

**"REPEATS" AND THE MODERN THEORY OF THE
GENE**

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Bridges introduced the term "repeats" for those sections of the salivary gland chromosomes of *Drosophila* which seem to be completely identical with other sections, the minimum extent of a repeat being a single band. He assumed that a section had once been actually reduplicated and had been inserted into the normal structure of the chromosome as a repeat, tandem or otherwise. He went one step further by suggesting that such repeats might account for the origin of new genes, if the repeated "gene" would change its function in the new position. Because the origin of new genes is completely mysterious, and because phylogeny without some such process is hardly conceivable within the framework of the gene theory, many geneticists have been found willing to accept this suggestion. This is rather surprising because the assumption is irreconcilable with the basic facts and tenets of classical genetics. A gene is supposed to reproduce its kind except when it mutates. The mutant gene, i.e., a member of a pair of alleles, has an action different from that of the original gene, and the same is true for any number of mutational changes, i.e., multiple alleles, but always affecting the same kind of process which, by way of extrapolation, is assumed to be controlled also by the original gene. Genes have never been known to mutate at different occasions into different directions, only into different grades of one effect. There is only one case known (the alleles spineless and aristapedia in *Drosophila melanogaster*) in which this relation does not seem to hold. To assume that a "repeated" gene can develop into a completely new type of gene, amounts, against the background of the classical conception of the gene and the facts of genetics, to mysticism. If it is pointed out that the new position of the gene makes a new effect possible—a vague allusion to the position effect—this is again an assumption which contradicts all known facts. Position effect produces the phenotype of a mutant of an adjacent locus (where known) as dominant or recessive effect, or, in special cases, as a mosaic effect. No fact is known which would justify the assumption that a change of position could make a known locus act otherwise than by producing its typical mutant effect, which includes the effects of multiple alleles.

Recently a number of facts have come to light which have been accounted for by the assumption of "repeats." The general type of these facts is this: Two or more mutants are found which behave like multiple alleles. Both produce, if homozygous (recessives), a definite effect, similar

but slightly different for each. In a compound the same effect is produced, which points to the presence of three multiple alleles. But careful experimentation reveals crossing over between the mutants, all other interpretations being excluded. Thus they behave as different "genes," though acting as alleles (pseudo-alleles, Lewis), and the conclusion is reached that they originated as repeats of one pre-existing gene. A number of such cases have now been studied (Lewis, Laughnan, Green and Green, Raffel and Muller, Komai) and others are suggested (Dunn and Caspari). An analysis of the facts, especially those unearthed in the remarkable work of Lewis and the Greens is apt to show the difficulties which the classical theory of the gene has to face and the superiority of a more modern concept.

Because Green and Green's work has thus far gone furthest inasmuch as a set of three "repeated" loci was found, we may use it as the basis of discussion. The decisive points are these: Among many lozenge alleles, all of which affect the quantity of the eye pigment, the eye structure, and the absence of the female spermathecas, and all of which behave as a typical series of multiple alleles, three could be shown thus far to exhibit a small amount of crossing over (resulting in one normal chromosome and one with more than one lozenge locus.) Thus they behave like individual loci, in close proximity, but permitting cross-over breaks between them. Nevertheless they act as alleles. This is best realized if different combinations are compared with at least one allele in both chromosomes with those in which one, two, or three alleles are present only in one chromosome. In a standard case of Mendelian inheritance individuals $\frac{a + c}{+ b +}$, $\frac{a b +}{+ + c}$ or $\frac{a b c}{+++}$, etc., should all be normal. But here only the last one is normal, the others show the compound lozenge effect, i.e., a , b and c behave as pseudo-alleles. The assumed "repeats" thus break the elementary rules of genetics and Green and Green know of no way out but to assume that in the first two cases the b or c , if separated from its mates, produces a position effect, thus giving the idea of position effect a quite new and doubtful definition, which was possibly suggested by a superficial resemblance to the original Bar position effect.

In my opinion these facts fit simply and without any new assumption into the modern picture of the basic features of the chromosome at the "genic" level. A group of facts are known (see especially Demerec 43 and Goldschmidt 44, full review and discussion in Goldschmidt 49) which show that the real genetical units of the chromosome are sections of different size, containing a number of bands in the salivary chromosomes, the maximum of which is not yet known. These units are characterized by the fact that whatever happens within this section produces a mutant effect of the same kind and that all these effects behave as multiple alleles. If we take, e.g.,

the "yellow" section invisible changes of a smaller order than one band, so-called point mutations, produce the mutant yellow. Translocation, inversion or deficiency breaks within this section act like mutants (position effect), also producing yellow, and all the point mutants and position effects behave as a series of multiple alleles. One may conclude that the invisible changes, the point mutants, are therefore also rearrangements, but within a single band. Whether this conclusion is drawn or not, it becomes clear that the whole section acts in some respects as a unit. Whatever happens within it, produces the same effect, or one very similar. If we should try to account for these facts by means of the classical theory of the gene, the whole section should be the gene because all changes within it are allelomorphous. The individual bands and their invisible mutations would become subgenes. But the position effects would also be subgenes. In addition, crossing over within the section seems possible. This is very unsatisfactory and the conclusion is obvious that at this level the classical theory of the gene does not work (see my former papers loc. cit.).

If we return now to the work on "repeats" it is seen to fit very easily into the group of facts and the concept just reported. At a former occasion (loc. cit.) I mentioned a disagreement between Muller and Demerec in regard to which band in the salivary chromosome should be regarded as the yellow locus. (There are similar discrepancies for other loci; see Bridges and Brehme, 1944.) The facts just reviewed led to the conclusion that there is no reason why both these authors should not be right. An invisible mutant change (point mutation) in any band of the yellow section would produce yellow. There can be at least as many point mutants of the same kind (and allelic) within any such section as there are bands. The application of this conclusion to the lozenge case is obvious: The lozenge effect is localized in a section which contains at least three bands which can mutate as so-called point-mutations. (Additional position effect alleles are bound to be discovered.) All must have a lozenge effect, all must be allelic just as it is proved for the yellow and scute sections, etc. (see Demerec and Goldschmidt, loc. cit.). No "repeats" are needed and no position effects. All facts fall in line simply if we forget about the classical theory of the gene and look at the facts dispassionately. Actually the work on the so-called repeats is a new proof of the correctness of that part of the newer ideas concerning the basic elements of genetics, which has been discussed here.

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ABSENCE OF MUTAGENIC ACTION OF X-RAYED CYTOPLASM IN *HABROBRACON*

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The literature concerned with x-ray effects on cells includes few records of attempts to separate injury induced in chromosomes from that induced in cytoplasm. Vintemberger¹ working with frog eggs concluded that it is the nucleus of the cell which is sensitive to x-rays. "L'irradiation de la région nucléaire a donc les mêmes effets que l'irradiation de la cellule entière." Dose used was 115 r. Zirkle² found that injury to fern spores by α -particles can be induced by extra-nuclear irradiation alone if dose is sufficiently large but that it is much greater when the nucleus is treated. Astaurov³ obtained androgenetic males from x-rayed *Bombyx* eggs fertilized by untreated sperm. These males (from untreated chromosomes in treated cytoplasm) were normal and their production continued after doses completely lethal to the expected types of progeny, biparental males and females. Henshaw⁴ found a direct correlation between the presence of a nucleus at time of irradiation and the manifestation of an effect, delay in cleavage. He worked with nucleated and non-nucleated fragments of *Arbacia* eggs. Petrova⁵ compared results of exposure to α -particles of entire cells of the alga *Zygnema* with those obtained by the treatment of the cytoplasm alone. She found that the mean lethal dose of the former ("Kerntod") was to that of the latter ("Plasmatot") as 1 to 700. Types of response differed under the two conditions of treatment. Transmissible changes were induced only when the entire cell had been irradiated.

What appears to be a striking exception to the conclusions of these inves-