GENETIC DIFFERENCES IN REACTIVITY OF LYMPHOID TISSUE DURING REGENERATION OF THE LIVER IN DIFFERENT STRAINS OF MICE

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Transplantation of lymphocytes from partially hepatectomized CBA and C57BL mice, together with sheep's red cells, into lethally irradiated syngeneic mice showed that the CBA mice acquired the ability to increase the number of antibody-forming cells much sooner after the operation (4 h) than C57BL mice (17 h). Transplantation of the lymphocytes in a semisyngeneic system led, as a result of the graft versus host reaction (GVHR), to a decrease in the number of antibody-forming cells during subsequent immunization of the recipients with sheep's red cells. The GVHR was less severe in the hepatectomized mice than in the controls. These changes also appeared sooner after the operation in CBA mice than in C57BL mice.

KEY WORDS: regeneration of the liver; antibody-forming cells; graft versus host reaction.

Regenerative processes in the liver and kidney are accompanied by a combination of changes in the functional properties of the lymphocytes [1-3], cells which are considered to be responsible for the development of the regenerative process [1].

The rate of regeneration of the liver is known to differ widely in animals of different strains [4]. Whereas in CBA mice the weight of the liver is almost completely restored on the seventh day after resection, and the increase in mitotic activity is observed at the normal times, in C57BL mice regeneration of the liver takes place more slowly as reflected in both these indices.

It was decided to investigate whether differences in the regenerative capacity of the liver in different strains are connected with differences in the reactivity of the lymphoid tissue.

EXPERIMENTAL METHOD

Experiments were carried out on 165 male CBA and C57BL mice and (CBA × C57BL) F_1 hybrids.

The index of reactivity of the lymphoid tissue was the latent period after removal of two thirds of the liver before which the first changes in the functional properties of the spleen cells could be observed: the antibody-forming ability of the cells and their ability to induce a graft versus host reaction (GVHR).

A cell suspension was prepared from the spleens of 5-7 mice from which two thirds of the liver was resected 4 and 17 h after the operation; $1 \cdot 10^7$ cells of this suspension were injected together with the antigen ($2 \cdot 10^8$ sheep's red cells), intravenously into lethally irradiated syngeneic recipients. On the eighth day after transplantation of the cells and antigen the number of antibody-forming cells (AFC) in the recipients' spleen was determined by Jerne's method [5]. Spleen cells from intact mice were injected together with the antigen into the control recipients.

The ability of the cells to induce the GVHR was studied at the same times after the operation by Möller's (1971) method [6]. For this purpose, $5 \cdot 10^7$ spleen cells of mice of one of the parental strains (hepatectomized in the experimental series, intact in the control) were injected into (CBA × C57BL/6) F_1 hybrids. The recipients

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TABLE 1. Number of AFCs in Spleen of Lethally Irradiated Mice Receiving Injection of Spleen Cells of Partially Hepatectomized Syngeneic Mice and Immunized with Sheep's Red Cells

Time after operation (in h)	Strain	Group	Number of recipients	Number of AFCs (M ± m)
4	CBA	Experimental	10	4112±760
		Control	8	1824±206
4	C57BL/6	Experimental	12	1990±340
		Control	8	1855±209
17	CBA	Experimental	9	6782±450
		Control	10	2084±350
17	C57B/6	Experimental	6	4281,2±380
		Control	6	2186,6±348

TABLE 2. Number of AFCs in Hybrid Mice Immunized with Sheep's Red Cells and Hybrid Recipients of Spleen Cells from Hepatectomized and Intact Mice

Strain of mice donating lymphocytes	Time after operation (in h)	Group	Number of recipients	Number of AFCs (M ± m)
—	—	Experimental	10	160 500±6 400
CBA	4	Control	10	14 872±860
		Experimental	11	5 720±361
C57BL/6	4	Control	7	7 110±454
		Experimental	7	6 190±484
CBA	17	Control	5	14 440±2 800
		Experimental	6	4 680±484
C57BL/6	17	Control	7	15 290±2 560
		Experimental	5	5 040±576

were immunized with sheep's red cells seven days later. The number of antibody-forming cells in the recipients' was determined by Jerne's method on the fourth day after immunization.

The intensity of the GVHR was judged from the degree of inhibition of antibody formation in the recipients of the spleen cells after injection of red cells compared with mice into which no spleen cells were injected.

EXPERIMENTAL RESULTS

In CBA mice the ability of the spleen cells to form antibodies varied depending on the time of the operation in the same way as in (CBA × C57BL) F_1 hybrids studied by the writers previously [3].

As Table 1 shows, the number of AFCs 4 h after the operation in the spleen of CBA mice receiving spleen cells of syngeneic donors was 2.25 times greater than in recipients of cells from intact mice. The number of AFCs in the spleen of the CBA recipients was even greater 17 h after partial hepatectomy.

By contrast with the CBA mice, injection of spleen cells 4 h after partial hepatectomy into C57BL mice, also in a syngeneic system, caused virtually no change in the number of AFCs compared with the control. Not until 17 h after the operation did their spleen cells acquire the ability to potentiate antibody formation to the same degree as in CBA mice 4 h after partial hepatectomy.

In other words, the latent period of stimulation of lymphoid tissue caused by the operation was much shorter in CBA mice than in C57BL mice. The number of AFCs was about equal to control recipients of the two strains.

As Table 2 shows, injection of immunocompetent cells of either parental strain caused a sharp depression of antibody formation in response to injection of sheep's red cells compared with mice not receiving lymphocytes (a decrease of about 30 times). However, this depression of the immune response was much less marked in recipients of lymphocytes of hepatectomized mice.

Special experiments showed that antibody-forming cells in this model were chiefly of recipient origin.

The operation produced the ability of the lymphocytes to induce a GVHR much sooner in the CBA than in the C57BL mice. Accordingly the number of antibody-forming cells was higher in the experimental recipients of CBA lymphocytes 4 h after the operation than in recipients of C57BL lymphocytes.

Virtually no difference in the ability of the spleen cells to induce the GVHR was present in the two strains 17 h after hepatectomy.

These results thus indicate that the lymphoid tissue of CBA mice is more labile and responds more rapidly by the modification of its functional properties and cell proportions characteristic of regeneration of the liver than in C57BL mice.

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REVERSIBILITY OF STRUCTURAL CHANGES IN CHROMATIN OF INTERPHASE NUCLEI OF PERIPHERAL BLOOD LYMPHOCYTES OF PATIENTS WITH DOWN'S SYNDROME UNDER THE INFLUENCE OF HEALTHY HUMAN SERUM

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A luminescence-microscopic investigation of short-term human cell cultures stained with Acridine Orange showed that the melting curve of the cell chromatin DNA in the region from 78 to 85°C depends on changing external environmental conditions, i.e., on the composition of the blood serum.

KEY WORDS: Down's syndrome; interphase chromatin; lymphocytes; thermal denaturation; Acridine Orange.

A previous luminescence-microscopic study of short-term (1 h) cell cultures stained with Acridine Orange revealed a clear difference between the melting profiles of the chromatin DNA of lymphocytes from healthy persons and patients with Down's syndrome [2, 3]. The melting curves of chromatin from healthy human lymphocytes have two maxima in the region of 78 and 85°C. Lymphocytes of patients with Down's syndrome were found to have one diffuse maximum in the region of 85°C. The absence of a decrease in fluorescence between 78 and 85°C is considered to be due to the greater degree of condensation of certain regions of the chromatin complex in cells with an altered karyotype (47, XY-21 and 47, XX-21).

The object of this investigation was to study the genesis of the following phenomena: Are the changes observed caused by stable disturbances of the structure of the chromatin in trisomic cells (as is indicated in

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