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CORRECTION OF IMMUNE RESPONSE TO SHEEP'S ERYTHROCYTES BY POLYELECTROLYTES IN DIFFERENT STRAINS OF MICE

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Inbred mice of strain C57BL, A, C57BR, C3H, and CBA, with low, medium, and high reactivity to sheep's red cells (SRBC), were injected with the polymers poly-4-vinylpyridine (P4VP) and polyacrylic acid (PAA) and immunized with SRBC; production of antibody-forming cells (AFC) in their spleen was then determined. Injection of P4VP into C57BL mice was shown to produce a fivefold increase, and injection of PAA a fourfold increase in the immune response. Injection of P4VP and PAA into mice of strain A increased the immune response by 2.5 and 2.8 times respectively. The immune response in C57BR mice was increased fourfold by P4VP and by 4.7 times by PAA. Treatment of C3H mice with P4VP increased the immune response by twice, and treatment with PAA by 2.4 times. Injection of P4VP and PAA into CBA mice did not affect the intensity of the immune response. With an increase in the immunological reactivity toward SRBC in the mice of these strains a decrease in the potentiating effect of polymers on the immune response was thus observed.

KEY WORDS: immune response; polyelectrolytes; genetic differences.

The height and development of the immune response during immunization by various antigens are genetically determined [2, 3]. After many years of study in the writers' laboratory a series of strains of mice with high or low reactivity to a particular antigen has been selected. For example, during immunization with sheep's red cells (SRBC) mice of strain CBA show high reactivity but C57BL mice low reactivity. Mice of strains A, C57BR, and C3H occupy an intermediate position between these two extreme strains [2, 3]. Genetic differences in the height of the immune response are determined at the level of populations of immunocompetent cells [2]. The writers have shown that the accumulation of fewer antibody-forming cells (AFC) in the spleen immunization with SRBC in C57BL mice compared with CBA is largely due to the low intensity of migration and cooperation of T and B lymphocytes in strain C57BL [5].

It is therefore reasonable to suggest that the immune response in C57BL mice, with low reactivity, can be strengthened by methods stimulating migration and cooperation of T and B lymphocytes.

Reports have recently been published that the synthetic compounds poly-4-vinylpyridine (P4VP) and polyacrylic acid (PAA) stimulate migration of B lymphocytes and increase the effectiveness of cooperation between T and B lymphocytes [1].

The object of this investigation was to study the effect of P4VP and PAA on the immune response to SRBC in mice with low, medium, or high levels of reactivity to that antigen.

EXPERIMENTAL METHOD

Mice of strains CBA, C3H, C57BR, A, and C57BL aged 2-3 months and weighing 20-22 g were used. The animals received a single intravenous injection of P4VP or PAA in a dose of 50 mg/kg. The methods of

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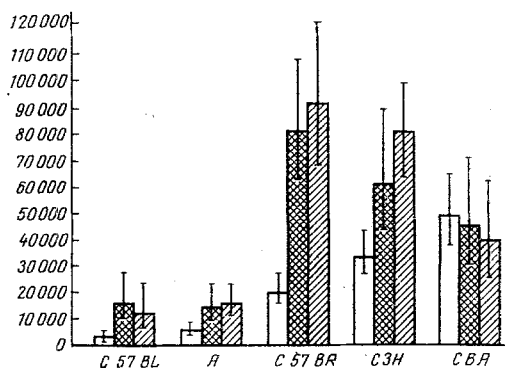


Fig. 1

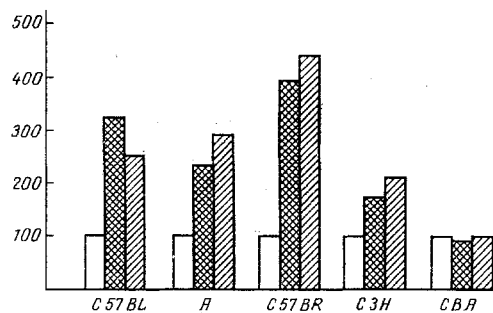


Fig. 2

Fig. 1. Effect of polyelectrolytes on AFC production in mice of different strains immunized with SRBC. Abscissa, strain of mice; ordinate, number of AFC in spleen. Unshaded columns - SRBC; cross-hatched columns - SRBC + P4VP; obliquely shaded columns - SRBC + PAA. Vertical lines mark 95% confidence limits ($P \leq 0.05$).

Fig. 2. Correction of immune response in different strains of mice by polyelectrolytes. Abscissa, strain of mice; ordinate, number of AFC (in % per 10^6 spleen cells). Remainder of legend as in Fig. 1. Height of immune response of mice receiving SRBC only taken as 100%.

preparing solutions of the substances were described previously [1]. Immediately before injection of the compound the mice were immunized intravenously with $2 \cdot 10^8$ SRBC. The number of AFC in the spleen was counted on the fourth day after immunization by Jerne's method [8].

The experimental results were subjected to statistical analysis with calculation of the geometric mean and confidence interval (I_p) with a probability of 95% ($P \leq 0.05$).

EXPERIMENTAL RESULTS

As Fig. 1 shows, in their ability to produce AFC against SRBC the mice of the strains used were distributed as follows. The smallest immune response to SRBC was observed in strains C57BL and A. C57BR mice produced more AFC. The maximal immune response to SRBC was observed in CBA mice. The C3H mice occupied an intermediate position in this series.

Injection of P4VP into C57BL mice immunized with SRBC led to a sharp (fivefold) increase in the immune response (Fig. 1). When PAA was injected into these mice, the increase in the immune response was fourfold.

Injection of P4VP and PAA into mice of strain A immunized with SRBC led to an increase in the number of AFC in their spleens by 2.5 and 2.8 times respectively.

After injection of P4VP into C57BR mice the immune response was increased fourfold, whereas PAA caused an increase of 4.7 times (Fig. 1); in C3H mice the increase was 2 and 2.4 times respectively.

Injection of P4VP and PAA into CBA mice during immunization with SRBC did not affect the height of the immune response.

Similar results were obtained when AFC were counted per 10^6 spleen cells. Results showing the correcting effect of the polymers on the immune response to SRBC are given in Fig. 2. The original height of the immune response in mice of each genotype was taken as 100%. As Fig. 2 shows, a marked increase in the immune response was observed in mice with low reactivity. In mice with high reactivity the polymers had either little or no stimulating action.

On the whole, with a decrease in the immunological reactivity to SRBC, an increase in the potentiating effect of the compounds P4VP and PAA on the immune response in these strains of mice was observed.

Genes of the immune response (IR genes) are known to exhibit their action at the level of T and B cells [6, 9, 10]. The immune response to concrete antigens in mice with low reactivity, connected with a defect of the T or B cells or macrophages, can be increased by transplantation of T or B lymphocytes or macrophages

respectively [4, 7]. However, injection of these cell populations into highly reactive mice, deficient in none of the above-mentioned types of cells, did not increase their immune response.

In the present experiments P4VP and PAA stimulated the immune response most in C57BL, A, and C57BR mice, with low reactivity to SRBC. The immune response of highly reactive CBA and C3H mice to SRBC was increased by a lesser degree as a result of injection of P4VP and PAA, or in CBA mice it was not increased at all.

The results indicate that the potentiating effect of the synthetic compounds P4VP and PAA on the immune response depends on the genotype of the mice. The compounds were very effective when injected into mice with low reactivity to SRBC.

The results thus confirm the hypothesis expressed previously that modern approaches to immunostimulation (or, conversely, to immunodepression) must be based on control of the individual stages of immunogenesis: migration and settling of stem cells and T and B lymphocytes, and interaction between T and B cells [1].

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