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SHORT PAPER

A new allele at the patch locus in the mouse

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SUMMARY

Evidence is presented for the existence of a new allele at the patch locus called patch-extended (symbol Ph^e). Crosses of Ph^e with Ph, W^v and Rw produce double heterozygotes that are different from those resulting from the original patch allele. Besides the different coat colour in these mice, all the $W^v+/+Ph^e$ animals that were tested resembled W^v+/W^v+ and proved to be sterile. However, the two patch alleles interact to produce a split-face phenotype which resembles the presumed Ph/Ph.

1. INTRODUCTION

The dominant spotting locus (W) in the mouse has long been known to have several mutant alleles, but two closely linked loci with similar effects, patch (Ph) and rump-white (Rw) have, so far, had only one known mutant each. This paper presents evidence for a new allele at the patch locus. The name suggested is patch-extended (symbol Ph^e).

The extent of the white spotting in the coat of $Ph/+$ mice varies from animal to animal. At one extreme mice have a large, clearly defined belly spot, while at the other they are pigmented only over the head and thorax. In some of these animals islands of pigmented fur may occur on the back in the white areas. Selection results in an increase in the extent of the white area with a concomitant decrease in fertility (Grüneberg & Truslove, 1960). Crosses of $Ph/+$ animals with either $W^v/+$ or $Rw/+$ produce double heterozygotes with a characteristic distribution of pigmented hairs which are diluted when W^v is present, but not when Rw is in the cross (Searle & Truslove, 1970). W^v/W^v animals are black-eyed white with sooty ears and are practically sterile; Ph/Ph embryos have split-faces and only rarely live to birth (Grüneberg & Truslove, 1960) and Rw/Rw embryos have not so far been identified.

2. OBSERVATIONS

The present Ph^e stock derives from two very white females (Fig. 1) which were noticed in an illegitimate litter containing five animals, four females with white patches and one normal male. The mother was $Ph/+$ and of the three possible fathers, one was $Ph/+$ and two $W^v/+$. The two very white animals were each mated to a $+/+$ male; one of them had one litter which was not reared and she died aged 152 days. The other produced eight litters containing 11 normal mice and 18 with extensive areas of white fur (Table 1) who all resembled the mother. This was noticeably different from the situation in the old patch stock where there is usually some variation in the extent of

the white patches amongst the offspring of a mating and it appeared that there might be a new mutant present in the stock at the patch locus.

Crosses of the suspected new mutant with $W^v/+$ or $Rw/+$ (Table 2) generated mice of an unexpected colour. $W^v+/+Ph^e$ (Fig. 1) were black-eyed white animals (looking like W^v/W^v) and so far none of them (three males and three females) has bred. $Rw+/+Ph^e$ (Fig. 1) looked much more like the old $W^v+/+Ph$ with diluted fur restricted to the sides

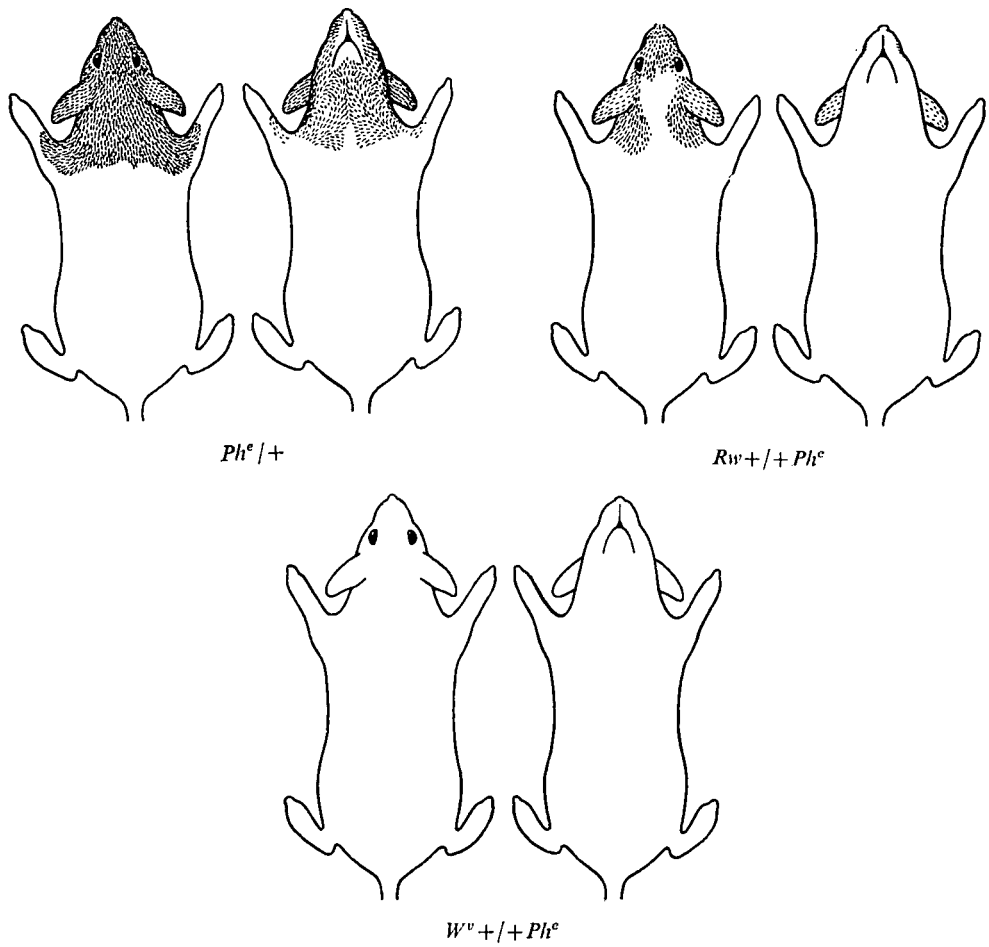

Fig. 1. The appearance of $Ph^e/+$ and of the compounds $Rw+/+Ph^e$ and $W^v+/+Ph^e$.

of the face and ears. $Rw+/+Ph$, on the other hand, always had an extensive area of undiluted fur over the head and shoulders although there was usually a head dot. Reciprocal matings of $Rw+/+Ph^e$ with $++/++$ have produced nine litters containing 27 $Rw+/++$ and 31 $++/+Ph^e$ animals, but no crossovers.

Mating $Ph/+$ with $Ph^e/+$ to test for possible allelism produced litters which could be classified for both alleles (Table 3). In order to confirm this classification use was made of the marked difference in the appearance of $W^v+/+Ph$ and $W^v+/+Ph^e$ mice. With this criterion 8 animals were confirmed as carrying the original patch allele (with 8 untested) and three as $Ph^e/+$ (with 10 untested). Seven litters of embryos of ~ 14

Table 1. *Segregation of* Ph^e

Mating	No. of litters	No. born	Mean litter size	*Ph^e*/+ ♂	*Ph^e*/+ ♀	+/+ ♂	+/+ ♀	*n*
+/+ ♂ × *Ph^e*/+ ♀								
1*	8	54	6·75	7	11	8	3	29
2	8	52	6·5	13	14	11	14	52
3	1	6	6·0	3		3		6
Ph^e/+ ♂ × +/+ ♀								
1	1	5	5·0	2	0	0	3	5
Total	18	117	6·5	51		41		92

* Original *Ph^e*/+ ♀.

Table 2. *Results of mating* Ph^e/+ *with* W^v/+ *or* Rw/+

Mating	No. of litters	No. born	Mean litter size	$\frac{Ph^e\ +}{+\ M}$	$\frac{+\ +}{+\ M}$	$\frac{Ph^e\ +}{+\ +}$	$\frac{+\ +}{+\ +}$	*n*
$\frac{W^v+}{+\ +} \times \frac{+Ph^e}{+\ +}$	12	65	5·4	8	8	10	7	33
$\frac{Rw+}{+\ +} \times \frac{+Ph^e}{+\ +}$	10	63	6·3	14	10	9	13	46

M = *W^v* in the first cross and *Rw* in the second.

Table 3. *Segregation of* Ph/+ *and* Ph^e/+

(Numbers tested and confirmed in parentheses.)

Mating	No. of litters	No. born	Mean litter size	+/+	*Ph*/+	*Ph^e*/+	*Ph*/*Ph^e*	*n*
Ph^e/+ ♂ × *Ph*/+ ♀	4	22	5·5	7	7(4)	5(1)	0	19
Ph/+ ♂ × *Ph^e*/+ ♀	4	26	6·5	6	9(4)	8(2)	0	23

days from $Ph/+ \times Ph^e/+$ matings gave 40 normals, 1 split-face and 21 solid moles. The split-face is probably Ph/Ph^e and as with Ph/Ph there is a high intra-uterine mortality. There was also a single split-face born from a mating of $Ph^e/+ \times Ph^e/+$ and so it looks as though both alleles produce similar homozygotes.

3. DISCUSSION

The genetic constitution of the original very white animals can probably be explained as a mutation at the old patch locus. It is very close to the *W* locus and resembles W^v in the phenotype of $W^v+/+Ph^e$ mice and in sometimes causing a slight dilution of the pigmented fur and in producing a head dot in some animals. The original mutation could have occurred in either parent of the two original unusual animals. The mother was certainly $Ph/+$ and the father probably also, unless he was $W^v/+$ but only transmitted the normal allele or the new mutant allele to his offspring. No $W^v/+$ animals were found among the descendants of the original abnormal mice. The mutation is similar to patch in many respects including that of producing a split-face embryo when crossed with $Ph/+$ and a new-born split-face when crossed with $Ph^e/+$.

The white spotting in patch was shown to be dependent on the genetic background and its extent was under genetic control (Grüneberg & Truslove, 1960). There was a parent–offspring correlation, but in no case did all the offspring resemble a parent with an extensive white patch consistently. Ph^e on the other hand shows a complete correlation between parents and offspring and it is possible to classify animals for either allele.

The differences in the double heterozygotes when $Ph^e/+$ is crossed with $W^v/+$ or $Rw/+$ form an interesting series. $W^v+/+Ph^e$ animals are more like W^v+/W^v+ and look slightly anaemic at birth, while $Rw+/+Ph^e$ are more like $W^v+/+Ph$ which $Rw+/+Ph$ never were. Dilution of the fur is a feature of $W^v/+$, but is not seen in either $Ph/+$ or $Rw/+$ mice. Neither is there dilution in $Ph+/+Rw$ although the extent of the white area is increased and the animals usually have a head dot (Searle & Truslove, 1970).

The apparent sterility of $W^v+/+Ph^e$ is unexpected as $W^v+/+Ph$ and $W^v+/+Rw$ are fertile in both sexes, but they both have more pigmented fur than $W^v+/+Ph^e$. This is in agreement with the results of selection for increased white spotting in $Ph/+$ animals where it was found that fertility decreased with an increase in the amount of unpigmented fur.

The embryological data are consistent with *Ph* and Ph^e being alleles with an increase in the early mortality of the Ph/Ph^e genotype. The patch stock has always had a high degree of background mortality. The survival of a presumed Ph^e/Ph^e split-face mouse to birth argues in favour of a less severe form of abnormality than on the old background, although in other respects the new allele appears to be more severe.

Grüneberg (1966) has drawn attention to the fact that freshly arising mutations in the mouse and other mammals have often been observed as clusters of several individuals in the first instance. The discovery of Ph^e similarly involved two heterozygotes in the first litter, but as so often, the underlying mechanism remains in doubt.

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