ON THE CAUSES OF MOSAICISM ASSOCIATED WITH HETEROCHROMATIC CHROMOSOME REGIONS

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THE hypotheses attempting to explain the mechanism of mosaic formation in cases of mosaicism caused by "eversporting displacements" fall into two groups. According to the hypotheses of the first group, the original chromosome aberration, peculiar to the given mosaic strain, causes the occurrence in somatic cells of secondary changes in the chromosome structure, such as the losses of chromosome pieces (Patterson, 1932; Schultz, 1936), the changes of the size of laterally attached translocated pieces (Stern, 1935), or the occurrence of gene mutations (Sidorov, 1936; 1940; 1941; Demerec and Slizinska, 1937). According to all these hypotheses a mosaic organism is considered a chimera.

The alternative point of view is expressed in the hypotheses of the second group, all of which explain mosaicism in terms of position effect, either the interchromosomal (Muller, 1935; Ssacharov, 1936) or intrachromosomal (Dubinin, 1936; Belgovsky, 1938; Prokofyeva-Belgovskaya, 1939a, 1939b; Panshin, 1938; Khvostova, 1939) one. According to this point of view, the somatic cells of a mosaic organism are all genotypically alike, the differences in characters they display depending solely upon the differences in biochemical reactions taking place in the immediate vicinity of genes responsible for mosaicism.

In 1938 I suggested that mosaicism of the type under discussion is to be ascribed chiefly to two causes: (1) the weakening of the biochemical efficiency of the gene primarily responsible for mosaicism, this weakening resulting from the interaction of substances produced by the

gene in question with those produced in heterochromatic regions, and (2) the increased variability of heterochromatic and heterochromatized chromosome regions in response to various internal and external influences. If the biochemical activity of the gene is lowered almost down to the critical level assuring a normal development of the character, the variations in the degree of heterochromatization of the chromosome section in which the gene in question is located should sometimes result in a still greater weakening of its efficiency and in an alteration of the normal process of character development. Thus mosaic spots similar to hypomorphic somatic mutations must develop in the body of the organism.

According to this view, the degree of mosaicism must depend not only upon the properties of the gene primarily responsible for mosaicism, but upon the general physiological conditions in the organism as well, and particularly upon the nature of other genes of this organism, influencing the same morphogenetic processes which the gene responsible for mosaicism controls. These other genes may be either allelic or not allelic to the gene in question. Furthermore, a mosaic allele must act as a hypomorphic mutation and an accumulation of identical mosaic alleles in the genotype must decrease the degree of mosaicism, shifting the phenotype toward wild type.

Experiments were carried out in order to check these expectations. Several mosaic forked mutations and a bristle-affecting gene "*If*" were chiefly used in the work. The mosaic alleles were: f^{B15}, f^{B27}, f^{B59} and f^{B168}. All of them occurred in chromosomes carrying the B^{M2} inversion and in all, except f^{B27}, reinversions occurred with the left break to the left of *f* and the right in the heterochromatic region. As a result, the *f* locus became transferred to the spindle fiber attachment and inserted into the heterochromatic region. Cytological studies of the f^{B15} and f^{B59} chromosomes, carried out by Prokofyeva-Belgovskaya, substantiated the genetic interpretation of their structures. The f^{B27} chromosome was not sufficiently studied.

The *If* gene (chromosome 2; 86.5) is evidently a gene affecting the some morphogenetic process which the *f* gene affects, combinations of the two genes giving the following phenotypes: f^+/f^+ If/If = forked-like bristles, f/f^+ If/If^+ = forked bristles, f/f If/If^+ = intensified forked, f/f If/If = very intensified forked bristles, almost lethal. In combinations with other bristle-affecting genes, *f* and *If* give similar results. Heterozygous *f* and heterozygous *If* both intensify the effect of *Bl* and of *Sb*, and neither of them influences the effect of *sn* or of *sbd*.

In accordance with the expectation, the heterozygosity for *If* shifts the degree of mosaicism for *f*, decreasing the number of normal bristles. Thus $v\ f\ f^{B59}$; *Cy*/+ males have 11.18 ± 0.597 normal bristles, while $v\ f\ f^{B59}$; *If*/+ have $4.08 + 0.396$. ($v\ f\ f^{B59}$ chromosome is a crossover chromosome having the f^{B59} allele along with an ordinary recessive *f* in its normal position). f^{B15}; *Cy*/+ males have 13.02 and f^{B15}; *If*/+ have 4.18 ± 0.423 normal bristles. In the f^{B27} case the exact classification of forked and normal bristles was not possible, but the shift was in the same direction.

The dependence of this effect of *If* on the mosaicism for *f* upon the similarity of the mode of action of these two genes is proved by the ineffectiveness of *If* in the case of eye color mosaicism caused by w^{m5}.

Another test of the dependence of the degree of mosaicism upon the general physiological conditions in the organism was performed on different compounds of mosaic and non-mosaic *f* alleles. The non-mosaic alleles used were the following: f^{B38} and f^{B37}—the strongest alleles of approximately equal strength; f^{B26}—a somewhat weaker allele; f^{B87}, f^{B68}, and f^{B92}—three still weaker alleles of approximately equal strength; and f^{B19}—the weakest allele. It was expected that the stronger the non-mosaic allele entering into the compound with the given mosaic one, the higher will be the degree of mosaicism of the heterozygous flies. The compounds of f^{B15} with different non-mosaic alleles gave the following average numbers of

normal bristles: with f^{B38}, 6.58 ± 0.395; with f^{B37}, 10.76 ± 0.441; with f^{B26}, 12.20 ± 0.632; with f^{B87}, 8.90 ± 0.695; with f^{B92}, 15.92 ± 0.568; with f^{B19}, 16.66 ± 0.546. It can be seen that the degree of mosaicism in this series tends to decrease with the decreasing strength of the non-mosaic alleles. The f^{B168} allele gave the following results: with f^{B38}, 2.06 ± 0.191 normal bristles; with f^{B26}, 2.24 ± 0.179; with f^{B68}, 1.64 ± 0.172; with f^{B92}, 1.69 ± 0.155; with f^{B19}, 3.36 ± 0.225. In this series only the f^{B168}/f^{B19} compound differs significantly from all the others, the degree of mosaicism of the rest being approximately the same. This result may be satisfactorily explained by the very high degree of mosaicism of the f^{B168} allele masking the effect of strong and intermediate non-mosaic f alleles.

The possibility of obtaining crossover chromosomes carrying in addition to a non-mosaic f allele a mosaic one inserted into the heterochromatic region provided the opportunity of comparing the degree of mosaicism of flies having one and two mosaic alleles, and thus to find out whether the mode of action of the latter is, as expected, similar to that of hypomorphic mutations. The degree of mosaicism of $f^{B36}f^{B59}/f^{B36}f^{B59}$ and $f^{B36}f^{B59}/w\ f^{B36}B$ flies hatching in the same bottles was compared. The average numbers of normal bristles in these two classes were found to be (with a correction for crossing-over in the B–f^{B59} region) 7.99 and 2.01, respectively, the difference between these averages being significant. It is thus evident that the effect of the mosaic allele f^{B59} is similar to that of the f^{+} allele, differing from it only in its intensity.

The experimental data presented here show that the degree of mosaicism does actually depend not only upon the nature of the gene primarily responsible for it, but upon the nature of other, both allelic and not allelic genes influencing the same morphogenetic process, as well. They also show that alleles producing mosaicism are hypomorphic. All this agrees with the hypothesis outlined in the beginning of this article, and if we add to these data those of Demerec (1940), who found that

mosaic facet alleles do not cover the lethal changes of the same locus and deficiencies for it, we shall have sufficient body of evidence proving that mosaicism is to be explained in terms of changed gene potencies and random variations of physiological conditions in different parts of the organism during its development, rather than to be ascribed to secondary changes in the chromosome structure in somatic cells.

The variability of biochemical reactions taking place in heterochromatic and heterochromatized regions was not the subject of the present investigation, but the existence of such a variability is evidenced by the high structural variability of these regions (Prokofyeva-Belgovskaya, in press) and by Mather's (1939) finding that the heterochromatic regions are responsible for the increased variability of crossing-over in the proximal chromosome regions. As heterochromatization, according to Prokofyeva-Belgovskaya, is equivalent to heteropycnosis, and as it is generally accepted in modern cytology that chromosome sections in heteropycnotic condition are physiologically inactive, all variations in the degree of heterochromatization must lead to similar variations in the physiological activity of the genes located in the corresponding chromosome regions.

Cases of mosaicism caused by the separation of a given gene (*e.g.*, *lt* or *ci*) from the inert region do not contradict the point of view here developed. Since the normal activity of genes normally situated in the immediate proximity of heterochromatic regions must depend upon their interaction with the latter, their separation may be expected to disturb the normal course of chemical reactions and in most cases to weaken the morphogenetic efficiency of the gene in question. More rarely, as in the cases of brown mosaics, the change in the gene's activity may happen to be of an antimorphic nature.

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