SPONTANEOUS CHROMATIN REARRANGEMENTS AND THE THEORY OF THE GENE

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Spontaneous chromatin rearrangements in *Drosophila* are considered to be rare. In the few cases known they have a visible phenotypic effect comparable to so-called gene mutations whereas many of the experimentally produced rearrangements show no visible effect. The general opinion of geneticists seems to be that in such cases either a gene mutation has occurred at or near the break or that a position effect is involved. Elaborate theories have been presented to account for such a position effect on the basis of the theory of the gene (Muller, Offerman). It has not escaped notice that these position effects include many of the phenotypes of so-called gene mutations, and some geneticists have put the question whether or not all mutations are position effects. But the answer was in the negative (e.g., Muller). A series of observations, which I made during the past four years, tend to show that gene mutations do not exist and therefore no genes. Owing to enforced interruptions the analysis of my material is not yet finished, but enough is known to make a strong case.

About four years ago I found that a standard *Drosophila* stock of pure plexus had changed its phenotype into extreme plexus and partly blistered individuals. A remarkable asymmetry combined with this drew my attention, and in trying to analyze this in hundreds of lines, selections and crosses the following events occurred. One of the one-pair-broods of the plexus blistered stock yielded only a few individuals. This seemed suspicious, and another generation was bred. This consisted of typical plexus, normal and rudimentary flies, to which in the next generation a type with pointed wings and one with spread, plexus and blistered wings was added (also short bristles, which were not followed up). The former plexus blistered had disappeared simultaneously in the whole brood. It was then found that rudimentary was identical with the classic one, and that the pointed wings behaved like a recessive mutant at the left end of the *X*-chromosome. (It may be added that very rarely single rudimentary males appear in F_2 of crosses involving the plexus-blistered line, after the fashion of so-called gene mutations.) Obviously here a complete rearrangement had taken place in which simultaneously three "mutant" types appeared, plexus reappeared and both plexus and blistered disappeared (or wild appeared). As the whole brood was changed simultaneously, the rearrangement must have taken place in the germ tract. Following this, the plexus-blistered stock was analyzed and seemed first to contain

both plexus and blistered (or an allele of the latter). The sex ratios, however, indicated something in the *X*-chromosome, and it turned out that the echinus and rudimentary loci were involved (occasionally also white). At present—the analysis is not yet finished—it seems as if the echinus locus were inserted at the *bs*-locus of one plexus-containing chromosome, and the rudimentary locus into the other. The third chromosome is also involved, at least at the ebony locus. One of these insertions (*rud*) produces an ordinary *bs*-effect, the other an extreme *bs*-effect, both behaving like alleles. It is not yet clear which further rearrangement produces the other types, and the detailed facts are very complicated.

It is remarkable that the same line since gave other rearrangements resembling mutations. Thus a "mutation" was produced located in the *X*-chromosome and characterized by soft wings with blisters behind the cross vein; and in a few crosses between *pxbs* and the stock *bs*, the "mutant" ebony was produced, further abnormal abdomen, scute and broad wings.

While working with these rearrangements it became necessary to inquire into the stock *bs* (blistered). Among the many crosses made with this "mutant," one again (with Oregon wild) yielded a simultaneous rearrangement in all individuals of a brood: blistered disappeared, and there appeared in the following two generations plexus, dumpy vortex, thoraxate, purple and a few apparently new types, all behaving like "gene mutations" in the second chromosome but involving all members of a brood and not single individuals as had also been true in the *pxbs* case. As blistered is again involved, both cases belong together and demonstrate a large series of "gene mutations" to be produced by a series of chromatin rearrangements within the same or between different chromosomes. There are many remarkable additional details. To mention only one: We mentioned the recessive type with pointed wings at the left end of Chrom. I. A phenotypically identical type was found after heat-treatment from wild type. It turned out to be situated at the same locus. When these two "alleles" with pointed wings were crossed (both breeding perfectly true), a series of types appeared in F_2, F_3, among them *pxbs*, *px*, spread wings, soft blistered wings.

After these findings I do not doubt that all so-called gene mutations will turn out to be chromatin rearrangements. This would make the idea of position effect absurd as this effect would be now synonymous with so-called gene mutation. In other words, there are no genes, no gene mutations and no wild type allelomorphs. One may call the production of a phenotypic effect by a locus a gene, if one chooses to, and the simultaneous effects of other loci involved in the rearrangement, modifiers. But then there is no wild type allele, the whole wild type chromosome being the allele for all "mutant genes" within this chromosome. The chromosome

then is the unit, and a definite order within its texture is required for normal development. It is obvious that this will lead to a reconsideration of all such things as modifiers, specific suppressors, dominance enhancers, etc. The details of further consequences will be elaborated in another place, where we shall try also to find a chemical model for such a situation and discuss the views of others.

Why, one may ask, did all the *Drosophila* workers not hit upon such facts before? There are a number of reasons. It seems that the type of experimentation which leads to the discovery of such cases is rarely used; namely, innumerable repetitions of pair-breeding in pure stocks or in simple crosses involving "mutants" which seem to be in a rather labile equilibrium. (Besides *bs* I have reasons to assume that plexus, Beaded, balloon, vestigial, cut, black, kidney belong to this category.) Such crosses are usually made only in class work, and in this case events such as the ones described would be considered an experimental error. That, however, the same results would easily be found if looked for may be concluded from a recent paper by Plough and Holthausen[1] who report facts resembling those here reported as occurring in class work; they describe their findings as a strange case of "mass mutation." And still more characteristic, the same loci in the second chromosome, black and blistered, are involved which were also involved in my cases, in addition to extreme plexus, scute and abnormal abdomen, all of which appear also in our group of changes.

There is now a strong suspicion, almost a certainty, that the explosion of "mutations," which I observed many years ago after temperature shocks[2] in a single case and which I described as my best case of heat effect (and which never could be repeated, neither by myself nor by others), involved the same comparatively rare phenomenon. The details which I have published thus far only in a summary way parallel closely the cases here reported: The rearrangement produced simultaneously the "mutants," ebony, rolled, kidney and aristapedia. The heat treatment probably had nothing to do with the spontaneous phenomenon. Such a solution could hardly be proposed in 1929 when the theory of the gene was held an indisputable fact. The details of the case are now worthy of publication.

I do not doubt that soon others will report similar cases (even from former experience, discarded because improbable), and that the gene then will disappear completely from genetics, except for teaching purposes. A full report upon the experiments will be published later.

[1] Plough, H. H., and Holthausen, C. F., "A Case of High Mutation Frequency without Environmental Change," *Amer. Nat.*, **71** (1937).

[2] Goldschmidt, R., "Experimentelle Mutation und das Problem der sogenannten Parallelinduktion. Versuche an Drosophila." *Biol. Centrbl.*, **49** (1929).