187. "Synthetic Lethals" in the Second Chromosome of *Drosophila melanogaster*

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Dobzhansky (1946)¹⁾ first pointed out that even lethals could be synthesized through intrachromosomal recombination in *Drosophila pseudoobscura*. The existence of such "synthetic lethals" was also reported in *D. prosaltans* (Dobzhansky *et al.* 1959)²⁾ and *D. willistoni* (Krimbas 1961).³⁾ In *D. melanogaster*, Wallace *et al.* (1953),⁴⁾ Gibson and Thoday (1962)⁵⁾ and others found "synthetic lethals" in the second chromosome, whereas Gantner (1958),⁶⁾ Spiess and Allen (1961)⁷⁾ and Allen (1964)⁸⁾ could not get conclusive evidence for their production in the chromosome. Hildreth (1956),⁹⁾ Spiess and Allen, and Allen were unable to detect such lethals in the third chromosome, and Hildreth could not demonstrate them in the sex chromosome. Accordingly, it is important to determine whether "synthetic lethals" really exist in *D. melanogaster* and to estimate the rate of the production of such lethals, if they do.

Six experiments, Exp. I–Exp. VI, were essential in order to study this question, because we could not deal with many sampled chromosomes in one experiment. The experimental plan was the same in all the six experiments. Throughout these experiments fifty five samples of wild second chromosomes of *D. melanogaster* were taken from a natural population in Yamanashi, Japan in 1965 and 1966, and tested for the viability effects in the homozygous condition with the aid of the usual *Cy*-method, only previously replacing the genetic background, namely, the first and the third chromosomes, of the *Cy/Pm* strain with those of the natural population. Out of the fifty five, eight chromosomes gave subvital homozygotes, but the others had normal viabilities. The mating scheme is presented in Fig. 1. In each experiment, all the possible crosses ($Cy/+_i \times Cy/+_j$) were made using ten chromosomes, normal or subvital, selected from the fifty five. In the following generation, one wild type female ($+_i/+_j$) carrying a pair of the original chromosomes was mated to *Cy/Pm* in each of 45 intercrosses to obtain recombinant chromosomes. Ten males bearing various recombinant chromosomes were taken from each of the 45 crosses and individually outcrossed to *Cy/Pm* in the next generation. Thus 450 (45×10) recombinants in one

Fig. 1. Mating scheme.

Table I. Number of the lethal chromosomes among the recombinant chromosomes

	Lethals	Recombinant chromosomes tested
Exp. I	0	330
Exp. II	9	275
Exp. III	26 (10)	338
Exp. IV	25 (10)	245
Exp. V	2 (1)	448
Exp. VI	13 (5)	435

Numbers in the parentheses indicate incomplete lethals.

experiment were tested for their relative viability in double dose. If wild type flies were less than 3.3% of total progenies in the final generation, the chromosome was designated as lethal. All cultures were maintained in vials on 20% boiled yeast medium. All experiments were carried at $25\pm 1^{\circ}\text{C}$.

The frequency of lethal chromosomes in recombinants is given in Table I. There are 49 complete lethals (0% viability) and 26 incomplete lethals (less than 3.3% viability) among the total 2021

recombinant chromosomes, 2.37% and 1.25% respectively. Many recombinants with lethal effects were seen in Exps. III, IV, and VI, whereas they were rare in Exps. I and V. Since subvital chromosomes were involved in Exps. III, IV, and VI as the original one, it might be presumed that the occurrence of "synthetic lethals" through recombination between linked genes and its frequency were affected by the viability of parental chromosomes. According to the viability of parental chromosomes, normal (N) or deleterious (D), 75 lethals gained in this investigation were assorted as follows:

Parental cross	Recombinant chromosomes	
	Tested	Lethals (%)
N×N	1494	32 (2.14)
N×D	462	34 (7.36)
D×D	65	9 (13.85)

The total frequency, 3.62%, is considered to show a higher rate than the expected rate due to lethal mutations in the second chromosome, and those obtained from N×D and D×D are apparently high. Therefore, it follows that lethals can be really produced by recombination of genes in somewhat deleterious chromosomes, whereas they are not necessarily expected to occur by recombination between normal chromosomes. In other words, the recombinants between normal and deleterious chromosomes and much more so those between deleterious ones can remarkably increase the lethal frequency.

It might be suspected that lethals arise as synergistic interaction of deleterious genes and polygenes. When Dobzhansky (1946) observed "synthetic lethals" in the second chromosome of *D. pseudoobscura* for the first time, the parental chromosome had not always normal viability. Furthermore, the tendency that lethal chromosomes were produced more frequently when subvitals were selected as parental chromosomes can be seen in the data obtained by Wallace *et al.* (1953), who reported "synthetic lethals" in the second chromosome of *D. melanogaster*.

Last, concerning this problem, Crow (1964)¹⁰⁾ wrote "...detrimentals and semilethals which, when two or more are present on the chromosome, may amount to a lethal effect, but presumably these are not classified as synthetic lethals". Following the statement of Crow, the lethals appeared in this study may not be referred to as "synthetic lethals". But if the concept of "synthetic lethals" covers the cases where lethals are produced through recombination between the chromosomes which are viable as homozygotes, irrespective of whether they are normal or deleterious, the results may be placed in the category of "synthetic lethals". Thus we are assured of the

existence of "synthetic lethals". Another experiment in which no crossing over is involved is necessary to confirm this point, and is now in progress.

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