Enhanced Tumor Homografts Following Pretreatment of Donor Mice.* (24770)

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On the premise that cancer in man is a form of spontaneous autografting our work has been directed toward a study of the enhancing (XYZ) effect(1,2) using the most comparable experimental tool available, namely isografting of tumors. Pretreatment of C57BL/6 host mice with frozen or with lyophilized isologous EO771 mammary carcinoma or with fresh supernate of EO771 tumor 2 weeks or more before isotransplant of EO771 tumor leads to more rapid growth of transplants and an earlier 50% point in the cumulative mortality among the animals(3-8) This could not be accomplished by pretreating with frozen extracts of other C57BL/6 tumors such as 755, 541-5, 541-14 or with frozen extracts of tumors from other strains of mice(3,8). The same degree of enhancement ensued without pretreatment of any kind if the donor tumor was from a second isotransplant of EO771 tumor made 10 days after a first transplant (9). Tumor tissue from such a second isotransplant when homotransplanted was capable of serial passage in foreign strains of mice without treatment of hosts or donors(9,10). Increased homotransplantability has been used as indicator of the altered status of isografts. The present paper reports that the first of double isografts also has an altered status and has an abiding capacity for homograft into foreign mice. It compares the altered status of the first with that of the second isograft of EO771 tumor, and discusses size and age of donor graft relative to homotransplantability.

Materials and methods. In our first series on double isografts in mice only the second isograft was tested for capacity to grow in foreign mice and the results were published (9; Table I, Exp. 1). In another series, the first isograft was also tested but it was not realized at the time that grafts from male donors into female recipients were inhibited(11), and this portion of the experiment was unsatisfactory (Table I, Exp. 2). Since then a third and larger series of experiments has been completed (Table I, Exp. 3). All mice were obtained from the breeding colony at Jackson Memorial Laboratory. The mice for homografting were divided into 3 groups and matched as to batch, age and sex. The first group, or controls, received EO771 tumor from a C57BL/6 mouse having single isograft; the second group from the first of a double isograft, and the third group from the second of a double isograft made 10-14 days after the first. No grafts in this series were taken from male donors. Tumor inocula were 0.1 cc of a 15% suspension of tumor cells in normal saline. Ulcerated donor tumors were not used.

Results. The first of a double isograft of EO771 into a C57BL/6 mouse acquires an altered status of comparable degree with that of the second, as determined by increased homotransplantability (Table I).

Discussion. If the results for isografting are comparable with those of autografting it is possible that cancer in man has acquired an altered status by the time the first metastasis occurs, and relative resistance of the host is diminished. Within conditions of our experiments neither size nor age of donor tumor was important(12); thus, a large (2-3 cm-d) and 20-25 day old and a small (0.5-0.7 cm-d) and 8-11 days old tumor had 9 times the homotransplantability of the control tumor of intermediate size and age (about 1.7 cm-d and 15 or 16 days). A common denominator in control and experimental series was the reaction of the isograft host. Selected mice from each homograft experiment were serially homografted without other treatment and the enhanced status of the tumor was consistently confirmed(9,13).

Conclusion. In 3 series of experiments em-

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TABLE I. Mice Dying from EO771 Homografts Taken from Single and from First or Second of Double Inoculations into an Isograft Host.

Exp.	Recipients strain	Sex	Tumor mortality according to Source of donor homograft: Single inoculation	First of double	Second of double	P
1*	BALB/c Jax		4/121		12/ 20	.01
2	"	♀	0/ 42	1/13	0/ 26	N.S.†
	"	♂	0/ 38	5/14	0/ 5	.01
3	"	♂	6/136	8/31	14/ 82	.01
	"	♀	2/149	2/20		.01
	C57BR/cd	♂	0/ 90	2/18		.01
	Sum‡ BALB/c		12/444	15/65	26/107	.01
			2.7%	23.1%	24.3%	

* First series of experiments(9).
† Donor tumor from a male with resulting low incidence among females(11).
‡ Values for male donor into female recipient (Exp. 2) omitted.

ploying 675 BALB/c, 108 C57BR/cd and 50 C57BL/6 mice, the first of double isografts of EO771 mammary carcinoma acquired an altered enhanced status comparable with that of the second of double isografts and each of the double isografts had 9 times the homotransplantability (24%) of single control isografts (2.7%). Within the conditions of the experiment neither size, nor age of the isograft was of importance. The altered enhanced status was abiding as determined by serial homotransplantability without further treatment.

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Nucleic Acid Levels of Rat Anterior Pituitary Glands Following Adrenalectomy.* (24771)

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The role of nucleic acids in protein synthesis has been reviewed by Brachet(1). Although endocrine organs are relatively poor in ribonucleic acid (RNA)(1), histochemical studies of the anterior pituitary gland demon-

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