Comparative Medicine
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Vol 64, No 5
October 2014
Pages 360–368

Original Research

Hereditary and Histologic Characteristics of the CF1/b cac Mouse Cataract Model

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A substrain of mice originating from the CF1 strain (an outbred colony) reared at Osaka Prefecture University (CF1/b cac mice) develops cataracts beginning at 14 d old. Affected mice were fully viable and fertile and had developed cataracts by 22 d of age. The incidence of cataracts did not differ between male and female mice. Histologically, 14-wk-old CF1/b cac mice showed vacuolated lens epithelial cells, swollen lens fibers, many pyknotic nuclei, and vacuolation of the lens cortex. To elucidate the mode of inheritance, we analyzed heterozygous mutants hybrids generated from CF1/b cac and wildtype BALB/c mice and the offspring of the backcrossed heterozygous mutants. None of the heterozygous mutants was affected, but the ratio of affected to unaffected mice was 1:3 among the offspring of the heterozygous mutants. The initial genomewide screen of 20 affected backcrossed offspring (CF1/b cac × [CF1/b cac × BALB/c]) indicated that the mutant gene resides on chromosome 16. For further mapping, we used affected progeny of CF1/b cac × (CF1/b cac × MSM/Ms) mice. We concluded that the cataracts in CF1/b cac mice are inherited through an autosomal recessive mutation and that the mutant gene is located on mouse chromosome 16 between D16Mit5 and D16Mit92 and between D16Mit92 and D16Mit201. The mapping of the mutant gene of the CF1/b cac mice to mouse chromosome 16 provides the positional information necessary to identify the candidate gene responsible for the CF1/b cac phenotype.

Cataracts cause lenticular opacity,[16] which may lead to eventual blindness.[11] In humans, the prevalence of cataracts increases markedly from the age of 45 y onward, and as many as 50% of 75- to 85-y-olds may be affected.[5] Approximately 10% to 38% of cases of childhood blindness are due to congenital cataracts,[22] and 25% to 33% of congenital cataracts are hereditary.[1] Furthermore, the clinical phenotype of cataracts varies, and according to current criteria, congenital cataracts can be divided into several categories based on the location and appearance of the opacities.[3] The establishment of an animal model of cataracts is an effective method to elucidate human cataractogenesis.[6] In particular, mouse models for congenital cataracts are useful for isolating cataract genes and analyzing the mechanism of cataract development,[15,21] and many types of cataracts, which may be inherited and which have been evaluated developmentally, histologically, and genetically, exist in mice.[12,21] Cataract lenses display various morphologic features, including the posterior dislocation of the nucleus,[13,29] swollen lens fibers,[14] vacuolation of the epithelium,[17] and vacuolation of the lens.[27] In the present study, we histologically and genetically investigated the characteristics of a mouse cataract model that originated from the CF1 outbred strain.

Received: 04 Dec 2013. Revision requested: 09 Jan 2014. Accepted: 09 Mar 2014.
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Materials and Methods

Animals and husbandry. CF1/b cac mice which are apportioned by Central Research Division (Takeda Chemical Industries, Osaka, Japan) in 2003 and are carrying out inhouse breeding in Osaka Prefecture University now, a new cataract strain derived from mice of the CF1 strain, were used. Normal BALB/c mice (wildtype) were purchased from CLEA Japan (Tokyo, Japan) and were used as controls and for genomewide screening. Normal ddY mice were purchased from Japan SLC, Inc. (Hamamatsu, Japan) and were used as controls in histological studies. MSM/Ms mice were kindly donated by Dr Moriwaki (National Institute of Genetics, Mishima, Japan) and used for mapping studies. All mice were maintained under controlled conditions of room temperature (24 ± 1 °C), humidity (55% ± 5%), and lighting (lights on 0600 to 2000). The mice received a commercial diet (CE2, Clea, Osaka, Japan) and water ad libitum. The present study was performed in accordance with the Guidelines for Animal Experimentation of Osaka Prefecture University, Japan.

Observations and histologic studies. Unanesthetized mice were monitored at least every other day after their eyes opened (approximately 12 d of age). For the histologic studies, neonatal (ages, 1, 7, 21, and 25 d) and adult (age, 14 wk) CF1/b cac mice and adult (age, 10 wk) ddY mice were used. Neonatal mice were anesthetized by using isoflurane and decapitated. The eyes were removed and fixed in 10% neutral buffered formalin for 2 d. Adult mice were anesthetized by using isoflurane and then infused with heparin–saline followed by 10% neutral buffered formalin, after which the eyes were removed and immersed in 10% neutral buffered formalin for 2 d. The eyes were dehydrated by a graded series of ethanol treatments, soaked in butyl alcohol,

Table 1. Linkage analysis of cataract gene (CF1/b cac) in affected backcrossed mice at selected loci

Chromosome	Locus	Distance (cM) from centromere	No. affected		χ^2	*P*
			CF1/CF1 allele	CF1/BALB allele		
1	D1Mit121	19.5	12	8	0.800	0.371
	D1Mit48	44	11	9	0.200	0.655
	D1Mit15	87.9	11	9	0.200	0.655
	D1Mit56	106.1	13	7	1.800	0.180
2	D2Mit64	18	8	12	0.800	0.371
	D2Mit102	53	11	9	0.200	0.655
	D2Mit412	78.7	13	7	1.800	0.180
	D2Mit52	99	12	8	0.800	0.371
3	D3Mit203	11.2	6	14	3.200	0.074
	D3Mit121	49.7	9	11	0.200	0.655
	D3Mit257	70.3	11	9	0.200	0.655
4	D4Mit 1	6.3	11	9	0.200	0.655
	D4Mit178	35.6	11	9	0.200	0.655
	D4Mit16	57.6	8	12	0.800	0.371
5	D5Mit13	20	11	9	0.200	0.655
	D5Mit10	50	11	9	0.200	0.655
	D5Mit409	81.3	8	12	0.800	0.371
6	D6Mit158	6	12	8	0.800	0.371
	D6Mit16	30.5	11	9	0.200	0.655
	D6Mit333	61	10	10	0.000	1.000
7	D7Mit229	23	11	9	0.200	0.655
	D7Mit181	37	10	10	0.000	1.000
	D7Mit10	66	11	9	0.200	0.655
8	D8Mit58	1	11	9	0.200	0.655
	D8Mit144	30	12	8	0.800	0.371
	D8Mit354	62	7	13	1.800	0.180
9	D9Mit229	11	9	11	0.200	0.655
	D9Mit347	56	9	11	0.200	0.655
	D9Mit18	71	9	11	0.200	0.655
	D10Mit87	16	11	9	0.200	0.655
10	D10Mit42	44	12	8	0.800	0.371
	D10Mit102	69	12	8	0.800	0.371
11	D11Mit51	18	13	7	1.800	0.180
	D11Mit320	43.8	14	6	3.200	0.074
	D11Mit168	63	13	7	1.800	0.180
12	D12Mit109	19	10	10	0.000	1.000
	D12Mit6	45	7	13	1.800	0.180
13	D13Mit88	19	11	9	0.200	0.655
	D13Mit159	45	12	8	0.800	0.371
	D13Mit204	71	5	15	5.000	0.025

Table 1. Continued

Chromosome	Locus	Distance (cM) from centromere	No. affected		χ^2	*P*
			CF1/CF1 allele	CF1/BALB allele		
14	D14Mit61	16.5	9	11	0.200	0.655
	D14Mit176	48	12	8	0.800	0.371
15	D15Mit226	10.4	13	7	1.800	0.180
	D15Mit123	30.6	11	9	0.200	0.655
	D15Mit219	65.6	11	9	0.200	0.655
16	D16Mit34	9.6	15	5	5.000	0.00250
	D16Mit4	27.3	18	2	12.800	0.00035
	D16Mit49	53	16	4	7.200	0.00729
17	D17Mit16	17.4	10	10	0.000	1.000
	D17Mit20	34	11	9	0.200	0.655
18	D18Mit94	17	6	14	3.200	0.074
	D18Nds1	55	9	11	0.200	0.655
19	D19Mit60	15	12	8	0.800	0.371
	D19Mit10	47	10	10	0.000	1.000

and embedded in paraffin (Tissue Prep, Fisher Scientific, NJ). Sections (thickness, 6 µm) were cut in a plane perpendicular to the anterioposterior axis of the eye and stained with hematoxylin and eosin.

Determining the mode of inheritance. To elucidate the mode of inheritance, CF1/b cac mice were mated with wildtype BALB/c mice to obtain heterozygous mutants, which then were mated to each other to obtain the segregation ratio of affected and unaffected mice. To determine the incidence of lenticular opacities, mice were examined more than weekly from 12 d until 5 mo of age.

Linkage analysis. Genomic DNA was extracted from tail tissue of affected backcrossed progeny (CF1/b cac mouse × [CF1/b cac mouse × BALB/c mouse]). For genome-wide screening, 54 polymorphic microsatellite markers (Sigma Aldrich Japan, Tokyo, Japan) typed polymorphisms between CF1/b cac and BALB/c mice were selected (Table 1). The primary screen comprised DNA samples from 20 affected mice. For additional mapping, genomic DNA was extracted from tail tissue of backcrossed progeny (CF1/b cac × [CF1/b cac × MSM/Ms]). For the region between D16Mit4 and D16Mit49, 9 microsatellite markers on chromosome 16 that had typed polymorphisms between CF1/b cac and MSM/Ms mice were selected (Table 2). For the secondary screen, 60 to 256 DNA samples from affected mice were used. PCR was performed in a 10-µL reaction mixture that contained 50 ng of template DNA, 1 mM dNTP, 0.5 U *Taq* polymerase (Takara Bio, Otsu, Japan), and 6.6 µM of each primer. Cycling conditions comprised initial denaturation at 94 °C for 3 min, followed by denaturation for 30 s, annealing for 45 s, and extension at 72 °C for 45 s (45 cycles), with final extension at 72 °C for 10 min. The annealing temperatures varied depending on the marker primers. Each PCR product was mixed with 3 µL loading buffer and electrophoresed in 8% polyacrylamide gels for 3 h at 120 V. Gels were stained with ethidium bromide or by using a silver staining kit (Daiich Pure Chemical, Tokyo, Japan). The significance of linkage was evaluated by using a χ^2 test of independence (degree of freedom, 1) of frequencies of hetero- and homozygotes in the affected backcrossed mice by using commercially available software (Microsoft Excel; Microsoft, Redmond, WA).

Results

Incidence of cataract. Table 3 shows the incidence of opacities with age in CF1/b cac mice. Opacity first appeared as white points or foci in the pink eyes of mice at 14 d of age (Figure 1 A). The rates of progression of opacity were almost equal between eyes, and the size of the opacity increased with age (Figure 1 B). The opacities were very similar in shape in each affected mouse. All CF1/b cac mice were affected by 22 d of age. The incidence of cataracts did not differ between sexes. All of the mice were fully viable and fertile, and it was impossible to distinguish between affected and unaffected mice by shape, size, or any other morphologic feature except lenticular opacity.

Histologic findings. *Adult mice*. ddY mice had normal lenses, whereas CF1/b cac mice had abnormal lenses (Figure 2 A and B). In CF1/b cac mice, the lens nucleus was moved to the posterior region of the lens. The bow and anterior regions of the lens contained many vacuoles (Figure 2 B), vacuolated lens epithelial cells, swollen lens fibers, and pyknotic nuclei (Figure 2 C and D). The posterior region of the lens demonstrated swollen fibers and liquefaction (Figure 2 E).

Neonatal CF1/b cac mice. At 1 d of age, CF1/b cac mice have normal lenses (Figure 3 A), whereas 25-d-old CF1/b cac mice have vacuolated lens epithelial cells, swollen lens fibers, and many pyknotic nuclei (Figure 3 B). The anterior region of the lens contained swollen fibers at 7 d after birth and thereafter (Figure 3 C, F, and I). In the bow region of the lens, vacuolated lens epi-

Table 2. Linkage analysis of cataract gene on chromosome 16 of affected mice

Locus	Distance (cM) from centromere	No. affected		χ^2
		CF1/CF1 allele	CF1/BALB allele	
D16Mit138	45.7	55	5	41.67
D16Mit42	49.6	157	4	145.40
D16Mit199	54.9	160	1	157.02
D16Mit127	55.5	255	1	252.02
D16Mit5	57.8	255	1	252.02
D16Mit92	60.2	255	1	252.02
D16Mit185	60.5	256	0	256.00
D16Mit115	61.2	256	0	256.00
D16Mit201	62.8	254	2	248.06

Markers D16Mit4 (36.2 cM) and D16Mit49 (78.2 cM) were nonpolymorphic between CF1 and MSM mice.

Table 3. Incidence of cataracts in CF1/b cac mice (total [no. female, no. male])

	Age (d)					
	12	14	16	18	20	22
Normal	186 (92, 94)	169 (83, 86)	106 (55, 51)	21 (10, 11)	3 (0, 3)	0 (0, 0)
Cataracts	0 (0, 0)	17 (9, 8)	80 (37, 43)	165 (82, 83)	183 (92, 91)	186 (92, 94)

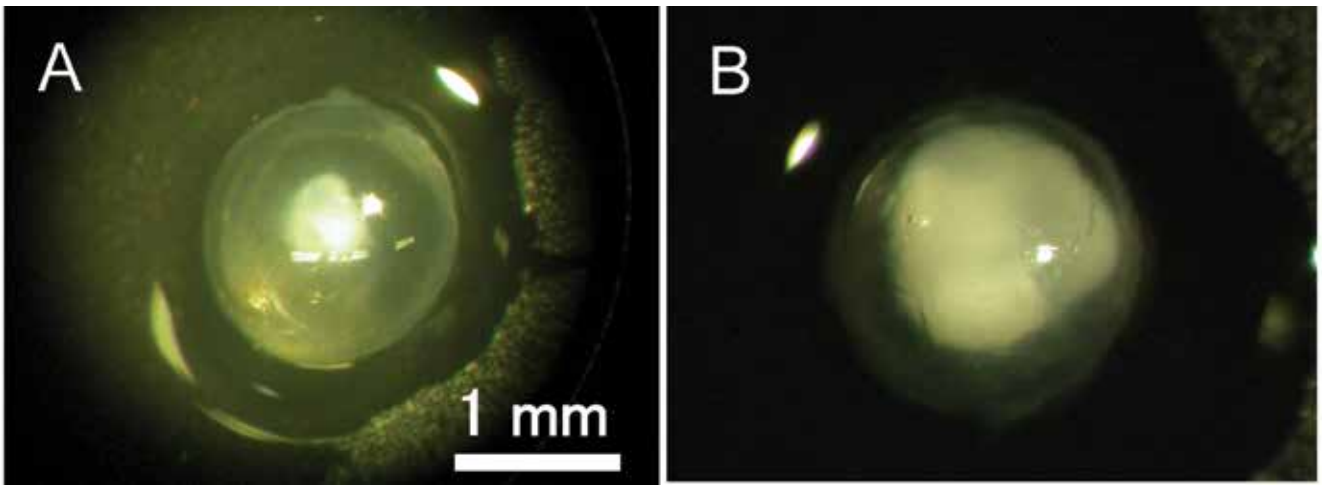

Figure 1. Stereomicroscopic features of the lenses of CF1/b cac mice. (A) A 14-d-old CF1/b cac mouse. The lens has a focal opacity. (B) A 20-d-old CF1/b cac mouse. The opacity in the mouse is larger than that in the 14-d-old mouse.

thelium was present at 14 d after birth and thereafter (Figure 3 E, H, and K). The posterior region of the lens demonstrated swollen, pale lens fibers in 14-d-old mice and swollen lens fibers and liquefaction of the lens in 21-d-old mice (Figure 3 D, G, and J).

Mode of inheritance. Heterozygous progeny from CF1/b cac and wildtype BALB/c mice were phenotypically normal; none of the 82 progeny (female, 40; male, 42) evaluated had cataracts. The ratio of affected to unaffected mice in the offspring of heterozygous mutants was approximately 1:3 (47 [female, 25; male, 22] mice had cataracts among the 189 [female, 94; male, 95] mice evaluated).

Linkage analysis. The results of genomewide screening of CF1/b cac and BALB/c mice are shown in Table 1. The χ^2 value for the polymorphic 54 microsatellite loci ranged from 0 to 12.8. In particular, the χ^2 values of the chromosome 16 markers D16Mit34, D16Mit4, and D16Mit49 were 5, 12.8, and 7.2, respectively, indicating linkage between the mutant gene of CF1/b cac mice and chromosome 16. We therefore performed additional linkage analysis by using CF1/b cac and MSM/Ms mice and 9 microsatellite markers known to be polymorphic in these strains (Table 2). The χ^2 values for these polymorphic 9 microsatellite loci ranged from 41.67 to 256.00. The 256 samples analyzed revealed four recombination events (Figure 4 A). Three offspring arose as a result of a single crossover event and 1 offspring as a result of double crossover events. Analysis of the haplotype distribution pattern enabled us to localize the cataract gene of CF1/b cac mice to the regions between D16Mit5 and D16Mit92 and between D16Mit92 and D16Mit201 (Figure 4 B). D16Mit5, D16Mit92, and D16Mit 201 are located at the coordinates 57773560 to 57773713, 60187187 to 60187335, and 62837628 to 62837739 on chromosome 16, respectively. The region between D16Mit5 and D16Mit92 includes 38

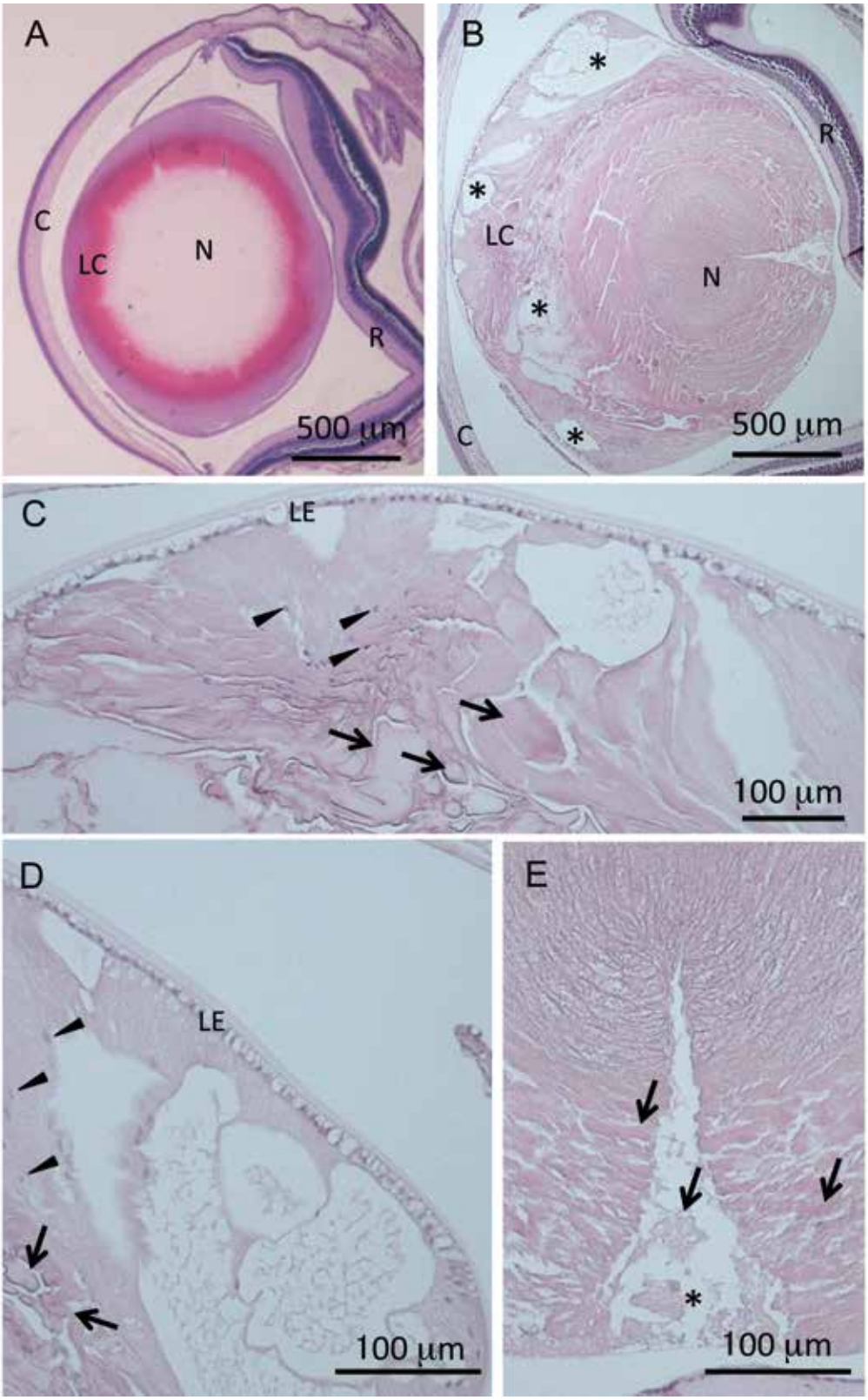

Figure 2. Eyes of adult (10-wk-old ddY (A) and 14-wk-old CF1/b cac mice [B through E]). (A) The eye is composed of several components (cornea, lens, retina, and so forth), with a normal lens. (B) The lens nucleus is dislocated posteriorly, and vacuoles (asterisks) are seen in the lens cortex. In the (C) anterior and (D) bow regions, vacuolated lens epithelial cells, piknotic nuclei (arrowheads), and swelling (arrows) of the lens fibers are seen. (E) The posterior region of the lens cortex shows swelling (arrows) of the lens fibers and liquefaction (asterisks) of the lens. C, cornea; LC, lens cortex; N, lens nucleus; R, retina; LE, lens epithelium.

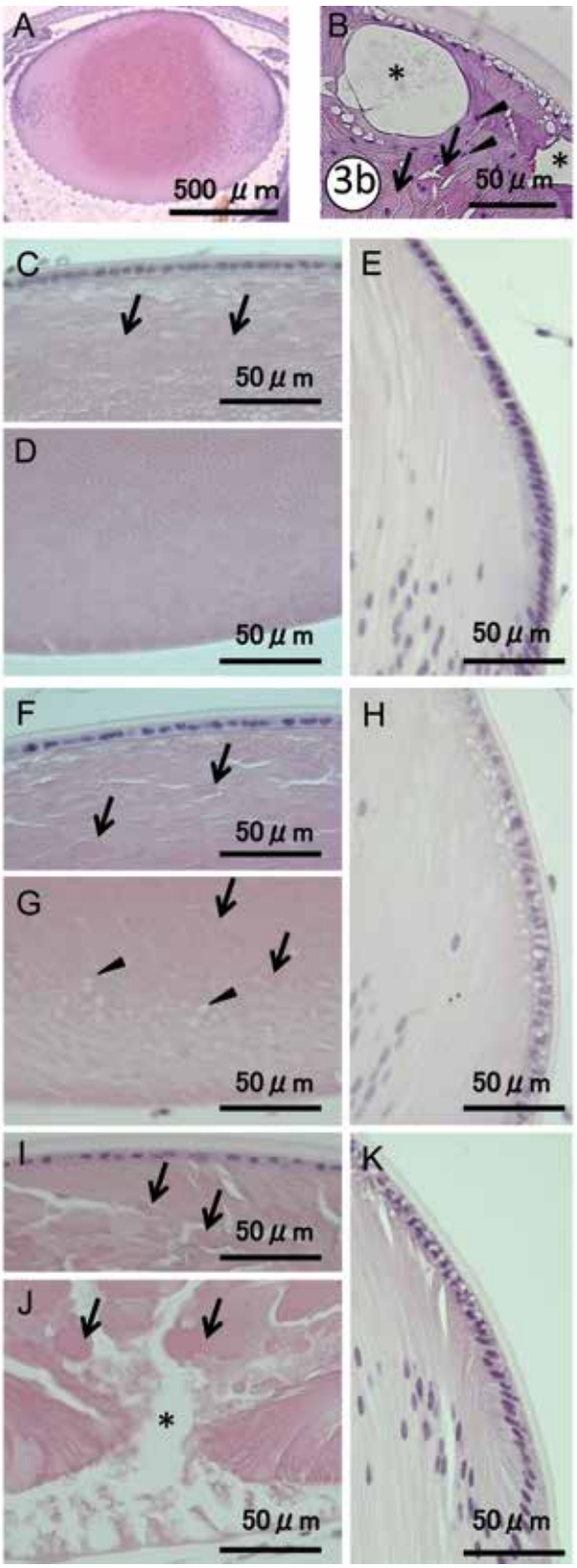

Figure 3. Lenses of neonatal CF1/b cac mice. (A) Lens of a 1-d-old CF1/b cac mouse is normal in appearance. (B) Transitional (anterior to bow) region of the lens of a 25-d-old CF1/b cac mouse demonstrates vacuoles (asterisks) in the lens cortex. In addition, vacuolated lens epithelial cells, piknotic nuclei (arrowheads), and swelling (arrows) of the lens fibers are present. (C) Anterior region of the lens of a 7-d-old CF1/b cac mouse. Swelling (arrows) of the lens fibers is seen. (D) Normal posterior region of the lens of a 7-d-old mouse. (E) Bow region of the lens of a 7-d-old mouse. Note the small vesicles beneath the lens epithelium. (F) Anterior region of the lens of a 14-d-old CF1/b cac mouse, with swelling (arrows) of the lens fibers. (G) Posterior region of the lens of a 14-d-old mouse shows swelling (arrows) of the lens fibers and pale lens fibers (arrow heads). (H) Bow region of the lens of a 14-d-old mouse, with small vesicles beneath vacuolated lens epithelium. (I) Anterior region of the lens of a 21-d-old CF1/b cac mouse. The lens fibers are swollen (arrows). (J) Posterior region of the lens of a 21-d-old mouse, in which swelling (arrows) of the lens fibers and liquefaction (asterisks) of the lens are seen. (K) Bow region of the lens of a 21-d-old mouse. Small vesicles are seen beneath the vacuolated lens epithelium.

protein-coding genes, and that between D16Mit92 D16Mit201 contains 3 (Table 4).

Discussion

The present study revealed that a new cataract model, CF1/b cac mice, is characterized by white foci in the pink eyes of mice 14 to 22 d after birth. The mutation is inherited in an autosomal recessive fashion, and the causative gene lies between 57.8 and 62.8 Mb from the centromere of chromosome 16.

The 4 major morphologies of mouse cataracts are nuclear, cortical, capsular–epithelial, and lens extrusion.[26] The various abnormal changes in cataract lenses include nuclear remnants in the lens fibers,[7] vacuolated epithelial cells,[13,24] degeneration of cortical fibers, and progressive condensation of the nucleus.[20] A cortical cataract involves the lens cortex and is associated with the breakdown of lens fiber cells and migration of lens nuclei to the posterior lens cortex.[26] In CF1/b cac mice, the lens nucleus was dislocated to the posterior cortex. Vacuolation of the epithelial cells and lens fiber cells involved the anterior surface of the lens. These results suggest that the abnormal lens feature of CF1/b cac mice is a cortical cataract.

Congenital cataracts have been classified into all 3 types of Mendelian inheritance: autosomal dominant, autosomal recessive, and X-linked.[23] In the present study, the incidence of cataracts in the heterozygous progeny between CF1/b cac and wildtype BALB/c mice was 0%, and the incidence of cataracts did not differ between male and female mice. These results indicate that the mutation in CF1/b cac mice is an autosomal recessive mutation. Among the offspring of the heterozygous mice, 47 mice had cataracts and 189 mice were healthy. This segregation ratio is well in line with the 1:3 ratio expected according to the hypothesis that the expression of cataracts in CF1/b cac mice is controlled by an autosomal recessive gene.

In this study, we found that the causative gene of cataract in CF1/b cac mice lies on chromosome 16, between D16Mit5 and D16Mit92 or between D16Mit92 and D16Mit201 (Figure 4 B). Candidate genes in these regions include *Opj* (opacity due to poor secondary fiber junction), *Coc* (coralliform cataract), and *Nct* (Nakano cataract). *Opj* is 22.8 Mb from the centromere of chromosome 16 and causes lenticular opacity and malformation due to a single-basepair mutation in the coding sequence of the Crygs gene, which encodes the major lens structural protein γS.[25] *Coc* is in the region between D16Mit134 and D16Mit63,[22] which are thought to lie between 32.9 and 49.8 Mb from the centromere of chromosome 16. The causative gene of CF1/b cac, however, lies in a location distinct from these 2 known cataract genes. The

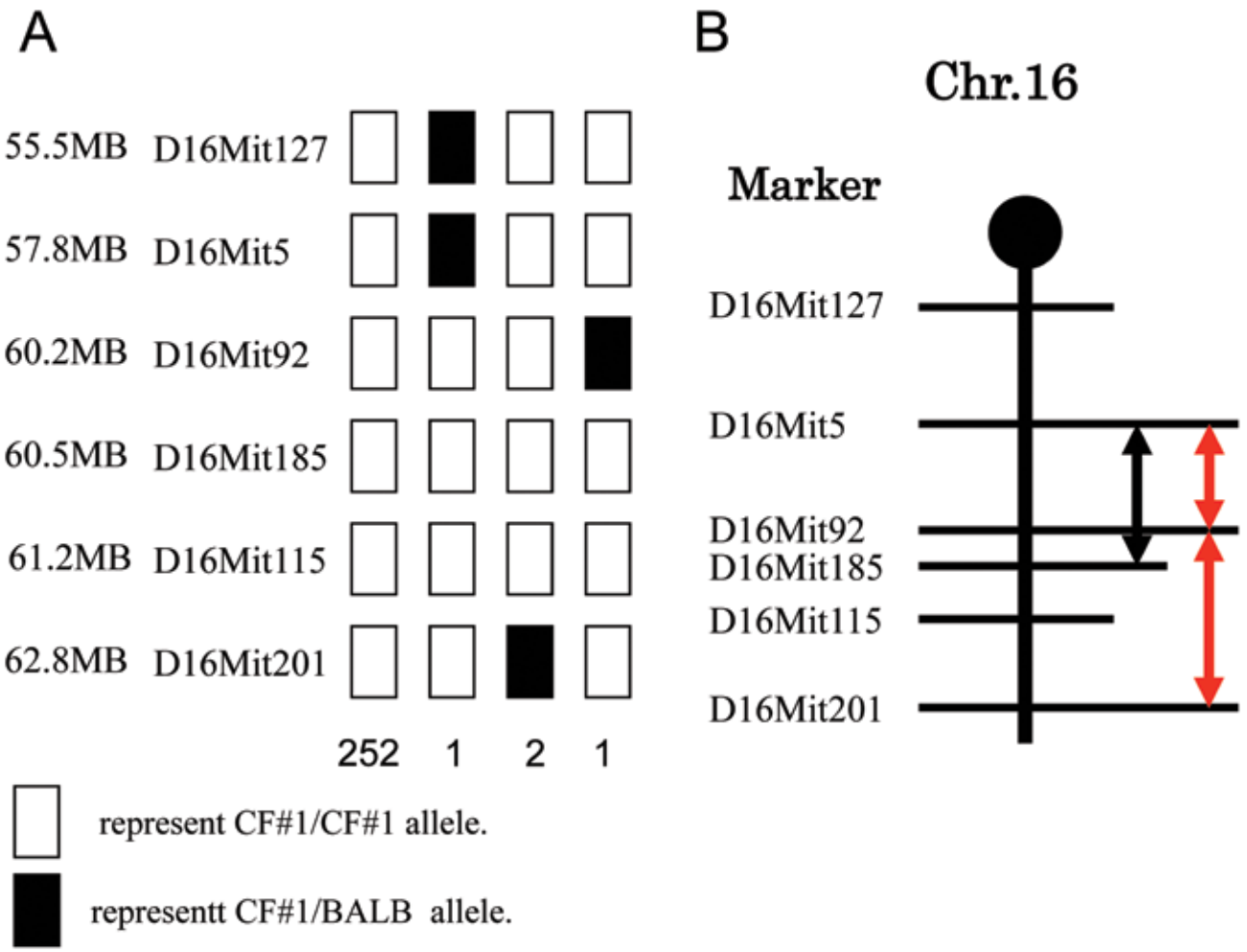

Figure 4. (A) Distribution of the haplotypes in a set of 256 affected offspring from the backcross (CF1/b cac × [CF1/b cac × MSM/Ms]). The typed loci are listed on the left. Columns denote specific chromosomes identified in affected backcrossed progeny. Values at the bottom of the figure are the number of progeny that inherited the indicated chromosomal haplotype from the F1 parent. Black squares represent the CF1/MSM allele; white squares represent the CF1/CF1 cac allele. (B) Genetic linkage map of chromosome 16. The map shows the location of the cataract gene of CF1/b cac mice (red arrows) and the *Nct* gene (black arrow). The typed loci are listed on the left.

present linkage analysis showed that the cataract gene of CF1/b cac mice is located the region between D16Mit 5 and 92 and between D16Mit 92 and 201, where 41 genes are located. However, 26 of the genes are olfactory receptor genes and unlikely to be the causative gene for cataracts of CF1/b cac mice. *Nct* lies between D16Mit5 and D16Mit185,[20] and its physical position is thought to be between 57.8 and 60.5 Mb from the centromere of chromosome 16. Given that the physical position of the causative gene of CF1/b cac is in the region between 57.8 and 62.8 Mb from the centromere of chromosome 16, *Nct* is a plausible candidate for the gene responsible for the cataracts in CF1/b cac mice. Recently, a hypomorphic mutation in the *Cpox* gene has been reported as a primary cause of hereditary cataract in the NCT mouse.[18] Therefore, 15 genes including *Cpox* and *Nct* are candidate genes of the cataract-causing mutation in CF1/b cac mice. In addition, the disruption of Eph-ephrin signaling leads to age-related cataracts in human and mice, and ephrin A5 knockout mice develop cataracts with severe defects in their epithelial cells and cortical fibers.[8] Furthermore, the Eph receptors and their ligands are critical regulators of lens development and maintenance.[2] Therefore, *EphaA6* may be involved in causing cataracts in CF1/b cac mice.

Several reports regarding the hereditary and morphologic characteristics of Nakano cataract mice are available. These mice demonstrate cataracts approximately 3 wk after birth and early histologic evidence of swelling at the distal portion of the lens fibers in the deep posterior suture area.[4] The Nakano cataract is characterized by the progression of a pinhead-sized opacity in the deep cortex 24 to 30 d after birth.[19] The first sign of opacity occurs 23 to 25 d after birth as a appeared as pinhead-sized opacity in the lens nucleus.[10] Homozygous mice develop a pinhead-sized opacity in the nucleus of the lens on postnatal day 24, and the anterior lens capsule is thicker than that of the normal lens.[28] Nakano mouse lenses show sustained transparency until 19 d after birth, fine opacity at day 20, and the development of a mature cataract around day 30.[9] Thus, cataract development in Nakano mice occurs at least 20 d after birth at the earliest. Although the cataract lenses of CF1/b cac mice showed swelling of the lens fibers in the deep posterior suture area, the histologic changes in the lens of

Table 4. List of candidate genes for CF1/b cac cataract gene

Gene name	Location (Mb)	Gene symbol	Accession no.[a]
Discoidin, CUB, and LCCL domain containing 2	58.41–58.47	*Dcbld2*	1920629
ST3 β-galactoside α-2,3-sialytransferase 6	58.47–58.52	*St3gal6*	1888707
Gene model 813	58.61–58.62		2685659
E330017A01Rik	58.64		3045360
Coproporphyrinogen oxidase	58.67–58.68	*Cpox*	104841
G protain-coupled receptor 15	58.72	*Gpr15*	1918473
Claudin 25	58.73	*Cldn25*	2447860
Olfactory receptor 172, 173, 177, 178, 180, 181, 183, 186, 187, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 201, 203, 204, 205, 206, and 207		*Olfr172~ Olfr207*	
γ-aminobutyric acid (GABA) receptor, rho 3	59.41–59.46	*Gabrr3*	3588203
Myc induced nuclear antigen	59.47–59.49	*Mina*	1914264
β-γ crystallin domain containing 3	59.49–59.56	*Crybg3*	2676311
ADP-ribosylation factor-like 6	59.61–59.64	*Arl6*	1927136
Eph receptor A6	59.65–60.61	*Epha6*	10834
NOL1/NOL2/Sun domain family member 3	62.73–62.79	*Nsun3*	2146565
ADP-ribosylation factor-like 13B	62.79–62.85	*Arl13b*	1915396
Syntaxin 19	62.81–62.82	*Stx19*	1915409

[a]Mouse Genome Informatics database

CF1/b cac mice were present mainly in the anterior and bow regions of the lens, and vacuolated lens epithelial cells and vacuoles were seen in the lens cortex. In addition, the first sign of lenticular opacity in CF1/b cac mice occurred at 14 d of age, and most mice developed cataracts by 18 d after birth. In the present study, the first microscopic sign of cataract formation was swollen lens fibers at 7 d after birth, with induction of epithelial cell vacuolation at 14 d and liquefaction of the lens in the posterior region at 21 d. Furthermore, vacuoles in the lens cortex were noted at 25 d after birth. Therefore, CF1/b cac mice seem to be phenotypically different from Nakano mice. Because the apparent difference may be due to differences in genetic background, additional studies are needed to clarify the relationship between the phenotypic and genetic characteristics of CF1/b cac mice.

The cataract-affected mice that we present here are fully viable and fertile, and a spontaneous cataract model derived from CF1 mice has not yet been reported. CF1/b cac mice will be a good tool for studying the molecular biology and genetics of cataractogenesis.

Acknowledgment

This work is supported in part by the Grant-in Aid 18500329 from the Ministry of Education, Science and Culture of Japan.

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