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# Inherited cataracts in inbred mice

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SUMMARY

Examination of the eyes with a slit lamp revealed that 101/H mice had a coloured cataract. Crosses to C3H/HeH indicated that this was inherited as a single recessive gene which we have designated *lop-2* (lens opacity-2). The related strain 129/Sv-$Sl^J$-*CP* had a phenotypically identical cataract and presumably also carries the *lop-2* gene. CBA/H, CBA/CaH-+/*p*, CBA/H-*kd* and CBA/H-T6 mice had a bright white or white/green cataract that typically extended from the nucleus to the anterior cortex of the lens. Crosses to C3H/HeH indicated that this was inherited as a semi-dominant gene. However, other crosses raise the possibility that the CBA cataract is also caused by *lop-2*. If so, the expressivity (and penetrance of the heterozygote) is affected by genetic background. Neither *lop-2* nor the gene responsible for the CBA cataract was linked to contrasted ($Sl^{con}$) on chromosome 10, so these are distinct from the *Lop* (lens opacity) gene. Further studies of genetic linkage are needed to clarify whether *lop-2* is responsible for both the 101/H and CBA/H cataracts.

## 1. INTRODUCTION

A cataract is an opacity in the normally transparent lens of the eye. Van Heyningen (1969) defined a cataract, for experimental purposes, as 'any lens change, however, small, that is visible *in vivo* by the use of optical instruments'. This definition embraces minor abnormalities that would not impair vision (and would not be considered as cataracts by clinical ophthalmologists) and mature cataracts that appear white to the naked eye. Cataracts are diverse in appearance and origin, and some are inherited. The causes of cataract include congenital defects, senility, metabolic disorders, infection and exposure to a variety of physical or chemical agents (van Heyningen, 1969). In many cases the opacity is the result of changes in lens hydration and swollen lens fibres (see, for example, Hazlett & Bradley, 1978, for discussion).

Genetic variants that cause cataracts in mice (reviewed by Robinson, Kuwabara & Zwaan, 1982) may provide insights into comparable conditions in man. In addition the accumulation and genetic mapping of such variants in the mouse should eventually provide a more reliable minimum estimate of the number of loci

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that can mutate to produce cataracts. This would be particularly useful for evaluating the information derived from the dominant cataract mutation test described by Kratochvilova & Ehling (1979).

In this paper we describe the inheritance of two cataract phenotypes found in inbred mice. These cataracts are not visible to the naked eye but are readily detected with a slit lamp in all mice examined from the affected strains.

## 2. MATERIALS AND METHODS

Mice of the outbred PT stock and the following inbred strains (with abbreviations in parentheses) were maintained at Harwell: 101/H (101), C3H/HeH (C3H), 129/Sv-*Sl*$^{J}$-*CP* (129), CBA/H (CBA), CBA/CaH-+/p, CBA/H-*kd*, CBA/H-T6, C57BL/0la, C57BL/10-*p*, DBA/20la and JU/FaCt. Mice from the 101/H and CBA/H colonies maintained by Dr E. P. Evans at the Sir William Dunn School of Pathology, Oxford were also examined. These colonies were derived from the Harwell substrains in 1971, and for the purposes of this paper are referred to as 101/HOxe and CBA/HOxe respectively. The Harwell CBA/H strain was derived from CBA/Ca, and eyes from five other CBA/Ca-based stocks, maintained in Edinburgh, were examined as described below.

Cataracts were detected using a Zeiss 30SL/M slit lamp (comprising a corneal microscope and slit illuminator) to examine the lens *in vivo*. A drop of 1% (w/v) atropine sulphate (Evans Medical Ltd) was applied to each eye of the mouse in order to dilate the pupil. Approximately 5 min later the mouse was restrained by hand and both eyes were examined, in turn, using the slit lamp in a darkened room. (Anaesthetic was neither necessary nor desirable.) The lenses were scanned with a narrow beam of light produced by the slit illuminator and observed through the corneal microscope using 20× magnification. The angle between illumination and observation was normally about 45°, but additional observations were made at narrower angles and in the 'red-reflex' position with the slit illuminator directly in line with the corneal microscope. In most cases mice were examined 3–5 weeks after birth, but adult mice were also examined.

In addition, eyes removed from mice maintained in the Zoology Department of the University of Edinburgh were examined as follows. A drop of 1% atropine sulphate was applied to each eye and 10 min later the mouse was killed by cervical dislocation. The mice were coded and the eyes were removed with curved scissors and placed in a vial containing Dulbecco's phosphate-buffered saline (PBS) with 0·6 mg/ml penicillin and 0·5 mg/ml streptomycin. The eyes were sent by mail from Edinburgh to Harwell, where each eye was separately mounted on a glass slide using a drop of 2% agar. The mounted eye was kept moist with a drop of PBS and the lens was viewed with a slit lamp as described above for eyes *in situ*. Some lenses from other eyes were dissected out and examined with a dissecting microscope.

Statistical tests were done using a Hewlett Packard programmable calculator, programmed by Mr D. G. Papworth to compute $\chi^2$ with Yates correction.

## 3. RESULTS

We discovered two cataract phenotypes in 101/H and CBA/H mice respectively. For the purposes of presentation of results in this paper we provisionally designate the genes responsible for the 101/H and CBA/H cataracts *lop-2* and *Lop-3* respectively.

### (i) *Cataracts in 101/H mice*

Examination of 16 101/H mice revealed that they all had cataracts. The cataract usually appeared as a dull green/brown translucent ring surrounding a black central region into which projected a brighter opacity that was variously coloured; often green or brown but sometimes white, blue, purple or pink. Examination of eyes with a slit lamp suggested that the cataract was located in the nuclear/perinuclear region of the lens. However, examination of a few excised lenses with a dissecting microscope revealed a small opacity in the anterior cortex but no cataract of the type seen with the slit lamp. The reason for this discrepancy is unclear but it is possible that the coloured cataract seen with the slit lamp is an interference phenomenon or an image of a smaller more anterior opacity.

An identical coloured-cataract phenotype was also detected with a slit lamp in mice of the inbred strain 129/Sv-*Sl*$^{J}$-*CP* and all 27 mice examined from the 101/HOxe colony maintained at the Sir William Dunn School of Pathology in Oxford by Dr E. P. Evans. The Oxford substrain of 101/H was separated from the Harwell colony in 1971 and the 129 strain was derived from the same general source as the 101 strain in 1928 by Dunn (see, for example, Festing, 1979). No such cataract was found, however, in the 101/El substrain that we imported from the Institut für Genetik at Neuherberg. In view of other genetic differences it seems likely that 101/El and 101/H are really different strains (West, Peters & Lyon, 1984).

No significant lens opacity was consistently seen in other Harwell stocks of mice that were examined. These included the outbred PT stock and the inbred strains C3H/HeH, C57BL/0la, C57BL/10-*p*, DBA/20la and JU/FaCt. However, sporadic minor opacities were seen, particularly in DBA/20la, and also in C57BL/0la and some related congenic strains.

The results of crosses between 101/H and C3H/HeH are shown in Table 1 (crosses 1–8). Overall the pattern of inheritance is compatible with a single autosomal recessive gene present in 101/H. We designate this gene *lop-2* (lens opacity-2). Cross 2 (Table 1) rules out the possibility that *lop-2* is X-linked because all the male progeny would be expected to have cataracts whereas the frequency among males was only 1/13). The crosses between 101 and PT (crosses 9-11, in Table 1) also conform to the general expectations of autosomal recessive inheritance.

The frequency of mice with cataracts in crosses 1–11 tends to be slightly higher than expected, and this is significantly higher for cross 6. This could either be attributed to cataracts of diverse origin or it may indicate that *lop-2*/+ heterozygotes occasionally express a cataract phenotype. (The frequency of cataracts

among control mice (Kratochvilova, 1981; Favor, 1983; West & Fisher, unpublished) ranges from 1% to 10%.) In our experiments we classified any lens opacity as a positive. Although the coloured cataract was the most common phenotype some mice had a dull opacity in or near the nucleus, others had anterior polar or anterior cortical cataracts either alone or in conjunction with a coloured or dull cataract, and a few had other minor abnormalities. Cataracts were almost always bilateral although, for example, one eye sometimes had a coloured cataract and the other an anterior cataract.

Crosses 12 and 13 in Table 1 indicate that the coloured-cataract phenotype in 129/Sv-*Sl*$^{J}$-CP is probably also caused by *lop-2*. Of the 41 mice in cross 13 with cataracts, 40 had bilateral coloured cataracts; two of these had, in addition, a unilateral anterior cataract, and the remaining mouse had a coloured cataract in one eye and an anterior cataract in the other.

Overall these results suggest that the *lop-2* gene is responsible for a variety of cataract phenotypes which may be influenced by the genetic background.

### (ii) *Cataracts in CBA mice*

We first observed the CBA cataract phenotype in three CBA/HOxe mice in Oxford. Subsequently we found an identical phenotype in the Harwell substrains of CBA/H, CBA/CaH-+/*p*, CBA/H-T6 and CBA/H-*kd*. Strains CBA/H and CBA/CaH-+/*p* have been maintained separately since 1948; CBA/H and CBA/H-T6 separated in 1960; CBA/H and CBA/H-*kd* separated in 1970 and CBA/HOxe separated from CBA/H in 1971.

The three CBA/HOxe mice examined all had bilateral bright white cataracts in the anterior cortex that extended to the lens nucleus. These were different from any cataract seen in the 101/H crosses, described above. Seven CBA/H-T6 mice all showed bilateral cataracts. Most were similar to the CBA/HOxe cataracts but 4/14 lenses (three mice) had a green/white cataract that resembled a more reflectant version of the coloured cataract seen in 101/H mice. All seven CBA/CaH-+/*p* mice had bright white, nuclear and/or anterior cataracts and six CBA/H-*kd* mice had white or white/green cataracts in the nucleus or anterior part of the lens. One cataract appeared to be an anterior pyramidal opacity.

The results of crosses between CBA/H and C3H/HeH are shown in Table 2. Most of the mice in the $F_1$ generation (crosses 14 and 15) had mild cataract phenotypes comprising either perinuclear specks or lamellar specks in the cortex. Backcrosses to CBA/H (crosses 18 and 19) produced some progeny with the more severe phenotype typical of the CBA strain. Overall the pattern of inheritance shown by the crosses in Table 2 indicates that the CBA cataract is caused by a single, autosomal, semi-dominant gene. None of the 10 males in cross 14 had normal lenses and none of the 24 males in cross 15 had severe cataracts, so the CBA cataract gene is not X-linked. The differences between observed and expected frequencies in Table 2 are probably attributable to the presence of cataracts of diverse origin and various classification errors as discussed in the previous section for *lop-2*.

The semi-dominant mode of inheritance and the more severe cataract phenotype suggested that the CBA cataract was not attributable to the 101/H, *lop-2* cataract

Table 1. *Cataracts among progeny of 101/H mice*

| Cross | | | | Progeny | | | | |
|---|---|---|---|---|---|---|---|---|
| Strains (♀×♂) | | Genotypes (♀×♂) | | Cataracts | Normal | % cataracts | Expected % cataracts | Significance |
| 1 C3H | × 101 | +/+ | × *lop-2/lop-2* | 0 | 30 | 0 | 0 | |
| 2 101 | × C3H | *lop-2/lop-2* | × +/+ | 1 | 23 | 4 | 0 | |
| 3 (C3H × 101) | × C3H | +/*lop-2* | × +/+ | 2 | 28 | 7 | 0 | |
| 4 (101 × C3H) | × C3H | *lop-2*/+ | × +/+ | 2 | 40 | 5 | 0 | |
| 5 (C3H × 101) | × 101 | +/*lop-2* | × *lop-2/lop-2* | 28 | 15 | 65 | 50 | $\chi_1^2 = 3{\cdot}35$ |
| 6 (101 × C3H) | × 101 | *lop-2*/+ | × *lop-2/lop-2* | 33 | 14 | 70 | 50 | $\chi_1^2 = 6{\cdot}89$* |
| 7 (C3H × 101) | × (C3H × 101) | +/*lop-2* | × +/*lop-2* | 11 | 23 | 32 | 25 | $\chi_1^2 = 0{\cdot}63$ |
| 8 (101 × C3H) | × (101 × C3H) | *lop-2*/+ | × *lop-2*/+ | 11 | 34 | 24 | 25 | $\chi_1^2 = 0{\cdot}01$ |
| 9 PT | × 101 | +/+ | × *lop-2/lop-2* | 0 | 21 | 0 | 0 | |
| 10 PT | × (PT × 101) | +/+ | × +/*lop-2* | 3 | 42 | 7 | 0 | |
| 11 (PT × 101) | × (PT × 101) | +/*lop-2* | × +/*lop-2* | 9 | 22 | 29 | 25 | $\chi_1^2 = 0{\cdot}10$ |
| 12 129 | × C3H | *lop-2/lop-2* | × +/+ | 0 | 32 | 0 | 0 | |
| 13 129 | × 101 | *lop-2/lop-2* | × *lop-2/lop-2* | 41 | 0 | 100 | 100 | |

*$P < 0{\cdot}05$.

Table 2. *Cataracts among progeny of CBA/H mice*

| Cross | | | | Cataracts among progeny | | | | | | Expected ratio | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Strains (♀×♂) | | Genotypes (♀×♂) | | Severe cataracts | Mild cataracts | Normal | % cataracts | Expected % cataracts | Significance | severe:mild:normal | Significance |
| 14 C3H | × CBA | +/+ | × *Lop-3/Lop-3* | 0 | 26 | 0 | 100 | 100 | | 0:1:0 | |
| 15 CBA | × C3H | *Lop-3/Lop-3* | × +/+ | 0 | 38 | 3 | 93 | 100 | | 0:1:0 | |
| 16 (C3H×CBA) | × C3H | +/*Lop-3* | × +/+ | 0 | 36 | 18 | 67 | 50 | $\chi_1^2 = 5{\cdot}35^*$ | 0:1:1 | $\chi_1^2 = 5{\cdot}35^*$ |
| 17 (CBA×C3H) | × C3H | *Lop-3*/+ | × +/+ | 1 | 32 | 30 | 52 | 50 | $\chi_1^2 = 0{\cdot}06$ | 0:1:1 | |
| 18 (C3H×CBA) | × CBA | +/*Lop-3* | × *Lop-3/Lop-3* | 16 | 21 | 0 | 100 | 100 | | 1:1:0 | $\chi_1^2 = 0{\cdot}43$ |
| 19 (CBA×C3H) | × CBA | *Lop-3*/+ | × *Lop-3/Lop-3* | 14 | 25 | 3 | 93 | 100 | | 1:1:0 | |
| 20 (C3H×CBA) | × (C3H×CBA) | +/*Lop-3* | × +/*Lop-3* | 10 | 26 | 5 | 88 | 75 | $\chi_2^2 = 2{\cdot}93$ | 1:2:1 | $\chi_2^2 = 4{\cdot}17$ |
| 21 (CBA×C3H) | × (CBA×C3H) | *Lop-3*/+ | × *Lop-3*/+ | 12 | 50 | 15 | 81 | 75 | $\chi_1^2 = 0{\cdot}97$ | 1:2:1 | $\chi_2^2 = 7{\cdot}10^*$ |

$^*P < 0{\cdot}05$.

Table 3. *Cataracts among progeny of crosses between 101/H and CBA/H mice*

| Cross | | | | Progeny | | | Expected % cataracts and Significance | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | If allelic | | If unlinked | |
| Strains (♀×♂) | | Genotype if unlinked (♀×♂) | | Cataracts | Normal | % cataracts | | | | |
| 22 101 | × CBA | *lop-2/lop-2* +/+ | × +/+ *Lop-3/Lop-3* | 34 | 1 | 97 | 100 | | 100 | |
| 23 CBA | × 101 | +/+*Lop-3/Lop-3* | × *lop-2/lop-2*+/+ | 28 | 4 | 88 | 100 | | 100 | |
| 24 C3H | × (CBA×101) | +/+ +/+ | × +/*lop-2 Lop-3*/+ | 5 | 33 | 13 | 50 | $\chi_1^2 = 19{\cdot}18^{**}$ | 50 | $\chi_1^2 = 19{\cdot}18^{**}$ |
| 25 CBA | × (CBA×101) | +/+*Lop-3/Lop-3* | × +/*lop-2 Lop-3*/+ | 50 | 3 | 94 | 100 | | 100 | |
| 26 101 | × (CBA×101) | *lop-2/lop-2* +/+ | × +/*lop-2 Lop-3*/+ | 49 | 0 | 100 | 100 | | 75 | $\chi_1^2 = 15{\cdot}03^{**}$ |
| 27 (CBA×101) | × (CBA×101) | +/*lop-2 Lop-3*/+ | × +/*lop-2 Lop-3*/+ | 48 | 3 | 94 | 100 | | 81 (13/16) | $\chi_1^2 = 4{\cdot}73^*$ |
| 28 (101×CBA) | × (101×CBA) | *lop-2*/+ +/*Lop-3* | × *lop-2*/+ +/*Lop-3* | 72 | 2 | 97 | 100 | | 81 (13/16) | $\chi_1^2 = 11{\cdot}48^{**}$ |

$^*P < 0{\cdot}05$ $^{**}P < 0{\cdot}001$.

gene. For the purposes of further discussion in this paper we provisionally designate the CBA cataract gene *Lop-3* (lens opacity-3).

### (iii) *Crosses between 101/H and CBA/H*

The frequency of cataracts among progeny of crosses between 101/H and CBA/H mice is shown in Table 3. The genotypes shown are those expected if *lop-2* and *Lop-3* are not genetically linked, and the expected frequencies shown assume either that *lop-2* and *Lop-3* are allelic or that they are unlinked. As expected most (101 × CBA)$F_1$ and (CBA × 101)$F_1$ mice (crosses 22 and 23) had cataracts. However, in most cases the phenotype resembled that of 101/H (*lop-2/lop-2*) rather than CBA/H (*Lop-3/Lop-3*). Only 5/38 mice from the C3H ♀ × (CBA × 101) ♂ cross (cross 24) had cataracts, which is significantly fewer than the expected 50 % + /*Lop-3* (compare with crosses 16 and 17 in Table 2). It seems likely that the mild cataract phenotype characteristic of + /*Lop-3* heterozygotes (e.g. cross 14, Table 2) may not be detected on the different genetic background of cross 24 (Table 3).

Different frequencies of mice with cataracts are expected from crosses 26–28 in Table 3, depending on whether *lop-2* and *Lop-3* are allelic, genetically linked or unlinked. The observed frequency is higher than the expected, if *lop-2* and *lop-3* are unlinked, in all three crosses. This suggests that the two genes may be genetically linked, allelic or even identical alleles that produce different cataract phenotypes on different genetic backgrounds (variable expressivity).

### (iv) *Tests for genetic linkage*

Tests to determine whether *lop-2* or *Lop-3* is genetically linked to $Sl^{con}$ (contrasted) were performed in order to evaluate whether either *lop-2* or *Lop-3* is allelic with *Lop*. (Lyon *et al.* 1981 reported a recombination frequency of 21·7 % between *Lop* and $Sl^{gbH}$ on chromosome 10.) The results (Tables 4 and 5) show that neither *lop-2* nor *Lop-3* is genetically linked to $Sl^{con}$ and so they are not allelic with *Lop*.

The linkage test between *Lop-3* and $Sl^{con}$ made use of the distinction between severe cataracts (*Lop-3/Lop-3*) on the one hand and mild cataracts or normal lenses (*Lop-3*/+ or + / +) on the other. An earlier attempt to treat *Lop-3* as a dominant gene and distinguish *Lop-3*/+ from + / + was less successful, because fewer than the expected 50 % cataract phenotypes were found among the progeny of crosses between C3H females (+ / + + / +) and *Lop-3*/+ + /$Sl^{con}$ males (9/39 + /$Sl^{con}$ progeny and 6/26 + / + progeny had cataracts). This is similar to the low frequency of cataracts found among the progeny of cross 24 (Table 3).

In addition, eyes from various CBA/Ca congenic stocks, maintained in the Department of Zoology of the University of Edinburgh, were examined as described in the Materials and Methods section. Three congenic stocks (CBA/Ca–*Gpi-1s*$^a$, CBA/Ca–*Igh-1*$^b$ and CBA/Ca–*Pgk-1*$^a$) were tested together with two positive controls (CBA/Ca and CBA/Ca–T6) and one negative control stock (C3H/HeHa–*Pgk-1*$^a$). (The genes *Gpi-1s* and *Igh-1* are located on chromosomes

Table 4. *Test for genetic linkage between* lop-2 *and* $Sl^{con}$

Cross: *lop-2*/+ +/$Sl^{con}$ × *lop-2*/*lop-2* +/+

| Progeny classes | |
|---|---|
| Parental | |
| Cataract, + | 21 |
| Normal, $Sl^{con}$ | 22 |
| Recombinant | |
| Cataract, $Sl^{con}$ | 18 |
| Normal, + | 23 |

Recombinant fraction (R.F.) = 41/84 = 48·8 ± 5·5 %
Expected R.F. if *lop-2* and $Sl^{con}$ are unlinked = 50 %; $\chi_1^2 = 0{\cdot}01$
Expected R.F. if *lop-2* is allelic with *Lop* = 52/240*; $\chi_1^2 = 21{\cdot}09$**

* R.F. for *Lop* and $Sl^{gbH}$ = 52/240 (Lyon *et al.* 1981).
**$P = 0{\cdot}001$.

Table 5. *Test for genetic linkage between* Lop-3 *and* $Sl^{con}$

Cross: *Lop-3*/*Lop-3* +/+ × *Lop-3*/+ +$Sl^{con}$

| Progeny classes | | |
|---|---|---|
| Parental | | |
| Severe cataract | + | 20 |
| Normal/mild cataract | $Sl^{con}$ | 22 |
| Recombinant | | |
| Severe cataract | $Sl^{con}$ | 13 |
| Normal/mild cataract | + | 20 |

Recombinant fraction (R.F.) = 33/75 = 44·0 ± 5·7 %
Expected R.F. if *Lop-3* and $Sl^{con}$ are unlinked = 50 %; $\chi_1^2 = 0{\cdot}85$
Expected R.F. if *Lop-3* is allelic with *Lop* = 52/240*; $\chi_1^2 = 13{\cdot}35$**

* See footnote to Table 4.
**$P < 0{\cdot}001$.

7 and 12 respectively and *Pgk-1* is on the X-chromosome.) Cataracts were found in eyes from all five CBA stocks but not in eyes from the C3H/HeHa–*Pgk-1*$^a$ negative control. If any of these three congenic stocks had not had cataracts this would have indicated that the wild-type allele of *Lop-3* was introduced along with *Gpi-1s*$^a$, *Igh-1*$^b$ or *Pgk-1*$^a$ and had displaced the *Lop-3* allele from the stock. This would have suggested the possibility of genetic linkage, between *Lop-3* and the relevant locus (*Gpi-1s*, *Igh-1* or *Pgk-1*), which could then have been tested. Since all of the CBA/Ca congenic stocks had cataracts, however, this does not help to decide a priority for future linkage tests.

## 4. DISCUSSION

The cataract present in 101/H mice is present in two 101/H colonies that were separated in 1971 and in a distantly related strain, 129. The CBA cataract was present in ten stocks of CBA, two of which were separated in 1948. These observations indicate that neither the 101/H nor CBA cataract genes are the results of recent mutation events.

The crosses with the unaffected strain C3H indicate that *lop-2* is recessive and

*Lop-3* is semi-dominant, and the phenotypes of the cataracts seen in 101/H and CBA/H mice appear, at least superficially, to be different. However, the penetrance of the mild cataract phenotype in *Lop-3*/+ heterozygotes seems to be low on some genetic backgrounds (cross 24 in Table 3 and the unsuccessful linkage cross between C3H and *Lop-3*/+ +/$Sl^{con}$ discussed above). Also the phenotype of the *lop-2* cataract is variable and includes anterior cataracts which may be a mild form of the cataract seen in CBA/H mice. Conversely, some CBA/H cataracts could be more severe forms of the coloured cataract seen in 101/H and the 129 strain.

These ambiguities raise the possibility that the cataracts in CBA/H, 101/H and 129 are all caused by the same gene (*lop-2*) and that the expressivity (and penetrance of the heterozygote) is affected by genetic background. This possibility is supported by crosses 26–28 (Table 3) which suggest that *lop-2* and *Lop-3* are allelic or at least genetically linked.

Not only is it unclear whether *lop-2* and *Lop-3* are different genes, but it is also not clear whether they are different from any of the other genes that cause cataracts in mice. There are now over fifty genetically determined lens abnormalities in the mouse (Table 6), but only ten of those listed have been genetically mapped. We have shown that *lop-2* and *Lop-3* are distinct from *Lop*, but until further linkage studies are done the linkage relationship between *lop-2* and *Lop-3* plus the number of separate gene loci involved in lens abnormalities will remain unknown. Two sets of recombinant inbred strains (NX129 and 129XB) exist that have a 129 strain as one of the progenitor strains (see Taylor, 1981). It may be possible to use these recombinant inbred strains as a first step to mapping *lop-2*. Once *lop-2* is mapped it would be a simple matter to test whether *Lop-3* is closely linked and perhaps determine whether *lop-2* and *Lop-3* are separate loci.

The existence of genetically inherited cataracts in laboratory mice should also be borne in mind when screening for new cataract mutations or testing for genetic linkage of cataract genes with other markers. For example, the *Bpa*/+ (bare patches) mice that were shown to have cataracts by Happle *et al.* (1983) were derived from a Harwell stock that was maintained by crossing *Bpa*/+ females to (C3H/HeH × 101/H)$F_1$ males. The *lop-2* gene was almost certainly present in the stock examined for cataracts by Happle *et al.* (1983) and could have been a source of confusion. However, these authors reported cataracts in 8/10 *Bpa*/+ females, but none in ten control littermates, which suggests that *Bpa* had a real effect. We have made limited observations on the Harwell *Bpa* stock and found nuclear or perinuclear opacities in 4/12 *Bpa*/+ ♀♀ but no similar opacity among 42 +/+ ♀♀ and +/Y ♂♂ from the same stock. However, various other types of opacities (including the coloured cataract characteristic of 101/H) were present in this stock. (Among the *Bpa*/+ ♀♀ we found 4/12 nuclear or perinuclear opacities; 1/12 coloured cataracts; 2/12 dull nuclear opacities and 5/12 normal. Among the +/+ ♀♀ and +/Y ♂♂ from the same stock we found 8/42 coloured cataracts; 1/42 anterior cataracts; 1/42 with a coloured cataract in one eye and an anterior cataract in the other; 3/42 dull nuclear opacities and 29/42 normal.) A more systematic study of both young and old mice, preferably on a different genetic background, is needed to clarify whether *Bpa* causes cataracts.

In conclusion we have shown that the inbred strains 101/H and some related

Table 6. *List of genes that affect the mouse lens**

| Gene symbol | Gene name | Effect on lens | Chromosome |
|---|---|---|---|
| Accepted gene symbols | | | |
| *ak* | Aphakia | Small eye lacking lens | 19 |
| *bh* | Brain-hernia | Mature cataract at 7–12 months | 7 |
| *Bld* | Blind | Lens absent or misshapen and attached to cornea | 15 |
| *Bpa* | Bare patches | Cataract (see Happle *et al.* 1983) | *X* |
| *bs* | Blind sterile | Cataract | 2 |
| *cac* (formerly *cat*) | Recessive cataract | Cataract at 1–3 months | |
| *Cat* (allelic $Cat^{Fr}$, formerly *Svl*) | Dominant cataract (formerly shrivelled) | Cataract, abnormal lens epithelium | |
| *Dey* | Dickie's small eye | Small lens with cataract | 2 |
| *dyl* | Dysgenetic lens | Small misshapen lens attached to cornea | |
| *ec* | Ectopic | Lens degeneration | |
| *Elo* | Eye lens obsolescence | Small eye with abnormal lens | 1 |
| *Eo* | Eye opacity | Eye opacity† and small eyes | |
| *lg* | Lid-gap | Eyes open at birth, lens vacuolated | |
| *Lop* | Lens opacity | Cataract | 10 |
| *lr* | Lens rupture | Lens degeneration | |
| *mi* | Microphthalmia | Small eye and cataract (see Tost, 1958, Packer, 1967) | 6 |
| *nct* (formerly *cat*, $Cat^{Na}$) | Nakano cataract | Cataract, abnormal lens fibres | |
| *nuc* | Nuclear cataract | Cataract at 3–4 weeks | |
| *Sey* | Small eye | Small eye, thick lens capsule | |
| *vl* | Vacuolated lens | Cataract | 1 |

| | | |
|---|---|---|
| Provisional gene symbols | | |
| *Acc* | Anterior capsular cataract | — |
| *act* | Adult cataract | Cataract at 2–3 months |
| *Alm* | Anterior lenticonus with microphthalmia | — |
| *Apo* | Anterior polar opacity | — |
| *Apoc* | Anterior polar cataract | — |
| *Apyc* | Anterior pyramidal cataract | — |
| *Cad* | Congenital cataract | — |
| $cat^{AA}$ | Cataract, Ann Arbor | Cataract at 1 month |
| *Cts* (formerly *Cs*) | Cataract and small eye | — |
| *Enc* | Embryonic nucleus cataract | — |
| *Iac* | Iris anomaly with cataract | — |
| *Idc* | Iris dysplasia with cataract | — |
| *Nuc* | Nuclear cataract | — |
| *Nzc* | Nuclear and zonular cataract | — |
| *pcs* | Polar cataract and small eye | — |
| *Vlm* | Vacuolated lens with microphthalmia | — |
| No gene symbol assigned | | |
| Philly mouse cataract strain | — | Cataract at 10 days |
| Emory, CFW mouse | — | Cataract at 8–18 months |
| In 20% of a group of *nu/nu* (nude) mice | — | Cataract at 5–6 weeks |
| Eighteen cataract mutations (plus one corneal opacity mutation) | — | See Favor (1983) |

* The list is based on information in *Mouse News Letter* **70**, 6–44 and 54–56 (1984), Green (1981) and Robinson, Kuwabara & Zwaan (1982). These sources give the original references.

† It is not stated whether the 'eye opacity' is a lens opacity.

strains have genetically inherited cataracts that are caused by an autosomal gene that we have designated *lop-2* (lens opacity-2). CBA/H mice also have inherited cataracts, but further genetic mapping studies are required to clarify whether this is caused by *lop-2* or a different gene. Until this is known the gene symbol *Lop-3* must be regarded as provisional.

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