the two companions to the Andromeda Nebula are of average size; the smaller Andromeda companion apparently is a dwarf galaxy, and the Large Magellanic Cloud is comparable in dimensions with the mean of the 125 largest in the twenty-five groups.

3. The mean angular diameter of the five largest galaxies in a group (if the group is not too small and scattered) is a fair criterion of distance when the diameters are measured on Bruce plates of long exposure. When current values are accepted for the integrated photographic absolute magnitudes of galaxies,[4] the mean linear diameter of the five largest galaxies in a group may be provisionally taken as 4.2 kiloparsecs.

4. On the basis of the angular-diameter method, the distances have been revised and new values derived for the mean density of matter in space in these twenty-five groups. The revision materially decreases the dispersion in density, but it confirms the earlier result that in the large groups the space density averages about 5×10^{-70} glx/cc, which corresponds probably to a total space density considerably higher than 10^{-28} g/cc.

[1] *H. B.* 873 (1930).
[2] *Mt. Wilson Contr.* 427 (1931).
[3] *H. B.* 874 (1930).
[4] These PROCEEDINGS, **19**, 591 (1933); H. Repr., 92 (1933).

LINKAGE INTERRELATIONS OF THREE GENES FOR REX (SHORT) COAT IN THE RABBIT

BY W. E. CASTLE AND HANS NACHTSHEIM

BUSSEY INSTITUTION, HARVARD UNIVERSITY, AND INSTITUT FÜR VERERBUNGSFORSCHUNG, BERLIN, GERMANY

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Three races of so-called rex rabbits (in German, Kurzhaarkaninchen) have been produced in recent years. The hair of such animals is abnormally short, soft and plush-like, and their whiskers (vibrissae) are bent or curly. The guard hairs are scarcely, if at all, longer than the other hairs and are often erroneously described as lacking.

Rex rabbits are now being extensively bred by rabbit fanciers. Hope has been entertained by many that the pelts of such animals would be valuable to the furrier, but a decision on this point must probably await the time when such pelts will be available in quantity and carefully graded.

Meantime these new mutations of the rabbit afford material of unusual interest to students of rabbit genetics. For convenience, the three races will be designated rex No. 1, rex No. 2 and rex No. 3. In Germany they are

known as Rex, Deutsch-Kurzhaar and Normannen-Kurzhaar, respectively.[1] All are phenotypically similar, indeed quite indistinguishable, when the residual heredity is the same, but they are all genetically different, so that crosses between any two of them produce rabbits with normal coats.

Rex No. 1 is the one best known to fanciers. It was discovered in France by Abbé Gillet in 1919 as a mutation occurring in a race of ordinary rabbits. Its inheritance, as well as that of the other two rex mutations, is that of a simple Mendelian recessive character.

Several years later, in 1926, a breeder in Hamburg, Germany, discovered a short-haired rabbit in the hutches of another breeder at Lübeck, Germany. He was able promptly to establish from this individual the race Rex No. 2 (Deutsch-Kurzhaar). Still later, in 1927, in another part of France a breeder of Himalayan rabbits, Madame Du Bary, observed that short-haired individuals were occurring among her animals. From these she established a race which we will call Rex No. 3 (Normannen-Kurzhaar).

Breeding stock of rex No. 1 and rex No. 2 was secured by Nachtsheim in Germany, and the initial crosses with ordinary rabbits were made by him. Later, F_1 crossbreds were brought by him or sent to Castle, in America, and crosses were made by Castle, as well as by Nachtsheim, between the two races and with race rex No. 3, which meanwhile had been obtained from Madame Du Bary in France.

In earlier publications both Nachtsheim and Castle have described breeding experiments with rex No. 1, in which it was shown to be a simple recessive character, and to recombine independently of all previously known genes of the rabbit. In other words, it was not linked with any other gene of the rabbit known at that time, and so must be supposed to have its locus in a different chromosome.

Similar linkage studies were undertaken with rex No. 2, and the results in this case also were negative, until a test was made for linkage between the two rex genes, rex No. 1 and rex No. 2. To our great surprise this test was positive, showing that these two rex mutations, due to different and complementary genes, had their loci in the *same* pair of chromosomes. The evidence for this conclusion is as follows.

A cross between rex No. 1 and rex No. 2 produces rabbits entirely normal in appearance, both mutations being completely recessive. When these F_1 normal animals are mated with each other, they produce mixed litters of normal and short-haired individuals, the latter being distinguishable from normals at birth by their curly whiskers.

A total of 391 F_2 young has thus far been recorded, of which 195 were normal and 196 short-haired. If the two genes were independent, located in different chromosomes, we should expect a 9:3:3:1 Mendelian ratio to be approximated in F_2, the last three classes all being short-haired.

The ratio of normals to short-haired would then be 9:7, a decided excess of normals. This does not occur. Instead, the two classes are approximately equal.

If, on the other hand, the two rex genes are completely linked, borne in the same chromosome at identical or closely adjacent loci, then we should expect them to behave like allelomorphs, and to give a 1:2:1 ratio in F_2; and of the three classes the first and last would be short, the middle class being normal. In other words, there should be equal numbers of normal and short-haired, as actually observed. It was not expected, accordingly, that crossovers would be detected among the F_2 individuals. Nevertheless, search was made for them, and, much to our surprise, they were found.

It is impossible, by inspection, to determine whether a particular F_2 short-haired individual is an r_1 or an r_2 individual, though it must be homozygous for one or the other gene, since otherwise its coat would be normal, like that of the F_1 individuals which are heterozygous for both genes.

Accordingly, breeding tests were made of F_2 short-haired individuals by backcrossing them to one or the other, or, if necessary, to both of the pure races. Tests of this sort have been completed for 51 F_2 short-haired individuals. Of these, 18 have proved to be pure r_1r_1 individuals which do not carry the r_2 gene. Their genetic formula is accordingly $r_1r_1R_2R_2$. A like number, 21, have proved to be pure r_2r_2 individuals, whose formula is $R_1R_1r_2r_2$. Five individuals are of the composition $r_1r_1R_2r_2$, i.e., they are homozygous for r_1 and heterozygous for r_2; and seven are of the constitution $R_1r_1r_2r_2$, homozygous for r_2 but heterozygous for r_1. No double recessives have as yet been identified, though their production in F_2 would be theoretically possible, and in F_3 would be expected to occur frequently, if the crossover individuals ($r_1r_1R_2r_2$ and $R_1r_1r_2r_2$) were mated one with another.

The F_1 normal individuals, as already stated, are double heterozygotes, $R_1r_1R_2r_2$. The gametes which they would be expected to produce are $r_1R_2 + R_1r_2$ (non-crossovers) and $R_1R_2 + r_1r_2$ (crossovers). A non-crossover gamete (r_1R_2) uniting with a crossover gamete, r_1r_2, would produce the "crossover class" $r_1r_1R_2r_2$, of which five individuals have been identified, one male and four females. The other sort of non-crossover gamete (R_1r_2) uniting with a crossover gamete, r_1r_2, would produce the "crossover class" $R_1r_1r_2r_2$, of which seven individuals have been identified, four being males and three females.

The question now arises, what percentage of crossover gametes do the F_1 individuals produce? In other words, what is the crossover percentage? Each of the 12 crossover individuals received one crossover gamete and one non-crossover gamete, as already indicated. The 39 other tested

F_2 short-haired individuals received only non-crossover gametes, two each. The total number of non-crossover gametes concerned in the production of the tested F_2 population of 51 individuals is accordingly 12 + 78, or 90; whereas the crossover gametes number 12. This is 11.7 ± 2.1 per cent of the total 102 gametes which entered into the production of the tested F_2 population. The indicated crossover percentage is accordingly between 10 and 12 per cent.

The foregoing calculation takes into consideration only the double recessive type of crossover gamete, r_1r_2. We should expect a second type of crossover gamete, the double dominant, R_1R_2, to be produced in like frequency by the F_1 parents. That it is actually produced has been experimentally demonstrated but not on a sufficient scale to give the results quantitative value. Two of the normal-coated F_2 individuals have been tested by appropriate matings with pure r_1 and pure r_2 races. One of them was found to be, like the F_1 parents, a double heterozygote, $R_1r_1R_2r_2$. It evidently arose from the union of two dissimilar non-crossover gametes, r_1R_2 and R_1r_2. The other individual was heterozygous for r_1 only, its constitution being $R_1r_1R_2R_2$. It could have arisen only from the union of a non-crossover gamete, r_1R_2, with a crossover gamete R_1R_2.

It is accordingly clear that crossing-over does occur between the genetic loci r_1 and r_2, and that they are distant from each other about 10 or 12 units, since about 10 or 12 per cent of crossing-over occurs. It seems surprising that if crossing-over occurs as frequently as this, the F_2 ratio of normal to short-coated young should indicate complete linkage by yielding approximate equality of the two classes. But upon calculating the expectation for F_2 with 10 per cent of crossing-over, it is found to deviate very little from equality, so little, indeed, that random sampling would be likely to conceal it completely. Thus, in an F_2 population of 400 individuals, the expectation is 201 normal to 199 short, if crossover gametes are to non-crossover gametes as 1:9. We have actually observed 195 normals:196 short in a population of 391 individuals. This is very close to the theoretical expectation.

A very different F_2 ratio of normal to short is obtained when either rex_1 or rex_2 individuals are crossed with the rex_3 race. The former cross has produced an F_2 population of 278 individuals, of which 159 are normal and 119 short-haired. A 9:7 ratio, expected if no linkage exists, would be 156.4:121.6, an even smaller excess of normal individuals than is observed. The deviation from expectation is only 2.6, the probable error being 5.6. Accordingly, the agreement with expectation is excellent.

If, however, we test the observed numbers for agreement with a 1:1 ratio, expected if close linkage exists between r_1 and r_3, we find the deviation to be 17.4 and the P. E. 5.58, a very poor fit. In all likelihood, there-

fore, the ratio is 9:7 rather than 1:1, and r_1 and r_3 are independent rather than linked.

The cross between rex$_2$ and rex$_3$ has produced an F_2 population of 166 individuals, of which 104 are normal and 62 short-haired, a considerable excess of the former. On a 9:7 basis the expected numbers would be 93.4:72.6, and the excess of normals would be 10 less than observed, the P. E. being 4.3. This is only fair agreement, but the deviation from expectation is in the opposite direction from what would be expected if there were linkage between r_2 and r_3, for in that case normals and shorts should be approximately equal. From this expectation the observed numbers deviate by 21 individuals, the P. E. being 4.3.

Accordingly, in both crosses agreement is better with a 9:7 than with a 1:1 ratio of normal to short-haired, the former ratio indicating complete independence, the latter linkage. Since r_1 and r_2 are linked with each other (lie in the same chromosome), it follows that if one of them is free from r_3 (lies in a different chromosome), then the other must be free also. Accordingly, it is legitimate, for statistical purposes, to combine the two F_2 populations obtained by crossing r_1 and r_2 with r_3. If this is done, we have a total of 444 individuals, of which 263 are normal and 181 short-haired. The expectation on a 9:7 basis is 249.7:194.3, from which the observed numbers deviate by 13.3, which is less than twice the probable error (7.0) and so not significant, since it may well be a consequence of random sampling. It should be noted, also, that the deviation is not in the direction to indicate linkage (toward equality of normal and short) but in an opposite direction toward inequality of the two classes, which is expected if no linkage occurs.

Further evidence that r_1 and r_2 assort freely with reference to r_3 (though not with reference to each other) is found in a few tests which have been made of the constitution of F_2 short-haired animals derived from the crosses $r_1 \times r_3$ and $r_2 \times r_3$. From the former cross, one individual has been found to be $r_1r_1R_3r_3$ and another $R_1r_1r_3r_3$. Each of these must have arisen from the union of a crossover (new combination) with a non-crossover (original combination) of an r_1 with an r_3 allelomorph.

From the $r_2 \times r_3$ cross, three F_2 short-haired individuals have been fully tested. One is of the constitution $r_2r_2R_3r_3$, another is $R_2r_2r_3r_3$ and a third is $r_2r_2r_3r_3$. Into the production of the first two there entered, in each case, one *new combination* and one *original combination* gamete. Into the production of the third, only *new combination* gametes entered.

It appears, accordingly, that *new combination* gametes are fully as frequent in occurrence as *original combination* gametes. We have evidence that in the production of these five tested F_2 individuals 6 of the former sort and 4 of the latter sort were concerned. If there were linkage between r_3 and the other rex genes, we should expect *new combinations*

to be less frequent in occurrence than *original combinations*, but they are not.

The somatic character of the individual homozygous for two rex genes, r_2 and r_3, is of interest. Each of these genes, by itself, is able to produce the same short-haired type. Together they produce apparently no greater effect than each would produce by itself.

Summary.—Three races of short-haired (rex) rabbits have originated, each by a recessive mutation in a different gene. The genes responsible for two of these rex mutations (r_1 and r_2) are borne in the same chromosome, since they are linked with about 10 or 12 per cent of crossing-over between them. The gene for the third rex mutation (r_3) lies in a different chromosome, since it recombines freely with both r_1 and r_2.

[1] In Nachtsheim's laboratory the genetic symbols used are:

rex = Franz. Rex = r_1
dek = Deutsch-Kurzhaar = r_2
nok = Normannen-Kurzhaar = r_3.

THE GENE THEORY IN RELATION TO BLENDING INHERITANCE

BY W. E. CASTLE

BUSSEY INSTITUTION, HARVARD UNIVERSITY

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Before the rediscovery of Mendel's law, Francis Galton had recognized two sharply distinct classes of inherited characters, those which are alternative and those which blend. He found examples of these in human eye color and human stature, respectively. When the parents differ in eye color, the children are like one or the other parent, the inheritance being characterized as alternative; but when the parents differ in stature, the children are of intermediate stature, a blending effect.

With the rediscovery of Mendel's law, it was recognized that an adequate explanation had been found for the inheritance of alternative characters, which were then commonly called unit-characters. But this terminology later fell into disrepute because it was found that literal-minded individuals conceived of the character itself as being inherited in the gametes rather than a single something which was necessary for the production of the character. So the term *gene* was introduced to designate the indispensable something in the germ cell necessary for the development of the character in the individual.

By a brilliant series of discoveries, Morgan and his pupils proved that the genes are located in the chromosomes of the germ cells where they