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SHORT PAPER

Genetic differences between substrains of the inbred mouse strain 101 and designation of a new strain 102

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SUMMARY

Genetic polymorphisms revealed two distinct substrains of the inbred strain 101. One group included substrains 101/Rl, 101/H and 101/HOxe; the other group comprised 101/El and 101/Sl. The two groups differed at 5 of the 8 genetic loci tested. The accompanying paper (Evans, Burtenshaw & Adler, 1985) shows that the two groups also differ for several chromosome polymorphisms. We suggest that genetic contamination occurred during the derivation of 101/El from 101/Rl and was already present in 101/El when 101/Sl was produced from this substrain. We further propose that these substrains be renamed 102/El and 102/Sl respectively.

1. INTRODUCTION

In a previous publication (West, Peters & Lyon, 1984) we reported genetic differences between substrains 101/H and 101/El of the inbred mouse strain 101. Both the 101/H substrain, maintained at Harwell, and the 101/El substrain, maintained at the Institut für Genetik at Neuherberg, were derived from 101/Rl at Oak Ridge. We now report genetic comparisons, and the accompanying paper by Evans, Burtenshaw and Adler describes cytogenetic comparisons, of these three substrains, together with substrains designated 101/Sl and 101/HOxe. Substrain 101/Sl was derived from 101/El and is currently maintained at Oak Ridge and substrain 101/HOxe was derived from the Harwell 101/H substrain and is maintained in Oxford. The genealogy of the various 101 substrains is shown in Fig. 1.

2. MATERIALS AND METHODS

Twelve 101/Rl and 12 101/Sl mice (6 of each sex of both substrains) were sent from Oak Ridge to Harwell for genetic tests and comparison with previously published results (West *et al.* 1984) for 101/H and 101/El substrains. Animals from the Harwell 101/H

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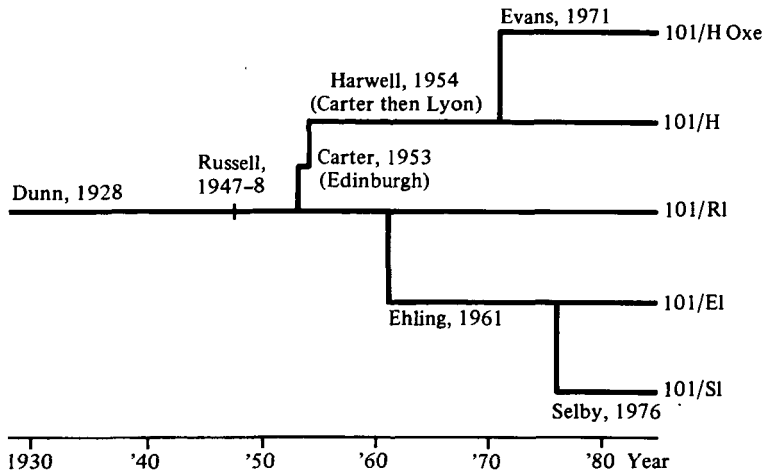

Fig. 1. Genealogy of the 101 substrains tested.

substrain were sent to Dr E. P. Evans in Oxford in 1971 and for the purpose of this paper will be referred to as 101/HOxe.

All 24 101/Rl and 101/Sl mice were typed for agouti (*a*), carbonic anhydrase-2 (*Car-2*), glucose phosphate isomerase (*Gpi-1s*), haemoglobin α-chain (*Hba*), haemoglobin β-chain (*Hbb*), lens opacity-2 (*lop-2*) and phosphoglucomutase-1 (*Pgm-1*) as previously described (West *et al.* 1984). Two 101/Rl and two 101/Sl mice, together with a C3H/HeH control, were killed, the eyes excised, coded and histologically sectioned in order to classify the 101/Rl and 101/Sl substrains for retinal degeneration (*rd*) as described earlier (West *et al.* 1984).

3. RESULTS

All twelve 101/Rl mice had bilateral cataracts identical to those found in 101/H and 101/HOxe mice and attributed to the *lop-2/lop-2* genotype (West & Fisher, 1985). Four of the 12 101/Sl mice tested also had cataracts but none was identical to 101/H and for this reason the 101/Sl substrain was classified as wild type for the *lop-2* locus. One female and one male 101/Sl had small unilateral opacities in the anterior cortex of the lens, one female had a significant unilateral nuclear cataract and one female had significant bilateral cataracts extending from the nucleus to the anterior cortex. The cause of these cataracts is unknown but cataracts that are not inherited are known to occur sporadically in mice (Kratochvilova, 1981; Favor, 1983). Both of the 101/Rl and the two 101/Sl mice that were typed for *rd* were rd^+ and all twelve of each substrain were homozygous for alleles at the other six genetic loci, as shown in Table 1.

The results of the genetic analysis show that 101/Rl is identical to 101/H and that 101/Sl is identical to 101/El at all eight loci tested.

4. DISCUSSION

Apart from the cataracts observed in some 101/Sl mice, all the mice tested from a given substrain were clearly homozygous for all the genetic and chromosome polymorphisms (Evans *et al.* 1985) that were considered. The results shown in Table 1 show that the 101 substrains fall into two distinct groups. One group includes 101/Rl, 101/H and 101/HOxe and the other group comprises 101/El and 101/Sl. Substrains within each group were identical for all genetic and chromosome polymorphisms that were tested but the two groups differed at 5 of the 8 genetic loci tested and for two chromosome

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Table 1. *Genetic and cytogenetic differences between various 101 substrains and the C3H/HeH mouse strain*

Genetic locus	Chromosome	Mouse strain					
		101/Rl	101/H*	101/HOxe	101/El*	101/Sl	C3H/HeH*
		Genetic polymorphisms (alleles present)					
Hbb	7	d	d	–	d	d	d
Pgm-1	5	a	a	–	a	a	b
rd	5	+	+	–	+	+	rd
a	2	A^w	A^w	A^w	A	A	A
Car-2	3	a	a	–	b	b	b
Gpi-1s	7	a	a	–	b	b	b
Hba	11	a	a	–	c	c	c
lop-2	?	lop-2	lop-2	lop-2†	+	+	+
		Chromosome polymorphisms‡					
—	8	Hc^s	–	Hc^s	Hc^l	Hc^l	Hc^l
—	13	Hc^l	–	Hc^l	Hc^s	Hc^s	Hc^s

* Genetic classification of 101/H, 101/El and C3H/HeH is taken from West, Peters & Lyon (1984).

† Classification of 101/HOxe as *lop-2* is from West & Fisher (1985).

‡ From Evans, Burtenshaw & Adler (1985). The C3H/HeHOxe substrain was used for the analysis of chromosome polymorphisms.

polymorphisms. In addition, Evans *et al.* (1985) found other minor chromosome polymorphisms which divided the two groups similarly. The distribution of chromosome polymorphisms supports the previous suggestion (West *et al.* 1984) that 101/El shares genetic material with both 101/H and C3H/HeH strains and may represent a recombinant inbred strain produced by an illegitimate mating between 101 and C3H strain mice.

If 101/El and 101/Sl have been genetically contaminated, reference to the genealogy of the various 101 substrains (Fig. 1) shows that the contamination could have occurred either (1l) at Oak Ridge, before 1961, in a 101/Rl subline that later became extinct at Oak Ridge or (2) at Neuherberg. Since both 101/El and 101/Sl were both homozygous for identical genetic and chromosome polymorphisms the 101/El substrain was probably completely inbred and homozygous by 1976 when the 101/Sl substrain was derived. (One possibility is that the 101/El substrain was established, in error, from a mating between 101/Rl and C3H/Rl in 1961 when these two strains were sent from Oak Ridge to Neuherberg.)

Given the degree of disparity between the two genetically distinct groups of 101 substrains it would seem advisable to designate these as two separate strains rather than variant substrains. The strain symbol 101 could be discontinued and two new strain symbols adopted. Alternatively, the similarity of strains 101/Rl and 101/H, which have been separated since 1953, could be considered as good evidence that these are descendants of the original 101 strain. The 101 symbol could be retained for them, with a new symbol for 101/El and 101/Sl. If this course was adopted the strain symbol 3H1 should be avoided since this is used as an abbreviation for F_1 hybrids produced by crossing C3H and 101 strains. We propose that the substrain symbols 101/Rl, 101/H and 101/HOxe be retained but substrains 101/El and 101/Sl be renamed 102/El and 102/Sl respectively.

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REFERENCES

Evans, E. P., Burtenshaw, M. D. & Adler, I. D. (1985). Chromosome differences between substrains of the inbred 101 mouse strain. *Genetical Research* **46**, 353–356.

Favor, J. (1983). A comparison of the dominant cataract and recessive specific-locus mutation rates induced by treatment of male mice with ethylnitrosourea. *Mutation Research* **110**, 367–382.

Kratochvilova, J. (1981). Dominant cataract mutations detected in offspring of gamma-irradiated male mice. *Journal of Heredity* **72**, 302–307.

West, J. D. & Fisher, G. (1985). Inherited cataracts in inbred mice. *Genetical Research* **46**, 45–56.

West, J. D., Peters, J. & Lyon, M. F. (1984). Genetic differences between two substrains of the inbred 101 mouse strain. *Genetical Research* **44**, 343–346.

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