within the uterus of another strain female the strain susceptibility, as shown by descendants of this mouse, was not altered toward a transplantable tumor from the mouse strain that developed the ovum. There was, however, a definite indication of an increased susceptibility for the tumor that came from the same mouse strain as was employed to protect and nourish the transferred ovum in its development.

The negative mice were kept for one year before they were discarded. Unfortunately, no negative mice were reinoculated. The reason was that the ultimate outcome of a single transplant of a tumor from an unrelated strain was difficult to determine in the pure stocks until considerable time had elapsed. Both of the tumors employed develop sizable masses in four to five weeks when implanted into the strain that originated them. However, many of the positive blacks with S91 implants showed no masses for several months following inoculation but had well established melanotic tumors at the end of one year. The descendants of transferred ova mice grew the tumors of unrelated strains at a faster rate than did the regular pure stock dba and C57 black mice.

Since the same female was used to foster each developing transferred ova mouse before and after birth, experiments are now under way to test the effect of foster nursing when taken alone. A considerable number of mice are being fostered, but finished data are available on only small numbers of mice as shown in Table 2. Here the JAX–A stock mice were

TABLE 2

TRANSPLANTATION OF TUMORS INTO FOSTERED MICE

Tumors	A stock	A stock young fostered by dba females	dba young fostered by black females
L946AII ..	0	0	5 = 5 + :0 – inoc. at 30 days
S91	6 = 0 + :6 –	4 = 4 + :0 – inoc. at 30 days 7 = 2 + :5 – inoc. at 60 days	5 = 5 + :0 –

fostered on JAX–dba females and JAX–dba young were fostered on JAX–C57 black females.

The six unfostered A stock mice inoculated with S91 first received implants at 30 days and were reinoculated at about 5 months. They were killed at the end of one year without any signs of tumor growth. The fostered A mice inoculated at 30 days all developed large masses and had extensive lung metastases. Where the mice were kept for 2 months before inoculation only two out of seven developed the transplanted tumors and these were delayed for a long time before developing. Unpublished data by Law show a similar result when he used older fostered mice to receive implants of tumors. This would indicate a lessening of the influence in older fostered mice.

In the above data where mixed ages were used for the descendants of transferred ova mice, a similar age influence may have been in operation. The non-transferred pure stock mice were all about 30 days of age when inoculated.

There appears to be an extra-chromosomal influence exerted by the foster female upon the ova of other stock females implanted into the uterus of such a female. One method of testing this influence by the use of transplantable tumors is described. The testing of the effects of foster nursing alone on transplantable tumors is under investigation.

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THE EFFECT OF FOSTER NURSING ON THE GROWTH OF A TRANSMISSIBLE LEUKEMIA IN MICE[1]

THE most extensive reports concerning the factors involved in susceptibility to transmissible leukemia[2,3] show that inoculated leukemic cells grow in practically 100 per cent. of mice of the susceptible inbred strain and in the first hybrid generation involving this strain. Leukemic cells fail completely to grow in mice of other unrelated or resistant strains. From the work that has been done the conclusion has been reached that susceptibility or non-susceptibility to leukemic tissue is dependent upon the relationship existing between the genetic constitution of both the host and the tumor cell. Only a very few exceptional inoculations, that is, negative inoculation in expected susceptible mice or positive inoculation in expected non-susceptible mice, have been recorded for the various types of transmissible neoplastic growths. These, however, have been adequately explained.[4]

The purpose of the present report is to record the behavior in transplantation of a lymphoid leukemia, line $\overline{LL}$ 449. This tumor was induced in ♀D2001, of the Jax dilute brown strain (D), subline 212 following painting with a 0.3 per cent. solution of 9:10 dimethyl-1:2 benzanthracene in benzene.[5] The carcinogen was applied to the back of the animal from occiput to mid-sacral region twice a week until tumor appearance. At 143 days following initial painting there appeared extreme bilateral axillary, cervical and inguinal lymphadenopathy. The animal appeared dyspneic and was killed *in extremis* a week

[1] The author is recipient of a Finney-Howell Foundation Medical Research Fellowship.

[2] E. C. MacDowell and M. N. Richter, *Jour. Cancer Research*, 14: 434, 1930.

[3] M. D. Schweitzer and J. Furth, *Am. Jour. Cancer*, 37: 224, 1939.

[4] John J. Bittner, *Jour. Genetics*, 31: 471, 1935.

[5] L. W. Law and Marjorie Lewisohn, *Proc. Soc. Exp. Biol. and Med.*, 43: 143, 1940.

later. At necrospy the liver was greatly enlarged, pale and nodular. The spleen, which measured 4.2 × 1.7 × 0.7 cms, was likewise pale and nodular. The mesenteric-intestinal, renal and lumbar nodes showed extreme lymphadenopathy. There existed connective tissue oedema and severe anasarca. The white blood count obtained from ventricle blood was 123,600, and the differential count showed 100 per cent. medium and large lymphocytes.

Inoculations of approximate one cubic millimeter pieces of tumor tissue were made subcutaneously into the right axilla, by use of a sterile trocar. Unless otherwise stated inoculations were made at one month of age.

In the first transplant generation only 4 of 6 D strain, subline 212, mice were susceptible to the leukemic cells. Subsequently, through the following 6 transplant generations there occurred 100 per cent. takes in 31 mice. On the other hand, only 1 of 41 D strain, subline 111, mice and none of 26 Jax C57 black strain (B) mice grew the leukemic cells. Four other distinct lines of lymphatic leukemia similarly induced in subline 212 of the D strain gave 100 per cent. takes in subline 212, nearly 100 per cent. takes in sublines 3 and 4, but grew in less than 10 per cent. of mice of subline 111.

Of 12 D strain, subline 111, mice foster nursed by a D, subline 212, mother 6 were positive to inoculations in the first generation transfer. These mice, however, were 2 months old when inoculated. All resistant D strain mice fostered by a susceptible D mother were positive to fourth generation inoculations. All B strain mice fostered by a susceptible D strain mother grew leukemic cells of the fourth generation transfer. There was complete resistance of 4 B strain fostered mice when inoculated with second generation leukemic cells. These mice, however, were 3 months old when inoculated. None of the 16 B strain mice fostered by the resistant D mother grew leukemic cells. That the failure of B strain fostered mice to grow leukemic cells of the second generation transplant is due to an age factor rather than a virulence factor is indicated by the results of Cloudman in an accompanying report. Experiments are now in progress to test this.

The clinical course of the disease as determined by invasion of leukemic cells, blood counts and length of life following inoculations was very similar in the B strain fostered mice, the resistant D strain fostered mice and in the control susceptible D strain mice.

TABLE 1

REACTIONS OF DILUTE BROWN D AND C57 BLACK B MICE TO INOCULATIONS OF LYMPHATIC LEUKEMIA LINE $\overline{LL}$ 449

Transplant generation	Donor	Host	Reaction	Length of life (days)
G 1	D Subline 212	6 D Subline 111	6 –	
		6 D Subline 212	4 +, 2 –	K31, K31, K31, D63
		10 B by D Subline 111	10 –	
		12 D Subline 111 by D Subline 212	6 +, 6 –	D31, D31, D36, D36, D38, D60
G 2 a)	D Subline 212	4 D Subline 111	4 –	
		4 B by Subline 212	4 –	
		6 B by Subline 111	6 –	
		14 D Subline 111	1 +, 13 –	D30
G 3	D Subline 212	11 D Subline 212	11 +	6 D19, 5 D24
G 4 a)	D Subline 212	5 D Subline 111 by D Subline 212	5 +	D18, D18, D20, D23, D25
		6 B by Subline 212	6 +	K12, K14, D23, D33, D40
		6 D Subline 111	6 –	
		5 D Subline 212	5 +	K12, K13, D24, D25, D33
b)		4 D Subline 111	4 –	
		4 D Subline 212	4 +	D19, D25, D24, D33
c)		6 D Subline 212 by B	6 +	K19, D19, D23, D23, D24, D25
G 5 a)	D Subline 111 by D Subline 212	7 D Subline 111	7 –	
b)	B by D Subline 212	10 B	10 –	
		5 D Subline 212	5 +	D12, 3 D19, D23
G 6	D Subline 212	3 D Subline 4	3 +	D15, D17, D22
G 7	D Subline 212	5 D Subline 3	5 +	K18, K18, K19, D20, D23

Leukemic cells which grew in resistant fostered hosts failed to grow when reinoculated into resistant non-fostered mice. See Table 1. This is further evidence that leukemia developing after inoculation does not result from a proliferation of the lymphocytes of the host.

Data are not yet complete relating to the reaction of susceptible D strain mice deprived entirely of "susceptible" milk. All mice removed within 12 hours following birth and fostered on a resistant B strain mother grew leukemic cells.

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