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A Test for the Identity of "Dysoptic" with "Blind" in Mice¹

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Abstract. A genetic test for the identity of two mutants "Dysoptic" and "Blind" was made. The results of breeding point to their identity, but the results are not absolutely conclusive. A study of the Dysoptic-Blind embryo may furnish the final evidence.

A spontaneous mutation for blindness occurred in a Bagg albino strain of mice in the laboratory of Dr. Ernst Caspari at Wesleyan University, Middletown, Connecticut. It proved to be a dominant mutation, with the homozygote lethal. The embryo of the homozygote dies at the end of the seventh day (1). The heterozygote is blind with opacity of one or both eyes, or with reduced size of eyeball in one or both eyes, or with opacity in one with reduced size in the other eye (2). This mutation was called "Blind."

Another mutation occurred in the laboratory of Dr. A. G. Searle at the Radiobiological Research Unit at Harwell, Didcot, Berkshire. The stock was agouti, carrying recessive traits of non-agouti, dilute, brown and albino. This mutation too was found to be a dominant, with the homozygote lethal (private communication). The embryology of the homozygote has not yet been investigated. The heterozygote shows corneal opacity, but Dr. Searle reported no microphthalmia or anophthalmia. He also found that when expression is unilateral, the right eye is more often affected than the left (private communication). This mutation was named "Dysoptic."

Dr. Searle sent eight Dysoptic mice, all of which had opaque corneas on both eyes, to the biology laboratory of Simpson College in order that we might make a straightforward genetic test for the identity of the two mutations.

Dysoptic mice were bred to Dysoptic to increase the stock. They were also mated to controls of the albino strain, and to Blind albinos.

The results of the breeding are shown in Table 1.

In every case the actual ratios are not in close agreement with the expected ratios perhaps because of lowered viability of the mutants or because of incomplete penetrance. In the blind stock,

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six genetically blind but phenotypically normal animals have been identified. In every case their eyes were opened before the 10th day. This lack of penetrance or low expressivity has not been definitely established among the Dysoptics.

TABLE 1
Breeding Results

Cross	Offspring			Expected Ratio
	Mutant	Normal	Ratio	
Dysoptic x Dysoptic	39	44	47%:53%	67%:33%
Dysoptic x Blind	52	63	45%:55%	75%:25% if different 67%:33% if alike
Dysoptic x Normal	39	64	38%:62%	50%:50%
Blind x Blind	108	212	34%:66%	67%:33%
Blind x Normal	228	570	35%:65%	50%:50%
Normal x Normal	1	272	0%:100%	0%:100%

In our laboratory, we have observed greater variability in the expressivity of Dysoptic than was reported by Dr. Searle. There is frequent microphthalmia, and often opacity of one eye, with reduced size in the other eye. When expression is unilateral, we found that the left eye is as often affected as is the right eye.

It is significant that the ratios of mutants to normals obtained in crosses of Dysoptic x Dysoptic are so close to those in crosses of Dysoptic x Blind. Using a X² test, the probability that the discrepancy would be this much or more, and still be examples of the same ratio, is 70%

Likewise, Dysoptic x Normal crosses give quite similar results to crosses of Blind x Normal. This is to be expected whether or not the two mutations are identical.

The similarity of the results of crosses of Blind x Normal to crosses of Blind x Blind is puzzling. The lack of penetrance, or lowered viability, or both, of the heterozygote may be the explanation.

Since both Dysoptic and Blind are lethal when homozygous, the size of the litter should be of significance in determining their identity. If they are examples of the same gene mutation, the mean litter size in matings of Blind x Dysoptic should be just as small as in mating of Dysoptic x Dysoptic, for both the Dysoptic-Dysoptic and the Dysoptic-Blind homozygote would die in utero and be reabsorbed. If they are examples of two different genes, the Dysoptic-Blind individual would be a double hetero-

zygote and presumably live. Table 2 shows the results of this study.

TABLE 2.
Size of Litter at Birth

Cross	Number of Litters	Mean Litter Size	95% Confidence Interval
Dysoptic x Dysoptic	19	4.63 ± .46	3.66 - 5.60
Dysoptic x Blind	23	5.00 ± .38	4.21 - 5.79
Dysoptic x Normal	16	7.25 ± .75	5.65 - 9.85
Blind x Blind	49	4.69 ± .35	3.99 - 5.39
Blind x Normal	66	6.41 ± .30	5.81 - 7.01
Normal x Normal	22	6.73 ± .63	5.42 - 8.04

Using Student's distribution, the 95% confidence intervals for the means of litter size indicate that the litter size from Dysoptic x Normal matings is significantly larger than from Dysoptic x Dysoptic. Also Blind x Normal and Normal x Normal litters are significantly larger than Blind x Blind litters. However, the difference in litter size between Dysoptic x Blind matings and Dysoptic x Normal is not quite significantly different at the 5% level.

DISCUSSION

At present our data seem to indicate that the two mutations, Dysoptic and Blind, in breeding act as the same gene. In crossing the two stocks, the litter size is reduced, but not quite significantly so at the 5% level. If they are in fact identical, we would expect the Dysoptic-Blind individuals to be lethal. Further breeding may clarify this situation.

The Blind homozygote shows a failure of mesoderm formation, and an enlargement of cells of the proximal entoderm (1). If the Dysoptic homozygote, and the Dysoptic-Blind embryo show these same abnormalities, it would indicate a probable identity. Therefore, a study of this embryology should follow.

Literature Cited

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