THE EYE-PIGMENTARY SYSTEM OF *DROSOPHILA*

VII. THE WHITE LOCUS

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I. INTRODUCTION

THE white locus of *D. melanogaster* (1·5 in the X-chromosome) is of great importance for the study of allelism since it has mutated to a large series of multiple alleles, although these are also thought to consist of at least two series of pseudoalleles. The function of this locus has been discussed (Beadle and Tatum, 1941; Nolte, 1952) and it is thought that the probable mode of action of the wild-type allele is at the level where a common substrate is differentiated for the formation of two specific substrates that combine with the red and brown chromogens respectively, to form the red and brown chromophore groups. In this investigation it was hoped to gain further information on the relations between mutation and the functions of a gene. Two types of genetic differences were studied. First, fourteen mutant genes in the multiple series, *i.e.*, satsuma (w^{sat}), coral (w^{co}), wine (w^w), coloured (w^{co^l}), blood (w^{bl}), cherry (w^{ch}), eosin (w^e), eosin² (w^{e2}), eosin³ (w^{e3}), apricot (w^a), apricot³ (w^{a3}), apricot⁴ (w^{a4}), tinged (w^t) and white (w), and second, two position effects of the mottled type, *i.e.* white-mottled-4 (w^{m4}) and white-mottled-5 (w^{m5}). The methods applied in this study have been fully described (Nolte, 1952, 1954a).

2. OBSERVATIONS

(i) Eye-colour phenotype

These mutants are described by Bridges and Brehme (1944) and some have been described in a previous study (Nolte, 1950). The allele w^{e3} was found to be a new allele after photometric analysis, although it had originally been extracted from a white-eyed strain and had been accepted as the usual eosin allele (Nolte, 1944). The female has a slightly darker eye-colour than the w^e female and the male is slightly pinker than the w^e male. The two alleles w^{co} and w^w are apparently indistinguishable phenotypically (Bridges, 1938) but have been found to differ in pigment content. The position-effect w^{m5} is more variable in eye-colour than w^{m4} (Nolte, 1950), generally showing mottling of garnet with colourless patches, and at reduced temperatures the eye is highly speckled.

(ii) *Histology*

Microscopically the white series of alleles seems to belong to the brown type of eye-colour mutants (Nolte, 1950). The pigment cell regions (primary, secondary, basal and post-retinal) in the eyes of females appear as follows. The mutant w^{sat} resembles the mutant brown (bw), the primary cells have a yellowish tone due to brown granules, while the other three regions have a purplish-brown colour in aggregate caused by brown granules; the granules appear to be small in size as in the mutant bw , the basal cells are smaller than normal, and the post-retinal region appears to be normal in extent. The pigment regions of the allele w^{col} have in aggregate a bright brown colour caused by medium brown granules throughout all four regions, these granules being indistinct in outline or smaller than normal; the basal pigment cells are small and about as compact as in w^{co} , while the post-retinal region is narrower than normal. The two alleles w^{co} and w^w resemble each other in histological eye-colour but the former is somewhat darker; they show less colour than the allele w^{col} but with a darker tone of brown, with the exception of the post-retinal region which is more purplish-brown. The granules, excepting those in the primary cells, are indistinct in outline and the basal cells are small rounded masses. The allele w^{bl} at 20° C. has primary cells with brown granules, the other pigment regions being a reddish-brown as in the mutant carmine (cm) (Nolte, 1950); all granules are more distinct in outline than in the other alleles, and the basal cells are more nearly normal in size. At 25° C. the colour is paler and more brownish, the granules being indistinct in outline excepting in the primary cells and the basal cells are very small rounded masses. The allele w^{e2} has a yellowish tinge to the brown of the primary cells and a more reddish- or purplish-brown in the other three regions; the granules are less indistinct than in w^{co} , and the basal cells are small. In w^{a3} the aggregate colour is a medium brown, and the granules in all regions vary in size, many being larger than normal; the basal cells do not show such compact masses of granules as in the other alleles. The allele w^e resembles w^{co} in all respects with the exception that it is much lighter in colour; and the primary cell granules are very distinct; the allele w^{e3} is very similar to w^e . In w^{eh} there is a similar picture, but the primary cell granules are not quite as distinct. The alleles w^a and w^{a4} are very light in eye-colour, and in w^t and w no colour can be detected histologically.

Like w^{m4} (Nolte, 1950) the position-effect w^{m5} also shows a very variable histological picture, the colour in aggregate being brown with varying numbers of ommatidia or parts of ommatidia unpigmented, but with a lesser number of the elements of an ommatidium pigmented than in w^{m4} , though the pigmented sector runs throughout all four pigment regions. The basal cells seem smaller or more compact than normal, while the post-retinal region has a reduced number of pigment cells visible.

FIG. 1.—Light-absorption curves of the red pigment extracted in AEA, for 10 heads per 1 c.c., in the whole range. 1, blood (w^{bl}) at 20° C.; 2, eosin² (w^{e2}) at 25° C.; 3, blood at 25° C.; 4, apricot (w^a) at 25° C.

FIG. 2.—Light-absorption curves of the red pigment extracted in AEA, for 10 heads per 1 c.c. 1, coloured (w^{col}); 2, the heterozygote coloured-wine (w^{col}/w^w); 3, wine (w^w).

(iii) *Photometric analysis*

All the strains were examined for types of pigment, and so also were certain compounds with other mutant genes; some of the light-

TABLE 1
Relative amounts of red and brown pigments in the eyes of the multiple alleles at the white locus

Allele	Red pigment	Brown pigment
w^+	0.8993 ± 0.0052	0.0866 ± 0.0007
w^{col}	0.1454 ± 0.00220	0.0182 ± 0.00043
w^{a2}	0.0616 ± 0.00110	0.0506 ± 0.00051
w^{a3}	0.0542 ± 0.00084	0.0091 ± 0.00025
w^{co}	0.0496 ± 0.00042	0.0302 ± 0.00027
w^{sal}	0.0321 ± 0.00047	0.1083 ± 0.00140
w^w	0.0308 ± 0.00054	0.0342 ± 0.00044
w^{a3}	0.0240 ± 0.00038	0.0290 ± 0.00078
w^{bl}	0.0188 ± 0.00060	0.0122 ± 0.00020
w^e	0.0142 ± 0.00020	0.0182 ± 0.00034
w^{ch}	0.0125 ± 0.00020	0.0285 ± 0.00046
w^a	0.0108 ± 0.00018	0.0089 ± 0.00020
w^{a1}	0.0100 ± 0.00027	0.0085 ± 0.00016
w^t	0.0034	0.0028
w	0.0024	0.0020

absorption curves of pigment extracts are given in figs. 1-4. The amounts of the red and brown eye pigments were determined for 10-12 cultures of each strain, the red pigment being absorbed in acidified

TABLE 2
Relative amounts of red and brown pigments in the eyes of w^{bl} , w^{m4} and w^{m5} at different temperatures

Strain	Temperature	Red pigment	Brown pigment
w^{bl}	18° C.	0.2012 ± 0.0056	0.0553 ± 0.0016
	20° C.	0.0950 ± 0.0038	0.0435 ± 0.0008
	21° C.	0.0705 ± 0.0026	0.0372 ± 0.0018
	24° C.	0.0255 ± 0.0008	0.0183 ± 0.0005
w^{m4}	25° C.	0.0188 ± 0.0006	0.0122 ± 0.0002
	20° C.	0.5516 ± 0.0226	0.0691 ± 0.0021
	22½° C.	0.7039 ± 0.0039	0.0757 ± 0.0001
	25° C.	0.8310 ± 0.0212	0.0845 ± 0.0001
w^{m5}	19° C.	0.0662 ± 0.0067	0.0209 ± 0.0011
	22½° C.	0.1593 ± 0.0243	0.0299 ± 0.0010
	25° C.	0.2248 ± 0.0202	0.0347 ± 0.0018

30 per cent. ethyl alcohol (AEA) and the brown pigment subsequently in acidified methyl alcohol (AMA). The amounts of pigment in extracts of the various strains are given in tables 1-3, the data being given as E at 480 $m\mu$ for the AEA extract and at 444 $m\mu$ for the AMA extract, for concentrations of 10 heads per 1 c.c. solvent.

FIG. 3.—Light-absorption curves of the brown pigment extracted in AMA, for 10 heads per 1 c.c. 1, wine (w^w), reduced extract; 2, apricot (w^a), reduced extract; 3, wine, oxidized extract; 4, wine, untreated extract.

FIG. 4.—Light-absorption curves of the red pigment extracted in AEA, for 10 heads in 1 c.c. 1, the combination eosin-sepia ($w^e; se$); 2, the combination wine-cardinal ($w^e; cd$); 3, the combination eosin-carnation ($w^e; car$).

3. DISCUSSION

The findings on the mutant changes at the white locus have yielded facts which are pertinent to the study of the nature of mutation as well as to that of the action of genes in general.

(1) In general mutants with mainly the brown pigment present in the eye appear to have small granules (Nolte, 1950, 1952), and such is the case with the alleles w^{sat} , w^w , w^e and w^{ch} in the present study. The brown pigment being deposited first and the amount being relatively small in comparison with the amount of red pigment in the wild-type, it would appear that the main increase in size of the granule is by an accretion due to deposition of red pigment. This seems

TABLE 3
Relative amounts of red and brown pigments in the eyes of certain mutants and their combinations with alleles of white

Strain	Red pigment		Brown pigment
	415 $m\mu$	480 $m\mu$	
w^w/w^{col}		0.0872	0.0242
$w^e car$		0.0045	0.0035
car		0.2829	0.0380
w^e	0.0189	0.0142	0.0182
$w^e se$	0.0810	0.0120	0.0390
se	0.3708	0.0556	0.1233
w^{w^o}		0.0308	0.0342
$w^{w^o} cd$		0.0457	0.0033
cd		0.9672	0.0131
w^+		0.8993	0.0866

proved by the presence of more distinct (or larger) granules in w^{bl} at 20° C., also in w^{e2} and w^{a3} which all have a higher red pigment content than the allele w^{co} , which has smaller granules. An exception is the granules in the primary cells which, in all the alleles, are more distinct and larger than the granules in the other pigment regions, and in all the alleles these granules appear to contain brown pigment only as in the mutant ruby (rb) (Nolte, 1950). In the allele w^{a3} the granules vary in size, with some larger than normal and with perhaps a reduction in number. It further appears that the size of the basal pigment cells, as judged by the masses of pigmented granules, may be based on the size of these granules; in w^{bl} at 20° C. these cells or their pigmented contents seem to be nearest to normal in size, while in the same allele at 25° C., with much smaller amounts of both pigments, these pigmented masses appear to be very small, as also occurs in other alleles with small amounts of pigments. However, there appear to be exceptions in w^{co} and w^{e2} , which possess comparatively large amounts of both pigments and yet in which the basal cells appear as small compact masses, though slightly larger in w^{e2} which has more pigment.

A consideration of all these facts leads to the conclusion that the alleles of white do not have as primary function the building up of the pigment granule, but that they rather affect its size secondarily through the amounts of pigment produced.

(2) The red pigment extracted by AEA in the wild-type and most mutants has been shown to have a light-absorption valley at 260 m μ and a peak at 275 m μ in the ultra-violet, as also a peak at 480 m μ in the visible range (Nolte, 1954a). A modified form of this pigment has been described for the mutants *sepia* (*se*) and *clot* (*cl*), i.e. a yellow pigment with the three points of absorption at 255, 270 and 415 m μ respectively (Nolte, 1954b). The photometric curves of the AEA extract of some of the alleles of white in figs. 1-2 appear to indicate the presence of a second modified form of the red pigment. The colour of these extracts varies from a very light to a darker yellowish tone and this is also reversibly reduced to a colourless state by sodium hydrosulphite, indicating that some of the properties of the pigment have not been altered. A comparison of the spectrophotometric curves of AEA extracts brings to light an interesting point, viz., that for the alleles with the greatest amount of this pigment these curves more nearly coincide with the curve of the normal red pigment (Nolte, 1954a); for example, for the alleles w^{e2} , w^{u3} , w^{eo} and w^{col} the three distinctive points of absorption are at 260, 275 and 480 m μ respectively. In fig. 2 it will be seen that the curve for the heterozygote w^{col}/w^w shows values between those of the two homozygotes. In general the AEA curves of alleles with low amounts of red pigment show that reduction in amount is correlated with a levelling-off of the ultra-violet peak of absorption and also of the peak at 480 m μ , though in several alleles the latter peak seems to be shifted back to 460-470 m μ .

AEA extracts of body fluids were made in order to test the presence of other substances dissolved from the head, and for this purpose the thorax was taken; for volumes more or less equivalent to those of the heads used for eye extracts an average E was calculated. For these fluids a valley appears in absorption at 237 m μ and a peak at 255 m μ , indicating the presence of a dissolved substance chemically different to the eye pigment. If the E values for this substance, presumably present in the body fluids, are subtracted from the data for the eyes it appears that for most of the alleles the three distinctive points of absorption are similar to that of the normal pigment. The data for an extract of the heads of a compound mutant with a low red pigment content, i.e. *rb car*, show light absorption similar to that obtained for some of the lower alleles of white. It thus appears probable that in the lower members of this series of alleles the absorption curves are modified by the relatively high fraction of other materials extracted from the head fluid by AEA, so that actually no modification of the red pigment has occurred. This conclusion invalidates that formed in an earlier investigation (Nolte, 1952) and also the conclusion of Ephrussi (1945) on the white alleles, i.e. that in the various alleles

various degrees of condensation of identical pigment molecules occur ; it must, however, be noted that Ephrussi worked with the alleles made homozygous for scarlet (*st*), that he found a flattening of the steeply sloping curve for w^{co} in the visible region with increase in pigment deposition, and that he noted that the absorption curves have a distinct change of slope at 480 $m\mu$. Maas (1948) working with white alleles homozygous for cinnabar (*cn*) did not reach the same conclusions as Ephrussi.

During the course of the present study it was discovered that the method of oxidizing or reducing the AMA extract of brown pigment affects the shape of the absorption curve in the ultra-violet, due to specific absorption by an excess of hydrogen peroxide and by some secondary product formed by the sodium hydrosulphite. This fact necessitates a modification of some conclusions which have been reached on the relationship between the red and brown pigments (Nolte, 1954a). Fig. 3 shows some of the effects of the oxidizing and reducing agents even in pure AMA, while the untreated AMA extract shows the type of absorption for the brown pigment. Though untreated extracts of brown pigment from the eyes of different alleles of white do not show absorption curves with such a clear-cut valley at 230 $m\mu$ and peak at 260 $m\mu$ as was found in the case of pupal eyes (Nolte, 1954a), it is possible that in adults these points are to some extent masked by the simultaneous extraction of increased amounts of impurities. In a previous study (Nolte, 1952) it was postulated that, because of a similarity in their peaks of absorption in the ultra-violet, the red and brown pigments had a part of their chromophore groups in common, and it was suggested that this part was produced by the action of the white locus. The findings of the present study do not substantiate this view, though such a part in common may still exist because the apparently partially oxidized state of the extracted brown pigment may have caused obliteration of double-bond structure and therefore loss of peak in ultra-violet absorption. A chromophore system may be very complex and absorption peaks produced in the ultra-violet would be summations of the effects of the partial chromophores. The conclusions arrived at, therefore, cannot be more explicit than that the white locus, in differentiating a common substrate, may cause the production of two constituents which may differ rather widely in regard to their spectrophotometric properties.

(3) An evaluation of the quantitative relationships between the multiple alleles and position effects may be arrived at by inspection of the data of tables 1-2 ; it should be noted that in a previous study (Nolte, 1952) the allele w^{co} was taken as identical with w^w . As point of reference is taken the amount of pigment occurring in the allele w^{bl} in which the content of both pigments is inversely correlated with rise in temperature. For the red pigment it was found that the increase in content is geometric, amounting to a factor of about 1.4 for each degree drop in temperature, while for the brown pigment the increase

is arithmetic, rising by an amount of about one-half of the amount present at 25° C. for each degree drop in temperature. Theoretically, if the curves of these increases are prolonged to 13° C., the amount of red pigment should be about 0.91 and of brown pigment about 0.086, *i.e.* approximately the amounts present in the wild type. Tests to confirm this showed that a critical temperature exists probably at about 15-18° C., at which the increase in pigment content with drop in temperature ceases due to metabolic upsets at the low temperature.

In comparing the quantitative relations between the various alleles of white two facts should be noted: first, the various strains are not isogenic for any series of genes that might affect the total amounts of the two pigments; secondly, the decrease in red pigment content is not correlated with decrease in brown pigment content for any specific allele. Comparing the red pigment content with that for w^{bl} at 25° C., the increase in the series is by a factor of approximately 1.2, *i.e.* the members of the series increase in content by a ratio approximately equal to that for w^{bl} for a drop of half a degree in temperature. For the brown pigment the increase is in an arithmetic series, rising by an amount approximately equal to that for w^{bl} for a drop of one degree in temperature. Some remarks must be made in regard to these general rules. First, some alleles are grouped together for pigment content, *e.g.*, w^{co} , w^{e3} and w^{ch} as a group with an equal content of brown pigment. Secondly, some gaps appear such as between w^{col} and w^{e2} for the red pigment, and between w^{sal} and w^{e2} and between w^{e2} and w^w for the brown pigment. Thirdly, the lower alleles do not seem to conform to these rules. For the higher alleles, however, the gaps could be accounted for if it could be predicated that these could be filled by alleles not easily distinguishable from those already known, in the way that coral and wine are not distinguishable in gross eye-colour.

Some kind of quantitative relation is therefore indicated as resulting from mutations at the white locus, and this relationship could support either an hypothesis for two differential functions of one locus or for the separate functions of two loci. Some evidence has been advanced for the hypothesis that the locus can actually be split into two, perhaps coinciding with the double band 3C2.3 in the cytogenetic map. In one investigation on crossing-over MacKendrick and Pontecorvo (1952) give evidence for crossing-over having taken place between w and w^{bl} , and between w and w^{co} . In the second instance Lewis (1952) has evidence of crossing-over between w and w^a , though implicit in this investigation is the hypothesis that if the two mutant genes are at different loci, a mutation at one locus blocks or impairs the functioning of the normal allele at the other locus when these two are in the same chromosome, *i.e.* $a +/+w$ has the mutant phenotype, a case of position pseudoallelism; these pseudoalleles may represent an established duplication of a single ancestral gene. Lewis assumes a simple model of one gene controlling the reaction $A \longrightarrow B$ and the

other $B \rightarrow C$, so that the position-effect can be assumed to result from the failure of substance B to diffuse readily from one chromosome to the other. If the white locus could be subdivided into two loci, a mechanism more acceptable of one gene having one product could be visualized for the differentiation of a common substance into two specific substrates; the two loci could respectively condition the reactions for the red and brown substrates. Thus for the genotype $a+/a+$ (apricot female) the mutant a would lower the production of one substrate and impair the function of the normal allele of the other locus; for the genotype $+e/+e$ (eosin female) the converse effect should then appear since in both mutants there is a reduction in both pigments. In such an event, however, the interaction would not be a simple one-way type as postulated by Lewis but rather a competitive relation (*cf.* the excess of brown pigment in w^{sat}). Some indications of possible evidence for the postulate of Lewis do exist. First, such a scheme may account for the fact that the alleles arranged in two series for descending order of red and brown pigment content do not coincide. Secondly, Lewis advances the hypothesis that the genes eosin and white belong to one locus since they are lightened by the modifier Pale, whereas apricot is darkened by the latter. Thirdly, if the alleles are divided into two groups according to which sex has the darker eyes, we find those with the male darker are: coral, wine, coloured, blood and apricot, while those with the female darker are eosin, cherry and white. In connection with a system of grouping Mainx (1938) noted that compounds such as coral/wine and blood/wine are intermediate in phenotype while those such as eosin/blood and apricot/white more nearly resemble the darker homozygote. It is also noteworthy that the first group, with the exception of wine, have relatively more red than brown pigment, while the second group, with the exception of eosin, have relatively more brown than red pigment.

In the two mottled position-effects the amounts of both pigments increase with a rise in temperature, that for red being more rapid than for brown. For both pigments the rate of increase is arithmetic so that it must be assumed that the action of the position-effect is different to that of a mutation at the locus.

(4) With the effect of temperature on the pigment content of the allele w^{bl} as point of reference, some conclusions may be drawn on the effect of mutation on the function of this locus. For this allele Ephrussi and Herold (1945) determined the critical period for qualitative variation at 40-48 hour after puparium formation, that is, before pigment is visible in the eye. Presumably the actual critical period is very short and during it the differentiation of the assumed substrates is initiated and reaches a maximum. Decrease in temperature increases the duration of this period and consequently the enzyme activity of the gene w^{bl} is allowed additional time in which to continue its work. Basically, therefore, the mutation to this allele reduces the activity of

the locus, perhaps by reducing the amount of enzyme involved; in a similar way mutation to other alleles results in a reduction of activity—the production of hypomorphs. A correspondence exists between the rate of increase in pigment content in w^{bl} with decrease in temperature, and the rate of increase in the multiple alleles arranged in series; the members of the series do not, however, retain the same order for the red pigment as for the brown. The white locus does not, therefore, appear to act through a simple splitting of a substance into two since then these hypomorphic mutants should show an equivalent decrease in both pigments. An alternative hypothesis is that of Beadle and Tatum (1941), *i.e.* the locus may control an enzyme catalysing basically similar reactions in two parallel chains. On the other hand, the action of the white locus may indeed be through the differentiation of two enzymes from one precursor if it is accepted that other genes may take part in the production chains of the substrates differentiated for the two pigments, *e.g.* the loci of karmoisin (*kar*) and cardinal (*cd*) in the brown chain and the locus of purple (*pr*) in the red chain (Nolte, 1954*a*, 1955). The excess of red pigment in the mutant *cd* and of brown pigment in the mutant *pr* may be due to the diverting of part of the basic substance to the alternative chain. The quantitative data show that the red pigment increases more rapidly than the brown, although the brown is fully deposited before the red; thus if mutations at the white locus result in changes in the velocity of reactions controlled by this locus the balance of reactions in the two chains could be disturbed, resulting in differences in the relative amounts of the two final products.

The position of various genes in the scheme of eye-pigmentary reactions as proposed in previous studies of this series may be tested by reviewing some data on their combinations with alleles of white (table 3; fig. 4). The combination of w^e with carnation (*car*) shows large sub-additive effects for both pigment quantities; the mutant *car* delivers some substance in reduced quantities for further elaboration, and by the action of the hypomorphic mutant at the white locus even lesser quantities of the final products result. The combination of w^w with *cd* shows a large sub-additive effect on the brown pigment but an additive effect of the red pigment—it has been postulated that *cd* diverts some of the substrate from the brown to the red pigment pathway. The combination of w^e with *se* shows the epistatic effect of the latter in producing a modified red pigment and in having an additive effect on the brown pigment; the normal allele of *se* has been placed in the production chain of the common precursor required for the action of the white locus (Nolte, 1954*b*).

4. SUMMARY

The sixth group of eye-colour mutants of *Drosophila melanogaster* to be studied is the series of multiple alleles at the white locus, these

being w^{sat} , w^{co} , w^w , w^{col} , w^{bl} , w^{ch} , w^e , w^{e2} , w^{e3} , w^a , w^{a3} , w^{a4} , w^t , w and also the position-effects w^{m4} and w^{m5} .

1. The eye-colour phenotypes vary from white to very dark ruby. Histologically the colour results from granules which generally are brown, with little red; the primary pigment cells contain brown pigment only. The pigment granules are generally very indistinct excepting in the primary cells; in the higher members, however, the granules are more distinct or larger, and in w^{a3} a scattering of granules larger than normal occurs. The basal pigment cells are generally small compact masses. All these are effects of the slowing down of pigment production.

2. The red pigment of the higher members of the series yield spectrophotometric curves identical with that of the normal red pigment; for those with low red pigment content the curves are modified due to the relatively high admixture of impurities in the extracts. The brown pigment is also identical with the normal. For most alleles the untreated brown pigment extract gives an ultra-violet peak at $260\text{ m}\mu$ (as for all pupal eyes) or at least a more rapid drop at this point.

3. The red pigment content of the allele w^{bl} increases geometrically with a drop in temperature by a factor of about 1.4 per 1°C .; the brown pigment content increases arithmetically with a drop in temperature by about half of that present at 25°C . per 1°C . If the alleles are arranged in separate series for increase in amount of the two pigments, these two series do not coincide. In the red series the increase is by a ratio approximately equal to that for w^{bl} for half a degree drop in temperature; in the brown series some of the alleles fall in groups and the rise in amount in these groups is arithmetic, being an amount approximately equal to that for w^{bl} for one degree drop in temperature. Some gaps occur in both series, and it is postulated that these missing members have not yet been recognised.

4. Possible pseudoallelism at the white locus is discussed, as well as the possible type of mutation at this locus, and the interrelations of its function with the action of other loci in the two chains of pigment production.

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ADDENDUM

After going to press a new white allele came to hand, with the wine or coral type of eye-colour. Its red pigment amounts to 0.0407 (thus filling the gap in the series between w^{sat} and w^{co}), while an amount of brown pigment of 0.0370 places it in a group with w^w .