Lethal Alleles in Mus musculus: Local Distribution and Evidence for Isolation of Demes

Abstract. *In the vicinity of Calgary, Alberta, 20.5 percent of wild house mice tested were found to be heterozygous for the lethal allele designated* t^{w5}, *and an additional 3.4 percent were heterozygous for one or more alleles not belonging to the* t^{w5} *group. The distribution patterns of wild-type and lethal alleles within and between clusters of small demes supports the postulate that random drift plays a significant role in the evolution of these populations. Distribution patterns also suggest that the demes are reproductively isolated to a greater degree than has been generally assumed.*

Lethal and male-sterile alleles at locus T on the 9th chromosome of the house mouse are characterized by transmission ratios averaging 0.96 in male heterozygotes caught in the wild state (*1*). This high frequency of the mutant allele in the effective sperm pool of such males is believed to be the factor responsible for the widespread distribution and high frequency of such alleles observed in samples taken from free-living populations, and has been described as an evolutionary force opposed to the selection against these alleles (*2*).

The evolutionary dynamics of this situation have been investigated by means of mathematical models based on the alternative assumptions that populations are large and panmictic (*3*), or that breeding units are small enough so that stochastic processes play a major role in determining equilibrium frequencies (*4*). In each case, evaluation of the adequacy of the model has been hampered by lack of information on the constitution and biology of local populations.

During the summers of 1962 and 1963, populations of *Mus* located on seven farms in the vicinity of Calgary, Alberta, were the subjects of ecological and genetic investigation. In the genetic part of the study, 214 male mice were captured in Sherman or Longworth traps and taken to the laboratory for test matings. Lethal alleles detected through these matings have been cross-tested to determine their relationship to balanced lethal lines carrying alleles obtained at other localities. Procedures for initial testing and subsequent cross-testing have been described in the publications of Dunn and his co-workers (*1, 5*).

Tests for heterozygosity were completed for 187 male mice. Of these, 176 came from established populations which had not been disturbed by previous sampling. Tests showed 42 of the 176 to be heterozygous at locus T. As shown in Table 1, the bulk of these heterozygotes carried alleles which were found by cross-testing to be identical with that designated by Dunn (*5*) as group 3, and represented in these cross-tests by Dunn's t^{w5} line. The overall frequency of heterozygotes shown in Table 1 is 0.238. This does not differ significantly from a value of 0.156 calculated on the basis of tests of 153 male mice from natural populations reported for a continent-wide sampling in the United States (*1*).

The transmission ratio of heterozygotes may be estimated as the proportion of mice receiving the dominant marker (an allele for brachyury designated as *T*) from the female parent of test stock which have also received the lethal (*t*) from the wild male being tested. For those heterozygotes carrying an allele of the t^{w5} group, the sample of offspring is sufficient for an examination of this ratio, with 214 tailless (*Tt*) to 13 brachyurous (*T*+), giving a ratio of 0.942. This is not significantly different from the ratio of 0.941 reported for t^{w5} heterozygotes from New York (*2*). Alleles identical with t^{w5} have been reported previously from Florida, Connecticut, Vermont, Texas, Arizona, Kansas, and Montana (*1*).

Six heterozygotes were found to carry *t*-alleles not identical with t^{w5}. These are still being subjected to cross-testing with other balanced lethal lines and are tentatively designated as t^{wx}. Table 2 shows that one t^{wx} allele was recovered from the Stryker farm in 1962, while the remaining five were found on the Perry farm. Mice heterozygous for t^{w5} were found on both of these farms. These two instances are the first in which *t*-alleles belonging to two different groups have been discovered in free-living populations inhabiting an area as small as that of a single cluster of farm buildings.

Table 2, together with Fig. 1, illustrates the local pattern of distribution of *t*-alleles. Mice were found primarily in buildings of small size: granaries, toolsheds, chicken houses, and small barns. The total number of mice found in inhabited buildings ranged from 1

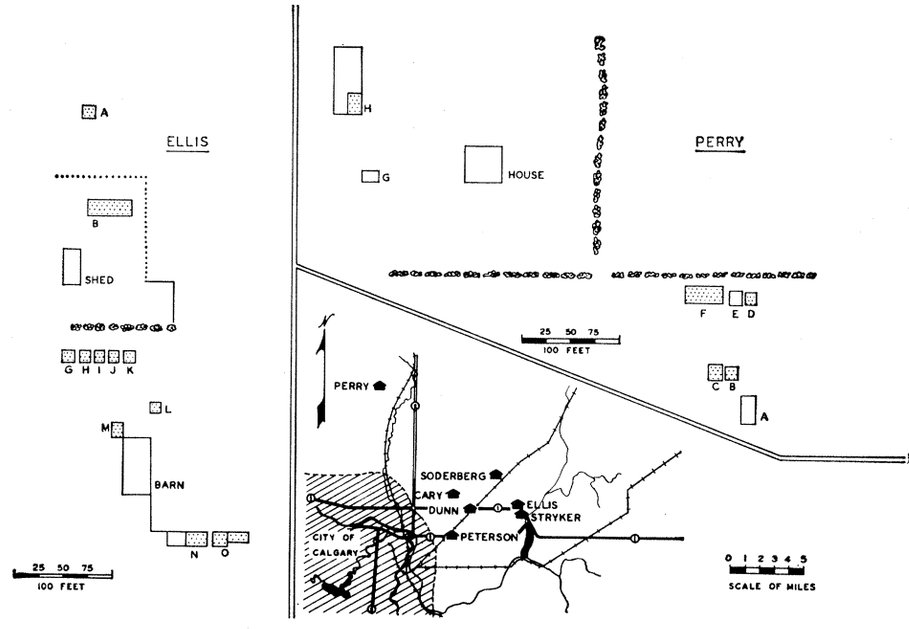

Fig. 1. The distribution of farms from which mice were taken is shown in the inset at lower right. Distribution of buildings on the Ellis and Perry farms is shown as typical of those studied. Stippled outlines indicate buildings from which samples were taken and letters relate these buildings to the data presented in Table 2.

Table 1. Overall frequency of *t*-alleles in male mice from the vicinity of Calgary, Alberta.

No. of mice	Genotypes	Frequency	Gene frequency
134	++	0.761	$+ = 0.081$
36	$+t^{w5}$	0.205	$t^{w5} = 0.102$
6	$+t^{wx}$	0.034	$t^{wx} = 0.017$

to 84, with a mean of 10.4 individuals for buildings where two or more mice were found. On the basis of the behavioral observations of Eible-Eibesfeldt (*6*) on *Mus*, and the segregation of social groups observed in a Norway rat colony by Calhoun (*7*), each building might be expected to contain one or more family groups reproductively isolated from other such groups through defense of communal territories. The pattern of gene distribution I have observed appears to support such a hypothesis. Adjacent groups differ in genetic composition and these differences have persisted for 2 years despite gross disturbances incurred when males were removed for testing in 1962. During these sampling operations, 65 percent of male mice known to be present through previous mark-and-release censuses were removed. Of 13 buildings inhabited in both years, none of six buildings where heterozygotes were not found in 1962 had acquired *t*-alleles in 1963. Of the seven buildings where heterozygotes did occur in 1962, all but two produced animals heterozygous for the same allele in 1963.

Table 2. Distribution of genotypes among male mice from seven sets of farm buildings.

Farms*	Genotypes 1962†			Genotypes 1963‡		
	++	$+t^{w5}$	$+t^{wx}$	++	$+t^{w5}$	$+t^{wx}$
			Ellis			
A	0	1	0	2	0	0
B	0	4	0	2	1	0
G				0	1	0
I	1	0	0	3	0	0
J				0	1	0
K	3	0	0	3	0	0
L				1	3	0
N	0	1	0	1	2	0
O	1	1	0	3	4	0
			Stryker			
A				1	0	0
B	0	0	0			
C				1	0	0
D	1	0	0	3	0	0
E				5	0	0
F	1	1	0			
G	2	0	0			
H				2	3	0
I	1	0	0			
J	5	1	1	2	0	0
			Dunn			
A				3	0	0
B	1	0	0	3	0	0
C	0	1	0	2	1	0
D	1	1	0	10	1	0
			Peterson			
A				0	1	0
B	3	0	0	1	0	0
D				4	1	0
			Soderburg			
A				0	1	0
			Cary			
B	0	1	0			
C	1	0	0	11	0	0
E				5	0	0
F				7	0	0
			Perry			
B				1	0	2
C				0	0	2
D				2	0	0
F				4	0	1
H				31	4	0
			Totals			
36	21	12	1	113	24	5

* Letters indicate individual buildings. † In 1962 some buildings were sampled a second time. Tests included in this table refer only to the first sampling in each specific building. ‡ In 1962 only adult males were tested. In 1963 juvenile and immature males were also retained for testing.

The pattern of distribution on the Perry farm is particularly interesting. There the very large population in building *H* produced mice heterozygous for t^{w5}, but almost certainly did not contain mice heterozygous for t^{wx}, which was carried by mice in buildings *B*, *C* and *F* only a few meters distant.

In 1962 one t^{w5} heterozygote was taken on the Cary farm, in building *B*. In 1963 this deme had become extinct, but a total of 23 males were tested from three other granaries and an abandoned hen house, all within 30 meters, without discovery of a heterozygote. It thus appears that no deme on this farm now carries the allele.

The patterns of local distribution observed suggest that immigration of mice into established populations is very rare. Such a possibility has been suggested by the work of Godfrey (*8*) with voles. The demes discussed herein are of very small size, and the random pattern of distribution of *t*-alleles may be interpreted as supporting the contention of Lewontin and Dunn (*4*) that stochastic processes may play a significant role in the evolutionary dynamics of these alleles.

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References and Notes

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Hypertensive Vascular Disease Produced by Homologous Renin

Abstract. *Administration of rat renin to uninephrectomized rats reproduced most, if not all, the changes (hypertension, vascular disease, hypertrophy of the zona glomerulosa of the adrenals) found after partial constriction of the renal artery. This is taken as evidence that the renal pressor system plays a major role in the pathogenesis of renal hypertension.*

On the assumption that renal hypertension results from increased release of renin, various, but unsuccessful, attempts have been made to reproduce the course of renal hypertensive disease by administering renin to normal animals. Subcutaneous injections or intravenous infusions of renin caused a slight rise in arterial pressure but no vascular lesions (*1*, *2*). These failures have been used as supporting evidence by those who believe that the renal pressor system has no part in the pathogenesis of hypertension.

Recently (*3*), we found that unlike hog renin, crude extracts of rat kidneys which had been subjected to reduced perfusion pressure reproduced the early manifestations of renal hypertension when injected subcutaneously into uninephrectomized rats. We then postulated that renal hypertension was caused by the release of renin and of a potentiating substance. The possibility remained, however, that the ineffectiveness of hog renin was due to its heterologous nature. We therefore decided to study the effects of rat renin alone or in combination with crude kidney extracts. By injecting renin into uninephrectomized animals we hoped to reproduce the changes associated with hypertension in rats with unilateral and partial clipping of the renal artery: if the injections were to replace the endocrine functions of the clipped kidney, the remaining kidney of the uninephrectomized rats should show the same changes as those seen in the one contralateral to the clipped kidney.