ANTIGEN-NONSPECIFIC SUPPRESSION OF FORMATION OF IMMUNOLOGIC MEMORY FOR FOREIGN RED CELLS

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The study of the influence of suppressor cells on immunologic processes is an interesting problem in modern immunology. Numerous investigations by Soviet and other workers have demonstrated the essential role of suppressor cells in the control of the immune response to various antigens, including xenogeneic red blood cells. It has been shown that depression of the primary immune response to sheep's red blood cells (SRBC) in mice is antigen-specific in character; this property is found both in suppressor cells and the suppressor factor isolated from them [2, 3, 6]. It was shown previously [1] that spleen cells of mice immunized with SRBC can suppress development of immunologic memory to this antigen.

Experiments were carried out on male CBA mice weighing 18-30 g, obtained from the "Rappolovo" Nursery, Academy of Medical Sciences of the USSR. The effect of suppressor factor of immune spleen cells, obtained by the following method, was studied. Mice were immunized by a single intraperitoneal injection of $2 \cdot 10^9$ SRBC. The animals were killed 14 days later and the spleen removed; a suspension of spleen cells was prepared in medium 199 with antibiotics (cell concentration $4 \cdot 10^8$/ml). The cell suspension was treated with ultrasound for 3 min on an MSE apparatus (England), then centrifuged at 20,000g for 30 min. The supernatant, which contains suppressor factor [2-5], was used.

Development of the immunologic memory was studied in an adoptive transfer system. Cyclophosphamide (from Saransk Medical Preparations Factory) was injected intravenously into recipient mice in a single dose of 200 mg/kg, and 4 h later normal syngeneic spleen cells ($5 \cdot 10^7$ cells) together with a small dose (10^6) of SRBC or of rat red blood cells (RRBC) were injected intravenously. After seven days a repeated injection of the corresponding red cells was given in the same dose, and after a further four days the number of antibody-forming cells (AFC) in the spleen was determined by the local hemolysis in gel method [7].

The action of the suppressor factor was studied by injecting the animals with supernatant obtained by the method described above intravenously in a dose of 0.5 ml 24 h after the first injection of antigen. Mice receiving antigen alone served as the control. Activity of suppressor factor against the primary immune response to SRBC and RRBC also was determined. For this purpose normal spleen cells ($5 \cdot 10^7$), together with extract of immune spleen cells (0.5 ml, intravenously) were injected into recipients after preliminary treatment with cyclophosphamide, and this was followed by intraperitoneal injection of SRBC or RRBC ($5 \cdot 10^8$ cells). The number of AFC in the mouse spleen was determined five days later.

The results were subjected to statistical analysis and geometric mean values of AFC and confidence intervals at $P \leqslant 0.05$ were calculated.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that suppression of the primary immune response was antigen-specific in character: Injection of suppressor factor into the mice sharply inhibited the response to SRBC, whereas the response to RRBC remained at the control level. Conversely, when suppressor factor was injected during sensitization of the mice their secondary immune response to both antigens (SRBC and RRBC) was significantly reduced. The differences from the control are highly significant.

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TABLE 1. Effect of Suppressor Factor of Immune Spleen Cells on Primary Immune Response and Formation of Immunologic Memory

Type of immune response	Antigen	Number of mice in group	Number of AFC in spleen (mean), percent of control
Primary	SRBC	17	3,6 (2,6—4,9)
	RRBC	18	114 (93,5—139)
Secondary	SRBC	12	19,5 (15,3—24,9)
	RRBC	12	29,6 (20,5—42,6)

Legend. Confidence intervals shown in parentheses.

The suppressor factor obtained from spleen cells of mice immunized with SRBC thus has the ability to inhibit the development of immunologic memory to another antigen (RRBC), without affecting the primary immune response to injection of that antigen. The reasons for this difference are not yet clear. It can be postulated that cells responsible for the formation of immunologic memory in the early stage of their development are more sensitive to the nonspecific influence of suppressor factor than cells responsible for the primary immune response. This problem requires further study.

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