GENETIC STUDIES OF THE SYRIAN HAMSTER

VII. INDEPENDENCE DATA

ROY ROBINSON
St Stephen's Road Nursery, Ealing, London, W.13

Received 27.ii.70

1. Introduction

A number of mutant genes are now known in the hamster, *Mesocricetus auratus*. The majority of these affect coat colour, either modifying the quality of the pigmentation or producing white spotting. The present report is concerned with a search for possible chromosomal linkage between seven genes. New independence data are presented and collated with data given in previous papers (Robinson, 1958, 1959*a*, *b*, *c*, 1962*a*, *b*, 1964). A general review of hamster genetics and details of the seven genes may be found in Robinson (1968).

2. Material and methods

Table 1 lists the genes investigated. Impenetrance is not a problem with these mutants but inviability was encountered. The genes *ru* and *s* are associated with marked inviability effects, the expression of which varies

Table 1

Symbols and description of mutant genes of the hamster

Symbol	Designation	Prime characteristic
b	Brown pigment	Coat colour
Ba	White band	White spotting
c^a	Acromelanic albino	Coat colour
e	Cream	Coat colour
ru	Ruby-eye	Coat colour
s	Piebald	Coat colour
Wh	Anophthalmic white	Coat colour

between genetic backgrounds. The new segregation data is summarised by tables 2 and 3. These are analysed by the scoring method described by Fisher (1946) and elaborated by Bailey (1961). Inviability effects can upset the regular gene ratios but these can be allowed for by the appropriate analysis (Robinson, 1958; Bailey, 1961). Table 5 gives the main features of the analyses. This tabulation gives the estimated recombination fraction for the combined data, together with the resultant score and information which may be useful for future amalgamations. The column headed *phase balance* shows the percentage of information derived from coupling segregation.

3. Analysis of new data

In general, the analysis has revealed negative results (table 4). Several of the crosses did produce significant associations but in each case it is doubtful if these are due to linkage. The three cases are the *e-ru* test of cross XX and *ru*-male tests for crosses XX and XXI. For instance, it may be noted

TABLE 2

Assortative data on c^d, e, ru *and* s *genes*

Cross	Type	Sex	+	*e*	*ru*	*eru*	*s*	*es*	*rus*	*erus*	c^d	$c^d ru$
XIII	$c^d+++Y/+erusX\times$	male	73	22	17	3	11	4	0	0	46	10
	$c^d+++X+erusX$	female	74	29	13	14	11	2	2	0	38	12
XIV	$++Y/eruX\times$	male	56	17	15	6	—	—	—	—	—	—
	$++X/eruX$	female	45	14	12	3	—	—	—	—	—	—
XV	$e+Y/+ruX\times$	male	231	67	49	25	—	—	—	—	—	—
	$e+X/+ruX$	female	235	81	45	15	—	—	—	—	—	—
XVI	$+Y/ruX\times$	male	181	—	107	—	—	—	—	—	—	—
	$ruruXX$	female	197	—	141	—	—	—	—	—	—	—
XVII	$e+Y/eruX\times$	male	—	150	—	15	—	—	—	—	—	—
	$ee+ruXX$	female	—	164	—	24	—	—	—	—	—	—
XVIII	$+sY/ru+X\times$	male	102	—	13	—	15	—	0	—	—	—
	$+sX/ru+X$	female	13	—	16	—	26	—	2	—	—	—
XIX	$+ruY/e+X\times$	male	23	20	12	11	—	—	—	—	—	—
	$eeruruXX$	female	23	21	19	9	—	—	—	—	—	—
XX	$c^d+++Y/+erusX\times$	male	203	57	30	16	30	12	3	0	113	17
	$c^d+++X/erusX$	female	185	67	38	24	23	11	5	2	91	27
XXI	$++Y/eruX\times$	male	24	5	4	1	—	—	—	—	—	—
	$++X/eruX$	female	14	4	11	6	—	—	—	—	—	—

that comparable associations are not apparent for the same pairs in other crosses. The result for the *e-ru* pair could be due to chance (in part at least) but it more probably stems from the inviability of *ru*. The linkage-like lack of association between *ru* and male is almost certainly due to differential inviability. These conclusions will emerge more clearly from the analysis of the whole 22 crosses.

4. Analysis of combined data

The data from the 22 crosses undertaken during the course of these experiments have been analysed as a whole, with the results of table 5. None of the pairs of genes examined has yielded unequivocal evidence for linkage. However, several of pairs have given curious results which deserved to be discussed in detail.

Data on the segregation of the *e-ru* pair of genes have produced significant associations on two occasions (cross V, $\chi^2 = 5{\cdot}73$, d.f. = 1; and cross XX, $\chi^2 = 4{\cdot}56$, d.f. = 1). These results have not been substantiated over the 12

Table 3

Assortative data on b *and* Ba *genes*

Cross	Type	Sex	*Ba*	*Bab*	*Ba*	*b*
XXII	*bBaY*/++*X*×	male	103	28	35	6
	bBaX/*bBaX*	female	83	32	27	8

crosses in which the two genes have assorted simultaneously. The χ^2 value for the 12 crosses is $\chi^2 = 18{\cdot}74$ (d.f. = 12), with a deviation χ^2 of 2·50 (d.f. = 1), and a heterogeneity χ^2 of 16·24 (d.f. = 10). None of these values is significantly high. The result for the two significant cases are due to unusually poor viability of the +*ru* progeny (a recombinant class). Examination of the two non-*ru* classes did not disclose a departure from independent segregation.

The *ru*-male comparison reveals a highly significant association between *ru* and sex. The resaon is differential inviability between the sexes. Most *ruru* animals display impaired vitality in terms of significantly lower body weight for both sexes (Robinson, 1958), progressive infertility of the male (Bruce, 1958) and, now, significantly greater pre-natal mortality of the male. The *ru* gene has featured in 16 crosses, most of which produced *ruru* animals in a 3 : 1 ratio, the remainder in 1 : 1. The estimated viabilities for each cross are similar for each ratio but modified by sex. The viability for males is $0{\cdot}546 \pm 0{\cdot}024$ and for females is $0{\cdot}691 \pm 0{\cdot}028$, producing the significant difference of $0{\cdot}145 \pm 0{\cdot}037$. The sterility of the male *ruru* has meant that only females have been mainly used for breading, hence in the segregating F_2 and backcrosses, the male represents a crossover class. The differential mortality is great enough to influence the recombination fraction. Two other items point to the same conclusion. Cross XIV was produced from young *ruru* males before these became sterile. The number of backcross offspring is small, but consistent, in showing a deficiency of *ruru* males (now a non-recombinant class) and a recombination fraction ($0{\cdot}515 \pm 0{\cdot}043$) in excess of 0·5. Finally, an estimate of the recombination fraction, based on the two non-*ruru* classes, of all the relevant 16 crosses, gave the non-significant

TABLE 4

Estimated recombination fractions and associated viabilities

Cross	Loci	Recombination fraction	Viability
XIII	*c*^{a}-*e*	0·443 ± 0·078	—
	c^a-*ru*	0·525 ± 0·042	0·687 ± 0·091
	c^a-*s*	0·344 ± 0·141	0·294 ± 0·069
	c^a-male	0·457 ± 0·044	—
	e-*ru*	0·553 ± 0·050	0·650 ± 0·102
	e-*s*	0·566 ± 0·067	0·367 ± 0·063
	e-male	0·411 ± 0·052	—
	ru-*s*	0·665 ± 0·094	u = 0·565 ± 0·097
			v = 0·337 ± 0·068
	ru-male	0·422 ± 0·049	0·687 ± 0·091
	s-male	0·544 ± 0·065	0·367 ± 0·062
XIV	*e*-*ru*	0·487 ± 0·061	0·818 ± 0·154
	e-male	0·512 ± 0·067	—
	ru-male	0·513 ± 0·070	0·818 ± 0·154
XV	*e*-*ru*	0·541 ± 0·031	0·655 ± 0·063
	e-male	0·508 ± 0·032	—
	ru-male	0·550 ± 0·035	0·655 ± 0·063
XVI	*ru*-male	0·486 ± 0·020	0·656 ± 0·054
XVII	*ru*-male	0·469 ± 0·060	0·332 ± 0·589
XVIII	*ru*-*s*	0·375 ± 0·099	u = 0·472 ± 0·086
			v = 0·334 ± 0·067
	ru-male	0·428 ± 0·621	0·454 ± 0·080
	s-male	0·488 ± 0·066	0·328 ± 0·065
XIX	*e*-*ru*	0·478 ± 0·043	0·586 ± 0·103
	e-male	0·529 ± 0·043	—
	ru-male	0·514 ± 0·043	0·586 ± 0·103
XX	*c*^{a}-*e*	0·447 ± 0·049	—
	c^a-*ru*	0·506 ± 0·207	0·614 ± 0·053
	c^a-*s*	0·443 ± 0·058	0·381 ± 0·050
	c^a-male	0·479 ± 0·028	—
	e-*ru*	0·432 ± 0·032*	0·614 ± 0·053
	e-*s*	0·497 ± 0·035	0·381 ± 0·050
	e-male	0·449 ± 0·033	—
	ru-*s*	0·563 ± 0·049	u = 0·568 ± 0·060
			v = 0·400 ± 0·048
	ru-male	0·415 ± 0·032*	0·614 ± 0·053
	s-male	0·522 ± 0·040	0·381 ± 0·050
XXI	*e*-*ru*	0·395 ± 0·090	—
	e-male	0·391 ± 0·104	
	ru-male	0·159 ± 0·104*	—
			—
XXII	*b*-*Ba*	0·458 ± 0·042	—
	b-male	0·571 ± 0·048	—
	Ba-male	0·503 ± 0·048	—

u = viability of *ru*, v = viability of *s*.
* Significant, see text.

value of 0·497 ± 0·014. This value is evidently more realistic than that of table 5 and has been utilised to calculate the closest linkage compatible with the data shown in fig. 1.

The *ru* and *s* genes also display a significant linkage-like association. It is unlikely that the association is due to linkage but to an inviability interaction. Both of the genes are individually inviable as shown by significant deficiencies of *ruru* and *ss* segregants in all of the crosses. The inviability is also shown by weight relationships between the genes (Robinson, 1958). At

TABLE 5

Combination of data for independent segregation

Loci	Recombination fraction	Score	Information	Phase balance	References
b-ba	0·458 ± 0·042	−24·00	572·44	0	This paper
b-e	0·502 ± 0·037	1·33	773·33	0	Robinson (1962*a*)
b-ru	0·505 ± 0·041	3·00	599·08	0	Robinson (1962*a*)
b	0·564 ± 0·032*	64·67	1009·33	0	Robinson (1962*a*, this paper)
Ba-e	0·532 ± 0·027	44·89	1404·89	100	Robinson (1962*b*)
Ba-ru	0·548 ± 0·071	9·56	197·33	100	Robinson (1962*b*)
Ba	0·536 ± 0·022	72·67	2000·00	100	Robinson (1962*b*, this paper)
c^d-*e*	0·493 ± 0·026	−10·67	1512·30	0	Robinson (1959*a*, this paper)
c^d-*ru*	0·498 ± 0·019	− 4·14	2879·64	0	Robinson (1959*a*, this paper)
c^d-*s*	0·423 ± 0·046	−35·90	463·66	24	Robinson (1959*a*, this paper)
c^d-male	0·503 ± 0·015	13·44	4573·30	0	Robinson (1959*a*, this paper)
c-ru	0·482 ± 0·012	−136·33	7421·60	68	Robinson (1958, 1959*a*, *b*, this paper)
e-s	0·481 ± 0·014	− 94·22	4834·73	90	Robinson (1958, 1959*a*, 1962*b* 1964, this paper)
e-Wh	0·466 ± 0·026	− 50·00	1460·00	100	Robinson (1964)
e-male	0·486 ± 0·011	−139·67	9158·00	82	Robinson (1968, 1959*a*, *b*, 1962*a*, *b*, this paper)
ru-s	0·434 ± 0·029*	− 79·06	1206·34	44	Robinson (1958, 1959*a*, 1962*b*, this paper)
ru-male	0·477 ± 0·032*	−236·00	10102·42	94	Robinson (1958, 1959*a*, *b*, 1962*a*, *b*, this paper)
s-Wh	0·551 ± 0·030	58·00	1132·00	100	Robinson (1964)
s-male	0·512 ± 0·017	42·67	3662·02	66	Robinson (1958, 1959*a*, 1962*b*, 1964, this paper)
Wh-male	0·500 ± 0·026	0·00	1460·00	100	Robinson (1964)

Standard error, score and information are computed for the recombination fraction of 0·5.
* Significant, see text.

21 days of age, the *ruru* and *ss* weigh 80 and 77 per cent., respectively, of normal. Of more interest is that the *ruruss* animals weigh only 45 per cent. of normal, which is below the expected 64 per cent. on the assumption of a simple proportional decrease. The male *ruruss* nearly always are sterile while the females are exceedingly poor mothers.

In most of the crosses, *ru* and *s* have always entered in repulsion phase. This has meant that the *ruruss* phenotype is a recombinant class and a deficiency could be due either (1) to linkage or (2) to the suspected inviability interaction. By preserving with *ruruss* females and fostering of young to normal mothers, F_1 offspring in coupling phase (+ +/*russ*) were obtained (crosses XIII and XX). The number of offspring could not fully balance the larger numbers obtained from repulsion phase crosses (II, III, VI and XVIII). However, by deleting one of the crosses, the respective amounts of

information can be made approximately equal. Subject to the amounts of information closely balancing, the combination of crosses chosen (II, VI and XVIII) were those with the largest score, on the principle if these failed

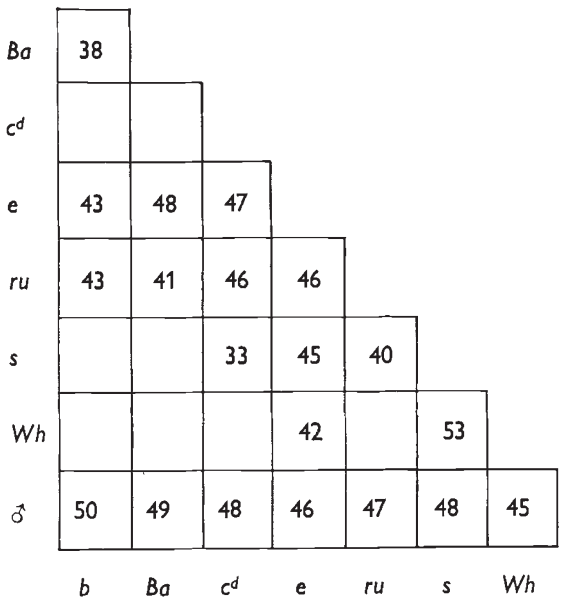

FIG. 1.—Summary of extent of linkage tests. The percentages within each cell show the closest linkage compatible with the breeding data.

to produce a significant result, the other combinations would not. The results are shown by table 6. Although each of the coupling and repulsion entries are significant, the total score is not. The recombination fraction for

TABLE 6

Evidence that the association between ru *and* s *is due to inviability interaction and not to linkage*

Phase	Score	Information	Recombination fraction	χ^2
Coupling	45·909	528·011	0·587 ± 0·044	3·99
Repulsion	−85·563	518·690	0·335 ± 0·044	14·12
	−39·654	1046·795	0·497 ± 0·014	1·50

this data is 0·462 ± 0·031 and is probably the most realistic estimate available at this time. For this reason, it has been used to calculate the closest linkage compatible with the data as shown by fig. 1.

5. SUMMARY

1. Evidence is presented for the independent inheritance of the seven genes *b*, *Ba*, c^a, *e*, *ru*, *s* and *Wh*. Genes *b* and *Ba* are shown to assort independently for the first time.

2. The association between *ru* and *s* is shown to be due to an inviability interaction, rather than to linkage.

3. The association between *ru* and sex is due to differential inviability between the sexes.

4. All linkage data has been statistically combined to give final estimates and the closest linkage compatible with the observed random assortment.

6. References

BAILEY, N. T. J. 1961. *Introduction to the Mathematical Theory of Genetic Linkage*. London: Oxford University Press.

BRUCE, H. M. 1958. Genetic infertility in ruby-eye male hamsters. *Studies in Fertility, 9*, 90-98.

FISHER, R. A. 1964. A system of scoring data with special reference to pied factors in mice. *Amer. Nat., 80*, 568-578.

ROBINSON, R. 1958. Genetic studies of the Syrian hamster. I. The mutant genes cream, ruby-eye and piebald. *J. Genet., 56*, 85-102.

ROBINSON, R. 1959*a*. Genetic studies of the Syrian hamster. II. Partial albinism. *Heredity, 13*, 165-177.

ROBINSON, R. 1959*b*. Genetic studies of the Syrian hamster. III. Variation of dermal pigmentation. *Genetica, 30*, 393-411.

ROBINSON, R. 1959*c*. Genetic independency of four mutants in the Syrian hamster. *Nature, 183*, 125-126.

ROBINSON, R. 1962*a*. Genetic studies of the Syrian hamster. IV. Brown pigmentation. *Genetica, 33*, 81-87.

ROBINSON, R. 1962*b*. Genetic studies of the Syrian hamster. V. White band. *Heredity, 17*, 477-486.

ROBINSON, R. 1964. Genetic studies of the Syrian hamster. VI. Anophthalmic white. *Genetica, 35*, 241-250.

ROBINSON, R. 1968. Genetics and karyology. In Hoffman, R. A., Robinson, P. F., and Magalhaes, H. (Editors), *The Golden Hamster: its Biology and Use in Medical Research*. Ames: Iowa State University Press.