THE LINKAGE RELATIONS OF SIX FACTOR LOCI IN GUINEA-PIGS

by

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INTRODUCTION

The number of linkage studies made with the higher animals is small when compared with the work done with plants. Bateson and Punnett (1911) reported a case of reduplication (the English term for linkage). Emerson (1911) reported the first case of linkage in corn. Since then linkage has been found in the snap-dragon, primula, wheat, oats, sweet-pea, garden-pea, tomatoes, and many other plants.

One of the first linkage papers on animals was published by T. H. Morgan working with *Drosophila melanogaster*. The four linkage groups are known in *Drosophila melanogaster* and many factors are known in each group.

Linkage has been reported in such rodents as rabbits, rats, and mice, but not in guinea-pigs. There seem to be parallel series of factors in the rodents; this fact makes the lack of linkage in guinea-pigs the more remarkable.

Ibsen (1923) furnished evidence of the independent assortment of six pairs of factors in guinea-pigs. Wright (1928) presented further evidence of the independent assortment of the same six factors and also two additional ones.

The present experiment has been in progress ten years, and at the present time 1,592 animals have been analyzed, a far larger number than has been previously used in linkage experiments with guinea-pigs.

PURPOSE

The purpose of the experiment was to determine the linkage relations of the six major color and coat pattern factors. They are:

1. P - normal allelomorph of p; p - pink eye.
2. E - complete extension of black or chocolate in pigmented part of coat; e^p - partial extension; e - non-extension.
3. C - intense pigmentation, red present; Cr - non-yellow, (absence of red - white).
4. A - agouti; a - non-agouti.
5. B - black; b - chocolate.
6. R - rough fur (rosettes present); r - smooth fur (absence of rosettes).

METHODS

When the linkage relations of two or more factors are studied the usual procedure in animals is to produce animals which are heterozygous for the desired factors. Then mate these heterozygous individuals to multiple recessive animals (the common term for this mating is the backcross). The linkage relations are obtained from the distribution of the offspring from the backcross mating.

In producing the heterozygous males used in this experiment all the dominant factors came from the same parent, sometimes the male and sometimes the female parent. Heterozygous females were produced in the same manner. In the following diagrams <u>A</u> represents an animal carrying two or more dominant factors; <u>aa</u> represents an individual that is homozygous recessive for all the six factors used in this experiment. The four diagrams represent the four backcross matings employed, and show the kind of heterozygous animals used in each mating:

1. $\dfrac{A\,\text{♂}}{aa\,\text{♀}}$ ♂ x aa ♀ 3. aa ♂ x $\dfrac{A\,\text{♂}}{aa\,\text{♀}}$ ♀

2. $\dfrac{aa\,\text{♂}}{A\,\text{♀}}$ ♂ x aa ♀ 4. aa ♂ x $\dfrac{aa\,\text{♂}}{A\,\text{♀}}$ ♀

The heterozygous animals are produced, as before mentioned, with the dominant factors from one parent and the recessive factors from the other parent so that when the gametes are produced the non-crossover gametes will contain either only dominant or only recessive factors. The crossover gametes, on the other hand, will contain one dominant and one recessive factor.

When an animal which is heterozygous for six pairs of allelomorphs is mated to a sextuple recessive it is possible to study the linkage relations of fifteen combinations of factors, two at a time. Many times it was impossible to produce an animal which was heterozygous for all six factors. This impossibility coupled with the epistatic effect of some of the factors made it necessary at times to study only part of the linkage relations.

REVIEW OF LITERATURE

Very few papers have been published on the linkage relations in guinea-pigs. Ibsen (1923) presented a paper upon the "Evidence of the Independent Inheritance of Six Pairs of Allelomorphs in Guinea-pigs." The factors worked with were: $\underline{P}$ and $\underline{p}$, $\underline{C}$ and $\underline{Cr}$, $\underline{e}^{p}$ and $\underline{e}$, $\underline{B}$ and $\underline{b}$, $\underline{A}$ and $\underline{a}$, and $\underline{R}$ and $\underline{r}$. The evidence, though incomplete in some cases, indicates that all the factor pairs are inherited independently of each other.

In a more comprehensive paper, Wright (1928) presented the linkage relations of eight pairs of allelomorphs in the guinea-pig. Analysis of the data showed independent inheritance of the eight pairs of factors. The factors with which he worked were : P and p, E and e^p, C and Cd, A and a, B and b, S and s, R and r, and M and m.

After analyzing the offspring from several matings in which the male parent was heterozygous for all eight pairs of factors and the female was a multiple recessive, he concluded that none of the factors were sex linked. Further proof of this conclusion was derived from the offspring of a female heterozygous for all eight pairs of factors that had been mated to a multiple recessive male.

In Wright's data the monohybrid and dihybrid ratios show fifty per cent crossingover, or independent assortment in nearly every case. The apparent exception appeared in the crossover values between C and P. The heterozygous females produced 46.1 per cent crossover gametes, while the males produced 56.6 per cent crossovers. The crossover value for both sexes combined, however, is 50.6 per cent.

The octohybrid ratio he obtained from 398 young showed no tendency for litter-mates to resemble each other any more than is expected by chance. The distribution of factors was random as well as the distribution of sex.

DISCUSSION

The results of Ibsen (1923) and Wright (1928) showed independent inheritance of the factors P and p, E and e, C and Cr, A and a, B and b, and R and r. Further proof of the independent inheritance of these factors is furnished by the present experiment.

In Table I is found a summary of the four crosses. An inspection of the table shows that none of the factors are sex-linked. The table also shows that there is no linkage between any of the six pairs of factors used in this experiment. There are several instances in which the two non-crossover classes are unequal in size. Sometimes the two crossovers are also unequal.

Table II is a condensation of the four crosses shown in Table I. In this table the variation in the size of the two non-crossover and the two crossover classes is more apparent. Some of these cases are due to the epistatic effect of one of the factors. This is especially true for the factors E and A. A acts only on B or b when they are extended by E or e^p; e is the non-extension of black (B) and chocolate (b). In an ee animal the black or chocolate is not extended, and so, since there are no black or chocolate hairs present it is seldom possible to tell whether A or a is present. As a result of this interaction of factors the classes e a and e A are necessarily small.

The genotypes carrying B show, in several instances, what appears from the per cent of crossingover to be linkage. That it is not linkage can be seen by the inequality in numbers of the two non-crossover and the two crossover classes. In every case there is an excess of B's. Another proof that this is not linkage is the fact that the factors which appear to be linked with B do not show any linkage with each other.

The crossover values between P and C show a great deal of variation in the four crosses (See Table I). The cross in which the heterozygous male receives his dominant factors from his sire shows 52.9 per cent crossingover. The cross in which the heterozygous female receives her dominant factors from her dam shows only 39.8 per cent crossing over. The total of the four crosses is 45.6 per cent. Similarly Wright (1928) found that P and C appeared to be linked in the F_1 females but not in the F_1 males. When the results from the two sexes were combined the appearance of linkage was lost.

There is no satisfactory explanation at present for the discrepancies in size of the two non-crossover and the two crossover classes in the genotypes involving B nor for the apparent linkage of P and C.

Although none of the factors seem to be linked there is a possibility that they might be linked in certain individuals - if translocation has occurred. Translocation is the breaking off of a piece of chromosome and the attaching of this piece to another chromosome. The test, to see whether translocation has occurred, would be to study the offspring of a heterozygous individual that had produced a large number of progeny. If translocation has taken place there is a possibility that for the individuals studied two factors would be linked.

The offspring of several individuals heterozygous for all six pairs of factors were studied individually. None of these gave any positive evidence of translocation having taken place. The distribution of factors was random as well as the distribution of sex.

SUMMARY

The analysis of 1,592 animals for the six factor loci P and p, E and e, C and Cr, A and a, B and b, R and r show that:

1. There is no linkage between any of the factors.
2. There is no evidence of sex-linkage.

3. Translocation has not taken place. This conclusion was reached after the offspring of individuals heterozygous for all six pairs of factors had been analyzed individually.

4. In some instances there is a large discrepancy in the numbers of the two non-crossover classes and sometimes of the two crossovers. The epistatic relationships explain some of the discrepancies, but for the others there is no satisfactory explanation at present.

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Table I

	A ♂/aa ♀ ♂ x aa ♀: Non-cross-overs ♂ : ♀	Cross-overs ♂ : ♀	aa ♂/A ♀ ♂ x aa ♀: Non-cross-overs ♂ : ♀	Cross-overs ♂ : ♀	aa ♂ x A ♂/aa ♀ ♀: Non-Cross-overs ♂ : ♀	Cross-overs ♂ : ♀	aa ♂ x aa ♂/A ♀ ♀: Non-Cross-overs ♂ : ♀	Cross-overs ♂ : ♀
PE	54:40		56:48		43:51		51:42	
pe	43:46		44:44		44:36		54:46	
Pe		50:47		45:38		44:45		46:50
pE		29:33		47:43		35:36		40:40
PC	23:20		57:36		29:33		49:53	
pCr	15:13		46:53		25:25		41:44	
PCr		24:19		43:45		21:28		27:34
pC		15:23		50:43		26:13		31:30
PA	15:19		24:14		16:11		17:16	
pa	12:13		18:15		4:13		10:15	
Pa		18:13		17:15		13:15		12:16
pA		9:8		16:13		9:13		6:3
PB	39:29		37:25		31:32		29:33	
pb	11:14		17:9		9:12		5:8	
Pb		41:36		27:33		41:36		31:38
pB		18:19		28:21		25:16		18:18
PR	13:12		23:18		14:11		4:4	
pr	9:15		26:20		11:13		7:4	
Pr		17:8		20:17		10:20		2:4
pR		9:5		12:14		7:15		4:3
EC	24:15		47:30		28:27		30:39	
eCr	24:20		40:51		20:22		34:34	
ECr		16:15		42:39		23:26		26:28
eC		15:28		42:16		29:19		38:38
EA	23:26		32:35		23:27		22:19	
ea	4:3		7:2		1:3		3:2	
Ea		25:24		31:26		19:26		18:28
eA		1:1		0:0		0:0		1:0
EB	35:24		44:36		41:43		31:32	
eb	22:26		22:18		24:16		22:19	
Eb		26:26		26:18		27:33		17:25
eB		22:14		21:11		13:14		14:17
ER	9:6		10:7		9:18		2:1	
er	14:13		17:15		10:14		3:2	
Er		11:9		18:9		13:18		5:3
eR		11:10		14:8		10:12		6:5
CA	8:4		14:15		10:10		11:10	
Cra	4:8		13:12		5:8		9:11	
Ca		6:8		13:19		9:10		3:17
CrA		7:4		20:14		11:10		7:6
CB	13:10		34:15		25:20		22:31	
Crb	14:6		18:15		17:15		12:16	
Cb		11:7		25:22		15:17		16:24
CrB		7:11		23:26		14:16		14:14
CR	2:1		15:11		5:3		1:2	
Crr	5:1		16:20		3:6		1:0	
Cr		2:7		20:12		4:8		0:3
CrR		2:3		13:16		2:3		0:0
AB	10:12		26:20		20:14		14:10	
ab	15:19		17:12		9:13		11:10	
Ab		7:11		11:6		11:7		6:9
aB		14:11		16:14		12:12		10:15
AR	0:1		5:2		3:4		0:0	
ar	0:0		5:2		1:5		2:1	
Ar		2:0		8:4		3:4		0:0
aR		1:1		5:1		3:2		1:0
BR	12:3		11:3		5:7		0:0	
br	8:7		8:5		4:6		2:1	
Br		6:4		11:5		3:11		0:1
bR		2:6		6:4		3:3		0:1

Table II

	NC*	C*	%	D/PE
PE	392		52.7	3.0
pe	358			
Pe		370	47.3	
pE		305		
PC	304		54.4	4.23
pc	262			
Pc		244	45.6	
pC		231		
PA	133		53.8	2.3
pa	100			
Pa		123	46.2	
pA		77		
PB	258		43.3	5.58
pb	85			
Pb		286	56.7	
pB		163		
PR	100		54.6	2.66
pr	107			
Pr		100	45.4	
pR		72		

	NC*	C*	%	D/PE
EC	251		53.0	2.73
ec	248			
Ec		217	47.0	
eC		227		
EA	208		53.1	1.93
ea	25			
Ea		203	46.9	
eA		3		
EB	290		60.0	8.26
eb	172			
Eb		183	40.0	
eB		126		
ER	65		48.1	1.0
er	90			
Er		88	51.9	
eR		80		
CA	83		47.2	1.48
ca	71			
Ca		87	52.8	
cA		79		

	NC*	C*	%	D/PE
CB	173		52.2	1.53
cb	114			
Cb		138	47.8	
cB		125		
CR	40		48.9	0.45
cr	53			
Cr		57	51.1	
cR		40		
AB	127		57.0	4.14
ab	101			
Ab		68	43.0	
aB		104		
AR	15		46.4	4.06
ar	17			
Ar		21	53.6	
aR		16		
BR	41		55.3	1.93
br	43			
Br		41	44.7	
bR		27		

*NC - Non-crossovers. C - Crossovers.

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