

STIMULATION OF MITOTIC ACTIVITY OF THE HEPATOCYTES
AND KUPFFER CELLS OF THE LIVER OF INTACT MICE BY
T- AND B-LYMPHOCYTES OF PARTIALLY HEPATECTOMIZED
SYNGENEIC DONORS

A. G. Babaeva, N. A. Kraskina,
and N. V. Yudina

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T-lymphocytes from the spleen of partially hepatectomized CBA mice enhance the mitotic activity of hepatocytes and Kupffer cells of the liver in nonoperated recipients. The proliferation induced by these cells is equal to the inductive capacity of the whole suspension of lymphocytes from the spleen of partially hepatectomized animals, which contain T- and B-lymphocytes. The proliferation induced by B-lymphocytes from the spleen of operated mice is significantly lowered and is displayed chiefly in relation to Kupffer cells.

KEY WORDS: regeneration of the liver; T- and B-lymphocytes; proliferation.

Transplantation of splenic lymphocytes of partially hepatectomized or unilaterally nephrectomized mice into intact syngeneic recipients has been shown to stimulate mitotic activity of their liver and kidney cells [1, 2, 5, 6]. It is interesting to discover which lymphocyte population has the property of transferring the proliferative stimulus.

The object of this investigation was to study how transplantation of a suspension of T- or B-lymphocytes of partially hepatectomized animals is reflected in proliferative activity of the liver. To isolate these populations a suspension of spleen cells from hepatectomized mice was treated with specific antisera against B- and T-lymphocytes (ABS or ATS) respectively.

EXPERIMENTAL METHOD

Experiments were carried out on 114 CBA mice weighing 25-30 g. Two-thirds of the liver was removed from the group of mice subsequently serving as lymphocyte donors by the usual method. The animals were killed 16-19 h after the operation with chloroform vapor, a suspension of their spleen cells was prepared in medium No. 199, and it was then centrifuged at 1500 rpm. After treatment with the appropriate serum the suspension of lymphocytes was injected intravenously in a dose of 60-70 million cells into recipient mice. Specific rabbit sera against mouse T- or B-lymphocytes were used to treat the lymphocytes. The method used to obtain and test the sera was described previously [3, 4]. ATS or ABS (in a dose equivalent to 1 mg serum protein to 1 ml suspension) was added to a suspension of spleen cells in a concentration of 3×10^7 cells/ml, together with normal rabbit serum as the source of complement (0.03 ml to 1 ml suspension). The mixture was incubated for 45 min at room temperature and the cells were washed with medium No. 199 and injected into recipient mice. Intact mice of the same line were used as recipients. The animals were killed 49-50 h after transplantation of the lymphocytes with chloroform vapor. All the animals were given an injection of colchicine in a dose of 5 mg/kg 4 h before sacrifice.

The liver of the recipients was fixed in Carnoy's fluid. Sections 4-5 μ thick were stained with hematoxylin and eosin and the mitotic index was determined in the hepatocytes and Kupffer cells by the method described previously [1, 2].

Laboratory of Growth and Development, Institute of Human Morphology, Academy of Medical Sciences of the USSR. Laboratory of Immunology, Moscow Institute of Epidemiology and Microbiology, Ministry of Health of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 89, No. 1, pp. 69-70, January, 1980. Original article submitted March 2, 1979.

TABLE 1. Mitotic Activity of Hepatocytes and Kupffer Cells of Mice Receiving Different Lymphocyte Populations

Group of recipients	Donors of lymphocytes	Treatment with anti-serum	Cell population	Mitotic index, %	
				in hepatocytes	in Kupffer cells
1	Hepatectomized	—	T-lymphocytes + B-lymphocytes	0,42±0,09	2,61±0,42
2	»	ATS	B-lymphocytes	0,11±0,03	1,20±0,17
3	»	ABS	T-lymphocytes	0,42±0,08	2,06±0,47
4	Intact	—	T-lymphocytes + B-lymphocytes	0,02±0,01	0,33±0,10
5	Control	—	—	0,03±0,02	0,10±0,04

EXPERIMENTAL RESULTS

The results of experiments to determine the mitotic index are given in Table 1. They show that injection of splenic lymphocytes from hepatectomized mice (group 1) sharply increased proliferation of both Kupffer cells and hepatocytes (by 26 and 14 times respectively). Transplantation of spleen cells of intact mice (group 4) did not affect the mitotic activity of the hepatocytes and stimulated proliferation of Kupffer cells only weakly. The separated splenic lymphocyte populations of the hepatectomized donors differed in principle in their ability to induce cellular proliferation. This property was well marked in T-lymphocytes: The intensity of mitotic activity induced by them was not lower than that induced by the whole suspension of spleen cells containing both T- and B-lymphocytes.

Ability to induce proliferation was significantly weaker in the B-lymphocytes than in the T-lymphocytes from the spleen of the hepatectomized animals (group 2). Stimulation of mitotic activity in response to transplantation of B-lymphocytes was exhibited in the case of Kupffer cells, but was expressed very weakly in the hepatocytes.

It can be concluded from these results that the proliferative stimulus is transferred mainly by the T-lymphocytes of animals in which a process of reparative regeneration is taking place.

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