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The genetics of sex-linked anaemia in the mouse

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ORIGIN

The gene 'sex-linked anaemia' (*sla*) appeared first in the progeny of a daughter of a male that had been irradiated with 500 r. of X-rays. The daughter was born one month after the irradiation of her father. Mated to an unrelated wild-type male she produced sixteen sons of which six were anaemic. Her fertility was normal. Experience in subsequent matings showed the anaemia to be rather difficult to classify. In litters examined on the day of birth the anaemic young were usually clearly distinguishable by their pale colour. But in older litters, and even in a few at birth, the classification could not be made with confidence. The haematology of the anaemics is described by Grewal (1962).

SEGREGATION

The single-factor segregations of *sla* alone and in combination with Tabby, *Ta* (Falconer, 1952, 1953), are given in Table 1, from which it is clear that the anaemia

Table 1. *Segregation of* sla

	Parents		Offspring: Females		Offspring: Males	
Type of mating	♀	♂	*sla*	+	*sla*	+
(a)	+ +/+ +	+ *sla*	0	8	0	8
(b)	+ +/+ +	*Ta sla*	0	14	0	16
(c)	+ +/+ *sla*	+ +	4	54	29	17
(d)	+ +/*Ta sla*	+ +	0	13	9	4
(e)	*Ta* +/+ *sla*	+ +	0	15	8	8
(f)	+ +/+ *sla*	+ *sla*	2	3	1	2
(g)	+ +/*Ta sla*	+ *sla*	30	40	36	54
Totals for 1:1 expectation (♀♀ from f and g; ♂♂ from c–g)			32	43	83	85

is due to a single sex-linked recessive gene, though there is evidence of misclassification. Four females were classified as anaemic from matings which were not expected to produce homozygotes. Two of these were tested and proved to be heterozygotes. If the other two were also heterozygotes the penetrance in heterozygous females

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(4 out of 65 expected heterozygotes) amounts to 6%. Though the overall segregation in male progeny is close to the expected 1:1, there is heterogeneity between the different types of mating, according to how Tabby entered the cross. In matings without *Ta* (types c and f) the ratio of *sla*:+ in males was 30:19 ($\chi^2 = 2{\cdot}5$); in matings with *Ta* and *sla* in coupling (types d and g) it was 45:58 ($\chi^2 = 1{\cdot}6$). These two ratios are significantly different from each other ($\chi^2 = 4{\cdot}1$). With *Ta* and *sla* in repulsion (type e) the ratio was 8:8. The heterogeneity is probably due to reduced viability of *Ta* males, but there is also a suggestion that some normal males were classified as anaemic.

LINKAGE

The original mutation to *sla* occurred in a chromosome already marked with *Ta*. The recombination with Tabby was accordingly estimated first in two-point tests, the results of which are given in Table 2. Male progeny gave an estimate of 3·4%

Table 2. *Two-point linkage tests with* Ta

Parents			Offspring phenotypes					
♀	♂	Sex	*Ta sla*	*Ta* +	+ *sla*	+ +	Recombination	
$\frac{Ta\,sla}{+\ +}$	+ *sla*	♀♀	24	5	6	35	15·7%	
		♂♂	33	2	2	53	4·4%	
$\frac{Ta\,sla}{+\ +}$	+ +	♂♂	9	0	0	4	0·0%	3·4%
$\frac{Ta\,+}{+\,sla}$	+ +	♂♂	0	8	8	0	0·0%	

for the recombination between *sla* and *Ta*, but the female progeny showed 15·7% recombination, the difference being significant at the 1% level. Since the estimate from the males agrees with that from the three-point tests it seems probable that the estimate from the females is biased by misclassification. Three-point tests were made with Tabby and Brindled Mo^{br} (Fraser, Sobey & Spicer, 1953; Falconer, 1954). The symbol *Br* will be used here in place of Mo^{br}. The results are given in Table 3. They show, from the absent cross-over class, that the order of the genes is *Br–Ta–sla*. The recombination frequencies were 2·9% between *Br* and *Ta*, and 2·1% between *Ta* and *sla*. These, however, are probably underestimates of the true values because there is evidence of viability interaction. More reliable estimates are probably to be obtained from the non-Brindled progeny only. These give 4·2% for recombination between *Br* and *Ta*, and 3·2% between *Ta* and *sla*. The 5% confidence limits of the *Ta–sla* recombination are 1·2% and 6·8%.

The other genes so far located on the X-chromosome are jimpy, *jp* (Phillips, 1954), which is 21 cross-over units from *Ta* on the side remote from *sla*; and Bent-tail, *Bn*

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Table 3. *Three-point linkage tests, from matings of* $\frac{\text{BrTa}+}{++\text{sla}}$ ♀♀ by ++sla ♂♂

Region of cross-over	Phenotype of offspring	♀♀	♂♂	Totals	
None	*BrTa* +	86	61	147	323
	++*sla*	80	96	176	
Br–Ta	*Br* + *sla*	2	0	2	10
	+ *Ta* +	5	3	8	
Ta–sla	*BrTasla*	1	0	1	7
	+ + +	1	5	6	
Double	*Br* ++	0	0	0	0
	+ *Tasla*	0	0	0	
	Totals	175	165		340

(Garber, 1952), which lies on the same side of *Ta* as *sla*. The recombination between *Bn* and *Ta* is about 13% (11% reported by Falconer, 1954; 15% reported by Phillips, 1954). Recombination of 3·2% between *sla* and *Ta*, with an upper limit of 6·8%, therefore proves that *sla* must lie between *Bn* and *Ta*. The linkage map of the X-chromosome of the mouse is therefore as follows:

Bn—10—*sla*—3—*Ta*—4—Mo^{br}—17—*jp*

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