ALLOGENEIC STIMULATION OF THE IMMUNE RESPONSE TO MENINGOCOCCAL POLYSACCHARIDE GROUP A ANTIGEN

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Meningococcal polysaccharide antigens (MPA), like other bacterial polysaccharides, can be classed on the basis of several properties among the thymus-independent antigens [1]. The immune response of mice to MPA is insufficiently high even if a wide range of doses is used [3]. The reason for this may be both high activity of T suppressors and the small number of antigen-specific clones of B cells. Investigations of the graft versus host reaction have shown that injection of allogeneic cells significantly increases the number of antibody-forming cells (AFC) synthesizing antibodies against both thymus-dependent [6] and thymus-independent [7] antigens. It appears interesting to study the possibility of enhancing the immune response of mice to MPA with the aid of the allogeneic reaction.

The object of this investigation was to determine the genetic conditions for manifestation of the phenomenon of allogeneic potentiation of the immune response to group A MPA (MPA-A) and also to study this phenomenon during the immune response to other antigens.

EXPERIMENTAL METHOD

Male mice aged 2-4 months belonging to lines CBA/CaLacSto (H-2^k), C57BL/6jSto (H-2^b), CC57BR/MvSto (H-2^b) and (CBA × C57BL/6)F_1 (H-2^{kb}) hybrids were used. Meningococcal polysaccharide vaccines of groups A and C, prepared by the production unit of the G. N. Gabrichevskii Moscow Research Institute of Epidemiology and Microbiology [2], and also typhoid Vi-antigen and sheep's red blood cells (SRBC) were used as antigens. Mice were immunized intravenously with MPA-A and MPA-C in the optimal dose of 0.5 μg [3], with Vi-antigen in a dose of 2 μg,

TABLE 1. Allogeneic Stimulation of Immune Response to MPAA

Group No.	Donors of NSC	Recipients	Number of AFC in spleen	Number of experiments	Number of mice
1	—	F_1	430 (278—665)	5	36
2	CBA	F_1	16710 (8730—31920)	2	12
3	C57BL/6	F_1	10140 (7551—13580)	5	33
4	—	CBA	2985 (1614—5508)	2	12
5	C57BL/6	CBA	1706 (775—3758)	2	14
6	—	CC57BR	1545 (977—2432)	3	21
7	C57BL/6	CC57BR	9616 (5585—16560)	3	20

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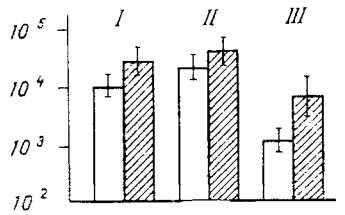

Fig. 1. Allogeneic stimulation of immune response to various antigens. Ordinate, number of AFC per spleen. Unshaded columns — initial level of AFC after injection of antigen; shaded columns — AFC level after injection of antigen + NSC. I) SRBC, II) Vi-antigen, III) MPA-C.

and with SRBC in a dose of 5×10^7 cells. Simultaneously with the antigen the mice were given an intravenous injection of 5×10^7 normal spleen cells (NSC) from allogeneic or semiallogeneic donors. The number of AFC in the spleen of the recipients and control mice was determined by the method of local hemolysis in gel [5], using intact red blood cells, and also red blood cells loaded with Vi-antigen [4] or with MPA [3]. The results were subjected to statistical analysis with determination of the geometric mean numbers of AFC and confidence intervals at the $P \leqslant 0.05$ level of significance.

EXPERIMENTAL RESULTS

The results of investigation of the immune response to MPA-A are given in Table 1. Injection of NSC of mice of the parental lines (groups 2 and 3) into (CBA × C57BL/6)F_1 mice caused a significant increase in their immune response to MPA-A (by 25-40 times) compared with the control (group 1). In these cases, incidentally, the donors and recipients were both similar and different with respect to H-2 antigens. In the absence of similarity with respect to the H-2 complex no allogeneic stimulation of the immune response to MPA-A was observed (groups 4 and 5), although allogeneic differences were the same as before.

In a separate series of experiments mice of lines C57BL/6 and CC57BR, identical as regards the H-2 complex but differing for other histocompatibility loci, were used as donors and recipients. As Table 1 shows, significant stimulation of the immune response was found in this case also (groups 6 and 7).

Manifestation of the phenomenon of allogeneic potentiation of the immune response using other antigens (SRBC, Vi-antigen, and MPA-C) in the allogeneic combination C57BL/6 → CC57BR was investigated in a series of experiments. It will be clear from Fig. 1 that the immune response of the recipients of allogeneic NSC to SRBC was enhanced a little (by 2.5 times, $P < 0.05$), to Vi-antigen it was unchanged, and to MPA-C it was increased by 8 times ($P < 0.05$).

The results suggest that allogeneic differences are an essential but not the only condition for manifestation of the phenomenon of allogeneic stimulation of the immune response to MPA. Effective enhancement of the immune response to this antigen depends on identity of donors and recipients with respect to the H-2 complex (Table 1). Allogeneic stimulation of the immune response is observed under these circumstances also when donors and recipients differ with respect to antigens controlled by genes outside the H-2 complex. The results agree with those obtained by Yaffe et al. [8], who shows that the action of the allogeneic factor (a product of cells activated by histocompatability antigens) is limited to the H-2 complex.

The different degrees of allogeneic stimulation observed on immunization by different antigens may depend not only on the chosen donor—recipient combination, but also on the structural features of the antigens themselves and also on the intensity of the initial immune response to the doses of these antigens used. If the immune response is sufficiently well developed the allogeneic effect is manifested only weakly (in the case of SRBC) or not at all (in the case of Vi-antigen). When less immunogenic antigens (MPA-A and MPA-C) are used, allogeneic stimulation is more marked. This stimulation can take place through activation of "silent clones," an increase in size of the clone, or acceleration of B cell maturation. The intimate mechanisms of allogeneic stimulation are perhaps linked with release of the B cells from control by T suppressors.

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USE OF THE BLAST TRANSFORMATION TEST TO STUDY IMMUNOLOGICAL MEMORY FOR INFLUENZA A VIRUS

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In 1977, for the first time in the "modern history of influenza," virus A (H1N1) returned into epidemic circulation after an interval of 20 years. Persons over 25 years of age, i.e., those who met this virus in 1949-1956, developed influenza eight to 10 times less frequently in 1977 than younger individuals [1]. It is not clear how universal is the rule that subtype-specific anti-influenzal immunity to influenza A virus, in the mechanism of which an important role is played by cellular immunity [3], persists for a long time.

Accordingly it was decided to study immunological memory in a system of cellular immunity to influenza viruses A (H0N1) and A (H3N2) in people of different ages.

EXPERIMENTAL METHOD

Observations were made on two groups of volunteers: 1) 31 subjects aged 21-30 years, and 2) 33 persons aged 45-60 years. Blood was taken in a volume of 10 ml from the cubital vein: 2 ml was used to obtain serum and 8 ml to isolate the monocytic fraction on a Ficoll-Agipak gradient [5]. The blast transformation test (BTT) was determined from incorporation of [^{3}H]thymidine, added to the culture for 24 h in a concentration of 1 μCi/ml. Purified A (H0N1) and A (H3N2) viruses, inactivated by UV light, were used in a concentration of 25 hemagglutinating units per test sample. The reaction was read after incubation of the cultures at 37°C for 72 h. The results of the BTT were expressed as the stimulation index (SI): the ratio between the number of counts per minute of the stimulated lymphocytes and the number of counts per minute of the unstimulated lymphocytes. To detect antibodies in the blood serum the hemagglutination inhibition test (HIT) was used, and was conducted by the method recommended by WHO [7]. The level of antineuraminidase antibodies was determined by the elution inhibition test (EIT) [2, 4].

As antigens in the HIT inhibitor resistant variants of viruses were used: A/swine/Iowa/15/30 (HSw1N1), A/PR/8/34 (H0N1), A/Khabarovsk/74/77 (H1N1), A/Singapore/1/57 (H2N2), A/Hong Kong/1/68 (H3N2), A/Victoria/3/75 (H3N2), A/Texas/1/77 (H3N2), A/Bangkok/1/79 (H3N2), A/Khabarovsk/74/77 (H1N1).

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