FURTHER INVESTIGATIONS ON THE ORIGIN OF TUMORS IN MICE.

II. Tumor Incidence and Tumor Age in Hybrids.

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We wish to report the results that we obtained in crossing the strains described in our preceding paper.[1] We used some of the hybrids thus obtained for further hybridization. Soon after the beginning of our studies of heredity in cancer in mice, we started experiments in hybridization in order to determine whether tendency to a high or a low tumor rate prevails in the offspring of two parents, one of which had a high, while the other had a low tumor rate; or, to state it differently, whether a tendency to develop cancer is a dominant or recessive character.[2] We referred to these experiments briefly in a former publication.[3] We stated that in mating a certain strain rich in tumors with a strain very poor in tumors we obtained hybrids which have so far been rich in tumors. In this case the male, which is itself not liable to have tumors, transmits the liability to have tumors to the daughters. We mentioned another strain rich in tumors which if mated to a strain poor in tumors produced hybrids rich in tumors. We stated that we intended to collect further data before arriving at a definite conclusion. We can now on the basis of a large number of experiments confirm our previous preliminary conclusion that the higher tumor rate may be dominant in crosses. But we found that the result of hybridization varies in

[1] Lathrop, A. E. C., and Loeb, L., *Jour. Exper. Med.*, 1915, xxii, 646.

[2] We use the terms "dominant," "recessive," and "unit factor" at present merely as convenient means of expression, without implying by the use of these terms the adoption of further going hypotheses concerning the mechanism of heredity in cancer.

[3] Lathrop, A. E. C., and Loeb, L., *Proc. Soc. Exper. Biol. and Med.*, 1913, xi, 34.

different crosses. We again gave special attention to the inheritance of the tumor age. Yet while the material on which our further conclusions are based is large, we repeat what we said in the preceding paper, that we are still continuing our experiments and that we are ready to modify our conclusions whenever our further work should fail to confirm our first results. We lay special stress on communicating the observations as such and regard some of our conclusions as only tentative. We take this attitude especially as we were often obliged, through lack of sufficient funds in this work, to direct the breeding in such a way that simultaneously with our scientific aims economic needs were satisfied. Otherwise the experiments could not have been completed.

Hybrids Produced.

European + 102 and 103: 16% (16%) + 30% (38%). I age class + II age class.[4]

Hybrids: total 21% (25%). Mixture of 102 and 103: 22% (26%), 29% (32%), 29% (33%). European + 102: 14% (18%), 17% (21%). European + 103: 10%. IV age class.

The European mice were imported. 102 and 103 were the offspring of an old male, the son of a tumor mouse, and plum-silver females which had mixed origin and gave origin to the No. 8 strain. The old male was later mated to his daughters (among them 102 and 103) and their offspring constituted the 8½ strain. 102 and 103 after having been mated to the European had young ones at the same time and their offspring could only be partly distinguished as to whether 102 or 103 was the mother of a certain mouse. 102 and 103 are there-

[4] Before discussing in each case the result of the hybridization, we mention the two parent strains which entered into the cross; the male parent is named first, then the female parent. In the case of the first group mentioned the European was the male and 102 or 103 the female parent. Then follows the tumor rate of the father, 16% (including all age classes), and the tumor rate of the II and III age classes only, in brackets (16%) of the father strain; in the case of the mother strain the figures are 30% for all age classes and 38% for the II and III age class. Then follows the age class of the father strain: I age class; and of the mother strain: II age class. In giving the tumor rate of the hybrids the figure for the second and third age class follows again in brackets. The age class of the hybrids is given last. In the case of the first hybrid group several figures are given for the tumor rate of the hybrids; in some of the offspring 102, in others 103 was the mother, in still others the offspring of 102 and 103 were mixed. The lists of the mice with and without tumors in the different generations and in different age classes are arranged in the same way as in the preceding paper (Lathrop and Loeb, *Jour. Exper. Med., loc. cit.*). On the left side of the page are the mice without, on the right side the mice with tumors; the Roman figures signify the age classes.

fore essentially of a similar character to the No. 8 and No. 8½ strain. Altogether a record was kept of 146 mice of this strain. The variations among the different strains and different families are relatively small. The tumor rate throughout is low, on the whole similar to European, or intermediate between the European and No. 8. The tumors appear late, and belong to the IV age class. They herein differ from their parents, where the tumors appeared early; namely, in the I and II age class. Both parents of these hybrids had a low or medium tumor rate, and the tumor rate of the hybrids agrees with that of the parents. In several cases these hybrids were used for further hybridizations.

(a) (European + 102) F_1 + 8½ F_4: 14% (18%), 17% (21%) + 17% (19%). IV + II age class.

In this case both parents had a similar, low tumor rate; the tumor rate of the hybrids is the same as that of the parents, 16% (18%). The tumors appear late, the fourth is dominant over the second age class. Five generations of these hybrids were observed, and the results in all agreed with each other in regard to tumor rate as well as to tumor age.

	Without tumors.	With tumors.
F_1	26 (3 I 8 II 15 III)	5 (2 I 3 III)
	84% (12% I 31% II 57% III)	16% (40% I 60% III)
F_2	96 (18 I 26 II 52 III)	26 (2 I 7 II 17 III)
	79% (17% I 27% II 56% III)	21% (8% I 27% II 65% III)
F_3	210 (49 I 66 II 95 III)	40 (4 I 11 II 25 III)
	84% (23% I 31% II 46% III)	16% (10% I 27% II 63% III)
F_4	47 (19 I 9 II 19 III)	3 (3 III)
	94% (40½% I 19% II 40½% III)	6% (100% III)
F_5	16 (11 I 3 II 2 III)	3 (1 II 2 III)
	84% (70% I 18% II 12% III)	16% (34% II 66% III)
Total:	396 (101 I 112 II 183 III)	77 (8 I 19 II 50 III)
	84% (25% I 28% II 47% III)	16% (10% I 25% II 65% III)
	II + III 82%	II + III 18%

(b) 101 (English) + (European + 103): 71% (72%) + 10% or total 21% (25%). I age class + IV age class.

In this case males from a strain rich in tumors (101 English) were mated to females from a strain poor in tumors (European + 103). In the strain of the father the tumors appeared early, in the strain of the mother late. In the hybrids the tumor rate is intermediate, 34% (46%). The tumors in the offspring belong to the IV age class; the late appearance of the tumors seems again to be dominant. The hybrid mice were observed through three generations and the results in the various generations agreed well, on the whole. The figures for the sum of all the generations are as follows:

Without tumors.	With tumors.
101 (49 I 25 II 27 III)	51 (61 I 27 II 18 III)
66% (49% I 25% II 26% III)	34% (12% I 52% II 36% III)
II + III 54% III 60%	II + III 46% III 40%

(c) London + (European + 103) F_3: 28% (27%) + 10% (European + 103) or + 21% (25%) European + 102 and 103 (total). II age class + IV age class.

The parents have here a low or medium low tumor rate. In the father the tumors belonged to the II, in the mother to the IV age class. In the hybrids the tumor rate is low (5%), even slightly lower than in the mother. The tumors appear late.

The total figures are:

Without tumors.	With tumors.
74 (12 I 31 II 31 III)	4 (2 II 2 III)
95% (16% I 42% II 42% III)	5% (50% II 50% III)

The IV age class is again dominant.

(d) (European + 103) F_1 + III daughter of No. 10 : 10% or total 21% (25%) + ?30% (38%). IV age class + ?II age class.

In order to understand the character of these and the following hybrids, it will be necessary to state the character of the family of No. 10. No. 10 was a female mouse which was found to have a tumor on Sept. 8, 1910. She belonged probably to the No. 8 strain. She was in all probability mated to a male from the No. 8 strain. Sept. 10, 1910, she gave birth to three daughters, which are designated as follows: I (Nov. 3d), II (Nov. 8th), and III. The third daughter failed to grow for a considerable period of time, but later grew to normal size. Daughter I (Nov. 3d) was first mated to a European male 151, afterwards to an English Silver male, and last to a Cream male. Daughter II (Nov. 8th) was first mated to the same European male 151, and later to a male from the No. 8½ strain. The III daughter was mated to a son of European + 103. The European 151 was later crossed with females of No. 8 F_5. These various crosses are represented in Table I.

TABLE I.

No. 10 ♀ + No. ?8 ♂

151 European ♂ mated to:

♀ I Nov. 3d	♀ II Nov. 8th	♀ III
(a) + I Nov. 3d ♀	(a) + 151 European ♂	(a) + 151 European ♂	(a) + (European + 103) F_1 ♂
(b) + II Nov. 8th ♀	(b) + English Silver ♂	(b) + 8½ ♂	
(c) + No. 8 F_5 ♀	(c) + Cream ♂		

The offspring from the cross (European + 103) F_1 + III daughter of No. 10 gave a tumor rate of 17% (22%). The tumors belonged to the IV age class. The tumor rate and tumor age of the father were dominant in this case. About the tumor rate of the No. 10 family we have no definite knowledge, although we must assume that the I and II daughters had a very high tumor rate.

Without tumors.	With tumors.
F_1 8 (2 II 6 III)	0
F_2 94 (35 I 22 II 37 III)	11 (4 II 7 III)
90% (37% I 23% II 40% III)	10% (36% II 64% III)
F_3 38 (15 I 13 II 10 III)	17 (3 I 7 II 7 III)
69% (39% I 34% II 27% III)	31% (18% I 41% II 41% III)
Total: 140 (50 I 37 II 53 III)	28 (3 I 11 II 14 III)
83% (36% I 27% II 37% III)	17% (11% I 39% II 50% III)
II + III 78% III 79%	II + III 22% III 21%

(e) English Sable (son of Tumor Mouse 198) + [(European + 103) F_1 + III daughter of No. 10] F_2: 70% (69%) + 17% (22%). I age class + IV age class.

In this case only a few of the offspring were obtained, but the tumor rate is high, the tumors appear late, and the hybrids belong to the IV age class.

	Without tumors.	With tumors.
F_1	1 (1 I)	5 (3 II 2 III)

83% tumor rate, IV age class.

Here the high tumor rate of the English Sable male was dominant over the low tumor rate of the two females of the [(European + 103) F_1 + III daughter of No. 10] F_2 to whom they were mated. The latter had a very low tumor rate. On the other hand, it is probable that the age class (IV) of the females prevailed over the age class of the English Sable (I).

Summary.—In considering these six crosses, we shall distinguish tumor rate and age class. In two hybrids we find marked divergence of the tumor rate in the two parents; namely, 101 + (European + 103), where the tumor rate was intermediate, and English Sable + [(European + 103) F_1 + III daughter of No. 10] F_2. In this case the higher tumor rate seemed to dominate. In the other four crosses the tumor rates of the parents were either very similar to each other or differed not very markedly. In two of these cases perhaps the lower tumor rate dominated; in the two other the tumor rate of the offspring was similar to that of the parents. In the case of the age classes, on the other hand, the higher age class (later tumors) dominated in all cases. Every time the presence of the combination European + 102 or 103 called forth the IV age class, independently of the behavior of the tumor rate in the hybrids. This was already noticeable in the first cross: European + 102, 103. The age class was here higher than in either of the parent strains. It appears, therefore, that the age classes are determined by unit factors different from those determining tumor rate, and that dominance of the higher tumor rate may be combined with dominance of the higher age class (lateness of tumors).

(a) 151 (European) + No. 8 F_3: 16% (16%) (?) + 30% (38%). I age class (?) + II age class.

The hybrids had a tumor rate similar to No. 8: 30% (34%). The age class is likewise that of No. 8; *viz.*, II. The tumors appear, however, slightly earlier than corresponds to Age Class II. Four generations were observed which agreed fairly well.

Without tumors.	With tumors.
Total: 88 (31 I 19 II 38 III)	37 (8 I 20 II 9 III)
70% (35% I 22% II 43% III)	30% (22% I 54% II 24% III)
II + III 66% III 87%	II + III 34% III 19%

(b) 151 (European) + I daughter of No. 10 (Nov. 3d): 16% (16%) (?) + high tumor rate. I age class (?) + II or III age class (?).

The hybrids show a tumor rate of 72% (81%); they belong to the II age class. We may assume that daughters I and II of No. 10 had the tendency to a high tumor rate and that it was dominant over the lower tumor rate of European. However, there is not combined with the high tumor rate an early appearance of the tumors; they belong to the II age class. The figures for these hybrids were given in our preceding paper.[5]

(c) [151 (European) + I daughter of No. 10 Nov. 3d] + 101: F_2 72% (81%) + 71% (72%). II age class + I age class.

In this class both parents have a high tumor rate, and the hybrids have also a high tumor rate (55%), although not quite as high as the parents. This slight decrease in the tumor rate of the hybrids may be accidental, due to the relatively small number of observed mice. The tumors belong to the I age class.

Without tumors.	With tumors.
12 (8 I 2 II 2 III)	15 (10 I 5 II)
45% (66% I 17% II 17% III)	55% (66⅔% I 33⅓% II)

Four generations were observed. The results in the various generations agreed.

(d) 151 (European) + II daughter of No. 10 (Nov. 8th): 16% (16%) (?) + high tumor rate. I age class (?) + II or III age class (?).

The II daughter of No. 10 had probably a similar tendency to a high tumor rate as the I daughter. The hybrids have here again a high tumor rate, but their rate is not quite as high as that of the preceding strain of hybrids, the offspring of the same European father and the I sister. The tumor rate of the hybrids was 65% (69%), the tumors belonged to the II age class.

Without tumors.	With tumors.
F_1 3 (3 I)	0
F_2 4 (2 I 2 II)	3 (2 I 1 III)
F_3 24 (8 I 14 II 2 III)	44 (17 I 23 II 4 III)
35% (33⅓% I 58⅓% II 8⅓% III)	65% (39% I 52% II 9% III)
F_4 3 (2 I 1 III)	15 (1 I 10 II 4 III)
16% (66⅔% I 33⅓% III)	84% (7% I 67% II 26% III)
Total: 34 (15 I 16 II 3 III)	62 (20 I 33 II 9 III)
35% (44% I 47% II 9% III)	65% (32% I 54% II 14% III)
II + III 31% . III 25%	II + III 69% III 75%

The same European male and two sisters produced therefore hybrids with a similar tumor rate and a similar age class.

(e) English Silver + I daughter of No. 10 (Nov. 3d): 7% + ? high tumor rate. I age class + ?II age class.

[5] Lathrop and Loeb, *Jour. Exper. Med., loc. cit.*

After the I daughter of No. 10 had been mated to European 151, she was mated to an English Silver male with a very low tumor rate, but belonging to an early age class. The hybrids have a tumor rate of 36% (38%) which is much higher than the tumor rate of English Silver and intermediate between the tumor rate of the English Silver and the tumor rate of the descendants of this female and the European 151 male. The tumor mice belong to the II and not to the I age class, as do the tumor mice of the English Silver. The detailed figures for the various generations of these hybrids are given in the preceding paper.[6]

(f) English Sable + (English Silver + I daughter of No. 10, Nov. 3d) : 70% (69%) + 36% (38%). I age class + II age class.

Here a strain with high tumor rate is crossed with one with medium tumor rate. The descendants have a high tumor rate, 69%, similar to the strain of the father. The tumors stand probably somewhat between the I and II age class.

Without tumors.	With tumors.
5 (4 I 1 II)	11 (5 I 6 II)
31% (80% I 20% II)	69% (45% I 55% II)

The high tumor rate is here dominant.

(g) Cream + I daughter of No. 10 (Nov. 3d) : 2% (3%) + high tumor rate. IV age class + ?II or III age class.

The hybrids have a tumor rate of 36% (38%). The tumors belong to the IV age class. Tumor rate of the hybrids is similar to the tumor rate of the English Silver + I daughter of No. 10 (Nov. 3d). English Silver and Cream have a similar tumor rate, and the hybrids also have a similar tumor rate. But while the tumors of the English Silver belonged to the first age class, the tumors of the Cream belong to the IV age class and correspondingly the tumors of the English Silver hybrids belong to the II age class, and the tumors of the Cream hybrids belong to the IV age class. As far as the age of the tumors is concerned, the higher class (lateness of the tumors) is dominant; while as far as the tumor incidence is concerned, the hybrids show an intermediate condition between both parents. Neither in this case nor in the case of the English Silver hybrids with the I daughter of No. 10 does the lower tumor rate dominate. The various generations of this hybrid strain agree very well with each other.

	Without tumors.	With tumors.
F_1	13 (1 I 2 II 10 III)	5 (5 III)
	There may be a few mice of the F_2 generation included.	
	72% (8% I 15% II 77% III)	28% (100% III)
F_2	27 (2 I 17 II 8 III)	13 (3 I 7 II 3 III)
	68% (7% I 64% II 29% III)	32% (23% I 56% II 23% III)
F_3	54 (11 I 6 II 37 III)	40 (1 I 14 II 25 III)
	58% (20% I 11% II 69% III)	42% (2½% I 35½% II 62% III)
F_4	18 (4 I 8 II 6 III)	4 (2 II 2 III)
	82% (22% I 44% II 34% III)	18% (50% II 50% III)
Total:	112 (18 I 33 II 61 III)	62 (4 I 23 II 35 III)
	64% (16% I 29% II 55% III)	36% (6% I 37% II 57% III)
	II + III 62% III 64%	II + III 38% III 36%

[6] Lathrop and Loeb, *Jour. Exper. Med., loc. cit.*

(h) No. 8½ + II daughter of No. 10 (Nov. 8th) : 17% (19%) + ? high tumor rate. II age class + ?II or III age class.

The hybrids show here a high tumor rate, similar to that of the mother, possibly slightly lower: 49% (50%). The tumors belong to the III age class. Here again it seems that greater tumor incidence and lateness of the tumors are dominant. The various generations were as follows:

	Without tumors.	With tumors.
F_1	2 (1 I 1 II)	0
F_2	5 (1 II 4 III)	2 (1 II 1 III)
F_3	27 (4 I 10 II 13 III)	28 (6 I 13 II 9 III)
	49% (15% I 36% II 49% III)	51% (21% I 47% II 32% III)
F_4	8 (3 I 2 II 3 III)	10 (5 II 5 III)
	44% (37% I 26% II 37% III)	56% (50% II 50% III)
Total:	42 (8 I 14 II 20 III)	40 (6 I 19 II 15 III)
	51% (19% I 33% II 48% III)	49% (15% I 47½% II 37½% III)
	II + III 50% III 57%	II + III 50% III 43%

(i) A subgroup of this strain was formed. After the aged 8½ male of the preceding group had died, the II daughter of No. 10 (Nov. 8th) was mated with one of her sons. [8½ + II daughter of No. 10 (Nov. 8th)] + II daughter of No. 10 (Nov. 8th) : 49% (50%) + high tumor rate. III age class + ?II or III age class.

Here the tumor rate is somewhat lower than in the preceding strain; but this is mainly due to the greater mortality in earlier periods of life in mice of this strain.

	Without tumors.	With tumors.
Total:	46 (19 I 19 II 8 III)	26 (5 I 9 II 12 III)
	64% (41% I 41% II 18% III)	36% (19% I 35% II 46% III)
	II + III 56% III 40%	II + III 44% III 60%

Summary.—In all probability there was in no instance a low tumor incidence dominant, while in several cases a high tumor rate was dominant, and in others an intermediate tumor rate prevailed. It is almost certain that the I and II daughters of No. 10 had a tendency to a high tumor rate, and we may assume that the European male 151 had a tendency to a tumor rate perhaps somewhat higher than the average European. It is interesting that the two daughters of No. 10 gave with the English Silver and Cream, which had both very low tumor rates, a lower tumor rate than with European, which had apparently a somewhat higher tumor rate. The high tumor rate is again dominant in the hybrids between English Sable and English Silver + I daughter of No. 10. The high tumor

rate is also dominant or almost dominant in the crosses between 8½ + II daughter of No. 10. The dominance of the high tumor rate in this group is, however, not complete in each case. It is of interest that the crosses with the Cream and English Silver males, in which the males had in both cases very low and similar tumor rates, showed also similar tumor rates, and that these tumor rates were lower than in the hybrids between either 8½ or European with the I or II daughter of No. 10. Again the age class of tumors appears to be transmitted to hybrids as a distinct unit factor at least partly independent of the tumor rate, and the lateness of tumors may dominate, when at the same time a high tumor rate is dominant. We found in this class undoubted instances in which a low tumor incidence did not prevail.

Hybridizations in Which the Tumor Incidence of the Two Parent Strains Differed Markedly.

(a) Grandson of Tumor Mouse 121 (English Tan) + 3 Cream females: 73% + 2% (3%). I age class + IV age class.

The Cream mothers were without tumors. The hybrids had a tumor rate intermediate between those of the parent strains; *viz.*, 42% (41%). The age class of the hybrids was also intermediate; *viz.*, II.

	Without tumors.	With tumors.
F_1	1 (1 I)	5 (3 I 2 II)
F_2	27 (12 I 9 II 6 III)	17 (5 I 7 II 5 III)
	61% (45% I 33% II 22% III)	39% (29% I 42% II 29% III)
F_3	18 (2 I 11 II 5 III)	13 (6 I 7 II)
	58% (11% I 61% II 28% III)	42% (46% I 54% II)
F_4	7 (5 I 2 II)	4 (2 I 2 II)
	64% (71% I 29% II)	36% (50% I 50% II)
Total:	53 (20 I 22 II 11 III)	39 (16 I 18 II 5 III)
	58% (37% I 42% II 21% III)	42% (41% I 46% II 13% III)
II + III	59% III 69%	II + III 41% III 31%

In this case the father that does not have a tendency to tumors influences the tumor rate of the female children.

(b) In another case an English Sable male (No. 4,444) was mated to Cream females. English Sable + Cream: 70% (69%) + 2% (3%). I age class + IV age class.

In this case the hybrids, three generations of which were observed, were without tumors. Here the low tumor incidence of the Cream was apparently dominant over the high tumor incidence of the English Sable.

Without tumors.	With tumors.
25 (7 I 11 II 7 III)	0
100% (28% I 44% II 28% III)	0%

(c) No. 8½ + English Sable: 17% (19%) + 70% (69%). II age class + I age class.

The English Sable females used in this experiment were the daughters of the male No. 4,444 used in the preceding experiment, in which the English Sable was mated to Cream females. The hybrids in Experiment (c) had a tumor rate of 61% (60%); the tumors belonged to the I age class. The high tumor incidence and early tumor age of the English are here dominant.

(d) European + English Tan (daughter of Tumor Mouse 146, granddaughter of Tumor Mouse 121): 16% (16%) + 73%. I age class + I age class.

In this case the hybrids have a tumor rate of 28% (31%). The tumors belong to the II age class. The low tumor incidence of the European seems to be dominant. The tumors appear later than in the English strain. In this case a remarkable decrease in the tumor rate is found in the third generation.

Without tumors.	With tumors.
F_1 2 (1 II 1 III)	6 (1 I 3 II 2 III)
25% (50% II 50% III)	75% (17% I 50% II 33% III)
F_2 21 (5 I 11 II 5 III)	12 (2 I 8 II 2 III)
64% (24% I 52% II 24% III)	36% (17% I 66% II 17% III)
F_3 30 (8 I 11 II 11 III)	3 (2 II 1 III)
91% (26% I 37% II 37% III)	9% (66% I 34% II)
Total: 53 (13 I 23 II 17 III)	21 (3 I 13 II 5 III)
72% (24% I 43% II 33% III)	28% (14% I 62% II 24% III)
II + III 69%	II + III 31%

(e) Michigan Wild + English 101 F_2: (?) + 71% (72%). (?) age class + I age class.

In this experiment a male gray wild mouse, which had been caught in Michigan, was mated with English 101 females. Nothing definite is known about the tumor incidence of the strain to which the gray mouse belonged; there are, however, indications that the tumor incidence of wild gray mice is much lower than that of English 101. The offspring have here the tumor incidence and tumor age of the English 101. Hybrids 58% (70%). I age class.

Without tumors.	With tumors.
F_1 4 (1 I 3 III)	6 (1 I 5 III)
F_2 9 (7 I 2 II)	5 (1 I 2 II 2 III)
F_3 6 (4 I 2 II)	14 (7 I 7 II)
F_4 2 (2 I)	4 (4 I)
Total: 21 (14 I 4 II 3 III)	29 (13 I 9 II 7 III)
42% (67% I 19% II 14% III)	58% (45% I 31% II 24% III)
II + III 30%	II + III 70%

It is possible that as a result of some accident a few mice of the first generation of hybrids were the offspring of hybrid males (Michigan Wild and English

101 F_2) F_1 and the English mother: (Michigan Wild + English 101 F_2) F_1 + English 101 F_2. They may, therefore, have been ¾ instead of ½ English. But inasmuch as these particular females had no offspring, all the other generations were entirely ½ English.

(f) Cream + European 2% (3%) + 16% (16%). IV age class + I age class.

A black colored Cream male was mated to a pure European female (which became later Tumor Mouse No. 428). While No. 428 had tumors she raised three young mice, all females and very wild. These three daughters all developed tumors. In this case it is improbable that the low tumor incidence of the Cream was dominant. The higher rate of the European mother which herself had a tumor was evidently dominant.

Summary.—By combining Cream and two English strains, the tumor rate and age class in one case are intermediate, in the other case the low tumor incidence of Cream is dominant. The same English strain mated to 8½ is dominant. In a similar way the I daughter of No. 10 if mated to Cream gave a tumor rate similar to the intermediate one of the hybrids (English Tan + Cream), while the cross of the I daughter of No. 10 with a European, or of the II daughter of No. 10 with 8½, gave a high tumor rate. In a cross between European and English Tan the lower rate of the European is dominant, the tumors appear also later, while in a cross between Cream and European and probably also between a wild gray mouse and 101 English, the higher tumor incidence prevailed.

Waltzer Group.

(a) Waltzer + No. 8. In the autumn of 1909 a pure waltzing mouse was obtained from the Harvard Laboratory of Experimental Psychology. Tumors among these waltzing mice were extremely rare. This waltzing mouse was mated to a female of a Cream strain, with yellow color.[7] The offspring of this pair were black and did not waltz, a fact in accordance with the recessive character of the waltzing. These F_1 females were again mated to a pure male Waltzer. These offspring F_2 (¾ Waltzer) were in part black, some were spotted, none were waltzing. The females of F_2 were again mated to a pure male Waltzer. The offspring F_3 (⅞ Waltzer) were spotted black and white; there were no yellow mice among them; they were not waltzing.

An F_3 male (⅞ Waltzer and ⅛ Cream) was mated to white females of the No. 8 strain. Their offspring, which comprised mainly black mice or black mice with very little white are the first generation of the Waltzer + No. 8 hybrids. Mice with yellow color appeared only in the II generation of the hybrids. These mice were propagated through six generations; they were sensitive and died early and the number observed is therefore not great.

[7] These Creams were not identical with the Cream strain mentioned in the preceding paper or in other crosses, but they were equally poor in tumors.

⅞ Waltzer ⅛ Cream + No. 8: 1 to 5% (?) + 30% (38%). (?) age class + II age class.

The hybrids have a tumor rate of 31% (33%). The tumors appear early. The tumor rate of No. 8 is here apparently dominant.

Without tumors.	With tumors.
22 (12 I 4 II 6 III)	10 (5 I 4 II 1 III)
69% (55% I 18% II 27% III)	31% (50% I 40% II 10% III)
II + III 67%	II + III 33%

(b) (Waltzer + 8) + English 101 F_2: 31% (33%) + 71% (72%). Early tumor + I age class.

A male of the preceding group was mated to a female of the English 101 strain. Only a small number of the offspring were observed, but the indications are that there is a high tumor rate, probably a higher rate than in the Waltzer + No. 8.

Without tumors.	With tumors.
5 (2 I 3 II)	4 (1 II 3 III)

German Group.

In a number of crosses the German strain was used as one of the parent strains. Owing to the prevailing infection, the number of German mice observed was not very large, but the indications are that the German strain is fairly rich in tumors and that the tumors belong to the II age class.

(a) No. 8 + German: 30% (38%) + 50% (60%). II age class + II age class.

The hybrids show a tumor rate of 41% (41%). The tumors belong to the II age class. The tumor rate is therefore perhaps somewhat higher than that of No. 8 and not quite as high as that of the German mice. But the difference between the rates of the two parent strains is not great enough to make these results decisive. The age class is the same as that of the parents. The tumor rate in the second generation was in this case lower than that of the following generations.

Without tumors.	With tumors.
F_2 31 (2 I 14 II 15 III)	6 (4 II 2 III)
84% (6% I 45% II 49% III)	16% (66% II 34% III)
F_3 83 (27 I 24 II 32 III)	64 (12 I 32 II 20 III)
56% (32% I 29% II 39% III)	44% (19% I 50% II 31% III)
F_4 19 (5 I 5 II 9 III)	20 (4 I 10 II 6 III)
49% (26% I 26% II 48% III)	51% (20% I 50% II 30% III)
F_5–F_7 11 (6 I 3 II 2 III)	10 (5 I 5 II)
52% (55% I 27% II 18% III)	48% (50% I 50% II)
Total: 144 (40 I 46 II 58 III)	100 (21 I 51 II 28 III)
59% (28% I 32% II 40% III)	41% (21% I 51% II 28% III)
II + III 59% III 68%	II + III 41% III 32%

(b) German + Carter: 50% (60%) + 39 % (35%). II age class + I age class.

In our preceding paper we gave the tumor rate and tumor age of the various generations of these hybrids. This cross represents the only case in which the tumor rate and tumor age of the hybrids did not resemble that of either both or one of the parents. The hybrids had a tumor rate of 9% (10%). The tumors belonged to the IV age class.

Without tumors.	With tumors.
326 (79 I 88 II 159 III)	32 (4 I 11 II 17 III)
91% (24% I 27% II 49% III)	9% (12½% I 39% II 48½% III)

The result in this case is difficult to explain. We may have had accidentally to deal with recessives on one or both sides.

(c) English Tan (son of Tumor Mouse 121) + German 73% + 50% (60%). I age class + II age class.

Both parents have here a high tumor rate. The hybrids have also a high tumor rate, but apparently a somewhat lower rate than the English Tan. They belong to the age class of the English Tan (I age class).

Without tumors.	With tumors.
20 (11 I 7 II 2 III)	19 (10 I 7 II 2 III)
51% (55% I 35% II 10% III)	49% (52% I 36% II 12% III)

(d) German + (German + English Tan 143) F_1. The German father was mated to his daughters.

The English female which was mated to the German was Tumor Mouse 143: 50% (60%) + [50% (60%) + 73%]. II age class + I age class.

Without tumors.	With tumors.
2 (2 I) One of these two mice died at the age of 7 mos.	5 (3 I 2 II)

A strain probably rich in tumors and with early tumors.

(e) English + (8 + German) F_4. In this cross two English males were used, one belonging to the substrain English A, the other to the substrain English Sable: 77% (71%) and 63% (74%) + 41% (41%). Total (8 + German) or 51% (53%) : (8 + German) F_4. I age class + II age class.

The hybrids have a tumor rate similar to that of the English: 63% (76%). The tumors belong to the I age class. The crosses with both males gave similar results.

Without tumors.	With tumors.
Total: 30 (22 I 7 II 1 III)	52 (27 I 25 II)
37% (74% I 23% II 3% III)	63% (52% I 48% II)
II + III 24%	II + III 76%

In this strain the animals died young.

(f) German + 108. 108 was a white mouse of old Granby stock. She was related to the mice from which the father of the No. 8 strain was derived. 50% (60%) + ? low tumor rate. II age class + (?) age class.

In this case the hybrids had a low tumor rate (8%).

Without tumors.	With tumors.
22 (7 I 10 II 5 III)	2 (1 I 1 (?))
92% (32% I 45% II 23% III)	8%

It is probable that the low tumor rate of 108 prevailed.

(g) German + 6 F_4. No. 6 was a strain in which tumors occurred, but were apparently not very frequent, probably considerably lower than in the German strain. 50% (60%) + ?. II age class + (?) age class.

In this case the F_3 and F_4 generations of the hybrids had less tumors than the F_1 and F_2 generations. In the hybrids the tumor rate was 37% (41%) and the tumors stood somewhere between the II and III age class.

Without tumors.	With tumors.
33 (11 I 10 II 12 III)	19 (4 I 6 II 9 III)
63% (33% I 30% II 37% III)	37% (21% I 32% II 47% III)
II + III 59% III 57%	II + III 41% III 43%

Summary.—If German and English mice are crossed, there is a high tumor rate in the hybrids; both parents have in this case a high tumor rate and the tumors appear on the whole early. In crossing No. 8 with German, the crosses seem to have an intermediate tumor rate. In crossing the (No. 8 + German) with English the high tumor rate of the English prevails and the tumors are early. In crossing German with 108 a very low tumor rate results. It is probable that 108 belonged to a family poor in tumors and that a low tumor rate was dominant. The tumor rate in the crosses of German and 6 F_4 is apparently intermediate between that of the parents. It seems then that in this group there may occur a dominance of the high as well as of the low tumor rate and an intermediate tumor rate may also occur. An unusual result was obtained in the case of the German + Carter in which the tumor rate was considerably lower than in either of the parents, and in this case the tumors appeared also much later than in the parents. This is the only case in which such an abnormality was observed in our experiments.

Summary of Table II.—In hybrids in which the English are one of the parent strains, the high tumor rate of the English is dominant in the majority of cases. An intermediate tumor rate prevails in hybrids in which the other parent has a very marked tendency to low tumor rate (Cream, European + 103 European) or where the other parent has a medium rate (⅞ Waltzer ⅛ Cream + No. 8). When the second parent has a very low tumor rate (Cream), the

TABLE II.

Behavior of Various Strains in Hybridization Experiments.

English.	Tumor rate.	Age class.
101 + (European + 103) d_1	i !	L !
English Sable (198) + [(103 + European) F_1 + III daughter of No. 10] d_1	h !	L !
(European 151 + I daughter of No. 10) F_2 + 101 F_2 d_1	c !	h !
English Sable d + (Silver + I daughter of No. 10)	h !	i (?)
English Tan (121) + Cream. (3 females)	i !	i !
English Sable (4,444) + Cream d	L !	
8½ + English Sable (4,444) d d_1	h !	h !
European d d_1 + English Tan (daughter of 146, granddaughter of 121)	L (i) !	< L !
Michigan Wild + 101 F_2 d d_1	h (?)	h (?)
(⅞ Waltzer ⅛ Cream + No. 8) d_1 + 101 F_2	i	L ?
English Tan (121) d_1 + German d	L	h
German + (German + English Tan 143) F_1 d d_1.	h	h
English d d_1 + (8 + German) F_4	h !	h !

d indicates dominance of tumor rate of a parent strain.

d_1 indicates dominance of age class of a parent strain.

c indicates tumor rate or age class of parents which is similar.

i indicates a tumor rate or age class intermediate between both parents.

L indicates the tumor rate or age class of the parent with lower tumor rate or late tumor dominant.

h indicates the tumor rate or age class of the parent with the higher tumor rate or early tumors dominant.

! indicates fairly definite results.

? indicates doubtful results.

< indicates that tumors in a cross are later than in either of the parent strains.

low tumor rate may prevail. The age class of the English strain is not to the same extent dominant as their tumor rate.

TABLE III.

European + 103 or 102 (L) (10% to 25%). IV age class.	Tumor rate.	Age class.
1. London + (European + 103) F_2 d d_1	L (c)	L !
2. (European + 102) F_1 d_1 + 8½ F_4	c !	L !
3. 101 + (European + 103) d_1	i !	L !
4. (103 + European) F_1 d d_1 + III daughter of No. 10	L (c) ?	L
5. English Sable (198) d_1 + [(103 + European) F_1 + III daughter of No. 10] d_1	h !	L !

Summary of Table III.—European + 103 (102) is a strain in which the rather low rate did not become entirely recessive in the offspring; the tumor rate of this parent strain was either dominant or the result was intermediate. The tendency of this strain to very

late tumors prevailed in all cases, even when its low tumor rate did not entirely prevail.

TABLE IV.

European.	Tumor rate.	Age class.
European d d_1 + 103, 102	L (?)	L
European d d_1 + English Tan (daughter of 146)	L (i) !	< L !
Cream + European	h (?) !	

Summary of Table IV.—The low tumor rate of the European had a tendency to be dominant with those strains which did not have a very high tumor rate. With the English it was dominant or intermediate; but the higher tumor rate of the European dominated over the lower tumor rate of the Cream.

TABLE V.

European 151.	Tumor rate.	Age class.
European 151 d_1 + 8 F_5 d	h (c) ?	i (L)
European 151 + I daughter of No. 10 d	h !	L
(European 151 + I daughter of No. 10) F_3 + 101 F_2 d_1	c !	h !
European 151 + II daughter of No. 10 d	h !	L ?

Summary of Table V.—The lower tumor rate of European 151 was recessive in crosses whose mother was the first or second daughter of No. 10.

TABLE VI.

No. 8.	Tumor age.	Age class.
European 151 + 8 F_5 d	h (c) ?	i (L)
7/8 Waltzer 1/8 Cream + No. 8 d d_1	h !	h
(7/8 Waltzer 1/8 Cream + No. 8) d_1 + 101 F_2	i !	< L (?)
No. 8 F_3 + German	i !	c
English d d_1 + (8 + German) F_4	h !	h !

Summary of Table VI.—The higher tumor rate of No. 8 prevailed probably over the lower tumor rate of European 151; it also prevailed over 7/8 Waltzer 1/8 Cream.

TABLE VII.

I and II daughters of No. 10.	Tumor rate.	Age class.
European 151 + I daughter of No. 10 d d_1	h !	L (?)
(European 151 + I daughter of No. 10) + 101 F_2 d_1	c !	h !
European 151 + II daughter of No. 10 d d_1	h !	L (?)
Silver d + I daughter of No. 10 d_1	i !	L !
Cream d_1 + I daughter of No. 10	i !	L !
8½ + II daughter of No. 10 d	h (i) !	c (L) ?
(8½ + II daughter of No. 10) d + II daughter of No. 10 d_1	L (c)	L

Summary of Table VII.—The high tumor rate of the I and II daughters of No. 10 was dominant over the lower rate of European 151 and No. 8½. It was intermediate with the very low tumor rates of Silver and Cream. Here we find again that various strains with a very low tumor rate depress the dominance of the parent with tendency to high tumor rate more than strains with a tendency to not as low a tumor rate. The independence of the inheritance of the age class from that of the tumor rate is here apparently quite definite.

TABLE VIII.

Cream.	Tumor rate.	Tumor age.
Cream d_1 + I daughter of No. 10	i !	L !
English Tan (121) + Cream (3 females)	i !	i !
English Sable (4,444) + Cream d	L !	
Cream + European d	h (?) !	
⅞ Waltzer ⅛ Cream + No. 8 d	h !	h
(⅞ Waltzer ⅛ Cream + No. 8) d_1 + 101 F_2	i	L (?)

Summary of Table VIII.—The low tumor rate of the Cream is apparently only in one case quite recessive, *viz.*, with European; in other cases it is dominant or the result is intermediate. The age class can be intermediate, when the tumor rate is intermediate, but the lateness of the tumors in the Cream mice can prevail with an intermediate tumor rate.

TABLE IX.

Silver.	Tumor rate.	Tumor age
Silver + I daughter of No. 10 d_1	i !	L !
English Sable + (Silver + I daughter of No. 10) d_1	h !	i (?)

Summary of Table IX.—The Silver strain resembles in its behavior the Cream. With a strain with a high tumor rate it produces crosses with an intermediate tumor rate. The greater lateness again prevails. In a further cross between such an intermediate strain and a strain with a high tumor rate, the high tumor rate of the English dominates.

TABLE X.

No. 8½.	Tumor rate.	Age class.
8½ + II daughter of No. 10 d	h (i) !	c (L) ?
(European + 102) F_1 d_1 + 8½ F_4	c !	L !
(8½ + II daughter of No. 10) d d_1 + II daughter of No. 10	L (c) !	L
8½ + English Sable (4,444) d d_1	h !	h !

Summary of Table X.—The tumor rate of the No. 8½ strain is recessive in combination with a strain with high tumor rate or intermediate crosses result. In these crosses the I age class can also prevail over the later tumors of No. 8½. In combination with (European + 102), however, the late tumor age of the (European + 102) prevails.

TABLE XI.

German.	Tumor rate.	Age class.
No. 8 F_8 + German	i (?)	c !
German + Carter	< L !	< L !
English Tan (121) d_1 + German d	L	h !
German + (German + English Tan 143) F_1	h	h
English d d_1 + (8 + German) F_4	h !	h !
German + 108 (= No. 8 ?) d	L	
German + 6 F_4	i (?)	c (?)

SUMMARY AND CONCLUSIONS.

1. In crossing strains known to differ in their tumor rates, the hybrids show in a considerable number of cases a tumor rate corresponding to the parent with a high tumor incidence; in some cases the offspring have the tumor rate of the parent with the low tumor incidence; in certain cases the tumor rate of the offspring is intermediate between those of the parents.

That these results are not accidental follows from the fact that we could show in some cases that two sisters crossed with the same strains or with the same male give similar offspring, and in other cases we could show that the same individual crossed successively with two strains that behave similarly produces hybrids with a similar tumor incidence.

2. There exists some evidence for the conclusion that different strains in being crossed with other strains differ in their power to impress their tumor rate upon the crosses. Thus the English strain and the I and II daughters of No. 10 have the tendency to transmit to the offspring a high tumor rate, while Cream, Silver, and some European other than 151 have a tendency to transmit a low tumor rate. While crosses of these daughters of No. 10 with European 151 or with No. 8½ show the high tumor rate of the mothers, the crosses of one of the same females with Cream or Silver show an intermediate tumor rate.

3. We find further evidence for our conclusion previously stated

that age class of the tumors and tumor rate are not dependent on the same factor. The age class enters into the crosses as a factor independent of the tumor rate. Thus we find in the crosses between the first daughter of No. 10 and Cream, and in the crosses between the same female and English Silver a similar tumor rate, but the age classes differ in conformity with the difference in the age classes of the parents.

We find, furthermore, that while in some cases a tumor rate and an age class that correspond to each other (high tumor rate, early tumors—low tumor rate, late tumors) are transmitted to the offspring, in other cases tumor rate and age class transmitted to the crosses diverge.

4. It seems that certain strains with very late tumors if mated with strains with earlier tumors have a tendency to transmit to the offspring their own tendency to very late tumors. With a certain strain lateness of the tumors seems to be dominant, while a low tumor rate is not necessarily dominant in the same crosses. This was noticeable in the crosses into which the strain European + 102 or 103 entered as one of the parents.

5. If both parents have a similar tumor rate the offspring have usually a similar tumor rate. There was, however, one exception to this rule in the case of the German + Carter mice, in which the offspring showed a much lower tumor rate and higher age class than either of the parent strains.