Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

Edited by James F. Crow and William F. Dove

Meiosis as an "M" Thing: Twenty-Five Years of Meiotic Mutants in Drosophila

R. Scott Hawley

Department of Genetics, University of California, Davis, California 95616

FIVE years ago, at the Annual Drosophila Conference in New Orleans, talks on Drosophila meiosis were squeezed into a session entitled *Muscles, Meiosis and Morphogenesis* (in other words, meiosis as an "M" thing; hence, the title of this piece). Although that session represented perhaps the nadir of interest in meiotic phenomena by Drosophila workers (there were simply too many more interesting slides of zebra-striped embryos to watch), the field has significantly regained its momentum in the ensuing years. Papers on meiosis in flies are now common in major journals and the number of labs working on meiosis seems to increase each year. Perhaps now, as the field matures, it is worth looking back at the publication that continues to guide work on the genetic analysis of meiosis in Drosophila.

This month marks the 25th anniversary of the publication of SANDLER, LINDSLEY, NICOLETTI and TRIPPA (1968), the paper that has served as a cornerstone of the genetic analysis of meiosis in *Drosophila melanogaster*. What follows is an appreciation of that paper and also of its intellectual companion, BAKER and CARPENTER (1972). It is not intended to be a review of the genetic study of meiosis in Drosophila (I have done that elsewhere: HAWLEY and THEURKAUF 1993 and HAWLEY, MCKIM and ARBEL 1993), but rather an attempt to put SANDLER *et al.* (1968) and BAKER and CARPENTER (1972) into perspective as truly fundamental works. My comments are based on the works themselves, a series of oral histories of varying reliability, and a yellowed copy of DAN LINDSLEY's application for the sabbatical funding that supported this study.

SANDLER *et al.* (1968) as a classic paper: In a parochial sense, SANDLER *et al.* (1968) remains the standard for the mutational analysis of meiosis in Drosophila; it served as the first report of a direct screen for meiotic mutations in flies and it established the standards by which future mutations would be characterized. In a more general sense, the paper represents one of the first heralds of modern genetic analysis in higher eukaryotes; it reframed the process by which genetics in Drosophila was done.

As noted by B. S. BAKER, SANDLER *et al.* (1968) is one of the earliest examples of a *systematic* search for, and study of, mutations affecting a complex regulatory process in higher eukaryotes. To the best of my knowledge, the only precedents for this systematic mutational approach in higher eukaryotes were the screens for early embryonic lethals at the *t* locus performed by SALOME WAELSCH and her colleagues in the mouse and the studies of mutations at the *bithorax* complex by ED LEWIS.

Those notable exceptions aside, much of the prior work in this century had focused on the analysis of mutations encountered by chance. Moreover, in many cases the focus was centered more on the nature of the mutants and the mutational processes themselves than on the biological function of the wild-type gene and the role of genes in regulatory hierarchies.

This was certainly true of the genetic analysis of meiosis. Although STURTEVANT, DOBZHANSKY, NOVITSKI, GRELL, SANDLER and LINDSLEY had certainly conducted detailed studies of the meiotic behavior of existing chromosome aberrations, there were very few data on mutations that affected meiosis in Drosophila. Indeed, there were only three recessive mutations known to affect the meiotic process (*c(3)G*, *cand* and *eq*). Although each of these mutations had been studied in detail, all of those studies were based on the analysis of single alleles. Moreover, there is no published evidence of an attempt to determine whether or not these mutations were true null alleles.

Certainly there had been no systematic approach to

identify other, perhaps equally important genes in the meiotic process. To quote from the grant proposal that funded this work, "The existence of these three autosomal recessive mutations that profoundly affect meiosis, which were encountered purely by chance, encourages one to suspect that a systematic search for meiotic genes might prove fruitful."

How the screen for new meiotic mutants was done: The mutations were recovered from wild populations collected in and around Rome at such locales as a winery in Salaria and the city's wholesale fruit market. LARRY SANDLER claimed for years that the collections were made entirely by DAN LINDSLEY while LARRY conversed with the vintners or the fruit merchants. (Having been LARRY's student, I have no reason to doubt this description of the division of labor). In a story that, until recently, I had always viewed as too apocryphal to be repeated in print, LARRY also claimed that while the fruit sellers were initially suspicious of DAN and his butterfly net, they were reassured by LARRY's claims, in the vernacular, that this was the only therapy that DAN's physicians at the asylum found effective. DAN did not speak Italian and was thus fortunately unaware of these conversations.

The decision to search for meiotic mutations in natural populations was based on the assumption that recessive mutations would be found as heterozygotes in natural populations at a frequency equal to the square root of their mutation rate, a frequency high enough to be detected in screens. To quote from LINDSLEY's grant application, "In ordinary ranges of mutation rates this should lead to an incidence of such mutations in nature in excess of that obtainable with most mutagens." Given that EMS would not be introduced to Drosophila geneticists until 1968, this frequency of mutations seemed greatly in excess of what could be obtained with existing mutagens such as γ- or X-rays. Moreover, a screen of wild populations seemed desirable because in addition to providing the desired mutations, it would also provide information on the types and prevalence of such mutations in natural populations.

The basic scheme was straightforward. Using a *2-3* translocation and crossover-suppressing marker chromosomes, lethal-free second and third chromosome complements would be extracted from several natural populations in Italy, and homozygotes for these *2-3* complements would be tested for their effects on segregation in both males and females and on recombination in females. Indeed, a significant number of meiotic mutants were recovered; of the 118 *2-3* complements tested in females, 11 significantly increased the rate of nondisjunction. Some 123 such *2-3* complements were tested in males, along with 177 half-complements (either *2* or *3*), and of these, four had strong effects on segregation. In addition a new *Segregation Distorter* chromosome was found.

As successful as these screens were, it is reasonable to ask why SANDLER and LINDSLEY felt the need to do them in Rome (as opposed to their home institutions in Seattle and San Diego). LINDSLEY's grant application presents two justifications for this decision. First, "If the incidence of autosomal recessive lethals in North America can be considered general, then southern populations might be expected to have more mutations than northern ones." Given that Rome is well north of San Diego, this rationale only makes sense if one is already committed to a European sabbatical. I find more truth in his second justification, "As an investigator demonstrates competence in his chosen field, the demands for him to devote his efforts to nonresearch efforts become incessant. This is especially true as long as he is at his home institution." (It might help us to consider the significance of this statement during the next 10 or so committee meetings.)

The recovered mutations: As stated above, SANDLER *et al.* (1968) recovered 15 mutations that affected disjunction in one or both sexes. Of these, only one, *mei-S332*, affected disjunction in both sexes; the remainder affected only females (11) or males (3). Two of these mutations, both of which specifically affect the disjunction of chromosome *4*, proved to be allelic and to define the *mei-S8* locus. Of the mutations affecting female meiosis, the most notable are *mei-S282* and *mei-S51*, both of which are described below.

As important as these mutations have subsequently proven to be, an equal or perhaps even greater yield was produced by the screen of EMS-treated *X* chromosomes performed by B. S. BAKER and A. T. C. CARPENTER who were, at that time, graduate students in LARRY SANDLER's laboratory (BAKER and CARPENTER 1972). This screen of 209 EMS-treated *X* chromosomes yielded a set of meiotic mutations whose study has supported much of the last 20 years of work on meiosis in Drosophila. These include *mei-9*, *mei-41*, *mei-218*, *mei-352* and *nod*.

There also appear to have been at least two small screens of EMS-treated autosomes in the SANDLER lab, one of which is reported in SANDLER (1971). Although these screens examined a very limited number of chromosomes, 35 in the first instance and 24 in the second, they yielded a number of very important mutations, namely *c(3)G68*, *pal*, *mei-W68* and *ord*. These mutations, as well those produced in the two screens described above, were to provide research materials for generations of students in LARRY's laboratory (cf. BAKER 1975; HALL 1972; PARRY 1973).

What did these mutations tell us? There was more at issue in this search than simply finding the mutations. At the time this work was initiated, the existing cytogenetic work had begun to lead to some rather

specific models of meiotic processes in Drosophila.

For example, it was widely accepted at that time that there were two systems for ensuring segregation in Drosophila females: a chiasmate system, and the so-called distributive system (GRELL 1976) that guaranteed the segregation of homologous or heterologous achiasmate chromosomes. According to GRELL, the choice of partners in the distributive system was determined not by homology, but rather in a manner that was determined by the availability, size and shape of these chromosomes. Buried in LINDSLEY's grant proposal, and thus presumably in the intent of the authors, is a direct test of that hypothesis. To quote again from the proposal, "If indeed there are two distinct pairing processes that obey different rules, then there should be different though probably overlapping, constellations of genes that control these phenomena."

Indeed, two mutations serving exactly this function, *nod* and *mei-S51*, were found in the course of these initial screens. The *mei-S51* mutation was found in the screen of natural populations reported in the SANDLER *et al.* (1968) paper. The *nod* mutation was found in the parallel screen of EMS-treated chromosomes by BAKER and CARPENTER (1972). Studies of *nod* would indeed confirm that the process of achiasmate disjunction was truly separate from that which ensured chiasmate segregation (CARPENTER 1973). Moreover, in a manner not appreciated for almost two decades, the study of *mei-S51* by L. G. ROBBINS would provide the first evidence that there was not one but rather two separate processes of achiasmate segregation in females (ROBBINS 1971; HAWLEY *et al.* 1993).

The work reported in SANDLER *et al.* (1968) also revealed that, although the control of meiosis I appears to be quite different between males and females, the processes that ensure sister chromatid adhesion and segregation at meiosis II appear to be under common control in the two sexes. This is exemplified by the *mei-S332* mutation, first reported in this paper, which affects the control of sister chromatid separation in both sexes. A second mutation, *ord*, which also affects sister chromatid cohesion in both sexes, was recovered in a separate screen of 24 EMS-treated second chromosomes performed by JIM MASON (1976) as a graduate student in LARRY SANDLER's laboratory. Work on both *mei-S332* and *ord* was continued by L. S. B. GOLDSTEIN (1980) and the loci are now under intensive study in the lab of T. ORR-WEAVER (KERREBROCK *et al.* 1992; MIYAZAKI and ORR-WEAVER 1992).

Finally, the phenotypes of several of the male meiotic mutations suggested the existence of at least some chromosome-specific functions acting during male meiosis. Most notably, the two alleles of *mei-S8* recovered by SANDLER *et al.* (1968) affect only the disjunction of chromosome *4* in males. Similarly, BAKER and CARPENTER (1972) recovered a large number of mutations that affect only the disjunction of the sex chromosomes. This may define a crucial difference between the two meiotic processes in that, with the quite possibly spurious exception of *mei-1*, there are no chromosome-specific meiotic mutations in females.

Most crucially, the analysis of the original set of mutants recovered in the screen of natural populations allowed SANDLER *et al.* (1968) to produce a pair of flow charts, or pathways, describing the deduced pathway of wild-type functions (see their Figures 3 and 4). The descriptions of these pathways are couched in terms, such as *landmarks* and *control points*, which seem to presage more modern discussions of the cell cycle. The term *landmark* was used to describe major events in the meiotic cycle, while the term *control points* was defined by SANDLER *et al.* (1968) as "points at which a genetic effect is necessary for the normal process of meiosis to continue." The analysis of the mutants recovered by BAKER and CARPENTER (1972) allowed these diagrams to be refined to the point where they became invaluable road maps of the meiotic processes in Drosophila, for example Figure 6 of BAKER and HALL (1976).

I might, however, point out that Figure 3 was more a source of anxiety than pride to LARRY SANDLER. He opened his issue of GENETICS only to find that this figure was upside down. Apparently, LARRY was concerned that someone had played an elaborate practical joke on him, and checked with his colleague DAVID STADLER, whose issue also contained the inverted Figure 3. I am told that LARRY was eventually calmed and reassured by the conviction that the defective copies had only been sent to those individuals whose last name started with S. I am happy if LARRY was indeed reassured by that conviction. However, honesty requires me to note that the copy on the desk next to me, which belongs to and was sent to M. M. GREEN, also contains an inverted Figure 3, as does the copy in our library.

Where are the mutants now? In the decade or so after their recovery, these mutations provided investigators with an incalculable wealth of information. This is perhaps best understood in terms of the use of these mutations to elucidate both the genetic control of recombination and the mechanism of the process itself.

CARPENTER used the existing array of recombination-defective mutants in genetic studies of both the recombination process itself and the mechanisms that control the number and distribution of recombinants. She also exploited these mutations in the course of detailed ultrastructural studies on the formation of the synaptonemal complex and analyses of recombi-

nation nodule structure (CARPENTER 1988, 1989). Finally, her detailed analysis of the effects of several recombination-defective mutations on various parameters of gene conversion provided crucial insights into the underlying mechanism (CARPENTER 1982). Taken together, and in light of data arising from the study of meiosis in yeast, these studies of recombination-deficient meiotic mutations in Drosophila served as linchpins in the modern synthesis of the relationship between chromosome pairing and the initiation of recombination (CARPENTER 1987; HAWLEY and ARBEL 1993).

In addition, the detailed analysis of the relationships between exchange and segregation in females homozygous for recombination-defective mutations provided crucial details for the now commonly accepted notion that normal levels of exchange are both necessary and sufficient to ensure regular segregation (BAKER and HALL 1976; HAWLEY 1988). They also provided data on the mechanisms that control the number and distribution of exchanges, which would have been impossible to glean in the absence of the mutations. More crucially, they also generated important insights into the functional significance of those controls: the extraordinary control of chiasma position probably reflects a compromise between the difficulties inherent in resolving proximal chiasmata and the low ability of very distal chiasmata to ensure disjunction.

These studies of the phenotypes of recombination-defective mutations were augmented by the finding that the set of recombination-defective mutations in Drosophila overlapped significantly with the set of mutagen-sensitive or repair-defective mutations (BAKER *et al.* 1976). Initially this finding generated enormous enthusiasm, both because it linked together two emerging new areas in Drosophila genetics and because it seemed to predict that the ongoing biochemical studies of repair would provide rapid insights into the nature of the recombinational defects, and thus into the nature of the recombination process itself. Although much has been learned, that later promise remains to be fulfilled. Recent progress on the cloning of such genes (*mei-41* and *mei-9*) by BOYD and his collaborators seems likely to provide truly significant insights into the mechanisms of both recombination and repair.

Finally, in a series of collaborative papers, BRUCE BAKER and MAURIZIO GATTI elegantly demonstrated that many of the recombination-defective or repair-defective strains also exhibit severe defects in mitotic chromosome behavior (BAKER, CARPENTER and RIPOLL 1978; GATTI and BAKER 1980). This work again served to interlock two emerging fields and to provide significant new insights into the roles the wild-type alleles of these genes play in the proper development of the fly.

With all of this work in the literature, why did only four or five labs present at the 1988 meeting in New Orleans? What happened? Perhaps the loss of apparent interest reflected refocusing of major workers in the field toward new problems. Perhaps the field was simply eclipsed by exploding developments in the study of various aspects of gene function during embryogenesis. Regardless of the cause of that decline, the last five years have witnessed a renaissance in the analysis of meiosis.

This rebirth has been characterized by three types of efforts. The first has been the detailed characterization of many of these loci at the genetic level: large searches for additional alleles have been reported for *nod* (ZHANG and HAWLEY 1990), *mei-S332* (KERREBROCK *et al.* 1992), *ord* (MIYAZAKI and ORR-WEAVER 1992) and *mei-218* (K. S. MCKIM and R. S. HAWLEY, unpublished data). Second, the development of confocal microscopy has allowed detailed analysis of the normal meiotic process in females, which had previously been impossible (THEURKAUF and HAWLEY 1992).

Perhaps the most instructive case of the power of combining the new microscopy with the analysis of a well characterized meiotic mutation is the analysis of the *nod* mutation. In this case the cytological description of the nod phenotype, together with the finding that the *nod* locus encodes a kinesin-like protein (ZHANG *et al.* 1990), provided truly important insights into the role that the wild-type *nod* protein plays in the process of achiasmate segregation.

But perhaps the most important addition to the field has been the application of the now traditional methods of molecular genetics to the genes defined by meiotic mutations. As noted above, this process has been accomplished for the *nod* mutation (ZHANG *et al.* 1990) and for the *ncd* mutation (MCDONALD and GOLDSTEIN 1990; ENDOW, HENIKOFF and NIEDZIELLA 1990). To the best of my knowledge, none of the genes defined by the mutants recovered by SANDLER *et al.* (1968) have so far been characterized at the molecular level. However, *mei-S332* has been characterized extensively at the cytological level by GOLDSTEIN (1980) and by KERREBROCK *et al.* (1992). In addition, multiple alleles of this mutation have now been obtained and the molecular analysis should be considered as imminent, if indeed it has not been completed at the time of this writing. A similar set of assertions can be made about the *ord* mutation which, like *mei-S332*, defines a crucial component of sister chromatid separation (MIYAZAKI and ORR-WEAVER 1992).

This molecular assault on the mutations provided by the original screen even extends to reviving the

dead. Sadly, both alleles of *mei-S8* were lost shortly after the paper was published. I'm aware of at least two laboratories seriously looking for new alleles of this locus. Similarly, my own laboratory has become deeply interested in recovering new alleles of *mei-T3*, a semi-sterile line recovered in the original SANDLER *et al.* (1968) screen.

Reflections from a cloudy crystal ball: One hopes that the enormous progress in the study of meiosis observed during the last five years is predictive of the next 25. Curiously, though, my strongest perception of the present is an uneasy feeling that we are running out of the past. The legacy of meiotic mutants left to us by SANDLER *et al.* (1968) and by BAKER and CARPENTER (1972) is nearly exhausted. It is clear that to take the next few steps in this process, we will once again need to perform large screens for meiotic mutations in both sexes. My own laboratory, and I suspect those of others as well, has now begun exactly this task.

Perhaps the most significant praise I can place on SANDLER *et al.* (1968) and on BAKER and CARPENTER (1972) is to note that they still serve as the most useful guide-posts as we embark in this effort. These more modern searches will use higher-tech mutagens (enhancer-traps and the like) and they will be combined with a more molecularly oriented and technically sophisticated analysis. Unlike SANDLER *et al.* (1968) and BAKER and CARPENTER (1972), our most immediate goals will be molecular descriptions of the genes in question.

Nonetheless, both the general schemes and the rationales remain unchanged. We still seek to dissect the meiotic process through the systematic collection and analysis of a large number of meiotic mutants. I suspect that those of us involved in these mutant hunts secretly hope that the mutants recovered in our screens will prove as valuable in the next 25 years as did those of our predecessors in the last 25 years.

I wish to thank BRUCE BAKER, ADELAIDE CARPENTER, JIM MASON and especially DAN LINDSLEY for sharing their memories and insights. I also thank DEAN PARKER, from whose reprint collection I unearthed the sabbatical grant application written by DAN LINDSLEY. Finally, I want to thank ADELAIDE CARPENTER, BRUCE BAKER, KENNETH BURTIS, BARRY GANETZKY, JENNIFER FRAZIER and KIM MCKIM for their valuable comments on the manuscript. Due to space limitations I have had to omit references to many of the studies done by various students in the SANDLER laboratory and by other workers. I deeply regret this limitation. This paper is dedicated to the memory of LARRY SANDLER, whose presence remains undiminished.

LITERATURE CITED

BAKER, B. S., 1975 Paternal loss (*pal*): a meiotic mutant in *Drosophila melanogaster* causing loss of paternal chromosomes. Genetics **80:** 267–296.

BAKER, B. S., and A. T. C. CARPENTER, 1972 Genetic analysis of sex chromosome meiotic mutants in *Drosophila melanogaster*. Genetics **71:** 255–286.

BAKER, B. S., A. T. C. CARPENTER and P. RIPOLL, 1978 The utilization during mitotic cell cycle of loci controlling meiotic recombination and disjunction in *Drosophila melanogaster*. Genetics **90:** 531–578.

BAKER, B. S., and J. C. HALL, 1976 Meiotic mutants: genic control of meiotic recombination and chromosome segregation, pp. 351–434 in *Genetics and Biology of Drosophila Ia*, edited by E. NOVITSKI and M. ASHBURNER. Academic Press, New York.

BAKER, B. S., J. B. BOYD, A. T. C. CARPENTER, M. M. GREEN, T. D. NGUYEN, *et al.*, 1976 Genetic controls of meiotic recombination and somatic DNA metabolism in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA **73:** 4140–4143.

CARPENTER, A. T. C., 1973 A mutant defective in distributive disjunction in *Drosophila melanogaster*. Genetics **73:** 393–428.

CARPENTER, A. T. C., 1982 Mismatch repair, gene conversion and crossing-over in two recombination-defective mutants in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA **79:** 5961–5965.

CARPENTER, A. T. C., 1987 Gene conversion, recombination, and the initiation of meiotic synapsis. BioEssays **6:** 232–236.

CARPENTER, A. T. C., 1988 Thoughts on recombination nodules, meiotic recombination and chiasmata, pp. 526–548 in *Genetic Recombination*, edited by R. KUCHERLAPATI and G. SMITH. American Society for Microbiology, Washington, D.C.

CARPENTER, A. T. C., 1989 Are there abnormal recombination nodules in the *Drosophila melanogaster* meiotic mutant *mei-218*? Genome **31:** 74–80.

ENDOW, S. A., S. HENIKOFF and L. S. NIEDZIELLA, 1990 Mediation of meiotic and early mitotic chromosome segregation in *Drosophila* by a protein related to kinesin. Nature **345:** 81–83.

GATTI, M., S. PIMPINELLI and B. S. BAKER, 1980 Relationships between chromatid interchanges, sister chromatid exchanges, and meiotic recombination in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA **77:** 1575–1579.

GOLDSTEIN, L. S. B., 1980 Mechanisms of chromosome orientation revealed by two meiotic mutants in *Drosophila melanogaster*. Chromosoma (Berl.) **78:** 79–111.

GRELL, R. F., 1976 Distributive pairing, pp. 435–486 in *Genetics and Biology of Drosophila Ia*, edited by E. NOVITSKI and M. ASHBURNER. Academic Press, New York.

HALL, J. C., 1972 Chromosome segregation influenced by two alleles of the meiotic mutation *c(3)G* in *Drosophila melanogaster*. Genetics **71:** 367–400.

HAWLEY, R. S., 1988 Exchange and chromosome segregation in eukaryotes, pp. 497–525 in *Genetic Recombination*, edited by R. KUCHERLAPATI and G. SMITH. American Society for Microbiology, Washington, D.C.

HAWLEY, R. S., and T. ARBEL, 1993 Yeast genetics and the fall of the classical view of meiosis. Cell **72:** 301–303.

HAWLEY, R. S., K. S. MCKIM and T. ARBEL, 1993 Meiotic segregation in *Drosophila melanogaster* females: molecules, mechanisms, and myths. Annu. Rev. Genet. **27:** 281–317.

HAWLEY, R. S., and W. E. THEURKAUF, 1993 Requiem for the distributive system: achiasmate segregation in Drosophila females. Trends Genet. **9:** 310–316.

HAWLEY, R. S., H. IRICK, A. E. ZITRON, D. A. HADDOX, A. LOHE, *et al.*, 1993 There are two mechanisms of achiasmate segregation in *Drosophila*, one of which requires heterochromatic homology. Dev. Genet. **13:** 440–467.

KERREBROCK, A. W., W. Y. MIYAZAKI, D. BIRNBY and T. L. ORR-WEAVER, 1992 The Drosophila *mei-S332* gene promotes sister-chromatid adhesion in meiosis following kinetochore differentiation. Genetics **130:** 827–841.

MASON, J. M., 1976 *Orientation disrupter (ord)*: a recombination-defective and disjunction-defective meiotic mutant in *Drosophila melanogaster*. Genetics **84:** 545–572.

MCDONALD, H. B., and L. S. B. GOLDSTEIN, 1990 Identification

and characterization of a gene encoding a kinesin-like protein in Drosophila. Cell **61:** 991–1000.

MIYAZAKI, W. Y., and T. L. ORR-WEAVER, 1992 Sister chromatid misbehavior in Drosophila *ord* mutants. Genetics **132:** 1047–1061.

PARRY, D. M., 1973 A meiotic mutant affecting recombination in female *Drosophila melanogaster*. Genetics **73:** 465–486.

ROBBINS, L. G., 1971 Nonexchange alignment: a meiotic process revealed by a synthetic meiotic mutant of *Drosophila melanogaster*. Mol. Gen. Genet. **110:** 144–166.

SANDLER, L. M., 1971 Induction of autosomal meiotic mutants by EMS in *Drosophila melanogaster*. Genetics **39:** 365–377.

SANDLER, L. M., D. L. LINDSLEY, B. NICOLETTI and G. TRIPPA, 1968 Mutants affecting meiosis in natural populations of *Drosophila melanogaster*. Genetics **60:** 525–558.

THEURKAUF, W. E., and R. S. HAWLEY, 1992 Meiotic spindle assembly in *Drosophila* females: behavior of nonexchange chromosomes and the effects of mutations in the *nod* kinesin-like protein. J. Cell Biol. **116:** 1167–1180.

ZHANG, P., and R. S. HAWLEY, 1990 The genetic analysis of distributive segregation in *Drosophila melanogaster*. II. Further genetic analysis of the *nod* locus. Genetics **125:** 115–127.

ZHANG, P., B. A. KNOWLES, L. S. B. GOLDSTEIN and R. S. HAWLEY, 1990 A kinesin-like protein required for distributive chromosome segregation in *Drosophila*. Cell **62:** 1053–1062.