such tests, using either Dp(I → VI)/NM103 or other, moderately stable, duplications. However, suitable controls should be done to guard against this error before concluding that a resistance allele is dominant.

F. REARRANGEMENTS IN OTHER EUKARYOTIC MICROORGANISMS

The pigment patterns in Neurospora asci provide a model of the inviability patterns to be expected in other eukaryotic microorganisms where the meiotic products are unpigmented and where chromosome aberrations may be revealed only by the inviability of deficiency spores.

1. Recognized Rearrangements

In spite of detection difficulties, evidence for rearrangements has been obtained in nine or ten cryptogamic organisms other than Neurospora. Information on these is given in Table 6. The nature and conclusiveness of the evidence varies, and is often tenuous. In four organisms it depends solely on the numbers of defective spores. Only in Aspergillus is the genetic evidence extensive. Only in Coprinus and Sordaria has there been cytological confirmation. Cochliobolus appears in Table 6 because of observations made during a study of mating behavior and fertility. Some progeny were initially dual mating type, inhibited, and barren, and this condition was unstable, suggesting in retrospect that they may have been heterozygous Duplications and that one of the parental strains may possibly have been a rearrangement resembling T(IL → II)/39311 or In(IL → IR)/H4250 in Neurospora. Sphaerocarpos appears in the table...
### Table 6

Chromosome Rearrangements in Eukaryotic Lower Organisms Other Than *Neurospora*

<table>
<thead>
<tr>
<th>Organism</th>
<th>Type of rearrangement</th>
<th>No. of rearrangements</th>
<th>Type of evidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydomonas eugametos</em></td>
<td>(Reciprocal translocations)</td>
<td>4</td>
<td>Tetrad patterns (viability)</td>
<td>d</td>
</tr>
<tr>
<td><em>Saccharomyces cerevisiae</em></td>
<td>(Reciprocal translocation)</td>
<td>1</td>
<td>Tetrad patterns (viability)</td>
<td>e</td>
</tr>
<tr>
<td></td>
<td>(Interstitial deletion)</td>
<td>1</td>
<td>Marker loss</td>
<td>f</td>
</tr>
<tr>
<td><em>Sordaria macrospora</em></td>
<td>(Reciprocal translocations)</td>
<td>2</td>
<td>Tetrad patterns (viability)</td>
<td>g</td>
</tr>
<tr>
<td><em>Sphaerocarpus donnellii</em></td>
<td>(Unknown)</td>
<td>Several</td>
<td>Spore lethality in heterozygous crosses</td>
<td>h</td>
</tr>
<tr>
<td><em>Ascocholus immersus</em></td>
<td>Translocation</td>
<td>1</td>
<td>Meiotic linkage</td>
<td>i</td>
</tr>
<tr>
<td><em>Aspergillus nidulans</em></td>
<td>Reciprocal translocations</td>
<td>Numerous (&gt;12 mapped)</td>
<td>Mitotic linkage; meiotic linkage; disomics from meiosis</td>
<td>j</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Coproina radiatus</em></td>
<td>Reciprocal translocation</td>
<td>1</td>
<td>Tetrad patterns (viability); pachytene pairing</td>
<td>l</td>
</tr>
<tr>
<td><em>Sordaria brevicollis</em></td>
<td>(Inversion?)</td>
<td>1</td>
<td>Tetrad patterns (pigment); meiotic bridges</td>
<td>m</td>
</tr>
<tr>
<td></td>
<td>Translocations</td>
<td>6</td>
<td>Tetrad patterns (pigment); meiotic linkage; cytology</td>
<td>n</td>
</tr>
<tr>
<td></td>
<td>(pericentric inversion?)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Sordaria fimicola</em></td>
<td>Reciprocal translocation</td>
<td>1</td>
<td>Tetrad patterns (pigment); cytology</td>
<td>o</td>
</tr>
<tr>
<td><em>Cochliobolus heterostrophus</em></td>
<td>(Duplication-generating rearrangement? See text)</td>
<td>1</td>
<td>Unstable barren bisexual progeny</td>
<td>p</td>
</tr>
</tbody>
</table>

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a Parentheses indicate that evidence is only presumptive.
b See Table 6 in Perkins (1974) for compilation of tetrad-pattern data.
c See Perkins (1974) for a critique of the evidence for inversion. A derivative of the same aberration strain was later diagnosed as a reciprocal translocation (Mu’Azu, 1973).
e McKey (1967).
f Hawthorne (1963).
g Heslot (1958).
h W. O. Abel (personal communication).
i F.-X. Francou (personal communication).
l Brygoo (1972).
m Ahmad (1970), Admad et al. (1972), Mu’Azu (1973).
Mu’Azu (1973).
o Cox and Gill (1967).
even though it is a bryophyte, because methods of culture and genetic tetrad analysis resemble those used with fungi.

A report of cytologically observed translocation heterozygosity in *Phytophthora* was inadvertently omitted from Table 6 (Sansome and Brasier, 1973).

2. Errors from Failure to Detect Rearrangements

There have been no reports of chromosome rearrangements in the other eukaryotic microorganisms and cryptogamic plants most used by geneticists—*Coprinus lagopus*, *Schizophyllum commune*, *Ustilago maydis*, *U. violacea*, *U. hordei*, *Venturia inaequalis*, *Glomerella cingulata*, *Ophiostoma multiannulatum*, *Podospora anserina*, *Schizosaccharomyces pombe*, or *Chlamydomonas reinhardtii*. It is difficult to imagine that rearrangements do not occur frequently in these organisms, in view of the fact that detectable rearrangements in *Neurospora* and *Aspergillus* are extremely frequent (Section V, B, 2).

Even in *Neurospora*, the presence of deficiencies may not always be detected if defective spores or asci disintegrate, or if deficiency spores become pigmented (as can happen with some rearrangements), or if microscope illumination is such that white ascospores cannot be seen. We know from experience in *Neurospora* that failure to recognize an aberration can lead to serious errors or misinterpretations. Some examples from *Neurospora* are given below.

a. Errors with Random-Isolated Ascospores. Markers in different chromosomes linked to a translocation will, of course, show pseudolinkage. A mutant trait that is linked to an unsuspected aberration may thus be assigned to an incorrect linkage group. (This happened with *T(1L;IVR)HK53 cut*. See Appendix.) Variability in crossing over from cross to cross could result from unrecognized rearrangements, and this would depend on whether the strains used as parents were homozygous or heterozygous for the rearrangement. Undetected aberrations such as small inversions or transpositions might well account for some of the crossing-over variability in *Neurospora*; if so, their identification will be complicated by the presence of different *rec* genes.

Progeny from a rearrangement that generates viable duplications may show distorted, apparently non-Mendelian, allele ratios for linked genes, depending upon the coupling phase and map location. Among viable progeny, allele ratios from $M \times m$ can range from $2M:1m$ to $1M:2m$. If two closely linked recessive genes are present when a duplication-generating rearrangement is crossed by normal sequence, and only one of them is covered by the duplication, one-third of the surviving progeny (the duplications) will appear to have undergone recombination, while the complementary recombination class is absent. (For data examples, see Table 3 of Perkins, 1972a.) Unorthodox results of this type might be interpreted invalidly in terms of selection, synthetic lethal genes, preferential segregation, or directed recombination.

b. Errors Due to Selective Tetrad Analysis. If tetrads containing fewer than four viable products fail to survive, or if they are excluded from analysis by the investi-
gator, the results for the remaining, complete tetrads may simulate chromatic interference for marked intervals linked to an undetected rearrangement. Specifically, an excess of 2-strand double exchanges relative to 3- or 4-strand might be expected. This is true of interstitial regions between centromeres and breakpoints when reciprocal translocations are heterozygous, and of regions included in heterozygous inversions. Emerson (1963, Addendum II) has considered the consequences in detail for translocations, with a probable example from yeast. Undetected rearrangements are undoubtedly responsible for some of the deviations attributed to chromatic interference in the literature.

c. Errors from Unstable Duplications. Because the Duplication progeny derived from duplication-generating aberrations by meiotic recombination are often unstable, heterozygous, cryptic markers from a recessive parent may appear as somatic sectors, or may reappear among the sexual progeny of an unrecognized duplication. Such behavior could be spuriously attributed to mutable genes or mutators, or interpreted as directed mutation.

d. Errors Due to Compound Rearrangements. The risk of failing to recognize a new rearrangement is not limited to the naive beginner, but is a problem even for the investigator who is experienced with rearrangements, because new chromosome breaks and rearrangements seem to occur with an appreciably greater frequency in strains and crosses where a simple rearrangement is already present. Progeny containing a new and unsuspected rearrangement may be encountered, or a stock known originally to be simple may spontaneously produce a derivative that is compound or complex. In our experience a sizable portion of newly detected rearrangements are complex or compound, even with very mild mutagen treatment. Failure to recognize extra complexities could result in false diagnoses or spurious conclusions regarding the correspondence between cytological chromosomes and genetic linkage groups.

VI. Summary

Progress in Neurospora cytogenetics has been speeded by advances in the cytology and genetics of chromosome rearrangements. Although DNA content is only ten times as great as in E. coli, individual chromosomes can be identified and their behavior readily observed by light microscopy during meiosis and related divisions in the ascus. Synapsis follows karyogamy. The largest bivalent elongates to 19 µm by pachynema. Synaptonemal complexes are present. Postmeiotic mitoses in the ascus are conventional. The haploid number is 7 and meiosis is similar throughout the genus, which includes hetero-, homo- and pseudohomothallic species. Only two mating-type alleles are known. Several known genes specifically affect meiosis. Three Spore-Killer genes are known which kill the meiotic products that do not receive them.

In N. crassa, over 400 genes and 167 rearrangements have been mapped to the seven linkage groups, which have been assigned cytologically to specific chromosomes. Functionally related genes are usually not closely linked, but several pairs or clusters are known, and several bifunctional
genes. Crossing over is highly variable in different genetic backgrounds. rec genes regulate meiotic recombination in one or more specific unlinked regions.

Ascospores containing deficiencies are inviable and white, while euploid ascospores and those containing duplications are viable and black. This greatly facilitates the detection and analysis of rearrangements. New aberrations can be diagnosed by determining the frequencies of asci that contain different numbers of white, deficiency spores. Typical reciprocal translocations are readily distinguished from insertional and quasi-terminal translocations, because only the latter two produce viable duplications, and these result in distinctive frequencies of ascus types.

Each known rearrangement is described. Nearly all are phenotypically normal and homozygous fertile. Reciprocal translocations are most common. There are two mutual insertions. The remainder produce viable nontandem duplications by meiotic recombination. These duplication generators are mostly insertional and quasi-terminal translocations, plus three quasi-terminal pericentric inversions and one transposition. Crosses between partially overlapping rearrangements also produce nontandem duplications. Some of the insertional translocations are inverted; these produce bridges and fragments. No paracentric inversion has been found.

Duplications obtainable from the duplication-generating rearrangements collectively cover more than half the genetic map. Most duplications are phenotypically wild but barren in crosses, and are unstable, reverting to euploid by segmental loss. With most but not all of eight duplications tested, the segment in rearranged position is lost preferentially so as to precisely restore the normal sequence. Genetic variants affect the instability. When new aberrations arise directly from wild type, the probability for a new nontandem duplication may be less than for a new balanced rearrangement which can later produce many Duplication progeny by recombination.

Except for Aspergillus, only a few rearrangements have been recognized in other eukaryotic microorganisms, where usually they are more difficult to detect than in Neurospora, with its pigmented spores. Failure to recognize an existing rearrangement can lead to spurious conclusions regarding linkage, recombination, interference, preferential segregation, or the presence of synthetic lethal genes.

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The importance of Barbara McClintock’s pioneering contributions to Neurospora cytogenetics cannot be overstated. The direction of our work has been influenced especially by her ideas and research, and by those of J. R. Singleton, Patricia St. Lawrence, and Dorothy Newmeyer. Dorothy Newmeyer has critically reviewed the
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Appendix: Chromosome Aberrations of Neurospora crassa

EXPLANATORY FOREWORD

Organization. The Appendix consists chiefly of summary descriptions of all analyzed rearrangements arranged in a single numerical sequence according to isolation number. The descriptions are preceded by two index tables (Appendix Tables 1 and 2) where the rearrangements are grouped in categories, according to type and linkage group.

Appendix Table 1 lists rearrangements that do not produce viable duplications. These are mainly reciprocal translocations.

Appendix Table 2 lists duplication-generating rearrangements under three subheadings: (1) Insertions, (2) Quasiterminal rearrangements, and (3) Less completely analyzed duplication-generators: aberrations about which knowledge is still inadequate for placing in (1) or (2). Duplications are not listed separately, but each is described under the rearrangement that produces it.

Isolation Numbers. Each rearrangement is permanently identified by a unique isolation number, which is usually the number of the strain in which the rearrangement originated or was first recognized. This may or may not include letters, depending on the usage of the discoverer. In all symbols for chromosome rearrangements the isolation number appears as the terminal item of the symbol, immediately following the parentheses. For example, in the symbols \( T(II \rightarrow I)NM177 \) and \( T(III;VII)Y112M4r \), the isolation numbers are NM177 and Y112M4r.

In arranging the descriptions according to isolation number, letters preceding the numerals are ignored unless the numerals are identical. If digits of the isolation number are interrupted by a letter, the order of listing is based on the digits preceding the letter.

The initial letters preceding the numerals in an isolation number usually indicate the worker or institution of origin of the isolate. In the rearrangements listed here, these are: ALS—Alice L. Schroeder; AR—A. Radford; B—Brookhaven National Laboratory (V. W. Woodward); C—California Institute of Technology; C—(with hyphen)—Cornell University (J. C. Murray, A. M. Srb); CJS—Carol J. Smarr; D—Duke University (S. R. Gross); EB—E. G. Barry; H—F. P. Hungate; HK—H. Kuwana; JH—Johns Hopkins University (Silver and McElroy, 1954); K—D. G. Catcheside; NM—Noreen E. Murray; P—D. D. Perkins; R—Rockefeller University (E. L. Tatum laboratory); S—Stanford University (Tatum laboratory after 1947); STL—Patricia St. Lawrence; T—Tokyo (Inoue and Ishikawa, 1970); Y—Yale University (Tatum or N. H. Giles laboratories); TM—Teresa M. Angel. Isolation numbers without letter prefixes refer to mutants in the original Beadle and Tatum (1945) numbering system, obtained chiefly at Stanford University before 1945. Strains prefixed ALS, NM, and AR were mostly discards from mutant hunts that were given to the first author to check for rearrangements.
Symbols and Conventions. The identifying symbol for each rearrangement consists of three elements, (1) an initial letter or combination of letters specifying the type of aberration (T—translocation, In—inversion, Dp—duplication, Tp—intrachromosomal transposition); (2) Roman numerals in parentheses indentifying the linkage groups involved; and (3) the isolation number—a unique number (or combination) identifying the specific rearrangement. The entire 3-element symbol is written in italics without spacing between elements.

Linkage groups are separated by a semicolon for ordinary reciprocal translocations, but by an arrow for insertional and quasiterminal rearrangements. A single arrow indicates that viable duplications are produced, and its direction indicates which component is the donor and which the recipient of the segment subject to duplication. The arrow is used in similar fashion in the genotype symbols for duplications, each of which bears the isolation number of the rearrangement from which it was obtained. Symbols for insertions do not specify whether the inserted segment is inverted with respect to the centromere. Double arrows are employed in symbols for mutual insertions.

Linkage group arms (R and L) may or may not be shown in symbols, depending on the type of rearrangement and the context. Where a mutant trait is inseparable from the rearrangement, an appropriate symbol for the trait follows the aberration symbol, separated by a space but not a comma, as for example T(I;II)4637 al-1. The trait may or may not be allelic with a known gene.

Standard chromosome sequence is designated Normal and symbolized N. Genetic linkage groups are designated by Roman numerals I—VII. Chromosomes are designated by Arabic numerals 1—7. For specific gene symbols, see the legend to Fig. 2.

Abbreviations: A, a: alleles at the mating-type locus mt; Ab: aberration of undefined or unspecified nature, or as a general term for rearrangements where the specific type is clear in context; B: black ascospore (usually viable); Dp: duplication (terminal or interstitial, inverted or noninverted); EMS: ethyl methanesulfonate; FGSC: Fungal Genetics Stock Center; In: inversion; L: left arm of linkage group (follows Roman numeral); mt: mating-type locus; N: number of asci scored for patterns of aborted ascospores; N: normal (standard) chromosome sequence; R: right arm of linkage group (follows Roman numeral); T: translocation; Tp: transposition (intrachromosomal); UV: ultraviolet light; W: white ascospore (usually inviable).
### APPENDIX TABLE 1

Rearrangements That Do Not Produce Viable Duplications, Listed by Linkage Groups

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Rearrangement</th>
<th>Linkage Group</th>
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<tr>
<td>I;II</td>
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<td>T(IR;II)AR216</td>
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<td>T(I;II)P4704</td>
<td>T(IR;VR)36703</td>
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<td>T(IL;II)P5890</td>
<td>T(IL;VR)47711</td>
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<td>I;III</td>
<td>T(IR;III)P73B101</td>
<td>T(IR;VI)AR13</td>
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<td>T(I;III)NM107</td>
<td>*T(I;VI)T51M158</td>
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<td>T(IL;III)NM109</td>
<td>T(I;VI)T51M166</td>
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<td>T(I;III)NM127</td>
<td>T(IR;VI)P54</td>
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<td>T(IR;III)AR180</td>
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<td>T(IR;III)AR208</td>
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<td>T(I;III)N3717</td>
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<td>I;IV</td>
<td>T(I;IV)HK53 cut</td>
<td>T(I;VII)K79 met-7</td>
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<td>T(IR;IV)T54M19</td>
<td>T(IR;VII)NM155</td>
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<td>T(I;IV)NM128</td>
<td>T(I;VII)ALS167</td>
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<td>T(IR;IV)NM132</td>
<td>T(IR;VII)TM429 his-3</td>
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<td>T(I;IV)NM137</td>
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<td>T(IR;IV)NM189 bs</td>
<td>T(I;VII)P1676</td>
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<td>(= NM147 bs, NM187 bs)</td>
<td>T(IR;VII)17084 thi-1</td>
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<td>II;III</td>
<td>*T(II;III)T54M140b</td>
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<td>(= NM162, NM167)</td>
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<td>II;IV</td>
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<td>T(I;IV)NM170</td>
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<td>T(IR;IV)NM172</td>
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<td>T(I;IV)AR180b</td>
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<td>T(I;IV)NM181</td>
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<td>T(I;IV)AR198</td>
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<td>T(IR;IV)AR212</td>
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<td>T(I;IV)D304</td>
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<td>I;V</td>
<td>T(IL;VR)AR18r</td>
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<td>T(II;VI)T27M9</td>
<td>T(II;VI)B362r</td>
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<td>T(IL;VR)AR18</td>
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<td>T(II;VI)T37M9</td>
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APPENDIX TABLE 1 (continued)

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<th>IV;VII</th>
<th>V;VI</th>
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<tr>
<td>T(IIR;VIIR)T51M143</td>
<td>T(III;IV)T42M36</td>
<td>T(IV;VI)B8</td>
<td>T(III;IV)P73B169</td>
<td>T(IV;VI)P73B12</td>
<td>T(IV;VII)AR10</td>
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<td>T(II;VII)NM134</td>
<td>T(III;IV)NM118</td>
<td>T(IV;VI)NM175</td>
<td>T(III;IV)NM131</td>
<td>T(IV;VI)AR207</td>
<td>T(IV;VII)NM158</td>
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<td>T(III;IV)AR211</td>
<td>T(III;V)NM101</td>
<td>T(IV;VII)STL384r</td>
<td>( = NM102, NM104, NM111, NM112, NM114, NM115)</td>
<td>T(IV;VII)AR5502</td>
<td>T(IV;VII)STL384b</td>
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III;V

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<th>III;VII</th>
<th>III;VIII</th>
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<tr>
<td>T(IIR;VI)1</td>
<td>T(III;VI)AR19</td>
<td>T(III;VII)Y112M4r</td>
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<td>T(IIR;VI)P670</td>
<td>T(III;VII)Y112M4r</td>
<td>T(IIR;VIIR)NM169r</td>
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</table>

<table>
<thead>
<tr>
<th>IV;V</th>
<th>IV;VI</th>
<th>IV;VII</th>
</tr>
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<tbody>
<tr>
<td>T(IVR;VR)AR11r</td>
<td>T(IV;V)T33M8</td>
<td>T(VR;VIIR)AR45</td>
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<td>T(IVR;VR)NM125</td>
<td>T(IVR;VR)NM141</td>
<td>T(V;VI)NM159</td>
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<td>T(IVR;VR)NM141</td>
<td>T(IVR;VR)AR221</td>
<td>T(VIR;VIIR)ALS7</td>
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<td>T(IVR;VR)R2355</td>
<td>T(IVR;VIIR)Y112M15 ad-3A</td>
<td>T(VI;VII)NM124</td>
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<td>Mutual insertions</td>
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<tr>
<td>T(IR ≡ IV)Y112M15 ad-3A</td>
<td>T(IR ≡ VR)S1325 nic-2</td>
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</tbody>
</table>

* Right and left arms are indicated only where they are known with certainty. Strains in parentheses appear to be identical with the translocation after which they are listed, and were probably derived from the same original mutational event. They are not included in the total count of 123 interchanges.

* Aneuploids are found among the progeny of T × N, probably as a result of 3:1 segregation. Except for these three exceptions, the translocations do not produce viable aneuploid progeny in substantial numbers.
APPENDIX TABLE 2
Duplication-Generating Rearrangements, Listed by Type and Linkage Group

<table>
<thead>
<tr>
<th>1. Insertions</th>
<th>2. Quasiterminal rearrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>*T(IL → IIIR)39311</td>
<td>In(IL → IR)AR16</td>
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<tr>
<td>T(IL → VIL)T51M156 un</td>
<td>(= AR94, AR111, AR153)</td>
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<tr>
<td>*Tp(IR → IR)T54M94</td>
<td>In(IL → IR)NM176</td>
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<tr>
<td>T(IR → IIIR)Y112M4i ad-3B</td>
<td>In(IL → IR)H4250</td>
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<td>T(IR → IIIR)4540 nic-2</td>
<td>T(IR → VIL)AR190</td>
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<tr>
<td>T(IR → VIL;I;V;VI)AR173</td>
<td>T(IR → VIIR)NM103</td>
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<tr>
<td>T(IR → IIIR;VI)AR217</td>
<td>T(IIL → VR)NM149</td>
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<tr>
<td>*T(IR → )ALS182</td>
<td>T(IR → V)ALS178</td>
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<tr>
<td>T(IIL → IIIR)AR18</td>
<td>T(IIR → IIIR;VIL)D305</td>
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<td>T(IIL → [IV;V];AR179</td>
<td>T(IVR → VIIR)ALS159</td>
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<tr>
<td>*T(IIL → VI)P2899</td>
<td>T(VIL → IR)T39M77</td>
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<tr>
<td>T(IIR → IL)NM177</td>
<td>T(VIR → IVR)AR209</td>
</tr>
<tr>
<td>T(I → IV)R2594</td>
<td>T(VII → IVR)T54M50</td>
</tr>
<tr>
<td>T(IIR → [IR;IIIR])AR17</td>
<td>T(VII → IVR)ALS179</td>
</tr>
<tr>
<td>*T(IVR → IIIR)S4342</td>
<td></td>
</tr>
<tr>
<td>*T(IVR → VII;IL;IIIR;IVR)S1229 arg</td>
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<tr>
<td>T(VR → VII)EB4</td>
<td>T(V → IVL)AR33</td>
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<tr>
<td>T(VIL → [I;IIIR])Y16329</td>
<td>T(IR;IIIR;IVR)R55</td>
</tr>
<tr>
<td>T(VIR → IVR)CJS1</td>
<td>T(VII → IV)ALS175</td>
</tr>
<tr>
<td>T(VII → IR)5536</td>
<td>T(IIR;VI;VII)AR176</td>
</tr>
</tbody>
</table>

- When these rearrangements are crossed by normal sequence, a class of viable Duplication progeny is produced regularly by meiotic recombination. Rearrangements are listed here in order of the linkage group from which the duplicated segment originated (the donor). Information on each aberration and duplication is summarized in the Appendix, where rearrangements of all types are given in a single numerical order. Figure 19 shows what is known of the segments included in the duplications. Some of the strains under 2 could be subterminal insertional translocations, but interchange of a terminal segment with a tip is the simplest hypothesis on present data.

- Production of bridges and fragments in meiosis indicates that the insertion is inverted with respect to centromere. Not all insertions have been examined for meiotic bridges and fragments.

### Descriptions of Individual Identified Rearrangements

Rearrangements are listed in a single numerical sequence according to isolation number (the number that follows the parentheses in the symbol). Information is given in the following order.

**Identifying symbol**
- Genetic basis (terse description; breakpoints)
- Vegetative phenotype
Fertility of $Ab \times Ab$ crosses
$Ab \times N$ crosses:
  Percent black ascospores
  Unordered asci:
    Percent ascis of the types: 8:0, 6:2, 4:4, 2:6, 0:8 (Black:White)
    Total number of ascis (in parentheses)
Cytology
Origin: strain, mutagen, discoverer
Other information
FGSC Numbers of $A$ and $a$ stocks
References

Additional information is given on the viable duplications from duplication-producing rearrangements:

**Duplication symbol**
Origin
Vegetative phenotype and stability
Fertility in crosses $\times$ non-Duplication
Derived products if unstable
Markers shown covered
Markers shown not covered

T(III;VI)1

T(VI $\rightarrow$ IV)CJS1
Insertional translocation. VIR segment distal to $trp-2$ is inserted in IVR (near $pan-1$). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 25% black; unordered ascis 1:1:34:27:37 (N = 164). Basis of the excessive defective ascospores is not understood. Cytology: Chromosome 2 is not abnormal. No bridges or fragments observed. Origin: Spontaneous as sector in a cross of $fl^b \times$ Normal-sequence $f$, from OR wild-type $\times$ T(IV $\rightarrow$ III)$S_{4342}$. Discovery and preliminary analysis by Carol J. Smarr. Further genetic analysis by Perkins. FGSC 2676, 2677.

Duplications: $Dp(VIR \rightarrow IVR)CJS1$. Less than one-third of surviving progeny from $T \times N$. Vegetatively scant or feeble. Barren in cross by nonduplication.
Markers shown covered: None. Markers shown not covered: $ylo-1$, rib-1, $trp-2$, $trp-4$, $pan-1$.

T(V $\rightarrow$ VII)EB4
Insertional translocation. A short VR segment near $al-3$ and $his-1$ is inserted into VII, probably left of $uc$. Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 99% black; a few percent are round. Unordered ascis 53:20:25:2:0 (N = 93). Cytology: Asynapsis of 2R is common at pachynema in $T \times N$. Breakpoint is
far out in long arm of 2. Second chromosome unidentified cytologically. Origin: Detected cytologically in 1971 by Barry as a minor component of a stock of 74-OR8-1 a, which had been preserved on anhydrous silica gel since received from F. J. de Serres in 1961. Genetic analysis by Perkins. FGSC 2179, 2180. Reference: Barry et al., 1972.

Duplications: \( Dp(VR \rightarrow VII)EB4 \). One third of surviving progeny from \( T \times N \). Vegetatively normal and stable. Crosses of duplication by nonduplication are scorable as barren; however, all produce ascospores, although in much smaller numbers than euploid crosses. Of the spores produced, some are round. Markers shown covered: None. Markers shown not covered: \( at, his-1, inl, al-3, bis, pab-1, met-3, his-6 \).

**T(II;IV)D5**

Reciprocal translocation. II;IV interchange with 17% recombination between \( bal \) and \( pdx \) in \( T \times N \). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 25:3:24:9:39 (\( N = 103 \)). Origin: \( inl \) (89601), UV. Detected and analyzed by Perkins. FGSC 2393, 1554.

**T(VI;VII)ALS7**

Reciprocal translocation. VIR (right of \( trp-2 \)) interchanged with VIIR (right of \( arg-10 \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50–75% black; unordered asci 31:21:37:5:7 (\( N = 272 \)). Many 5B:3W asci; evidently one duplication-deficiency class makes inviable black ascospores. Cytology: Producesacentric chromosome fragments (Barry). Origin: \( rg \) or \( a \), UV. Detected and analyzed genetically by Perkins. No viable duplications produced. FGSC 1993, 2916.

**T(IV;VI)B8**

Reciprocal translocation. IV;VI interchange with 9% recombination between \( pdx \) and \( ylo-1 \). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 23:19:19:14:24 (\( N = 78 \)). Origin: STA, UV. Detected and analyzed by Perkins. Originated with unlinked morphological mutant. FGSC 2394, 2395.

**In(IL \(
\)→ IR)AR9f**

See **In(IL \(
\)→ IR)AR16**.

**T(II;VI)AR9r**

Reciprocal translocation. IIR (between \( arg-5 \) and \( fl \)) interchanged with VII (near \( chol-2 \)). Growth slower than wild type. Homozygous-fertile, but ascospores ooze rather than shoot from perithecia. \( T \times N \) ascospores 50% black; unordered asci 18:0:68:3:11 (\( N = 238 \)). Origin: \( pyr-1 \) \( met-1 \) a (I263, 38706), UV. Detected and analyzed by Perkins. Strain of origin also contained unlinked **In(IL \(
\)→ IR)AR9f**. FGSC 2131, 2132.

**T(IV;VII)AR10**

Reciprocal translocation. IVR (near \( cot-1 \)) interchanged with VIIR (linked \( arg-10 \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black; unordered asci 15:52:22:6:4 (\( N = 208 \)). Origin: \( pyr-1 \) \( met-1 \) a, UV. Detected and analyzed by Perkins. Apparently one duplication-deficiency class is represented.
by inviable black ascospores; at least one-third of black spores from $T \times N$ are inviable, and no viable duplications are recovered. Generates viable duplications from intercross with $T(IVR; VIIR)NM158$. FGSC 2007, 2008.

**In(IL → IR)AR11i**

See $In(IL → IR)AR16$.

**T(IV; V)AR11r**

Reciprocal translocation. IVR (proximal to pdx) interchanged with VR (distal inl). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 14:2:42:16:26 ($N = 520$). Origin: $pyr-1$ met-1 a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercrosses with $T(IVR; VR)NM126$, $NM144$, $NM145$, and $R2355$. Duplications are pdx$^+$ from $AR11r \times NM144$; therefore $AR11r$ break is proximal to pdx. Strain of origin also contained $In(IL → IR)AR11i$. FGSC 2093, 2094.

**T(I; V)AR12**

Reciprocal translocation. IL (proximal to mt) interchanged with VR (near inl). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 11:13:53:13:11 ($N = 191$). Origin: $pyr-1$ met-1 a, UV. Detected and analyzed by Perkins, Beske, and Phillips (1968) first showed linkage in I or II and IV or V. Generates viable duplications from intercrosses with $T(IL; VR)P5401$ and 47711. These have an inhibited Dark-Agar phentotype typical of A/a; therefore $AR12$ breakpoinst is proximal to mt. FGSC 2006, 1462. Reference: Perkins, 1975.

**T(I; VI)AR13**


**In(IL → IR)AR15**

See $In(IL → IR)AR16$.

**In(IL → IR)AR16**

Pericentric inversion. A distal segment of IL (including ser-3 but not wn-3 and mt) is interchanged with the IR tip. No recombinant has been obtained with mating type. Wild phenotype. $In \times N$ ascospores 80% black; unordered asci 25:54:19:1:2 ($N = 177$). Origin: $pyr-1$ met-1 a, UV. Discovered by Perkins, analyzed by Turner. $In(IL → IR)AR9i$, $AR11i$, $AR15$, $AR16$, all from the same experiment, apparently have a common origin. Breakpoints and genetic behavior resemble $In(IL → IR)NM176$. The structure is formally similar to $In(1LR)sc^r$ in *Drosophila*. FGSC 1614. Reference: Turner *et al.*, 1969.

Duplications: $Dp(IL → IR)AR16$. About one-fourth of surviving progeny from $In \times N$. Slightly abnormal morphology of aerial mycelia, resembling $Dp(IL → IR)NM176$. Barren in crosses with nonduplication; fertile normal-sequence derivatives are produced by loss of the duplicated IL segment from the translocated

T(III \rightarrow [I;II])AR17


Duplications: Dp(IIIIR \rightarrow [I;II])AR17. One-third of surviving progeny from $T \times N$. Wild phenotype, stably barren. Many perithecia produce a few spores each. A high proportion of the spores are peculiar in shape, including some oversized. Markers shown covered: dow. Markers shown not covered: tyr-1, vel, trp-1, acr-2.

T(I \rightarrow III)AR18


Duplications: Dp(IIL \rightarrow IIIIR)AR18. One-third of viable progeny from $T \times N$. Very slow, feeble growth initially after ascospore germination, which cannot be attributed to heterozygous vegetative incompatibility alleles, but appears to be an intrinsic property of this duplication. Barrenness is exceptionally stable in crosses to nonduplication. The barren perithecia, with no beaks, progress only occasionally to form a few croziers (N. B. Raju). Markers shown covered: het-6. Markers shown not covered: pi, cys-3, pyr-4, het-c, ro-3, thr-2, arg-5.

T(III,VII)AR19


T(I,V)T27M9


T(II,V)AR30

Reciprocal translocation. II (probably L, near pi) interchanged with VI (unmarked segment far left of at). Wild phenotype. Homozygous-fertile. $T \times N$
ascospores 85–90% black; blackening increases with age; unordered asci 49:30:19:2:1 (N = 177). Origin: \(rg\ cr\); \(pyr-1\ met-1\) A, UV. Detected and analyzed by Perkins. Because duplication-deficiency ascospores become black, scoring of translocation by presence of nonblack ascospores is difficult. Less than half of black ascospores are viable. No viable duplications are recovered. FGSC 2004, 2005.

\(T(V \rightarrow IV)AR33\)

Translocation, either quasiterminal or insertional. An unmarked segment of V is translocated to IVL (near \(cys-10\)). (If translocation is quasiterminal, the segment is VL.) Wild phenotype. Homozygous-fertile. \(T \times N\) ascospores 70% black or less; unordered asci 36:32:28:2:2 (N = 117). Origin: \(rg\ cr\); \(pyr-1\ met-1\) A, UV. Detected and analyzed genetically by Perkins. FGSC 2021, 2396.

_Note added in proof:_ A distal segment of the short arm of chromosome 2, which carries the nucleolus organizer, appears cytologically to be translocated to the tip of another chromosome.

Duplications: \(D_p(V \rightarrow IVL)AR33\). One-third of viable progeny from \(T \times N\). Wild morphology. Barren in crosses by nonduplication, where perithecia contain all stages of meiosis, but few or no spores (N. B. Raju). Duplications are stable and may be transmitted through crosses. Markers shown covered: None. Markers shown not covered: \(lys-1\), \(at\), \(leu-5\), \(al-3\), \(his-6\).

\(T(IV;V)T33M8\)

Reciprocal translocation. IV (loosely linked \(pdz\)) interchanged with V (loosely linked \(at\)). Wild phenotype. Homozygous-fertile. \(T \times N\) ascospores 50% black; unordered asci 14:3:48:10:24 (N = 147). Origin 74A, UV. Detected and analyzed by Perkins. FGSC 2397, 2398.

\(T(VI \rightarrow I)T39M777\)

Quasiterminal translocation. A VIL segment including \(un-4\) and distal markers is translocated to the right end of I near R. Wild phenotype. Homozygous-fertile. \(T \times N\) ascospores 75% black; unordered asci 18:46:29:5:3 (N = 114). Origin: 74A, UV. Detected and analyzed by Perkins. Used as \(het-8\) tester to study vegetative incompatibility. FGSC 2133, 2134 (\(het-8^{or}\)). References: Mylyk, 1975, 1976.

Duplications: \(D_p(VIL \rightarrow IR)T39M777\). One-third of surviving progeny from \(T \times N\). Wild phenotype, but with slowly developing diffuse patchy dark pigment on surface of lower part of minimal slant. Crosses by nonduplication are scoreable as stably barren; however, all produce some ascospores, but far fewer than euploid crosses. Made unstable by \(mei-3\) (Newmeyer and Galeazzi, 1976b). Vegetative escapes from \(het-8\) inhibition remain barren (Mylyk). Markers shown covered: \(chol-2\), \(lys-5\), \(un-4\), \(het-8\). Markers shown not covered: \(cys-1\), \(ylo-1\).

\(T(III;IV)T42M36\)

Reciprocal translocation. III (probably left of \(acr-2\)) interchanged with IV (linked \(pdz\)). Wild phenotype. Homozygous-fertile. \(T \times N\) ascospores 75% black; unordered asci 16:53:23:7:1 (N = 100). Origin: 74A, UV. Detected and analyzed by Perkins. Evidently one duplication-deficiency class becomes black. Ger-
mination of black ascospores is low. No viable duplications are recovered. FGSC 2443, 2444.

T(V; VII) AR45
Reciprocal translocation. VL (near at) interchanged with VII (probably L, between thi-3 and met-7). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 75% black; unordered asci 37:25:34:2:2 (N = 92). Origin: rg cr; pyr-1 met-1 A, UV. Detected and analyzed by Perkins. Evidently one duplication-deficiency class makes inviable black ascospores. Germination of black ascospores is low. No viable duplications are recovered. FGSC 1760, 1761.

T(II; VII) T51M143

T(I \rightarrow VI) T51M156 un
Insertional translocation. An unmarked segment of IL near mt is inserted in VIIL between chol-2 and ad-8. Both the translocation and its duplication progeny are un phenotype, unable to grow at 34°C regardless of supplement, but capable of growth with wild-type morphology on minimal at 25°C. Fertility is limited in $T \times T$ crosses, but viable progeny are produced. $T \times N$ ascospores > 75% black; unordered asci 22:33:30:12:3 (N = 366). Origin: 74A, X-rays. Detected and analyzed by Perkins. S. Brody (personal communication) has shown that the closely linked chol-2* and ad-8* functions are not impaired in the rearrangement sequence. FGSC 2270, 2271.


T(I; VI) T51M158
Probably a reciprocal translocation that undergoes frequent 3:1 segregation at anaphase I. I (near centromere, linked arg-1 and cr) interchanged with VI (near rib-1 and ylo-1). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black, or less; unordered asci 20:7:40:9:25 (N = 258). Origin 74A, X-rays. Detected and analyzed by Perkins. FGSC 2759, 2760.

Duplications: 5%–10% or more progeny from $T \times N$ are duplications that can carry I and VI markers in heterozygous condition. Markers shown covered: rib-1, pan-2, del, trp-2 (when mt not heterozygous). ylo-1 (when mt heterozygous). Markers shown not covered: ad-8, cys-1, ylo-1, ad-1 (when mt not heterozygous), del, try-2 (when mt heterozygous). Some but not all duplications are detected as barren in crosses × Normal-sequence testers. The hypothesis of origin by 3:1 segregation is consistent with (a) a higher frequency of 4B:4W asci than ex-
pected when both break points are near centromeres, and (b) shifting patterns of marker coverage, depending on which member of the translocation complex is lost.

T(I;VI)T51M166

T(I;IV)HK53 cut
Reciprocal translocation. I (near arg-1) interchanged with IVL (distal to \( \bar{f} \)). Phenotype cut (osmotic-sensitive), scorably by morphology on minimal at 34°, or by no growth on minimal + 4% sodium chloride. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asc. 55:1:6:9:37 (N = 231). D. A. Smith (unpublished) has confirmed cytologically an exchange involving chromosome 1. Origin: Strain 4A (probably Abbott 4A), UV. Described as morphological mutant by Kuwana. Translocation recognized by Perkins. Original mutant strain also contained linked gene met-1 as well as a tol-like suppressor of the heterokaryon incompatibility associated with mating type, both separable from the translocation. An allelic point mutant, cut (LLM1), maps in IVL. Kuwana's cut has not previously been numbered. It is proposed from now on to use HK53 as isolation number, for convenience and to avoid confusion with allelic cut mutations. FGSC 2272, 2068. References: Kuwana, 1953, 1960; Smith and Perkins, 1972; Smith, 1975.

T(I;VI)P54
Reciprocal translocation. IR (near al-3) interchanged with VI (near ylo-1). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asc. 25:2:62:2:9 (N = 125). Origin: Recognized by Perkins in \( \bar{f} \), from cross aur cr A (Fincham stock F945-78) \( \times \) thi-1 a. FGSC 2445, 2446.

T(I;IV)T54M19
Reciprocal translocation. IR (linked mt) interchanged with IVR (linked pdz). Flat pe-like morphology. Female-sterile, with no perithecia. \( T \times N \) ascospores 50% black; unordered asc. 26:6:39:5:24 (N = 217). Origin: 74A, UV. Detected and analyzed by Perkins. Generates viable duplications from intercross with \( T(I;IVR)NM164 \). Therefore breaks must be in right arms. FGSC 2135, 2136.

T(VII \( \rightarrow \) IV)T54M50
Quasiterminal translocation. A VIII segment including thi-3 and markers distal to it is translocated to the right end of IV. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black, or more; unordered asc. 17:32:32:8:10 (N = 220). (Interpreted to be 21:58:21:0:0.) Origin: 74A, UV. Detected and analyzed by Perkins. Used for studying vegetative incompatibility. Translocation stocks containing het-e and het-E are used as testers. FGSC 2466, 2467 (het-e); 2603, 2604 (het-E). References: Perkins, 1975; Mylyk, 1975.

Duplications: \( \text{Dp}(VIII \rightarrow IVR)T54M50 \). One-third of viable progeny from \( T \times N \). Wild phenotype unless heterozygous for het-e alleles. Duplications are

Tp(II → IR)T54M94

Duplications: $Dp(\text{IR} \to \text{IR})T54M94$. Usually one-fifth or less of surviving progeny from $T \times N$. Wild phenotype. Highly barren in crosses by nonduplication. Barren condition is exceptionally stable. Markers shown covered: nil-1, cyh-1, os-5, al-2. Markers shown not covered: cr, thi-1, met-6, arg-6, al-1, hom.

T(II;III)T54M140b
Reciprocal translocation (probably). II (near arg-5) interchanged with III (between acr-2 and thi-4). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores > 50% black; unordered asci 49:5:35:2:9 ($N = 162$). Origin: 74A, UV. Detected and analyzed by Perkins. No barren duplications are produced. Cryptic aneuploids have been obtained from several crosses. These segregated acr-2, thi-4, or bal and are thought to originate as disomics, from 3:1 segregations. Black ascospores show good viability. Stock of origin also contained another probable rearrangement, tentatively $T(I \to III)T54M150$ un; this has probably been separated, but is inadequately analyzed. FGSC 2941, 2942.

T(I;II;IV)R55
A complex translocation showing linkage in IR near lys-3, in II near pe, and in IVR. (Not tested for linkage in group V.) Wild morphology, but slower growing. Homozygous-fertile. Cytology: Chromosomes 1, 2 and 6 are involved in the translocation. Breaks in 1 and 2 near centromere with arms exchanged, and in 2 through the nucleolus organizer with the tip of the organizer translocated to the long arm of 6. Origin: pe fl, X-rays. Detected and analyzed cytologically and genetically by P. St. Lawrence. Stock now lost. Reference: St. Lawrence (1953).

Duplications: Two types of probable duplications observed, called abnormal (abn) and abnormal-sterile (abn-s). The abn type crossed by standard chromosome sequence, R55 sequence, or other abn's produced asci developing to late meiotic prophase stages, but chromosome pairing appeared to be abnormal. Few asci completed the third division, and spore formation was rare and irregular. abn-s crossed to standard was barren, with perithecial development arrested prior to ascus formation.

T(II;III)AR62
T(II;IIIR)NM161. Strain of origin also contained an unlinked ascospore-color gene bs (AR62, in IR). FGSC 1545, 1546.

T(I;II)B66

T(IV;VI)P73B12

T(I;III)P73B101

T(II;VII)P73B169

T(I;II)STL76

T(I;VII)K79 met-7

T(III;V)NM101
Reciprocal translocation. III (linked ahr-2, trp-1) interchanged with VR (linked inl). Wild phenotype. Homozygous-fertile. T x N ascospores 50% black; un-
ordered asci 31:9:44:4:13 (N = 231). Origin: Em a, UV. Detected and analyzed by Perkins. Intercrosses indicate probably identical to III;V translocations NM102, 104, 111, 112, 114, 115 isolated from the same experiment. FGSC 1879, 1880.

T(III;V)NM102
See T(III;V)NM101.

T(I → VI)NM103
Quasiterminal translocation. A segment of IR including met-6 and distal markers is translocated to the right end of VI beyond trp-2. Wild phenotype. Homozygous-fertile. T × N ascospores 75% black, or more; unordered asci 26:42:27:4:1 (N = 219). Origin: Em a. UV. Detected by Perkins. Analyzed by B. C. Turner. Used as het-5 tester to study vegetative incompatibility. FGSC 2137, 2138 (het-5<sup>98</sup>). References: Turner, 1975, 1976; Mylyk, 1975, 1976. Duplications: Dp(IR → VIR)NM103. In one-third of surviving progeny from T × N. Duplications make relatively large, diffuse colonies on sorbose medium. In tubes, duplication resembles a slow wild type at 25°C but resembles f: fluffy at 34°. Sectoring (uncovering of recessive heterozygous markers) is apparent in some backgrounds. Initially highly barren. Marked crosses give no recovery of intact duplications. However, in many crosses a few perithecia are fully fertile through loss of one duplicated segment. Either segment—that in N or in T sequence—may be lost with equal probability. Euploid derivatives are always found in plantings of such partially fertile duplications. There is no evidence of delayed fertility, which might be expected if loss were stepwise. Markers shown covered: met-6, ad-9, nit-1, cyh-1, al-2, arg-13, R, un-18, het-5. Markers shown not covered: thi-1, un-1, cr, his-3, mt, fr.

T(III;V)NM104
See T(III;V)NM101.

T(I;III)NM107

T(I;III)NM109
Reciprocal translocation. IL (between un-5 and mt) interchanged with IIIR (between acr-2 and dow). Wild phenotype. Homozygous-fertile. T × N ascospores 50% black; unordered asci 20:0:63:2:15 (N = 54). Origin: Em a, UV. Detected and analyzed by Perkins. Intersexes show not identical with T(I;III)NM107, NM127, NM136, NM148. FGSC 2627, 2628.

T(I;V)ALS111
Reciprocal translocation. IR (near cr) interchanged with VR (between al-3 and his-6). Wild phenotype. Homozygous-fertile. T × N ascospores 70% black; unordered asci 39:16:35:3:6 (N = 148). Origin: rg cr a, UV. Detected and analyzed
by Perkins. No viable duplications are produced in crosses by Normal. Frequencies
of ascus types suggest the one inviable duplication-deficiency class darkens. How-
ever, germination is good among black ascospores. Possibly white spores degen-
erate. Produces viable duplications from intercrosses with $T(I;V)_{36703}$ and
$C-1670 ~ pk-1$. FGSC 2629, 2630.

T(III;V)NM111, T(III;V)NM112
See T(III;V)NM101.

T(I → III)Y112M4i ad-3B
Insertional translocation. IR segment including nic-2 is inserted in IIIR near vel.
ad-3B phenotype: requires adenine, accumulates purple pigment. $T \times T$ crosses
infertile, perhaps because of adenine requirement. $T \times N$ ascospores 75% black;
analysis by de Serres. III linkage identified by P. St. Lawrence. Separated from
T(III;VII)Y112M4r which was also present in original strain. FGSC 2637, 2638.
Reference: de Serres, 1957. (This is the first published account of an insertional
translocation in Neurospora.)

Duplications: $Dp(IR → IIIR)$Y112M4i. One-third of surviving progeny from $T \times N$.
$ad^*$ phenotype. Highly barren in crosses by nonduplication. Markers shown

T(III;VII)Y112M4r
Reciprocal translocation. III (near aer-2) interchanged with VII (linked wc). Wild
phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci
also contained T(I → III)Y112M4i ad-3B. Extracted, mapped and analyzed by
Perkins. FGSC 2631, 2632.

T(I ↔ IV)Y112M15 ad-3A
Translocation with breakpoints at or near ad-3A in IR and near pdx in IV.
Probably an inverted insertional I → IV, with mutual IV → I insertion postulated
to explain absence of viable duplications among progeny of $T \times N$. Pheno-
type ad-3A: requires adenine and makes purple pigment. Cytology: Chromosomes 1
and 3 reported aberrant by Griffiths et al. (but see Section IV, C). Acentric
chromosome fragments are formed, which persist in micronuclei and replicate
(Barry). Origin: 74A, X-rays. Aberrant recombination noted by de Serres. Aberr-

T(IV;VII)NM113
Reciprocal translocation. IV (linked pdx) interchanged with VII (linked met-7).
Sub-wild phenotype, pale pigment. Lysis and exudate at top of agar slant. Homo-
zygous-fertile. $T \times N$ ascospores 50% black; unordered asci 31:13:20:1:34 ($N =
70$). Origin: Em a, UV. Detected and analyzed by Perkins. Interccrosses show not
identical with T(IV;VII)NM156 or NM158, which originated from a different
experiment. FGSC 1917, 1918.

T(III;V)NM114, T(III;V)NM115
See T(III;V)NM101.
T(III;IV)NM118

T(I;IV)NM119

T(VI;VII)NM124
Reciprocal translocation. VI (linked ylo-I) interchanged with VII (near met-7). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 48:3:5:1:45 ($N = 361$). Origin: Em a, UV. Detected by Perkins. Analyzed and linkages established by Anna Kruszewska. Shot asci shift with time from excess 0B:8W to exceed 8B:0W. FGSC 2214, 1472.

T(IV;V)NM125
Reciprocal translocation. IVR (linked pdx) interchanged with VR (linked at). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 13:6:41:3:36 ($N = 63$). Origin: Em a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercross by $T;IVR;VR;AR;I1r$. Arm assignments were made on this basis. FGSC 2447, 2448.

T(II;IV)NM126

T(I;III)NM127
Reciprocal translocation. I (near mt) interchanged with III (probably R; loosely linked acr-2). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 17:1:53:3:25 ($N = 217$). Origin: Em a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercross with $T(I;III)NM126$. Arm assignments are based on this fact. Intercrosses show not identical with $T(I;III)NM107$, NM109 or NM146. FGSC 2405, 2406.

T(I;IV)NM128
Reciprocal translocation. I (linked mt) interchanged with IVR (near pt). pe-like morphology. $T \times T$ crosses nearly infertile. $T \times N$ ascospores 50% black; unordered asci 50:8:25:3:15 ($N = 93$). Origin: Em a, UV. Detected and analyzed by Perkins. Not tested for identity by crosses with NM140 or other pe-like I;IV translocations from the same source.
T(I;II)NM129
Reciprocal translocation. I (near his-2, probably right) interchanged with II (near arg-5). Morphology not wild: flat growth habit. Homozygous-barren (empty perithecia). $T \times N$ ascospores 50% black; unordered asci 30:5:9:6:51 (N = 661). Origin: Em a, UV. Detected and analyzed by Perkins. Progeny from $T \times N$ include a few percent of barrens, "Dark Agar" phenotypes (attributed to A/a heterozygosity), and in some crosses "Brown-flats" (attributed to het-C/het-c). These are thought to arise from 3:1 segregations. FGSC 2330, 2331.

T(I;V)NM130
Reciprocal translocation. I (linked arg-t) interchanged with VL (26 units left of at). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores > 50% black; unordered asci 36:16:30:4:15 (N = 230). Origin: Em a, UV. Detected and analyzed by Perkins. Not overlapping with $T(IR \rightarrow VL)AR190$, because no viable duplications are recovered from intercresses. This favors IL location of NM130 break point. Evidently some duplication-deficiency ascospores darken. FGSC 2407, 2408.

T(III;IV)NM131
Reciprocal translocation. III (linked och-2) interchanged with IV (linked pdz). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 17:3:69:0:11 (N = 36). Origin: Em a, UV. Detected and analyzed by Perkins. Intercross shows not identical with T(III;IV)NM118. FGSC 2409, 2410.

T(I;IV)NM132
Reciprocal translocation. IR (right of al-2) interchanged with IV (near pdz). "Creamy" morphology. Female-sterile. $T \times N$ ascospores 50% black; unordered asci 17:10:30:10:34 (N = 95). Origin: Em a, UV. Detected and analyzed by Perkins. Not tested for identity by intercrossing with similar I;IV translocations from the same source.

T(II;VII)NM134

T(I;II)NM135

T(I;III)NM136
Reciprocal translocation. I (near mt) interchanged with III (probably R; linked trp-1). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 29:4:46:2:19 (N = 94). Origin: Em a, UV. Detected and analyzed by Perkins. Original isolate contained a linked but separable arg-3 mutation. Generates viable but morphologically distinct duplications from intercross with
T(I;III)NM137

T(I;IV)NM139 bs
Reciprocal translocation. IR (near al-2 and proximal) interchanged with IVR (near pdx and distal). Wild vegetative morphology. $T$ ascospores are brown, yet viable. Homozygous-fertile. $T \times N$ ascospores 25% black; 25% viable brown, 50% white. Unordered asci 22:0:53:0:25 ($N = 271$), when brown ascospores are counted with black. Origin: Em a, UV. Detected and analyzed by Perkins. Alloclinal and identical with $T(I;IV)NM147$ and $NM187$, both of which show the same brown-ascospore phenotype. Not allelic with IR point mutant $bs-1$; brown ascospore (AR69). Generates viable duplications from intercrosses with $T(IR;IVR)NM140$ and $NM172$. Intercross shows not structurally identical with $T(IR;IVR)NM160$. FGSC 1565, 1566.

T(I;IV)NM140

T(IV;V)NM141
Reciprocal translocation. IVR (linked pdx) interchanged VR (near al-3). "Creamy" morphology. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 16:1:64:5:14 ($N = 163$). Origin: Em a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercrosses with $T(IV;VR)AR11r$, $NM145$ and $R2355$. $NM141$ break point assigned to IVR because $R2355$ maps in IVR. FGSC 2025, 1479.

T(I;V)NM143

T(I;IV)NM144
Em a, UV. Detected by Perkins, analyzed by Perkins, Kowles. Generates viable duplications from crosses with $T^{(IR;IVR)NM169}$, $NM164$, and $NM172$. Assignment of $NM144$ to right arm of IV is thus confirmed. Intercesses infertile with $T(I;IV)NM140$, $NM197$, $T54M19$. FGSC 1336, 1335. References: Kowles, 1972, 1973.

$T(IV;V)NM145$
Reciprocal translocation. IVR (linked $pdx$) interchanged with VR (between $at$ and $inl$). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 60-75% black; unordered asci 18:50:27:3:2 ($N = 277$). Origin: Em a, UV. Detected and analyzed by Perkins. Evidently some inviable duplication-deficiency ascospores from $T \times N$ become black. Germination of black ascospores is 60-75%. No viable duplications are recovered from $T \times N$. Generates viable duplications from intercrosses with $T(IVR;VR)AR11r$, $NM141$, and $R2355$. Breakpoint assigned to IVR on this basis. FGSC 2098, 2099.

$T(I;III)NM146$
Reciprocal translocation. I (loosely linked $mt$) interchanged with III (loosely linked $acr-2$). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 15:5:62:5:13 ($N = 61$). Origin: Em a, UV. Detected and analyzed by Perkins. Intercesses show not identical with $T(I;III)NM107$, $NM109$, $NM137$, or $NM136$. FGSC 2449, 2450.

$T(I;IV)NM147$ bs
See $T(I;IV)NM139$ bs

$T(II \rightarrow V)NM149$

Duplications: $Dp(III \rightarrow VR)NM149$. One-third of surviving progeny from $T \times N$. Wild phenotype unless heterozygous for vegetative incompatibility genes. The speed of somatic escape from inhibition in $het-c/het-C$ duplications is increased by $mei-3$ (Newmeyer and Galeazzi, 1976b). After escape, individual duplications vary from highly barren to relatively fertile, when crossed by nonduplication. Markers shown covered: $ro-3$, $het-c$, $pyr-4$, $het-6$, $cys-3$, $pi$, $col-10$. Markers shown not covered: $thr-3$, $thr-3$, $arg-5$. There is evidence also for a second class of duplications that are not heterozygous for III markers. Possibly these arise by 3:1 segregation, and they may involve VR.

$T(II;III)NM150$
T(IV → I)NM152
Insertional translocation. An extensive segment of IVR, including loci from <i>pyr-3</i> through <i>pyr-2</i>, is inserted in I, ten units from <i>arg-3</i> (probably IR). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores, 75% black, or less; unordered asci 18:16:44:9:13 (N = 324). Cytology: Preliminary cytological examination. Acentric fragments are produced which become pycnotic (Barry, 1973). However, their frequency is lower than would be expected if such a long insertion were inverted. Origin: Em a, UV. Detected and analyzed by Perkins. Data on IV breakpoint obtained by A. Radford. FGSC 1752, 1753.

Duplications: <b>D</b><sub>p</sub>(<i>IVR → I</i>)<i>NM152</i>. One-third of surviving progeny from <i>T × N</i>. Wild phenotype. Duplications scorable as barren with 90% confidence. Markers shown covered: <i>pyr-3</i>, <i>trp-4</i>, <i>met-2</i>, <i>cot-1</i>, <i>pyr-2</i>. Markers shown not covered: <i>pdx-1</i>, <i>col-4</i>, <i>cys-4</i>.

T(II;V)ALS154
Reciprocal translocation. IIIR (near <i>f</i>) interchanged with VR (near <i>inl</i>). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores > 50% black; unordered asci 11:40:32:6:11 (N = 88). Origin: <i>rg cr a</i>, UV. Detected and analyzed by Perkins. Poor germination among black ascospores and asymmetrical unordered ascus distribution suggest that some duplication-deficiency ascospores become black. FGSC 2062, 2063.

T(I;VII)NM155
Reciprocal translocation. IR (near <i>aur</i>, probably proximal) interchanged with VIIR (linked <i>mo(P1163)</i> and <i>met-7</i>). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores 50% black; unordered asci 36:3:22:8:31 (N = 74). Origin: Em a, UV. Detected and analyzed by Perkins. FGSC 1877, 1878.

T(IV;VII)NM156
Reciprocal translocation. IV (linked <i>pdx</i>) interchanged with VII (probably R; linked <i>we</i> and <i>arg-10</i>). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores 50% black; unordered asci 42:7:33:7:11 (N = 272). Origin Em a, UV. Detected and analyzed by Perkins. Intercrosses show not identical with <i>T(IV;VII)NM113</i> or <i>NM153</i>. FGSC 1921, 1922.

T(V;VI)NM157
Reciprocal translocation. VR (between <i>at</i> and <i>al-3</i>) interchanged with VIR (near <i>trp-2</i>, probably distal). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores 50% black; unordered asci 19:3:46:6:26 (N = 72). Origin: Em a, UV. Detected and analyzed by Perkins. Intercross shows not identical with <i>T(VR;VI)NM162b</i>. FGSC 2648, 2649.

T(IV;VII)NM158
Reciprocal translocation. IVR (linked <i>cot-1</i>) interchanged with VIIR (near <i>arg-10</i>, probably distal). Wild phenotype. Homozygous-fertile. <i>T × N</i> ascospores > 50% black; unordered asci 37:11:35:9:9 (N = 151). Origin: Em a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercross with <i>T(IVR;VII)AR10</i>. Assignment to IVR is based on this observation. Intercross shows not identical with <i>T(IV;VII)NM156</i>. FGSC 2026, 2027.
**T(IV → VI)ALS159**

Quasiterminal translocation. All IVR markers are translocated to the right end of VI beyond *trp-2*. Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 75% black; unordered asci 33:22:32:5:8 ($N = 259$). Origin: *rg cr a*, UV. Detected and analyzed by Perkins. FGSC 2100, 2101.

Duplications: $Dp(IVR \rightarrow VIR)ALS159$. One-third of viable progeny from $T \times N$. Usually recognizable by reduced conidiation on minimal slants at 34°C or patches of hyphae without conidia. Barrenness of duplications is exceptionally stable in crosses to nonduplications. A few individual perithecia become fertile. Markers shown covered: *pyr-1, un-8, pdx, pyr-3, cot-1, cys-4, uvs-2*.

**T(V;VII)NM159**

Reciprocal translocation. V (near *at*) interchanged with VII (near *wc*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black (defective spores become brown); unordered asci 25:2:44:3:25 ($N = 88$). Origin: *Em a*, UV. Detected and analyzed by Perkins. FGSC 2411, 2412.

**T(I;IV)NM160**

Reciprocal translocation. IR (right of *nic-2*) interchanged with IVR (near *col-4*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 31:6:15:6:42 ($N = 209$). Origin: *Em a*, UV. Detected and analyzed by Perkins. Intercrosses indicate identical sequence with $T(I;IV)NM162$ and with *NM167*, which is female-sterile. Generates viable duplications from crosses with $T(IR; IVR)NM140$, *NM144*, and *NM172*. Strain of origin also contained linked but separable point mutant *phe-1* (NM160). FGSC 1338, 1337.

**T(II;III)C161 aro**


**T(II;III)NM161**

Reciprocal translocation. II (linked *arg-5*) interchanged with IIIR (linked *trp-1*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 18:4:46:7:26 ($N = 179$). Origin: *Em a*, UV. Detected by Perkins. Beske and Phillips (1968) showed I or II linked with III or VI. Further analysis by Perkins. Generates viable duplications from cross with $T(II;IIIIR)AR02$. Intercross shows not identical with $T(II;IIIIR)NM180$. FGSC 2028, 2029.

**T(I;IV)NM162**


**T(V;VI)NM162b**

Reciprocal translocation. VR (linked *inl*) interchanged with VI (linked *ylo-f*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered

T(I;VI)NM163

T(I;IV)NM164

T(I;VII)ALS167
Reciprocal translocation. I (not separated from yg or cr) interchanged with VII (near we). T × T cross infertile because of markers. T × N ascospores 50% black or more; unordered asci 58:9:6:1:27 (N = 144). Origin: yg cr a, UV. Detected and analyzed by Perkins. FGSC 2413, 2529.

T(I;IV)NM167
Structurally identical with T(I;IV)NM169, q.v. Female-sterile. FGSC 1343, 1342.

T(I;II)NM168

T(I → )NM169d

Duplications: Dp(IR → )NM169d. Stably barren in crosses by nonduplication. Markers shown covered: un-18. Markers shown not covered: arg-13, so, aro-8, R. Duplications possess the vegetative morphology characteristic of R, and this is known from other rearrangements to be recessive when a duplication is heterozygous R/R⁺.
T(III;VII)NM169r
Reciprocal translocation. IIIR (linked *leu-1 trp-l*) interchanged with VIIR (near *uc to right*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 34:4:30:1:31 (N = 143). Origin: Em a, UV. Detected and analyzed by Perkins. Original isolate also contained $T(\text{IR} \rightarrow \text{NM169d}).$ FGSC 1816, 1817. Reference: Perkins, 1974.

T(I;IV)NM170
Reciprocal translocation. I (linked *mt*) interchanged with IV (linked *cot-l*). "Creamy" morphology. Female-sterile. $T \times N$ ascospores 50% black; unordered asci 11:4:54:9:22 (N = 46). Origin: Em a, UV. Detected by Perkins. Beske and Phillips (1968) showed I or II linked with IV or V. Further analysis by Perkins. FGSC 1489.

T(V;VI)NM171

T(I;IV)NM172

T(I → VII;I;V;VII)AR173

Duplications: $Dp(\text{IR} \rightarrow \text{VII};\text{I;V;VII})\text{AR173}.$ In one-third of surviving progeny from $T \times N.$ Stably barren in crosses. Markers shown covered: *un-2* *his-2.* Markers shown not covered: *fr, nit-2, leu-3, mt, arg-1, arg-3, sn, rg, nuc-1, lys-4, met-10, his-3; lys-1, at, al-3, mo(M184), mo(M193-1).* (Data on *nuc-1*-*his-3* from R. L. Metzenberg.)

T(V;VI)AR174
Reciprocal translocation. VR (linked *inl*) interchanged with VI (linked *ylo-l*). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores > 50% black; unordered asci 9:12:53:12:14 (N = 58). Origin: 74-OR23-1A, UV. Detected and analyzed by
Perkins. Original isolate also contained linked mutant gene resulting in nonblack perithecia and ascospores. FGSC 2678, 2679.

**T(VII–IV)ALS175**

A duplication-generating translocation involving VII (linked *wc*) and IV (linked *pdx*). Either IV is the recipient or *pdx* is covered by the duplication. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores < 50% black; unordered asci 0:3:28:19:51 (\( N = 75 \)). Origin: *rg cr*, UV. Detected by Perkins and early analysis by D. A. Smith. FGSC 2931, 2932.

Duplications: *Dp(VII–IV)ALS175*. Sub-wild vegetative phenotype. Barren in crosses with nonduplication.

**T(I;V)AR175**

Reciprocal translocation. I (linked *mt*) interchanged with V (near *at*). Near-wild phenotype (bleeds high in slant). Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 39:8:13:5:34 (\( N = 165 \)). Origin 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2593, 2594.

**T(IV;VI)NM175**

Reciprocal translocation. IVR (linked *pdx*) interchanged with VIR (linked *ylo-1*). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 49:0:5:5:42 (\( N = 41 \)). Origin: Em a, UV. Detected and analyzed by Perkins. Generates viable duplications from intercross with *T(IVR;VIR)*. Arm assignments are on this basis. FGSC 2295, 2293.

**T(II \( \rightarrow \) V)ALS176**

Translocation involving IIR (between *bal* and *arg-5*) and V (linked *at*; probably L). Probably quasiterminal. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black, or less; unordered asci 24:43:28:3:2 (\( N = 126 \)). Origin: *rg cr a*, UV. Detected and analyzed by Perkins. FGSC 2414, 2415.

Duplications: *Dp(IIR \( \rightarrow \) VL)ALS176*. In one-third of viable progeny from \( T \times N \). Initially thin, transparent, slow growth. Not stably barren in crosses by nonduplication, mostly behaving like normal sequence. Markers shown covered: *arg-5*, *aro-3*, *cpt*, *arg-12*, *fl*. (Other markers, in III, may be heterozygous in disomics from 3:1 segregations, which occur with frequencies of several percent.) Markers shown not covered in simple duplications: *bal*, *pyr-4*.

**T(I;III;VI;VII)AR176**

Complex rearrangement. Linked closely to *acr-2* (III), *ylo-1* (VI), and *wc* (VII) and less closely to *mt* (I). The structural basis is not understood. Wild phenotype. Homozygous-fertile. Ascospores oozed, few shot. \( T \times N \) ascospores < 25% black; unordered asci 8:5:30:20:36 (\( N = 154 \)). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2708, 2709.

Duplications: *Dp(VII? \( \rightarrow \) VI?)AR176*. In less than one-third of surviving progeny from \( T \times N \). Duplications are recognizable by flat morphology. Very stably barren. Markers shown covered: None. Markers shown not covered: *mt*, *acr-2*, *rib-1*, *met-7*, *nt*. 
In(II → IR)NM176

Pericentric inversion. A distal segment of IL (including ser-3 but not un-3 or mt) is interchanged with the IR tip. No bona fide euploid recombinant with mating type has been obtained. Wild phenotype. \( \text{In} \times N \) ascospores 75% black, or more; unordered asci 43:43:11:1:1 (\( N = 1362 \)). Cytology: Inversion in chromosome 1 confirmed cytologically (Barry). Origin: Em a, UV. Recognized aberrant by Perkins; genetic analysis by Turner and Taylor. Generates viable duplications from intercross with \( \text{In} (\text{IL} \rightarrow \text{IR}) H_{2} 250 \), and these are A/a heterozygotes which are phenotypically inhibited Dark-Agar types. Break points and genetic behavior resemble \( \text{In} (\text{IL} \rightarrow \text{IR}) A R 18 \). The structure is formally similar to \( \text{In} (\text{IL} \rightarrow \text{IR}) s c \) in \( \text{Drosophila} \). FGSC 1613. Reference: Turner et al., 1969.

Duplications: \( \text{Dp} (\text{IL} \rightarrow \text{IR}) N M 176 \). About one-fourth of viable progeny from \( \text{In} \times N \). Phenotype nearly wild, but with characteristic growth habit of aerial hyphae. Barren in crosses with nonduplications, eventually becoming fertile by loss of one duplicated IL segment, usually but not always that in the translocated position. Occasionally, duplication may be transmitted to progeny without breakage. Instability increased by mei-3 (Newmeyer and Galeazzi, 1976b). Markers shown covered: \( f t \), \( \text{un-} 5 \), \( \text{leu-3} \), \( \text{cyt-1} \), \( \text{cyg-5} \), \( \text{ser-3} \). Markers shown not covered: \( \text{un-3} \), \( \text{mt} \), \( \text{sce} \).

T(III;V)AR177

Reciprocal translocation. III (linked acr-2) interchanged with V (near at, probably VR). Wild phenotype. Homozygous crosses produce only a few spores. \( T \times N \) ascospores \( > 50\% \) black; unordered asci 37:16:34:4:9 (\( N = 153 \)). Origin: 74-QR23-1A, UV. Detected and analyzed by Perkins. Apparently one duplication-deficiency class consists of inviable black ascospores. Germination of black ascospores is 96%. No viable duplications recovered. FGSC 2680, 2681.

T(II → I)NM177


Duplications: \( \text{Dp} (\text{II} \rightarrow \text{I}) N M 177 \). In one-third of surviving progeny from \( T \times N \). Duplications are highly stable but sectoring may occur, with loss of material usually from the inserted location (Metzenberg et al., 1974). Vegetative "escapes" are still barren. Markers shown covered: \( \text{pcon} \) (nuc-2), \( \text{pe} \), arg-12. Markers shown not covered: \( \text{aro-3} \), \( \text{aro-1} \).

T(VII → IV)ALS179

Translocation, probably quasiterminal. An unmarked distal segment of VIII is translocated to IVR near \( \text{uvs-2} \). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black; unordered asci 18:96:13:2:1 (\( N = 141 \)). Origin: cr \( \text{rq} \) a, UV. Detected and analyzed by Perkins. FGSC 2264, 2265.
Duplications: \( Dp(\text{VI}L \rightarrow \text{IVR})\text{AL}S179 \). In one-third of surviving progeny from \( T \times N \). Wild phenotype; scorable as barren. Markers shown covered: \( \text{het-e, nic-3, thi-3} \).

\( T(\text{II} \rightarrow [\text{IV};\text{V}])\text{AR}179 \)
Complex insertional translocation. A IIII segment is inserted, with break points closely linked to \( \text{pdx} \) (IV) and \( \text{at} \) (V) in \( T \times N \) crosses. Near-wild phenotype, slightly less vigorous. Homozygous-barren. Forms perithecia but no ascospor. \( T \times N \) ascospor < 50% black; unordered asci 0:5:9:34:52 (N = 65). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2595, 2596.

Note added in proof: The short arm of chromosome 2, which carries the nucleolus organizer, is clearly involved cytologically.

Duplications: \( Dp(\text{III}L \rightarrow [\text{IV};\text{V}])\text{AR}179 \). In one-third of surviving progeny from \( T \times N \). Markers may come uncovered somatically. Barren in crosses. Some are fully stable. Markers shown covered: \( \text{pyr-4, het-c, ro-3, thr-2} \). Markers shown not covered: \( \text{arg-5} \).

\( T(\text{I};\text{IV})\text{AR}180b \)
Reciprocal translocation. I (linked \( \text{mt} \)) interchanged with IVR (near \( \text{col-4} \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospor 50% black; unordered asci 42:6:29:4:19 (N = 195). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. Separated from \( T(\text{I};\text{III})\text{AR}180r \), which was present in the same isolate. FGSC 2754, 2755.

\( T(\text{I};\text{III})\text{AR}180r \)
Reciprocal translocation. IR (linked \( \text{aur} \)) interchanged with IIII (linked \( \text{trp-1} \)). Wild phenotype. \( T \times T \) crosses show reduced fertility. \( T \times N \) ascospor 50% black; unordered asci 13:0:55:4:28 (N = 127). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. Separated from \( T(\text{I};\text{IV})\text{AR}180b \), which was present in strain of origin. FGSC 2939, 2940.

\( T(\text{II};\text{V})\text{NM}180 \)
Reciprocal translocation. IIR (near \( \text{arg-12} \), to right) interchanged with VR (between \( \text{lys-1} \) and \( \text{inl} \)). Flat vegetative morphology. \( T \times T \) crosses sterile with no perithecia. \( T \times N \) ascospor 50% black; unordered asci 25:9:41:4:22 (N = 69). Origin: Em a, UV. Detected and analyzed by Perkins. FGSC 2031, 1491.

\( T(\text{II};\text{VI})\text{AR}181 \)
Reciprocal translocation. IIR (linked \( \text{bai} \) and \( \text{fl} \)) interchanged with VI (linked \( \text{ylo-1} \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospor 50% black; unordered asci 21:7:42:11:20 (N = 189). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2453, 2454.

\( T(\text{I};\text{IV})\text{NM}181 \)
Reciprocal translocation. I (linked \( \text{mt} \)) interchanged with IVR (near \( \text{cot-1} \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospor 50% black; unordered asci 37:2:35:1:24 (N = 241). Origin: Em a, UV. Detected and analyzed by Perkins. FGSC 2933, 2934.
T(I \rightarrow )ALS182

Duplication-generating rearrangement, incompletely analyzed but probably with inverted insertion. A breakpoint in IR is between \textit{thi-1} and \textit{cyh-1}. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black; unordered asci 29:37:26:4:5 (\( N = 164 \)). Cytology: Bridges and fragments observed at meiotic divisions, but abnormal chromosomes not identified. Origin: \( rg \ cr \ a \), UV. Detected and analyzed genetically by Perkins.

\textit{Note added in proof:} The IR segment of \textit{ALS182}, which includes \textit{met-6}, is translocated to the tip of VL, distal to the nucleolus organizer. Viable duplications covering \textit{nic-2}, \textit{cr}, and \textit{thi-1} are produced in crosses of \textit{ALS182} \( \times \textit{AR190} \).

Duplications: \( Dp(IR \rightarrow )ALS182 \). In one-third of viable progeny from \( T \times N \), vegetative morphology of duplications is perhaps flat initially. If barren, only fleetingly; quickly become fertile and behave as normal sequence. When gene \( R \) is heterozygous, both \( R \) and \( R^+ \) ascospores result. When \( al \) is heterozygous, it sectors vegetatively. Markers shown covered: \textit{cyh-1}, \textit{al-2}, \textit{al-1}, \textit{R}, \textit{un-18}. Markers shown not covered: \textit{thi-1}, \textit{fr}, \textit{un-5}.

T(I;VI)AR182

Reciprocal translocation. I (linked \( cr \)) interchanged with VI (linked \( ylo-1 \)). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 37:8:29:9:17 (\( N = 194 \)). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2597, 2598.

T(III;V)NM183

Reciprocal translocation. III (linked \textit{acr-2}) interchanged with V (linked \textit{at}). Wild phenotype. Homozygous barren. \( T \times N \) ascospores \( > 50 \% \) black; unordered asci 45:11:29:4:11 (\( N = 160 \)). Origin: Em a, UV. Detected and analyzed by Perkins. Intercross shows not identical with \( T(III;V)NM101 \). FGSC 2633, 2634.

T(V;VI)AR184

Reciprocal translocation. V (near \textit{at}) interchanged with VI (near \textit{ylo-1}). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 35:13:20:8:24 (\( N = 143 \)). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 2416, 2417.

T(III;VI)AR186

Reciprocal translocation. III (linked \textit{acr-2}) interchanged with VI (linked \textit{ylo-1}). Wild phenotype. (Slightly flat on synthetic cross medium.) Homozygous-fertile. \( T \times N \) ascospores \(< 75 \% \) black; unordered asci 44:12:26:6:12 (\( N = 173 \)). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. Evidently some inviable duplication-deficiency ascospores darken. FGSC 1925, 1926.

T(I;IV)NM187 bs

See \( T(I;IV)NM139 \) bs.

T(I \rightarrow V)AR190

Quasiterminal translocation. Nearly the entire long arm of I, with all known IR markers except \textit{un-2}, is attached 35 units left of centromere in V. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 75% black or more; unordered asci 32:29:
31:5:3 (N = 211). Cytology: Break point in chromosome 1 at a or b chromomere, and in 2 in satellite distal to the nucleolus organizer. For pachytene cytology see Fig. 3 in Barry and Perkins (1969). Origin: 74-OR23-1A, UV. Detected and analyzed genetically by Perkins. FGSC 1951, 1952. References: Barry and Perkins, 1969; D. E. A. Catcheside, 1969.

Duplications: \( Dp(\text{IR} \rightarrow \text{VL})\) AR190. One-third of viable progeny from \( T \times N \). Duplications grow slowly after germination from ascospores. Somatic sectoring is often seen when albino is heterozygous. Duplications break down somatically and premeiotically to give normal sequence by complete loss of the IR segment from the translocation sequence. Barrenness is transient, making duplications difficult to score. The duplication is not transmitted to progeny. D. E. A. Catcheside has used AR190 to test complementation among albino mutants. Markers shown covered: his-2, nuc-1, me-10, ad-3A, nis-2, cr, c-yh-1, al-2, al-1, R. Markers shown not covered: un-2, sn, arg-1, mt. (Information on nuc-1 from R. L. Metzenberg.)

T(I;IV) AR193


T(I;V) AR207

Reciprocal translocation. IVR (linked pan-1, cot-1) interchanged with VI (near ylo-1). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black (variable); unordered asci 40:9:18:8:24 (N = 312). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. FGSC 1927, 1928.

T(I;III) AR208


T(VI \rightarrow IV) AR209


Duplications: \( Dp(\text{VIR} \rightarrow \text{IVR})\) AR209. In one-third of surviving progeny from \( T \times N \). Wild phenotype. Not detectably barren in crosses to non-duplication; duplications behave like fertile normal sequence, apparently by rapid loss of segment in T sequence. Markers shown covered: pan-2, trp-2, het-9, probably rib-1. Markers shown not covered: chol-2, lys-5, ylo-1, ad-1.
T(III;IV)AR211

T(I;IV)AR212

T(I;II)AR216
Reciprocal translocation. IR (proximal to ab-2) interchanged with II (between pvr-4 and bal). Wild phenotype. Homozygous-fertile. T × N ascospores > 50% black; unordered asci 44:8:16:0:32 (N = 262). Origin: 74-OR23-1A, UV. Detected and analyzed by Perkins. Original isolate also contained a linked but separable albino mutant. FGSC 1950, 1607.

T(I → ;II;VII)AR217
Complex insertional translocation. A central segment of IR, including ad-9 and nic-1, is inserted elsewhere. Other breakpoints are in II (near arg-5) and VII (near wc). Wild phenotype. Homozygous-barren. T × N ascospores 50% black or more; unordered asci 46:10:13:5:27 (N = 166). Origin: 74-OR23-1A, UV. Detected and analyzed genetically by Perkins. FGSC 2418.

Duplications: Dp(IR → ;II;VII)AR217. In one-third of surviving progeny from T × N. Slow to conidiate, pale pigment. Partially barren, with few ascospores shot from perithecia. Markers shown covered. ad-9, cyh-1, al-1, nic-1. Markers shown not covered: his-2, cr, os-1.

T(IV;V)AR221

T(I,VI)Y234M419

T(II;IV)Y256M230
Reciprocal translocation. II (near arg-5) interchanged with IV (near col-4). Wild phenotype. Homozygous-fertile. T × N ascospores 50% black; unordered asci

T(I;IV)D304

T(III → ;III;VI)D305

Duplications: Dp(IIR → )D305. From T × N. Slow or fluffy-like morphology. Variable fertility. Semibarren. Identification difficult, frequency uncertain. 3:1 segregations are not excluded as the cause of some duplications. Markers shown covered: phe-2, tyr-1, dow, het-7; vel (?) Markers shown not covered: acr-2, thi-2, trp-1.

T(IV → I)B362i

Duplications: Dp(IV → I)B362i. In one third of viable progeny from T × N. Stably barren. Markers shown covered: None (only pdx tested). Markers shown not covered: pdx.

T(II;VI)B362r

T(IV;VI)STL384b
Reciprocal translocation. IVR (near col-4 and to right) interchanged with VIIR (near sk). Wild phenotype. T × T sterile with no perithecia. T × N ascospores 75% black; unordered asci 23:42:28:4:3 (N = 803). Evidently one duplication-
deficiency class makes inviable black ascospores. Germination among black ascospores is low. No viable duplications. Origin: Detected by P. St. Lawrence in a single aberrant peritheium from a cross $mi-1$ 384a $\varphi$ (maternal inheritance) $\times$ 74-OR23-1A $\delta$. Ascus of origin also contained linked but separable T(V;VI) STL384r. Rearrangements resolved and mapped by Perkins. FGSC 2421, 2422.

**T(V;VI)STL384r**

Reciprocal translocation. IVR (near cot-1) interchanged with VI (linked ylo-1). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 25:6:53:4:12 ($N = 362$). Origin: Detected by P. St. Lawrence in a single aberrant peritheium from a cross $mi-1$ 384a $\varphi$ (maternal inheritance) $\times$ 74-OR23-1A $\delta$. Ascus of origin also contained T(V;VII)STL384b. Rearrangements resolved and mapped by Perkins. FGSC 2419, 2420.

**T(V;VI)A420**


**T(I;VII)TM429 his-3**

Reciprocal translocation. IR (at his-3) interchanged with VII (near met-7). Phenotype his-3; all three activities are missing. Wild morphology. Homozygous-fertile. $T \times N$ ascospores 50% black, or more; unordered asci 30:9:23:7:31 ($N = 627$). Origin: 429 cot-1 a, UV. Translocation identified and his-3 association shown by Angel. VII breakpoint mapped by Perkins. Inviable duplication-deficiency spores darken with aging. FGSC 2530, 2531. References: Angel et al., 1970; Angel, 1971; Catcheside and Angel, 1974.

**T(I;V)P649**

Reciprocal translocation. IR (near aur) interchanged with VI (near ylo-1). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 33:3:50:5:10 ($N = 224$). Origin: Spontaneous in backcross of cr thi-1 nit-1 aur nic-1 os-1 a $\times$ STA4. Detected and analyzed by Perkins. Generates viable duplications from intercross with T(IR;VI)AR13. FGSC 1608, 1609.

**T(I;VII)S1007**


**T(III;V;VII)P1156**

Complex interchange. Break points near lev-1 (IIIR), al-3 (VR), thi-3 (VIII). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores <50% black; unordered

Duplications: About one-fifth of progeny from T × N are stably barren. Their constitution is not understood. Failure to obtain consistent marker ratios among barrens suggests origin by nondisjunction (3:1 segregations).

T(IV → VII;I;II;IV)S1229 arg pe
Complex translocation. Interchange points in IL (near arg-3 and mt); in IIR at pe; in IVR, with markers between pdz and pyr-3 inserted in VII near thi-3. Arms of groups I, II, and IV translocated in progressive interchange. Inseparable from pe, which was present in the stock of origin, and from requirement for arginine, citrulline, or ornithine, which arose simultaneously with the aberration. Homozygous-barren. A few ascospores are produced, however. T × N ascospores 40% black; unordered asci 24:2:27:10:36 (N = 704). Cytology: Initial cytological examination (1960) found chromosomes 1, 2, 6, and 7 aberrant. However, chromosome 2 was later shown not to be involved (1969). Origin: pe fl Y8743-21-(13-7)a, X-rays. Identified as aberrant by Barratt and Garnjobst. Genetic and cytological analysis by Barry. FGSC 2946, 268. References: Barratt et al., 1954; Barry, 1960a,b; Barry and Perkins, 1969.

Duplications: Dp(IVR → VII)S1229. One third of viable progeny from T × N. Wild, but grows at slower rate. Crosses with either duplication or non-duplication strains are almost barren, producing very few spores. Duplications are stable through crosses, and segregate 1:1 in progeny from Dp × N. Markers shown covered: pt, met-1, cys(ozD'), col-4, arg-2. Markers shown not covered: pyr-1, pdz, pyr-3, his-5, trp-4, pan-1, cot-1, met-5, his-4, pyr-2. (FGSC 264, 265 are S1229 Duplications.)

T(I ↔ V)S1325 nic-2
Insertional translocation. A long central segment of IR is inserted in inverted order into VR between his-1 and inl. No viable duplications are produced; thus a short mutual VR → IR insertion is postulated. The rearrangement is inseparable from the nic-2 phenotype with which it arose. Wild morphology. Homozygous-fertile. T × N ascospores 50% black or less; unordered asci 5:0:71:3:21 (N = 223). Cytology: Singleton observed acentric chromosome fragments and dicentric bridges in the meiotic divisions in the ascus and concluded a paraacentric inversion was present, thus confirming St. Lawrence's genetic interpretation of an inversion in linkage group IR. Further genetic and cytological investigation by N. E. Murray, Perkins, and Barry showed the aberration to be actually an inverted insertion of a long segment from IR (chromosome 1) into VR (chromosome 2). The acentric fragments persist in micronuclei and replicate. Origin: pe fl Y8743-21(13-7)a, X-rays. Detected and I involvement analyzed by St. Lawrence. V involvement shown by Perkins and Murray following evidence of Newmeyer that another chromosome was involved. The inserted segment includes thi-1, met-6, ad-6, al-2, and al-1. FGSC 1558, 1557. References: St. Lawrence and Singleton, 1963; Murray, 1968a; Barry and Perkins, 1969; Barry, 1973.

T(I,V)C-1670 pk-1
Reciprocal translocation. IR (near centromere) interchanged with VR (at bis). Phenotype pk-1 (peak-1) morphology (allele of bis). Homozygous-fertile. T ×

**T(I;VII)P1676**


**T(V;VI)JH2003**

Reciprocal translocation. V (linked $at$) interchanged with VI (near $\gamma$lo-$I$). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores \(> 50\%\) black (probably because some defective white spores disintegrate); unordered asci $53:11:16:3:16$ ($N = 220$). Origin: Detected by Perkins in $\text{nit}(JH2003)$ (Silver and McElroy, 1954), which was obtained by FGSC from J. R. S. Fincham. Freed of $\text{nit}$ mutation. FGSC 2423, 2424.

**T(IV;V)R2355**


**T(II $\rightarrow$ IV)R2394**


Duplications: $Dp(\text{II} \rightarrow \text{IV})\text{R2394}$, present in one third of viable progeny from $T \times N$. Barren. Markers shown covered: None. Markers shown not covered: $\text{bal}$, $\text{pyr-4}$, $\text{fl}$.

**T(→ I)R2472 arg**

Duplication-generating translocation. A segment of unknown constitution is translocated to I (linked $mt$). Flat vegetative growth; not separated from a requirement for arginine or aspartate or asparagine. Not homzygous-fertile. $T \times N$ ascospores \(< 50\%\) black; unordered asci $4:30:23:26:17$ ($N = 100$). Origin: $\text{int}$ (89601), UV. Recognized aberrant by Garnjobst and Tatum (1967). Preliminary analysis by Perkins.

Duplications: $Dp(\rightarrow \text{II}L)\text{R2472}$, present in one-third of viable progeny from $T \times N$. Barren in crosses with nonduplication.
T(I;III)P2648
Reciprocal translocation. IR (proximal to aur) interchanged with III (linked trp-1). Wild phenotype. Homozygous-fertile. $T \times N$ ascospores 50% black; unordered asci 18:3:59:4:16 ($N = 192$). Origin: Found in a single $t$, from 74-OR23-1 A × arg-12 a. Beske and Phillips (1968) showed I or II and III or VI. Further analysis by Perkins. FGSC 1492, 2032.

T(II → VI)P2869


T(I;III)3717 vis
Reciprocal translocation. I (probably R) interchanged with IIIIR (near trp-1). Aconidial flat morphology, called vis (visible) and mapped in I by Houllahan et al. (1949). Homozygous-sterile with no perithecia. $T \times N$ ascospores 50% black; unordered asci 24:0:54:3:20 ($N = 119$). Origin: LA × La, X-rays. Aberration recognized and analyzed by Perkins. FGSC 2632, 2683.

In(II → IR)H4250

Duplications: $Dp(II \rightarrow IR)H4250$. About one-fourth of viable progeny from In × N (range 15–35%). Usually growth is drastically inhibited because of A/a heterozygosity, with spidery morphology and brown pigment; this "Dark Agar" phenotype is suppressed by the gene tol (Newmeyer, 1970). Duplications with tol are nearly wild, but with subtle "square" morphology. The speed of somatic escape from inhibition is increased by uvs-3 and mei-3. Duplications homozygous for mt alleles result occasionally from meiotic crossing over; these are not inhibited, but are subtly different from wild type in morphology, and
usually recognizable on this basis. Barren in crosses with non-duplications, eventually becoming fertile through loss of one duplicated II segment, usually that in the translocated position. Barren instability increased by mei-3 and by factor(s) from wild strain Adiopodoumé A (Newmeyer and Galeazzi). Markers shown covered: fr, un-5, nit-2, lev-3, cyt-1, ser-3, un-3, mt, la, acr-3, suc. Markers shown not covered: phe-1, sor, ad-5, eth-1, arg-3, un-2, mei-3, sn, rg, his-2, lys-4, R.

T(IV \rightarrow III)S4342

Insertional translocation. A long IVR segment distal to arg-2 and including markers pyr-3 through uvs-2 is inserted into IIIR proximal to ro-2, in inverted order. Wild phenotype. Homozygous-fertile. T × N ascospores 75% black, or less; unordered asci 15:47:28:6:3 (N = 467). Cytology: Chromosome 4 probably aberrant. About 50% of asci have bridges. Acentric fragments are frequent and persist in micronuclei but do not replicate as do fragments from some other insertional translocations. Origina: pe f/ Y8743-21(13-7)a, repeated X-rays (Colburn and Tatum, 1965). Translocation detected and analyzed by Perkins. Attempts to insert markers into the translocated segment have been unsuccessful. Strain of origin contained linked but separable mutation pt (S4342). FGSC 2064, 2065. Reference: Barry, 1973.

Duplications: Dp(IVR \rightarrow IIIR)S4342. In one-third of surviving progeny from T × N. Lighter growth than wild type at 2 cays, and tend to have yellowish aerial growth. Barrenness is exceptionally stable in crosses to non-duplications; perithecia have no beaks or ascospores. Markers shown covered: pyr-3, rib-2, trp-4, lev-2, pan-1, cot-1, his-4, cys-4, uvs-2. Markers shown not covered: pyr-1, pt, cys(oxD³), col-4, arg-2.

T(I \rightarrow III)4540 nic-2

Insertional translocation. A short segment of IR extending from nic-2 through cr is inserted between vel and tyr-1 in IIIR. Rearrangement inseparable from the nic-2 phenotype with which it arose. Wild morphology. Homozygous-fertile. T × N ascospores 75% black; unordered asci 16:64:18:1:1 (N = 275). Cytology: Preliminary cytological examination by St. Lawrence and by Barry, but chromosomes involved were not identified. Origin: LA × La, X-rays. Detected and analyzed by St. Lawrence. FGSC 766, 767. References: St. Lawrence, 1953, 1959.

Duplications: Dp(IR \rightarrow IIIR)4540. One-third of viable progeny from T × N. Duplications are nic⁺. Barren in crosses of duplication by non-duplication, where perithecial development is arrested prior to ascus development (P. St. Lawrence, unpublished observations, 1957). Markers shown covered: cr, cys-9, un-1. Markers shown not covered: thi-1, al-2.

T(1;II)4637 al-1

Reciprocal translocation. IR (at al-1) interchanged with IIIR (near pe). Phenotype al-1 (carotenoid deficient). Wild morphology. T × T perithecia are barren, but produce some ascospores which are viable but commonly malformed. T × N ascospores 50% black; unordered asci 20:1:63:2:14 (N = 237). Cytology: Reciprocal translocation confirmed. Break points, identified by McClintock, are far out in the long arm of chromosome 1, and near centromere in 6. Origin: LA × La, X-rays. Linkages determined by Houlaian et al. (1949), Hagerty (1952), and
Generates viable duplications from intercross with T(I; II)STL76, q.v. A component of alcoy linkage tester. FGSC 253, 252. References: McClintock, 1945, 1955; Singleton, 1948; St. Lawrence, 1953; Barry, 1967; Perkins et al., 1969.


Reciprocal translocation. IR (linked mt) interchanged with VR (distal to al-3). Wild phenotype. Homozygous-fertile. T × N ascospores 70% black; unordered asci 23:2:70:2:3 (N = 230). Origin: Detected by Perkins in cross of T(I → IV)T51M186 un A × intl; gyo-1; nt a. Generates viable duplications from intercross with T(IR;VR)NM143. IR arm assignment made on this basis. FGSC 2185, 2186.

Reciprocal translocation. IL (near mt) interchanged with IIL (distal to ro-3). Wild phenotype. Homozygous-fertile. T × N ascospores < 50% black; unordered asci 18:13:30:8:32 (N = 368). Origin: Found in a leu-t trp-1 a stock, and analyzed by Perkins. Barren progeny were produced in cross of original T × N, but not in subsequent crosses using extracted translocation. FGSC 2455, 2456.

Reciprocal translocation. IL (near un-5, proximal) interchanged with VR (near al-3). Wild phenotype. Homozygous-fertile. T × N ascospores 50% black with defective spores darkening with age; unordered asci 20:2:60:5:12 (N = 129). Origin: Found in a stock of his-4 (C141, FGSC No. 78), and analyzed by Perkins. Generates viable duplications from intercrosses with T(IL;VR)AR19 and 47711. These have an inhibited Dark Agar phenotype typical of A/a heterozygotes. FGSC 2427, 2428. Reference: Perkins, 1975.


Duplications: Dp(VIIR → IL)5936. One third of viable progeny from T × N. Normal vegetative morphology. Duplications are barren and highly stable in
crosses. Markers shown covered: arg-10, nt, sk, het-10. Markers shown not covered: wc, for.

T(III;VI)P6070
Reciprocal translocation. IIR (near tyr-1) interchanged with VI (near ylo-1). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 12:3:60:5:20 (\( N = 192 \)). Origin: Spontaneous, found in one segregant from his-2 un-2 A \( \times \) met-7 a. Detected and analyzed by Perkins. FGSC 2601, 2602.

T(VI \rightarrow [I;III])Y16329
Complex translocation, probably insertion. Breakpoints in I (near ml), IIR (near trp-1), and VII (between lys-5 and cys-1). A segment of VII including chol-2 and lys-5 is translocated to another interstitial or quasiterminal position. Vegetative growth sub-wild, with pale pigmentation and conidia in flecks. Female-sterile. No perithecia from \( T \times T \) crosses. \( T \times N \) ascospores <50% black; unordered asci 6:1:35:25:29 (\( N = 996 \)). Origin: col-1; pe; al-2 \( Y \)8743-6A, X-rays (Tatum et al., 1950). Rearrangement detected and analyzed by Perkins. Strain of origin contained linked but separable mutation phe-2 (Y16329). FGSC 2710, 2711.

Duplications: \( D_p(VII \rightarrow [I;IIR])Y16329 \). In one-third of surviving progeny from \( T \times N \). Wild phenotype, vigorous. Grow better than the parental translocation. Stably barren. Markers shown covered: chol-2, lys-5. Markers shown not covered: cys-1, ylo-1, trp-2.

T(I;VII)17084 thi-1

T(I;V)36703
Reciprocal translocation. IR (proximal to avr) interchanged with VR (proximal to bis). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 16:1:67:2:14 (\( N = 245 \)). Cytology: Chromosome 2 involvement (Phillips). Reciprocal translocation between chromosomes 1 and 2 determined by examination of pachytene chromosomes (Barry). Origin: 1A \( \times \) 25a, UV. I;V linkage detected by A. M. Srb. Generates viable duplications when intercrossed with \( T(IR;VR)ALS111 \), and C-1670 pk-1. Strain of origin contained linked mutant \( arg-1 \) (36703), and possibly also unlinked \( T(I;III)36703b \), q.v. FGSC 1445, 1446. References: Singleton, 1948; Phillips, 1967; Barry and Perkins, 1969; Perkins, 1971a.

T(II;III)36703b
Reciprocal translocation. II (near arg-5) interchanged with III (near acr-2). Arms not determined. Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 32:2:2:8:9:9:30 (\( N = 222 \)). Cytology: This may be the 36703 translocation examined by Singleton; see Barry and Perkins (1969) for discussion. Origin: Uncertain. May have been present with \( T(I;V)36703 \) in strain 36703.
lineage (UV), or may have arisen anew in a cross of 36703-5-9a×aur; bis A. Genetic analysis by Perkins. FGSC 1552, 1553. References: Singleton, 1948; Barry and Perkins, 1969.

T(I → II)39311


Duplications. \( Dp(IL → IIR)39311 \). One-third of viable progeny from \( T \times N \). Wild morphology. Barren in crosses. Duplications are usually drastically inhibited because of A/a heterozygozity, with restricted spidery morphology and dark brown pigment on complete medium; this "Dark Agar" phenotype is suppressed by the gene tol (Newmeyer, 1970). Duplications with tol are nearly wild, but slow-growing with subtle "square" morphology. The speed of somatic escape from inhibition is increased by wus-3. Markers shown covered: nit-2, leu-3, cys-1, ser-3, un-3, mt, suc, phe-1, arg-1, eth-1, arg-3, mei-3. Markers shown not covered: fr, un-5, sn, rg, un-2, his-2.

44105 thr-1

Probably not aberrant. McClintock (1945) examined this strain, regarded as showing genetic evidence of an aberration. Her cytological observations were inconclusive. Subsequent attempts have failed to show abnormal recombination of markers in VII, pseudolinkage of thr-1 with markers in other linkage groups, or other evidence of a rearrangement. References: McClintock, 1945; Singleton, 1948; Perkins et al., 1962.

T(IV;VI)45502

Reciprocal translocation. IVR (near pyr-3) interchanged with VIR (distal to trp-2). Wild phenotype. Homozygous-fertile. \( T \times N \) ascospores 50% black; unordered asci 21:2:56:0:20 (N = 225). Cytology: Cytological information conflicting. Examined by McClintock, Singleton, and Barry. For discussion see Section IV, C. Origin: Abb 4A×25a, UV. Strain of origin also contained closely linked point mutant pyr-3 (45502); IV;VI linkage of pyr-3 was reported by Houlihan et al. (1949). Generates viable duplications from intercross with \( T(IVR;VIR) \) NM175. FGSC 1067, 1876. References: McClintock, 1945, 1955; Singleton, 1948; Mitchell et al., 1952; St. Lawrence, 1953; Perkins et al., 1962; Murray, 1968a; Barry and Perkins, 1969; Perkins, 1974.

T(V;VI)46802 inl

Reciprocal translocation. VR (at inl) interchanged with VII (between chol-2 and ad-8). Phenotype inl (inositol requiring). Nonrevertible, even with mutagens (Giles, 1951). Wild morphology. Homozygous-fertile. \( T \times N \) ascospores 50% black;

T(I;V)47711
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