In the BC-8 mice which comprise the virus resistant strain coisogenic with C3H mice, the single gene differentiating the two strains appears to be the gene conferring virus resistance, and its presence is apparently expressed in macrophages which cannot support multiplication of West Nile and probably all other Arbor B viruses.

Summary.—Tissue cultures of peritoneal macrophages prepared from individual mice of the eighth generation of backcrossing between virus-resistant hybrids and virus-susceptible C3H mice were exposed to West Nile virus. Half of the cultures failed to support virus multiplication, while the remaining cultures yielded infectious virus. This distribution of resistance and susceptibility in macrophage cultures reflected on the cellular level genes segregating for virus resistance and susceptibility on the whole animal level.

* This investigation was supported in part by a PHS research grant No. C4534 from the National Cancer Institute, and Training Grant No. 2G-142, Public Health Service.

† Including 4 cultures probably resistant.

[1] Theis, G. A., R. E. Billingham, W. K. Silvers, and H. Koprowski, *Virology*, **8**, 264 (1959).

[2] Webster, L. T., *J. Exp. Med.*, **65**, 261 (1937).

[3] Goodman (Theis), G., and H. Koprowski, *Philos. Trans. Roy. Soc. London, Series B*, 1962 (in press).

[4] Little, C., in *The Biology of the Laboratory Mouse*, ed. G. D. Snell (New York: Dover Publications, Inc., 1956).

[5] Snell, G. D., *Transpl. Bull.*, **2**, 6 (1955).

[6] Manaker, A. R., P. C. Strother, A. A. Miller, and V. Piczak, *J. Nat. Cancer Inst.*, **25**, 1411 (1960).

[7] Clarke, D. H., and J. Casals, *Amer. J. Trop. Med. & Hyg.*, **7**, 561 (1958).

[8] Bang, F. B., and A. Warwick, these PROCEEDINGS, **46**, 1065 (1960).

---

*A NEW HYPOTHESIS ON THE NATURE AND SEQUENCE OF MEIOTIC EVENTS IN THE FEMALE OF DROSOPHILA MELANOGASTER**

BY RHODA F. GRELL

BIOLOGY DIVISION, OAK RIDGE NATIONAL LABORATORY,† AND ZOOLOGY DEPARTMENT, UNIVERSITY OF TENNESSEE

Communicated by Alexander Hollaender, December 28, 1961

A knowledge of the relation between synapsis, exchange, and disjunction is basic to an understanding of the meiotic process. That exchange in the female of *Drosophila melanogaster* is not a prerequisite for regular disjunction has been demonstrated by Sturtevant and Beadle[1] and by Cooper.[2] It is equally clear that when more than two chromosomal elements are mutually involved in disjunction, as happens with heterologues in the case of translocation heterozygotes[3] or with heteromorphs in the case of secondary nondisjunction,[1] the frequencies of exchange and regular disjunction are positively correlated. The role of a heterologue or of a heteromorph in these situations has been variously interpreted.

Bridges[4] postulated that competitive X,X,Y pairing, initiated prior to exchange (since secondary exceptions are almost invariably noncrossovers), is responsible

for X nondisjunction. Subsequent investigation indicated that the expectation of a general reduction in crossing over between the X's, correlated with the frequency of secondary exceptions, is not realized; instead, only a proximal reduction is observed.[5] Anderson's[6] study of XXY females, heterozygous for an X-autosomal translocation, disclosed a marked decrease in X-exchange among the exceptional progeny, an increase among the regular progeny, and a total exchange frequency equivalent to that found among the progeny from XX mothers. Anderson concluded that the Y acted only after synapsis and exchange to cause "the more loosely paired X chromosomes to be distributed to the same pole." Studies of heterozygous autosomal translocations led Dobzhansky[3] to propose that competitive pairing, incident to rearrangements, provokes a conflict between the attraction forces of homologous loci, weakens the intimacy of synapsis between these loci, and leads to decreased exchange and increased nondisjunction. An extension of this hypothesis to the case of secondary nondisjunction fails to account for the absence of crossovers among the exceptions since X,Y homology is limited to the most proximal regions. Sturtevant and Beadle's[1] studies with X inversion heterozygotes indicated that secondary nondisjunction is primarily dependent on the occurrence of noncrossover tetrads rather than the reverse. They considered that the Y acted in accordance with the hypothesis of competitive pairing to reduce proximal exchange in the X's.

The preceding observations and conclusions suggest that the Y functions in a dual capacity during meiosis, affecting exchange by reducing crossing over in the region of homology with the X's and affecting disjunction by associating with noncrossover X tetrads. If the assumption that the Y does play diverse roles in the exchange and disjunctive process is valid, it should be possible, as well as more satisfactory analytically, to employ a system for study in which one of these functions is inoperative. The discovery that nonhomologous elements are capable of very high frequencies of association,[7-9] as inferred from their segregation behavior, offers the possibility of such a system. In contrast to the X,X,Y situation, the relation of the Y to the autosome with which it associates is presumed to be uncomplicated by homology. The present work proposes to examine the relation between exchange in chromosome two and Y,2 association in order to determine if these represent simultaneous or sequentially related events.

The results suggest that these are sequential events, indicating that the meiotic process in the female of *Drosophila* is separable into two phases—that concerned with exchange and that concerned with disjunction. They further indicate that a nonhomologue is not involved in the first phase but may be highly involved in the second. To account for these relations, two kinds of pairing have been postulated: *exchange pairing*, preceding exchange, and *distributive pairing*, subsequent to exchange and preceding disjunction.

Materials and Methods.—Association between nonhomologues at meiosis has been shown to occur when two or more chromosomes or chromosomal elements are present without adequate homologous pairing partners.[10] It is recognized and measured by the nonrandom assortment of the nonhomologues. In the present experiments, nonhomologous association between the Y chromosome and an inverted second chromosome has been studied at the same time that crossing over between the second chromosomes has been measured.

It is known that when one of the four elements involved in a translocation heterozygote is inverted with respect to its homologue, it frequently behaves as a univalent[11] and in XXY females may regularly pair with the Y chromosome.[8] Induction of nonhomologous association between Y and two was accomplished by the utilization of the multiply inverted chromosome, Ins(2LR)Gla, in conjunction with a 2;3 translocation, T(2;3)A or T(2;3)101. Both T(2;3)A, which carries the inseparable, dominant marker Bristle (B*l*), and T(2;3)101 are reciprocal translocations with breaks very close to the spindle attachments. T(2;3)A gives the rearrangement 2L + 3L and 2R + 3R, whereas T(2;3)101 gives the rearrangement 2L + 3R and 2R + 3L. Although Ins(2LR)Gla is described[12] as a single pericentric inversion with one break at 27F and a second at 51D and should permit crossing over distal to the Gla breakpoints in 2L as well as in 2R, no crossovers were recovered in 2L among some 12,000 flies. This prompted a salivary gland chromosome analysis which disclosed the presence of two additional breaks, at 22D and 33F and identical to those present in In(2L)Cy. It appears likely that the Glazed inversion was originally induced in an In(2L)Cy chromosome. Crossing over was measured distal to the 2R inversion breakpoint with the aid of the recessive markers plexus (*px*) and speck (*sp*). The genotype of the males used in all the crosses was y^2; *al px sp/al px sp*.

The presence of the inseparable, easily classifiable and fully penetrant, dominant marker *Gla* in the inverted chromosome provided the means for following the segregation of the second chromosomes. Use of a marked y^+Y (= sc^8·Y)[13] that carries the normal allele of yellow (y^+) and the introduction of yellow-2 (y^2) into the X chromosomes of both parents permitted the distribution of the Y to be followed among the progeny.

The experiments were planned so that the test (XXY) females and the control (XX) females, in addition to being of the same genotype, were sisters, thus insuring uniformity of genetic background for the two groups. Virgin females, whose age did not exceed 10 hr, were placed, singly, in vials with three males for 24 hr and then transferred to bottles for a six-day period. The temperature was maintained at 25° ± 1°C throughout.

Results and Analysis.—The present experiments propose to answer the following questions:

1. Are those chromosomes participating in nonhomologous associations specifically noncrossovers?

2. Do nonhomologous associations that involve one of a pair of homologues reduce crossing over between those homologues?

The answer to the first question may be found by observing the distribution of the y^+Y among the crossover and noncrossover classes for chromosome two (Table 1). In each of the three experiments, the number of individuals in the four crossover classes is approximately equal. The only significant departure from equality occurs in the Y, translocation-bearing progeny and is attributable to reduced viability, since reduction is observed consistently both among the crossovers and noncrossovers of this genotype. It is most marked when the translocation carries all of the recessive markers, such as happens among the crossovers in Cross II, Experiment 3 and among the noncrossovers in Cross II, Experiment 2.

Since the y^+Y chromosome is recovered as frequently with the *Gla*-bearing as with

the translocation-bearing crossover types, it appears to be assorting independently of the second chromosome recombinants. On the other hand, among the noncrossover classes, the y^+Y shows a marked tendency to separate from the *Gla*-bearing chromosome. This is interpreted to mean that association between the Y chromosome and the nonrecombinant *Gla* chromosome preceded their segregation to opposite poles. It may be concluded that associations between the y^+Y and the *Gla*-bearing chromosome involve only nonrecombinants.

It now becomes necessary to determine whether noncrossovers arise as a consequence of Y, *Gla* associations. If so, a reduction in second chromosome exchange frequency is expected in the presence of a Y. The amount of reduction should be positively correlated with the frequency of nonhomologous association, and the expression, $a = 1 - 2n$ (where a = nonhomologous association between the Y and *Gla* chromosomes and n = nondisjunction of these chromosomes), is used to calculate this frequency.[10] The values for a, based upon the observed data, is given in Table 1 and turns out to be about 50 per cent in each experiment.

TABLE 1

ASSORTMENT OF THE NONHOMOLOGUE (y^+Y) WITH THE CROSSOVER AND NONCROSSOVER PROGENY

Cross I. Experiment 1: Progeny from $y^2/y^2/y^+Y$; Ins(2LR)Gla,*Gla*/T(2;3)101, *al sp*^{2} ♀ ♀ X y^2; *al px sp/al px sp* ♂ ♂.

Cross II. Experiment 2: Progeny from $y^2/y^2/y^+Y$; Ins(2LR)Gla,*Gla*/T(2;3)A, *al Bl px sp* ♀ ♀ X y^2; *al px sp/al px sp* ♂ ♂.

Experiment 3: Progeny from $y^2/y^2/y^+Y$; Ins(2LR)Gla,*Gla px sp*/T(2;3)A, *al Bl* ♀ ♀ X y^2; *al px sp/al px sp* ♂ ♂.

Experiment		y^+Y;T(2;3)	T(2;3)	y^+Y;Gla	Gla	n(%)	a(%)
1	Crossover	104	129	113	124	23.4	53.2
	Noncrossover	791	203	184	1042	(629/2690)	
	Total	895	332	297	1166		
2	Crossover	48	65	53	53	23.7	52.6
	Noncrossover	387	109	153	734	(380/1602)	
	Total	435	174	206	787		
3	Crossover	24	56	63	62	25.2	49.6
	Noncrossover	317	95	91	500	(305/1208)	
	Total	341	151	154	562		

n = cases where both y^+Y and Ins(2LR)Gla or neither y^+Y and Ins(2LR)Gla are recovered in the same individual.

a = nonhomologous association between y^+Y and Ins(2LR)Gla.

Translocation heterozygotes invariably give rise to a certain proportion of aneuploid gametes, and since this proportion may differ in the exchange and nonexchange types, the frequency of nonhomologous association calculated from the observed data may not measure the actual frequency. It is presumed that cells in which there is an exchange in chromosome two will have a chain of four elements at first metaphase and, judging from the results of Dobzhansky,[11] should produce about 50 per cent euploid gametes. Those cells that do not have an exchange in chromosome two are presumed to have a Y, *Gla* bivalent (or a *Gla* univalent) and a chain of three [T(2;3),3]. A chain of three should disjoin [i.e., separate T(2;3) $\leftrightarrow$ 3] about 80–90 per cent of the time,[14] but the random segregation of the *Gla* chromosome with respect to the T(2;3),3 trivalent should reduce the recovery of a euploid gamete from a nonrecombinant to 40–45 per cent. The incidence, then,

of euploid gametes from the second chromosome exchange and nonexchange types of oocytes is expected to be approximately equal, so that the observed frequencies should reflect fairly accurately the corresponding primary oocyte frequencies. Since there appears to be a slightly greater chance for the recovery of a euploid gamete among the recombinants (50%) than among the nonrecombinants (40–45%), the calculated frequency of about 50 per cent is probably an underestimate of the amount of Y, *Gla* association.

Crossover frequencies are given in Table 2. For each cross, A represents the presence of a y^+Y in the mother and B its absence. A comparison of A and B

TABLE 2

EFFECT OF A NONHOMOLOGUE ON CROSSING OVER BETWEEN HOMOLOGUES

Cross I. Experiment 1 $y^2/y^2(y^+Y)$*; Ins(2LR)Gla,*Gla*/T(2;3)101, *al sp*^{2} ♀ ♀ X y^2; *al px sp*/*al px sp* ♂ ♂.

Cross II. Experiment 2 $y^2/y^2(y^+Y)$*; Ins(2LR)Gla,*Gla*/T(2;3)A, *al Bl px sp* ♀ ♀ X y^2; *al px sp*/*al px sp* ♂ ♂.
Experiment 3 $y^2/y^2(y^+Y)$*; Ins(2LR)Gla,*Gla px sp*/T(2;3)A, *al Bl* ♀ ♀ X y^2; *al px sp*/*al px sp* ♂ ♂.

Experiment		Totals	Noncrossovers T(2;3)	Noncrossovers Gla	Crossovers T(2;3)	Crossovers Gla	Per Cent Crossing Over: Region 1 (Gla-px)	Region 2 (px-sp)	Total
1A	(y^+Y)	2690	994	1226	233	237			17.47 ± 0.73
1B	(no y^+Y)	4848	1834	2227	339	398			15.20 ± 0.52
2A	(y^+Y)	1602	496	887	113	106	9.18 ± 0.72	4.49 ± 0.52	13.67 ± 0.86
2B	(no y^+Y)	858	243	497	49	69	9.21 ± 0.99	4.55 ± 0.71	13.76 ± 1.18
3A	(y^+Y)	1208	412	591	80	125	11.92 ± 0.93	5.05 ± 0.63	16.97 ± 1.08
3B	(no y^+Y)	1521	533	749	105	134	11.37 ± 0.81	4.34 ± 0.52	15.71 ± 0.93

* ( ) designates present in A, absent in B.

shows that the observed crossover values for the second chromosomes are not reduced by the occurrence of a high frequency of association between one of the second chromosomes and the Y. In one case (Cross I), a small but significant increase is noted. In the two others, the frequencies are not significantly different, either when total or regional frequencies are compared. (Although Cross II was marked so as to detect double crossovers, only singles were recovered among some 5,000 flies.)

If the Y, *Gla* associations were in fact taking place at the expense of exchange, 50 per cent association should lead to a 50 per cent reduction in the number of primary oocytes with an exchange in the second chromosome. For the frequency of recovered crossovers in A and B to be the same, the presence of the Y would either have to increase the probability of recovery of a recombinant or decrease the probability of recovery of a nonrecombinant. The Y chromosome has been shown to segregate randomly with respect to the exchange types and should not affect their recovery. The alteration would, therefore, have to be accomplished by a drastic reduction in the recovery of gametes from nonexchange oocytes and, at the observed level of exchange, would involve a twofold reduction in the recovery of viable products from XXY females. That this is not the case is evident from a comparison of the fertility of XXY and XX females. The average number of progeny from a single XXY female is 149 and from a single XX female 186. As the presence of a Y *per se* is known to reduce fertility about one third,[15] these figures indicate the Y induces no increase in zygote lethality. Oksala, in an analogous situation, obtained a similar result.[8]

Discussion.—The above experiments suggest that nonhomologous associations

do not affect crossing-over frequencies despite the fact that nonrecombinants alone are involved in such associations. The results are interpreted to mean that nonhomologous associations occur subsequent to exchange and specifically between elements not participating in exchange. Parallel experiments, involving the X chromosomes,[16] show that the effect of the Y on crossing over between the X's is of the same magnitude whether secondary nondisjunction is high or low. Thus the effect of the Y on X exchange appears to be independent of its effect on X disjunction. Like nonhomologous association, this implies that XXY associations, which lead to secondary nondisjunction, occur subsequent to exchange and involve only nonrecombinant X tetrads.

On the basis of this evidence, the following sequence of meiotic events is postulated: (1) exchange pairing, (2) exchange, (3) distributive pairing, (4) disjunction. It is further postulated that the two kinds of pairing may be defined in the following way.

Exchange pairing is a prerequisite to exchange but does not necessarily lead to exchange. It occurs exclusively between homologous loci. If more than two such loci are present, it is competitive since the evidence indicates that at any particular level crossing over involves only two chromatids.[17, 18]

Distributive pairing is concerned with the segregation process. It occurs after exchange. Crossover elements remain associated; noncrossover elements pair with one another. When more than two noncrossover elements are present, pairing is competitive.[10] Pairing of this kind may be affected by homology but involves nonhomologues as well.

The possibility cannot be ruled out that if exchange pairing leads to the establishment of effective pairing sites[19] which virtually insure the exchange event, both exchange pairing and distributive pairing might then precede the actual act of exchange.

The present hypothesis provides a means of resolving a number of apparent paradoxes concerning the meiotic process. These include the facts that a decrease in exchange may lead to an increase in nondisjunction, yet exchange is not necessary for regular disjunction; that a heterologue or a heteromorph associates exclusively with noncrossover elements, yet does not increase the number of such elements; and that pairing for exchange must be highly specific, yet nonhomologues may pair very regularly.

According to the proposed model, distributive pairing is considered to be operative both when the genome is normal and when rearrangements or aneuploids are present. Under normal conditions, about 95 per cent of the X tetrads and probably a larger percentage of the major autosomal tetrads are crossovers. For these, the pattern of distributive pairing is set by exchange. The noncrossover residue, which might otherwise assort randomly, engage in distributive pairing. The importance of homology in this process is unknown. The coincidence of an X and a major autosomal nonrecombinant or of two major autosomal nonrecombinants in an oocyte should be the product of their occurrence singly, and the infrequency of this event provides little opportunity for nonhomologous association.

According to the hypothesis presented here, a Y chromosome, added to the normal genome, should compete for exchange pairing because of homology with the X's. Although the Y never participates in a crossover, its effect is measurable as a proxi-

mal decrease in X exchange. The Y should again be active at distributive pairing. At this time it competes for noncrossover X tetrads, that would in its absence pair distributively and disjoin from one another, and diverts a large fraction of these into secondary exceptions. Different heterozygous X inversions will, depending on their size and location, be effective in varying degrees for reducing X exchange.[1] The greater the number of noncrossover tetrads so produced, the greater should be the number participating in distributive pairing, or, if a Y is present, the greater should be the fraction of total tetrads that the Y diverts into secondary exceptions.

Association between nonhomologues at meiosis has been attributed to the absence of adequate homologous pairing partners for them.[10] This concept may now be more precisely defined. Associations between nonhomologues occur after exchange and between elements not participating in exchange. Such associations may be induced by increasing the number of nonhomologous elements that are nonrecombinant. Heterologous autosomal inversions, present heterozygously, effect such increases. Associations here are expected to lead to dominant lethals. If the heterologous inversions involve an X and an autosome, they should lead to X exceptions as well as dominant lethals.[20] Introduction of a chromosome that does not engage in exchange, such as a Y, should insure the complete availability of one element for distributive pairing. If autosomal, rather than X nonrecombinants associate with the Y, the detectable consequence should be only dominant lethals. Oksala[8] reports a great reduction in fertility of females heterozygous for Ins(2L + 2R)Cy when a Y is present. This suggests that dominant lethality occurs here as the result of associations between the Y and the nonrecombinant second chromosomes. When one of the autosomal nonrecombinants is involved in a translocation, so that it is frequently part of a recombinant element, the Y should associate only with the other autosomal nonrecombinant. These associations are detectable by the nonrandom assortment of the Y and the autosome.[8] Although nonrecombinant, the fourth chromosome is not available for distributive pairing with a nonhomologue unless present as an extra element or prevented by rearrangement from pairing homologously. Experiments (R. Grell, unpublished) have shown that the fours continue to segregate regularly when a Y is added to the female complement, whereas a free four will associate with a Y if a heterozygous or homozygous 3, 4 translocation is present.[7, 9]

These experiments provide no information as to the time of the meiotic events. The work of Plough[21] places crossing over at "the very earliest oocyte," which he believes probably corresponds to leptotene. If exchange is completed during leptotene and distributive pairing occurs some time subsequent to this, Pontecorvo's[22] speculation—that cytologically visible pairing may be only a mechanical device necessary for segregation—could well turn out to be true.

Summary.—1. To determine if crossover as well as noncrossover tetrads participate in nonhomologous associations, nonrandom assortment between a y^+Y and a multiply inverted second chromosome, Ins(2LR)Gla, has been studied at the same time that crossing over between Ins(2LR)Gla and its translocated homologue, T(2;3)A or T(2;3)101, has been followed. The results show that only noncrossover chromosomes participate in nonhomologous associations.

2. Crossing over between Ins(2LR)Gla and its translocation homologue, T(2;3)A or T(2;3)101, has been measured when the inverted chromosome is par-

ticipating in nonhomologous association with a y^+Y and when the y^+Y is absent. The frequency of crossing over appears not to be decreased by the occurrence of nonhomologous association. It is concluded that nonhomologous associations do not produce noncrossover tetrads but that these associations take place between noncrossover elements after exchange.

3. It is postulated that the probable sequence of meiotic events is (1) exchange pairing, (2) exchange, (3) distributive pairing, and (4) disjunction. *Exchange* pairing occurs between specific homologous loci; it is competitive if more than two such loci are present; it is a prerequisite for exchange but it does not necessarily lead to exchange. *Distributive* pairing occurs after exchange; crossover elements remain associated; noncrossover elements pair with one another; if more than two noncrossover elements are present, pairing is competitive; it may be influenced by homology but it involves nonhomologous elements as well.

4. The application of this model to normal females, to secondary nondisjunction, and to nonhomologous association is discussed.

The writer is indebted to D. L. Lindsley for his counsel and for his generous assistance in the preparation of the manuscript. She also wishes to express her appreciation to J. G. Carlson and E. H. Grell for many helpful suggestions and to E. B. Lewis, L. Sandler, D. Schwartz, D. Suzuki, B. Webber, and S. Wolff for their comments on the paper.

* From a dissertation submitted to the University of Tennessee in partial fulfillment of the requirements for the degree of Doctor of Philosophy. This work was done while the author was a holder of a U.S. Public Health Service Special Research Fellowship, GF-10, 916-Cl.

† Operated by Union Carbide Corporation at Oak Ridge, Tennessee, for the U.S. Atomic Energy Commission.

[1] Sturtevant, A. H., and G. W. Beadle, *Genetics*, **21**, 554 (1936).

[2] Cooper, K. W., *Genetics*, **30**, 472 (1945).

[3] Dobzhansky, Th., *Am. Naturalist*, **65**, 214 (1931).

[4] Bridges, C. B., *Genetics*, **1**, 1–52, 107–163 (1916).

[5] Bridges, C. B., and T. M. Olbrycht, *Genetics*, **11**, 41 (1926).

[6] Anderson, E. G., *Z. Induktive Abstammung-u. Vererbungslehre*, **51**, 397 (1929).

[7] Grell, R. F., *Genetics*, **42**, 374 (1957).

[8] Oksala, T., in *Exchange of Genetic Material: Mechanisms and Consequences*, Cold Spring Harbor Symposia on Quantitative Biology, vol. 23 (1958), p. 197.

[9] Grell, R. F., *Genetics*, **44**, 421 (1959).

[10] Grell, R. F., and E. H. Grell, these PROCEEDINGS, **45**, 51 (1960).

[11] Dobzhansky, Th., *Z. Induktive Abstammung-u. Vererbungslehre*, **64**, 269 (1933).

[12] Bridges, C. B., and K. S. Brehme, *The Mutants of Drosophila melanogaster* (Washington, D. C.: Carnegie Institution of Washington, 1944).

[13] Muller, H. J., and J. Valencia, *Drosophila Info. Serv.*, **21**, 69 (1947).

[14] Brown, M. S., University of Texas Publication No. 4032 (1940), p. 11.

[15] Grell, R. F., *Genetics*, **44**, 911 (1959).

[16] Grell, R. F., in preparation.

[17] Dobzhansky, Th., *Z. Induktive Abstammung-u. Vererbungslehre*, **68**, 134 (1934).

[18] Weinstein, A., *Genetics*, **21**, 155 (1936).

[19] Pritchard, R. H., *Genetical Research*, **1**, 1 (1960).

[20] Cooper, K. W., S. Zimmering, and J. Krivshenko, these PROCEEDINGS, **41**, 911 (1955).

[21] Plough, H. H., *J. Exptl. Zool.*, **24**, 147 (1917).

[22] Pontecorvo, G., *Trends in Genetic Analysis* (New York: Columbia University Press, 1958).