GONOSOMIC MOSAICISM INVOLVING A LETHAL

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During the course of an experimental study of the frequency of translocations, males of Beadle's Xc^2 and $\overline{yy}$ stock—which have a ring-shaped X-chromosome which they receive from their father, the females having attached X-chromosomes—were X-rayed and mated to virgin females $\overline{XX}Y$, i.e. females which carry attached X-chromosomes and a Y-chromosome. These females were $\overline{yy}$ *bw e ey*, i.e. having attached X-chromosomes homozygous for the gene yellow and the three pairs of autosomes homozygous for brown, ebony, and eyeless respectively. The stock was constructed by Muller in 1931. The F_1 heterozygous males, which, as was to be expected, were phaenotypically wild-type, were backcrossed individually to the same type of female, $\overline{XX}Y$. The progeny of these individual backcrosses were examined for the purpose of detecting translocations.

Two out of twelve thousand fertile backcrosses were remarkable for the reason that they produced only females—one about seventy, the other about eighty-two.

Since in this type of cross the mother has attached X-chromosomes, the sons receive their ring-shaped X-chromosome from their father and the daughters their attached X-chromosomes from their mother. The absence of males in the progeny is to be explained only by the presence of a lethal on the ring-shaped X-chromosome of the father in both cases. Such a lethal could have arisen in one of the following ways:

(1) as a mutation either dominant or recessive on the original material of the ring-shaped X-chromosome;

(2) as an autosomal dominant mutation, a piece of that autosome which carried the lethal being included in the ring as a result of a translocation involving the ring and that autosome, or a piece of the ring being included in the autosome;

(3) as a bobbed lethal mutation on the ring-shaped X-chromosome.

Of these three possible types of lethal mutations the second possibility was discarded from the beginning, for the reason that, judging by the random assortment of the characters in the progeny of the backcrosses, no translocation was involved.

As regards the third possibility, it would have to be assumed that the mother had no *Y*-chromosome (or at least no *Y* containing the normal allele of bobbed), in which case the putative sons would carry the bobbed lethal on their ring-shaped *X*-chromosome which they received from their father, but would get no *Y*-chromosome (or no effective *Y*-chromosome) from their mother to suppress the bobbed lethal. They would consequently fail to develop. In this case the daughters would be different from their mother in having *Y*-chromosomes of ordinary type received from their father. If this was the case, these daughters, on being mated to their father, would be able to supply their sons with *Y*-chromosomes, and it would be expected that such matings would give rise to sons carrying the bobbed lethal on their ring-shaped *X*-chromosome but having a *Y*-chromosome which suppressed the lethal. But when the daughters in both cases were actually backcrossed to their father, again only females were produced. So the possibility of a bobbed lethal had to be ruled out.

The first possibility, therefore, appeared to be the correct one. A lethal mutation—dominant or recessive—on the ring-shaped *X*-chromosome was received only by the sons—the mother having attached *X*-chromosomes—which consequently failed to develop. The daughters, like the mother, must have attached *X*-chromosomes and a *Y*-chromosome. When they were mated to their father the process was repeated. Unfortunately, owing to the nature of the cross—the females having attached *X*-chromosomes—it was impossible to ascertain whether the lethal was a dominant or a recessive one.

These two F_1 lethal-containing males looked normal in every respect. They were quite fertile, as in spite of their being mated to a single female each in a small vial they produced a large number of daughters. But since they produced no sons, the lethal must have been present throughout the gonads. Every cell of the gonads must have carried the lethal gene on the ring chromosome. This type of mosaic was designated a "gonosomic mosaic", since the soma must, in part at least, have been free from the lethal, otherwise the males would not have survived. It is suggested that this name should be applied to cases of this sort.

These two cases are similar to that found by Agol (1931) where a male carried in his somatic (eye) cells the genes apricot and the normal allele of ruby but possessed genotypically by mutation both apricot and ruby. When this male was mated to $\overline{XX}Y$ females, he produced none but phaenotypically white-eyed sons. This white-eye was shown to be the result of the interaction of the apricot gene and the new mutant gene for ruby, which must then have been present in all the cells of the gonads.

The first proved case of *Drosophila* mosaic involving the gonads was reported by Muller (1920). A male $\frac{H'}{tt}$ from a stock with red eyes had one red and one white eye. When he was mated to $\frac{tt}{tt}$ females with red eyes, all the offspring had red eyes. These were mated together in mass cultures and produced females, all of which had both eyes red, and males, half of which had both eyes red and the other half both eyes white. The new factor for white, therefore, must have been recessive and sex-linked, and the mutation in the original male was partly somatic, partly gonadic.

Another interesting case of mosaicism involving the gonads is that studied by Crew & Lamy (1937). This was a *pseudo-obscura* "triplo-X" female which was phaenotypically normal. She was a "triplo-X" in the sense that she possessed three different X-chromosomes though these were not present in the same cell. The result of crossing-over experiments showed the most plausible explanation to be that the two ovaries of this female differed in respect of their X-chromosome content, both possessing the grand-paternal X-chromosome but each having a different grand-maternal X-chromosome. It was later suggested by the authors that this female must have been the result of double-nuclear fertilization, i.e. of two X-bearing sperm with two female pro-nuclei of different constitutions. As this female was phaenotypically normal it was concluded that mosaicism was restricted to the germ cells and possibly other internal tissues.

Another case of mosaicism worth mentioning here is that of Panshin (1935). This was a bilateral mosaic male of *Drosophila melanogaster* whose left eye showed the character lz^{st} (a strong allele of the gene for lozenge, *lz*) and whose right eye showed the character lz^{ws} ("lozenge weak", a weak allele of *lz*). It resulted from a cross between an X-rayed yf male and a $\overline{yy}Y$ female. It is attributable to simultaneous origination of the two different alleles of the lozenge gene in two halves of a split X-chromosome of a spermatozoon.

In Agol's case, he rightly excluded the possibility of the new mutation, ruby, having been produced by the X-rays, the reason being that the unusual result—none but white sons—was obtained in the F_1 of the cross of the treated apricot male with $\overline{XX}Y$ females. This male, then, must have already carried the new mutation, ruby, in all the cells of his gonads before being treated.

In both the present cases, however, there is every reason to suppose that X-rays were the responsible factor, since the unusual result—absence

of males—occurred in the second generation of treated males. It is probable, therefore, that in each case the lethal mutation was produced by X-rays in the ring chromosome of a spermatozoon of the treated F_1 male. This spermatozoon, after fertilization, gave rise to the F_1 "gonosomic" mosaic now described.

The X-ray action in producing mosaics, as Muller (1927) suggested in interpreting the origin of mosaics, may be either a "fractional effect" or an "after effect". For the "fractional effect" we must assume that the ring-shaped X-chromosome was in a split state at the time the spermatozoon of the F_1 male was X-rayed and that the lethal mutation occurred in one only of the daughter chromatids. Later on, from derivatives of the daughter cell carrying the lethal mutation the gonads developed. On the other hand, the lethal mutation might have been the result of an after effect of X-rays during the ontogenesis of the egg fertilized by the treated sperms, the gonads developing from derivatives of the cell in which the lethal arose.

But no definite proof of "after effect" has yet been obtained. Patterson (1933) produced by X-ray sex-mosaics, in which the male parts carried, in addition to the marked maternal X, a broken or deleted X-chromosome. He assumed that the gametic chromosome must be in the two-strand stage at the time of treatment if a part of the fly is thus to receive a broken daughter X-chromosome and another part a whole X-chromosome, but the "after-effect" interpretation would be possible here too. An intermediate alternative, in all these cases, as Muller has pointed out to the author, is to suppose that breakage occurred at once in the unsplit chromosome of the spermatozoon, but reunion later, after splitting, and that the two chromatids might reunite differently.

On the other hand, we cannot absolutely exclude the possibility that this lethal mutation occurred spontaneously in the F_1 heterozygous males at an early stage of their embryonic development, probably the first or the second zygotic division, in one of the daughter chromatids. Since, however, X-rays are known to cause mosaics, they were probably responsible in this case for the mosaicism.

The two present cases are also of interest in connexion with the question of whether the origin of the gonads is uni- or multicellular. It may be recalled that when our F_1 gonosomic mosaic males were mated to $\overline{XX}Y$ females no sons were produced. Also, when the daughters were backcrossed to their father (the gonosomic mosaic), in each case again no sons were produced. It was then concluded that all the cells of the gonads of the two males must have carried the lethal on the ring-shaped

X-chromosome. This is difficult to explain on the hypothesis of a multicellular origin of these gonads. It suggests a unicellular origin. Agol's case, too, supports this view. When he mated his apricot male, which was also a gonosomic mosaic, to $\overline{X}\overline{X}Y$ females, he got only white sons.

These facts, however, are not necessarily in contradiction with the observations of Huettner (1923), who found that the polar cells which give rise to the germ cells were always at least five in number, for these may possibly be descendants of a single cell. On the other hand, in Panshin's and some other cases both gonads and soma were mosaic, so that the gonad is evidently of multicellular origin in some cases, and of unicellular origin in others.

As mentioned previously, the gonosomic mosaics described were both phaenotypically normal. They looked quite healthy and were fertile. Yet their breeding results can only be explained on the assumption that all the cells of the gonads carried the lethal. But does this mean that all the somatic cells were free from the lethal? There seems to be no reason to suppose so. In the light of the evidence of random movement of nuclei in the embryonic development brought forward by Parks (1936) and by others, it seems unlikely that the cells carrying the lethal produced nothing but the gonads. It is also not improbable that these gonosomic mosaics should survive carrying the lethal not only in their gonads but also in some of their somatic cells. The normal somatic cells—those free from the lethal—might be expected to counterbalance the effect of the cells carrying the lethal, and thus cause the survival of these males and their phaenotypic normality.

Patterson in his work on sex differentiation found that the male parts of the gynandromorphs tolerate a much longer duplication than was found to be the case in non-mosaics. In this case the gynandromorphs had a normal diploid half and a hyperploid male half, while the non-mosaics were *X*-hyperploids throughout. He also found that hypoploid tissue will survive with longer deficiencies in mosaic than in non-mosaic flies. These findings support the view mentioned above that the lethal gonosomic mosaics above described might have had the lethal contained in some of their somatic cells and were able to tolerate them because of their normal somatic cells.

Also in Agol's case it is likely that beside the gonads some of the somatic cells contained the new mutant ruby. The reason why the eyes of the mosaic male were apricot and not white-appearing can be explained by assuming that none of the somatic cells containing the ruby gene took part in the production of the eye pigments.

Summary

Two mosaic males are described which have a lethal in the *X*-chromosome throughout the germinal tissue. Each produced many daughters but no sons when mated to females with attached *X*'s. On the other hand, their soma must, in part at least, have been free from the lethal, otherwise these males themselves would not have survived.

Accordingly, this type of mosaic is designated "gonosomic mosaic". It is suggested that this name may be used for cases where mosaicism is due to a difference in genetical constitution between all or part of the soma and all or part of the gonads.

One explanation for these cases is that the *X*-chromosome in each of the spermatozoa from which the mosaic males were derived was in a split condition and that the lethal occurred in one of the daughter chromatids (most probably as a result of X-rays, as the father was irradiated).

Two other possible explanations were considered: (1) an autosomal dominant lethal which had become attached to the *X*-chromosome by translocation, and (2) a bobbed lethal in the *X*-chromosome. Both of these are shown to be non-valid in each case.

The question as to whether the origin of the gonads is uni- or multicellular is discussed, and it is decided that they must have had a unicellular origin in these cases.

It is argued that though the lethal was on the *X*-chromosome throughout the gonads, it need not be the case that all the somatic cells were free from the lethal. Some of them probably contained the lethal, and the healthy condition of the gonosomic mosaics was probably due to the counterbalancing effect of that part of the soma which was free from the lethal.

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