

CARTAS AL EDITOR

Selective Protection in BALB/c Mice Against Meth A Sarcoma Induced by Normal Allogeneic Tissues From H-2 Congeneic Mice

The sarcoma Meth A, induced by 3 methylcholanthrene in BALB/c mice (H-2^d) do have TSTA as detected by transplantation studies (8).

The nature and origin of tumour associated transplantation antigens, however, is obscure. Recently it has been described that tumour specific transplantation antigens crossreact with normal alloantigens (2, 6, 11). Furthermore some tumour cells express foreign H-2 like antigens detected by serology and cellular methods (1, 3). These *in vitro* and *in vivo* findings point to the possibility that TSTA consist of foreign histocompatibility antigens and require derepression of silent H-2 genes with a multigene H-2 system (4).

We present here data showing that preimmunization of BALB/c mice with normal allogeneic tissues from congenic mice of the B10 series induce selective protection in the growth of Meth A sarcoma. To assay the efficacy of immunization we have followed the survival of mice after lethal tumour challenge and have found that mice immunized with some allogeneic tissues survived more than controls.

Histocompatibility differences between B10 congenic mice are located within the H-2 system (10), so that variations in the survival of BALB/c mice challenged with a lethal dose of Meth A must be assigned to H-2 determinants.

BALB/c mice, 6-8 weeks old, were immunized with tissues from B10 (H-2^b), B10.A (H-2^a), B10.BR (H-2^k), B10.D2

(H-2^d), B10.HTT (H-2^u), BALB/c (H-2^b) mice and Wistar rats. Tissue suspensions were prepared one hour before inoculation. Kidney and liver were aseptically removed, minced, washed in cold PBS and resuspended in 5 ml of Eagle's Medium. The standard inoculum was a subcutaneous injection of 0.5 ml corresponding to approximately 1/3 of kidney-liver to each mouse. The syngeneic control preparations consisted of suspension of the kidney and liver from BALB/c mice.

Suspensions of Meth A cells were obtained by intraperitoneal puncture of BALB/c and diluted in Eagle's Medium. The dose of the Meth A tumour was 5×10^4 viable cells as determined by phase contrast microscopy. All tumour challenges were given subcutaneously to groups of ten mice fourteen days following immunization. The number of surviving mice in each group was checked every four days.

Fig. 1 illustrated the protection against Meth A sarcoma challenge, conferred to BALB/c (H-2^d) by immunization with allogeneic tissues from congenic mice.

Preimmunization with control BALB/c (H-2^d) and Wistar rat tissues gave less than 20% of protection 32 days after challenge. Preimmunization with B10.D2 (H-2^d), and B10.BR (H-2^k) gave 40% and with B10.A (H-2^a), 60%. The strongest protection was obtained with B10 mice (H-2^b): 80%. These results match other reports that have shown, by alloantisera

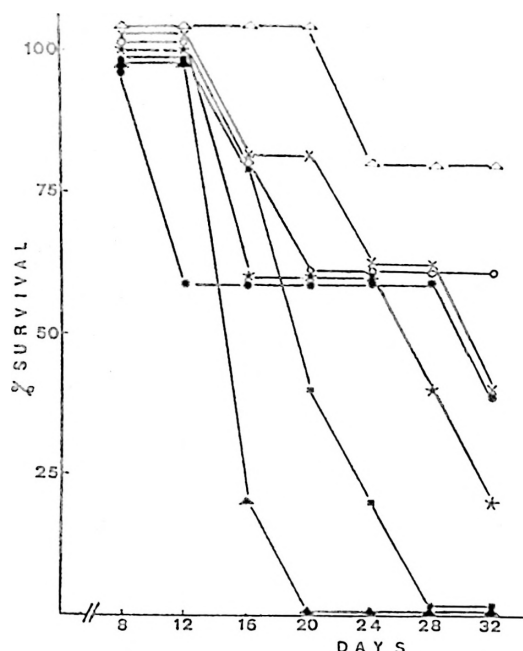


Fig. 1. Survival of groups of BALB/c mice immunized with normal tissues from B10 (Δ - Δ), B10.A (O-O), B10.BR (x-x), B10.D2 (●-●), B10.HTT (▲-▲), BALB/c (★-★) and Wistar rat (■-■) after challenge with 5×10^4 Meth A sarcoma cells.

and immunofluorescence techniques, the presence of H-2K.33, private specificity of H-2^b haplotype on the surface of Meth A sarcoma (5). This suggests the possibility that H-2K.33 alloantigen, and perhaps other non H-2 antigens of the B10 background, behave as TSTA on Meth A.

Surprisingly B10.HTT (H-2^d) did favour the growth of Meth A when compared with controls: 0 % survival 20 days after the challenge. It is known that the immune response can enhance tumour growth (9); so that H-2K.19, private specificity of H-2^d haplotype, also detected on Meth A (5), may induce an immune response that stimulates the growth of Meth A in BALB/c mice.

It is not known why some extraspecificities induce tumour rejection and some

others tumour enhancement. We could argue that qualitative and/or quantitative differences in these specificities on the immunizing tissues or on the membrane of Meth A sarcoma, might determine different immune responses.

The correlation observed between the foreign H-2 like antigens and the inhibition or enhancement of tumour growth after allogeneic immunization, suggests that Meth A tumour antigens are related to those specificities. Some of them behave as TSTA and some others as tumor enhancing antigens (TEA).

References

1. BACH, M. L., BACH, F. H. and ZARLING, J. M.: *The Lancet*, 1, 20-22, 1978.
2. BEAR, R. H., Jr., ROHOLT O. A. and PRESSMAN, D.: *Immunol. Comm.*, 6, 217-224, 1977.
3. GARRIDO, F., SCHIRRMACHER, V. and FESTENSTEIN, H.: *Nature*, 259, 228-230, 1976.
4. GARRIDO, F., FESTENSTEIN, H. and SCHIRRMACHER, V.: *Nature*, 261, 705-707, 1976.
5. GARRIDO, F., SCHMIDT, W. and FESTENSTEIN, H.: *J. Immunogen.*, 4, 115-122, 1977.
6. INVERNIZZI, G. and PARMIANI, G.: *Nature*, 254, 713-721, 1975.
7. MESCHINI, A., INVERNIZZI, G. and PARMIANI, G.: *Int. J. Cancer*, 20, 271-282, 1977.
8. OLD, L. J., BOYSE, E. A., CLARKE, D. A. and CARSWELL, E. A.: *Ann. N. Y. Acad. Sci.*, 101, 80-88, 1962.
9. PREHN, R. T.: *Transplant. Rev.*, 28, 34-49, 1976.
10. SNELL, G. D. and ROSCOE, B.: *J. Nat. Cancer Inst.*, 21, 843-858, 1958.
11. WRATHAMELL, A. B., GAUCI, C. L. and ALEXANDER, P.: *Br. Cancer J.*, 33, 187-192, 1976.

E. GARCÍA-OLIVARES and F. GARRIDO*

Departamento de Fisiología y Bioquímica
Facultad de Medicina
Granada

(Received on July 16, 1979)

* Present address: Departamento de Bioquímica. Facultad de Medicina. Córdoba.