tumors. However, the ages at which these animals develop neoplasms is strikingly higher than that at which the normal breeding animals develop cancer. (See Table I.)

It appears from these figures that the absence of hormone activity has a retarding effect on neoplasmic development, and may even inhibit tumorous growths, since practically all of the normal breeding females develop tumors if they live to 14.9 months of age, while in the castrated females only twenty in 210 have developed tumor, although they have all reached an age equal or greater than that at which the oldest breeding female developed neoplasms.

The complete absence of ovarian secretion has much the same effect on cancer incidence as does forced non-breeding.

It appears from this that the secretions of the ovaries under ordinary non-breeding conditions are not primarily the ones which stimulate tumor, but rather that it is commonly those conditions of hormone secretion in anticipation of the feeding of the embryo and young.

III. Do testicular hormones inhibit the growth of mammary tumors?

Since mammary cancer does not occur among the males of this race of mice, we might expect that possibly the testicular hormones inhibit these neoplasmic growths. If this is the case, the removal of the testes would remove the inhibitor and the operated individuals would be likely to develop tumor. In order to test this theory, 241 males of this race of mice were castrated at about four weeks of age and allowed to grow old under the same laboratory conditions as the stock animals.

The youngest of these animals lived to be fifteen months old and the oldest twenty-two months of age without developing a single tumor. The relief from inhibition caused by castration at four to five weeks of age is, therefore, not sufficient to allow the growth of mammary tumor. There is a possibility that the testes of these mice had begun to secrete in sufficient amounts to protect these mice against tumor after castration. Possibly, had they been castrated at an earlier age, different results might have been obtained. This, however, is very doubtful.

IV. Is it possible to grow mammary tumors in castrated males by transplanting ovarian tissue?

If it is the ovarian hormones which are causing the growth of tumors, ovarian tissue transplanted to castrated males encourages tumor development. With this in mind, 210 males were castrated and a whole ovary implanted subcutaneously in the abdominal region. The animals were then allowed to grow old. At the time of writing, when the youngest of these animals is ten months of age, *four have developed mammary tumors*—a thing never seen in the thousands of normal male mice of this inbred stock.

It would seem that the ages of cancer appearance in these animals should approach the curve of the virgin females, although the numbers are very small.

DISCUSSION

These results are interesting in that they correspond very closely with those reported by Dr. Carl F. Cori (1927). Our data, however, differ in several ways from his. Whereas he castrated his females at 15–22 days of age, we castrated ours at 28–35 days of age. Tumor was completely inhibited in his mice, while it was only partially inhibited in ours. This somewhat supports his conclusion that spontaneous cancer in the mouse is due to the lack of ovarian hormones after having had the use of it for a time.

Dr. Cori reports that in his castrated males, to which he transplanted two whole ovaries, no tumors appeared. Our experiment differed from his in that we transplanted but one ovary and obtained four males with mammary tumor from 210 animals treated in this manner. It is of interest to note that pathological diagnosis shows these tumors to be of the same type as those developed by the females in this strain of mice, namely, adenocarcinoma.

It is well known that in order to make successful transplantations of tissue, the animals involved must be very closely related. Possibly Dr. Cori's failure to feminize males was due to the fact that his stock was not sufficiently inbred, and the ovarian implant therefore degenerated.

CONCLUSIONS

(1) Non-breeding reduces tumor incidence in mice and delays the time of tumor appearance (207 mice used).

(2) Two hundred and ten female mice castrated at 28–35 days behave much the same as non-breeding females.

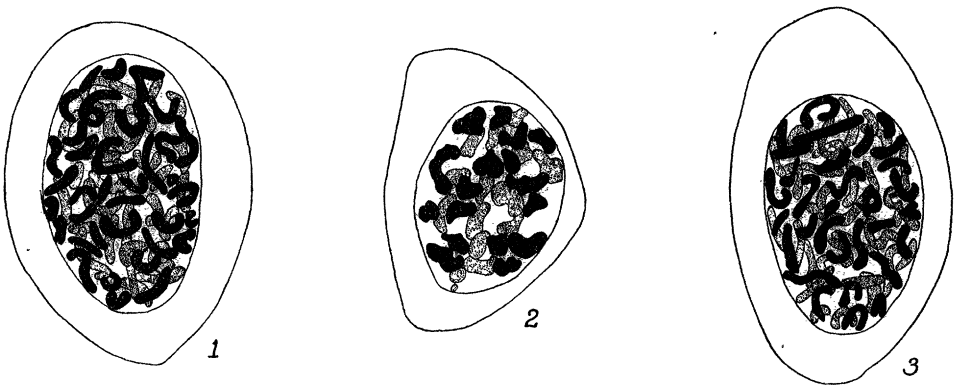
(3) Two hundred and forty-one males castrated at 28–35 days did not develop tumor, thus resembling non-castrated males.

(4) Spontaneous tumors, never obtained in thousands of normal males of the stock used, may develop in castrated males which have received subcutaneous transplants of ovarian tissue (210 operated—four tumors).

WILLIAM S. MURRAY
LABORATORY OF MAMMAL GENETICS,
UNIVERSITY OF MICHIGAN

THE CHROMOSOMES OF THE RAT

AN attempt to use the chromosomes of the rat as confirmatory evidence in certain phases of work on



human chromosomes brought out the fact that our mixed strain of laboratory rats shows an unusual situation in chromosomal behavior. The number of chromosomes of the albino rat as determined from three independent colonies of the Wistar strain is 42.[1] An examination of 38 rats from our colony shows that 21 of these possessed 42 and 17 had 62 chromosomes. The latter group is shown in Figures 1 to 3, Figure 1 being a prophase somatic group of 62 chromosomes from the nucleus of a mesenchyme cell in the testis of an embryo rat of 20 days; Figure 2 gives a tetrad group of 31 chromosomes from a primary spermatocyte from the testis of an adult rat; and Figure 3 a prophase somatic group of 62 chromosomes from a mesenchyme cell from the ovary of an embryo rat of 20 days. Thus two kinds of chromosome patterns occur in the same colony.

Since these rats had been mated indiscriminately, the natural expectation would be that the rats resulting from such unions would show 52 chromosomes. Rats with 52 chromosomes could not be found. Continued study of rat testes from the individuals of our colony, regardless of whether the diploid count was 42 or 62, showed that two kinds of secondary spermatocytes or spermatids are always present, one kind containing 21 chromosomes and the other 31. No variation in the number of chromosomes present in the spermatogonia or the first spermatocytes was found in any case. The changes producing a spermatid with 31 chromosomes in the 42 group or one with 21 chromosomes in the 62 group occur in the interkinetic period or early prophase of the second spermatocytic division.

The absence of rats with 52 chromosomes led to the conclusion that a sperm with 21 and an ovum with 31 chromosomes for some reason could not mate, like mating only with like. Confirmation of this was found in mating a strain of white rats obtained from Professor Slonaker, of Stanford University, which was found to possess only the normal number of 42 diploid and 21 haploid chromosomes, with individuals from the colony. Four such matings were made and the resulting 24 embryos fixed on the 16th day. All of these embryos had 42 chromosomes. Matings made at the same time among the individuals of the colony gave litters, some members of which had 42 and some 62 chromosomes.

Our rat colony has come from a cross made in Berkeley by Professor J. A. Long about 1912 between an albino (*Rattus rattus norvegicus albinus*) from the Wistar Institute mated with the common wild gray rat (*R. rattus norvegicus*), or what was considered this species at the time. Slides of the testes of the original strain of pure albino rats show 42 as the diploid and 21 as the haploid number of chromosomes. Unfortunately, no tissue is available from the original gray animal used as one of the parents of the hybrid stock.

It is interesting that two wild gray rats (*R. rattus norvegicus*) obtained by trapping in one of the warehouses in Oakland each gave a chromosome count of 42. The number of chromosomes in the spermatids of these has not yet been determined.

The following interesting facts, repeatedly confirmed, have emerged from these studies.

1. The albinous norway possesses 42 diploid chromosomes.

2. Two local wild gray norways were also found to possess 42 diploid chromosomes.

3. Our hybrid rat colony contains two types of members, those with 42 and those with 62 diploid chromosomes. Each produce two kinds of spermatids, one having 21 and the other 31 haploid chromosomes.

4. Matings are evidently possible only between sperm and ovum having a like chromosome number.

OLIVE SWEZY

ANATOMICAL LABORATORY,
UNIVERSITY OF CALIFORNIA

[1] Painter, T. S., 1926, SCIENCE, Vol. 64.