TWO CASES OF REVERSE MUTATIONS IN THE COLOUR FACTORS OF RABBITS.

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In a large litter of thirteen rabbits born in the autumn of 1931, and produced by a pair of pure-bred and prize-winning Chinchilla-Rex parents, a single individual differing markedly in colour from its litter mates was observed.

This individual was of a peculiar brownish hue, whilst all the other youngsters were either of the typical Chinchilla grey (Agouti-Chinchilla) colour, or turned eventually into so-called black Chinchillas. The exceptional individual became eventually a typical wild type coloured, or agouti, animal. Its pelage, however, like the fur of its parents and of all other members of the litter concerned, was that of a typical "Rex," with all the characteristic disturbances in the development of the outer coat.

In short, the exceptional individual was a typical "Castorrex" rabbit, though produced by a pair of Chinchilla-Rex animals.

The fact that our animal had the Rex type of hair formation is in itself a proof that no mistake concerning this individual could play any rôle in the case under discussion.

Since no other Rex-coated rabbits existed in the Institute at the time, it is obvious that any accidental and unrecorded mating of the Chinchilla-Rex female would result in at least part of the offspring becoming normal coated. This, as stated above, was not the case. The original pair subsequently produced a number of litters, comprising more than 100 individuals, which were all typical Chinchillas.

The original male was frequently mated with Chinchilla and Albino females, mostly Angoras, and produced nothing but Chinchilla, thus proving his homozygosity for Chinchilla albinism.

The original pair most likely belonged to the so-called "light" Chinchilla type, which has the desired brown eye colour. Since the Chinchilla-Rex is, as shown by Castle (1921), always of a darker shade than the normal-haired Chinchilla, the brown-eyed "light" Chinchilla conforms much more readily to show requirements under conditions of rexed

pelage, whilst the blue-eyed "dark" Chinchilla becomes almost black when rexed.

It is of course possible that one of these animals, at least, was of the "dark" type, possessing modifiers of eye colour. This assumption is, however, rather improbable and cannot be subjected to any direct proof.

A further possibility, that one of the original parents was a so-called "pale" Chinchilla, carrying the "pale" allelomorph of the Chinchilla factor, and that in consequence our exceptional individual is in reality a pale Chinchilla with unusually strongly developed brown pigmentation, could be subjected to rather extensive tests.

Since the exceptional individual was fortunately a male, he was tested with a number of females almost simultaneously.

The most critical tests are furnished by matings with Chinchilla and Albino females. From these matings the following classes of offspring were obtained:

From Chinchilla females		From Albino females		
Normal Agouti	Chinchilla	Normal Agouti	Chinchilla	Total
15	18	23	21	77

The above figures clearly show a 1 : 1 ration of Agoutis and Chinchillas, proving the animal under discussion to be heterozygous for full colour and Chinchilla dilution, producing both types of gametes in equal numbers.

Further, this animal cannot by any chance be an exceptionally brightly coloured "pale Chinchilla," as suggested above, since in this case all his offspring heterozygous for the mentioned Chinchilla allelomorph and true albinism would exhibit the characteristic "sable" coloration, which as stated was not the case.

Again, the back-crossing of an agouti-coloured son of the exceptional male bred from an Albino mother with Albinos yielded 11 albinotic young and 9 Agoutis, showing that this animal, like its father, carried two different members of the colour factor allelomorphs, namely the gene for full coloration and the factor for complete albinism.

These results form a sufficient proof that we are dealing here with a true reverse mutation from chinchilla albinism back to full coloration.

This mutation most likely took place in a rather late stage of gametogenesis in one of the parents of the unusual individual, possibly after the reduction division in one of the ova, or even during spermatid formation.

The rather unusual occurrence described in the preceding was followed

by a similar case in a line of rabbits somewhat related to the one that yielded the first reverse mutation.

In a litter produced by a pair of F_1 rabbits derived from a cross between Chinchilla-Rexes and White Angoras, born at the end of December 1932, two unusual individuals amongst three others of the expected classes were observed.

The cross mentioned above was undertaken in order to obtain the double recessive Angora-Rex compound, and was carried out on a rather extensive scale.

The Chinchilla-Rex rabbits used were mostly descendants of the original pair, mentioned in connection with the first case of reverse mutation.

The White Angoras, as found in former tests, carried the factor for yellow colour.

It was thus only natural that, amongst the F_2 products of the mentioned cross, there should appear chinchillated yellow rabbits, *i.e.* white animals with dark eyes and eventual dark pigment around the nose, in various combinations with respect to the type of fur.

Since our animals, unlike the "chinchillated yellows" of Castle which were grey eyed, have always brown eyes like the "yellow-chinchillas" of Nachtsheim, we have an additional proof that our material was, as a matter of fact, of the "light chinchilla" type, and further, that the reverse mutations mentioned in this paper did actually occur in the "light" member of the Chinchilla series of allelomorphs.

In the litter mentioned, produced as stated by a typical pair of Chinchilla-coloured F_2 rabbits, two typical Chinchillas, one "chinchillated yellow" and two fully pigmented yellow rabbits were found.

One of the yellows, which obviously form an entirely unexpected class, was normal haired and white bellied, evidently carrying the agouti factor, while the other was dark bellied, and a Rex.

The white-bellied yellow male died at the age of a few months, and could not be tested. The rex-haired dark-bellied doe has up to now produced the following two litters:

	Fully coloured	Chinchilla	Total
1. By a triple recessive Chinchilla-Angora-Rex male	2	1	
2. By a normal-haired pure Chinchilla	2	3	8

Though the figures are obviously very scanty, the above results are by themselves sufficient to prove that the yellow female is heterozygous for the normal colour factor, and without doubt must, just as her white-

bellied brother and the Agouti male mentioned at the beginning of this communication, be the product of a reverse mutation at the "light chinchilla" locus, which during germ-cell formation of one of the F_1 individuals restored its original internal balance, reverting to the original "colour factor" in its behaviour in inheritance. Physiologically the effect of the discussed reverse mutation is manifested in the affected organism by its ability to produce yellow pigment, which is totally inhibited in organisms homozygous for any of the known mutant allelomorphs of the gene responsible for full pigmentation.

Of course it is also possible that in the case last mentioned the recovery of the original genic balance occurred in the factor for complete albinism introduced by the White Albino ancestor of the mutant individuals, and not in the "light chinchilla" allelomorph.

This, however, does not seem probable, and certainly did not take place in the first reverse mutation mentioned.

The fact that both cases occurred in related stocks of rabbits, giving the impression of high incidence of an otherwise extremely rare phenomenon, may or may not be of further significance.

The successive occurrence of two reverse mutations among fewer than 500 individuals must be regarded as exceptionally frequent, but the total material is obviously too small to allow of any further inferences.

Though instances of reverse mutations in plant and animal organisms have been studied rather extensively in recent times, owing to the peculiar behaviour of certain "mutable" genes found in maize, *Drosophila virilis* and to some extent in *Drosophila funebris* (Timoféeff-Ressovsky, 1927), the phenomenon is unusual in Mammals.

A few instances of somatic reverse mutations of the colour factor in guinea-pigs, with one instance of a mutation which was in part somatic and in part genetic, were studied some time ago by Sewall Wright and Eaton (1926).

No such instance, so far as the writer is aware, has been recorded in the rabbit.

Since the case of albinism in rodents is often quoted as an example of irreversibility of the process of mutation, and an argument in favour of the so-called "presence and absence hypothesis," the writer considers that these cases may be of general interest, especially in view of modern concepts regarding the structure of the Mendelising gene.

SUMMARY.

1. Two cases of reverse mutation of the "light chinchilla" factor of the colour factor allelomorph in rabbits back to full pigmentation, together with respective breeding tests, are described.

2. The bearing of the observed phenomena on reverse mutations in other forms is briefly discussed.

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