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Inhibition of Tumour Growth in Irradiated Mice by Sensitized Homologous Spleen Cells

It is known that tumours possess antigens which differ from those in normal tissue. Experimental evidence for this has been obtained by workers using chemically-induced tumours and others with a virus-induced tumour and spontaneous tumours¹⁻³. It has also been shown, however, that the spontaneous A-strain carcinoma is not antigenic after repeated transplantation in the strain of origin⁴.

In this laboratory, where the long transplantable tumour L-5178 of DBA/2 mice was used, the cytotoxicity of immune serum produced in rabbits tolerant to normal DBA/2 mouse tissue was recently demonstrated⁵.

In the work recorded here it was decided to examine the effect of homologous immune spleen cells on the same mouse tumour. Fifteen DBA/2 mice were divided into three groups of five and treated as follows: (1) whole-body irradiation (600 r.) followed by intra-peritoneal inoculation of L-5178 tumour 3 days later, followed 1 h later by intra-peritoneal inoculations of homologous immune spleen cells; (2) whole-body irradiation followed by intra-peritoneal inoculation of L-5178 tumour 5 days later; (3) no irradiation, intra-peritoneal inoculations of L-5178 tumour at the same time as in groups (1) and (2).

The dose of tumour given to each mouse consisted of 500,000 ascites cells in normal saline. The spleen cell inoculation consisted of a normal saline suspension of 64×10^6 viable cells, these being obtained from strain 129 mice immunized with live L-5178 cells.

It was found that the mean survival time in each of the three groups of mice was essentially the same, approximately 9 days from the time of tumour inoculation. The mice in groups (2) and (3) developed marked ascites together with solid tumour in the peritoneal cavity and histological evidence of extensive tumour infiltration of other organs. The mice in group (1), however, which had been treated with immune spleen cells, showed no ascites or solid tumour and no histological evidence of tumour or infiltration whatsoever. These results are summarized in Table 1.

Table 1

Group	Day 0	Day 3	Survival times		Post-mortem findings
			Individual	Mean	
1	Irradiation	L-5178 in lymphoma cells and spleen cells	6, 8, 10, 10, 10	9	No tumour cells or ascites
2	Irradiation	L-5178 lymphoma cells	6, 6, 9, 10, 10	8	Heavy infiltration with tumour and marked ascites
3	No irradiation	L-5178	6, 10, 10, 10, 10	9	Heavy infiltration with tumour and marked ascites

It was considered that the failure to increase survival time in (1) was due to a graft-versus-host reaction rather than the effects of irradiation, and tumours played no obvious part in their deaths. Further experiments are being planned along lines suggested by Rabotti and Iossifides⁶. These workers suggested that the severity of the graft-versus-host reaction produced by a given dose of spleen cells was dependent on: (a) dose of irradiation; (b) degree of histo-incompatibility; (c) time interval between dose of irradiation and administration of spleen cells.

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HISTOLOGY

Birefringence of Lymph Node Cells

In the course of work on the role of the lymphatic system in the rejection of homologous skin grafts, histological sections of rabbits' lymph nodes, prepared by a standard paraffin embedding technique, were viewed under the microscope between two crossed polarizing filters. In certain sections, the nuclei of many cells were strongly birefringent (Fig. 1a, b, c). Perusal of the literature and conferences with colleagues have failed to uncover a previous description of this phenomenon. Because this finding might aid in investigations of nuclear structure, it is thought appropriate to report on it at this stage.

The cells which showed birefringence were most, but not all, of the large and small lymphocytes, as well as plasma cells and lymphendothelial cells. The nuclei of haemocyto blasts were optically inactive, but some of these cells contained 1-3 small, round, perinuclear, birefringent bodies (Fig. 1b). No cell in mitosis showed birefringence. The germinal centres of the nodes, except for a few scattered cells, were conspicuously devoid of cells with optical activity, and contrasted sharply with the cuff of birefringent small lymphocytes around them (Fig. 1a).

Anisotropy of nuclei could only be observed in sections of nodes that had been fixed in absolute alcohol or Carnoy's fluid; formalin fixation inhibited it. It was seen in all unstained deparaffinized sections, and to a varying degree in all sections stained with methyl green-pyronin. Staining with haematoxylin and eosin completely blocked it. Exposure of an unstained, deparaffinized and rehydrated section to 10 per cent formalin abolished the birefringence.

Touch preparations consisting of whole cells, whether fresh or alcohol fixed, or frozen sections of fresh or alcohol fixed lymph nodes, did not show birefringence. A possible strain artefact, derived from the cutting procedure, has been ruled out as the cause for the birefringence (by Mr. E. S. Emerson of the Polaroid Corporation, Cambridge, Massachusetts, whom I thank).

The meaning of this phenomenon is not yet clear. Because the observed anisotropy is entirely confined to