THE PARENTAL RESISTANCE PHENOMENON AND ITS GENETIC REGULATION

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Lymphocytes of \((CBA \times M523)F_1\) or \((A \times M523)F_1\) mice, if transplanted into CBA or A recipients irradiated in a dose of 1000 rad, react to test antigens (sheep's red cells, Salmonella typhi Vi-antigen) by the formation of only \(1/100-1/1000\) of the number of antibody-forming cells formed by syngeneic recipients. An intermediate result was observed after transplantation of the same cells into irradiated M523 recipients. Conversely, lymphocytes of \((A \times CBA)F_1\), \((CBA \times C57BL/6)F_1\), or \((A \times A.CA)F_1\) mice gave an equal immune response in syngeneic recipients and in CBA or A recipients. The ability of M523 lymphocytes or their hybrids to give an immune response to sheep's red cells did not differ from the immunoreactivity of lymphocytes of other lines either in situ or in a syngeneic adoptive system. Hematopoietic stem cells from \((CBA \times M523)F_1\) mice formed only \(40-50\%\) of the number of colonies in the CBA spleen as in the spleen of syngeneic recipients. It is concluded that the M523 mutation interferes with the proliferation and differentiation of hematopoietic cells and lymphocytes in nonsyngeneic irradiated recipients.

KEY WORDS: allogeneic inhibition; hybrid resistance; parental resistance.

Data on the possibility of a similar phenomenon in the reverse system \((F \rightarrow P)^*\) are few in number and contradictory in nature. In combinations of lines so far investigated, inhibition of hematopoiesis was only moderate in character [10, 12].

The present writers previously [5] found almost complete inability of lymphocytes of \((CBA \times CBA.M523)F_1\) mice to give an immune response to a foreign antigen (sheep's red blood cells – SRBC) in lethally irradiated CBA mice.

The object of the present investigation was to study this phenomenon and its link with the phenomenon of hybrid resistance.

EXPERIMENTAL METHOD

Mice of lines CBA/CaLacSto (abbreviated to CBA), CBA.M523/Y (M523), C57BL/6 YSto (C57BL/6), A/SnY (A), and A.CA/K1Y (A.CA), and their \(F_1\) hybrids, reared in the writers' own laboratories and also at the "Stolbovaya" Nursery, Academy of Medical Sciences of the USSR, were used as experimental animals. The M523 (H-2Ka) mutation appeared spontaneously in a population of CBA/CaLacSto mice [1] and was mapped in the H-2K locus [9]. The ages of the experimental mice ranged from 1.5 to 6 months.

*P stands for animals of the parental line.
Fig. 1 Immune response of F1 mouse spleen cells to SRBC in syngeneic irradiated recipients and recipients of parental lines. Here and in Fig. 2 abscissa is the number of AFC in spleen.

Fig. 2 Defectiveness of immune response of (CBA x M523)F1 spleen cells to S. typhi Vi-antigen in lethally irradiated CBA recipients.

SRBC and Salmonella typhi Vi-antigen, obtained from the Mechnikov Research Institute of Experimental Microbiology, Ministry of Health of the RSFSR, were used as antigens. A suspension of spleen or bone marrow cells was injected intravenously in a volume of 0.5-1 ml into recipients irradiated a few hours previously in a dose of 1000-1100 rad from a cobalt source. The donors and recipients were usually chosen to be of the same sex.

To obtain hematopoietic colonies, 5 x 10^4 bone marrow cells were injected into the recipients; the number of colonies was counted 8 days later. Vi-antigen was injected intravenously in a dose of 10 μg 0.5-1 h after transplantation of 1 x 10^8 donors' spleen cells.

SRBC were injected in a dose of 1 x 10^6 intravenously into the donors 6-30 days before the experiment and in a dose of 5 x 10^8 into the recipients 0.5-1 h after transplantation of 5 x 10^7 spleen cells.

On the 5th day after transplantation of the cells the number of antibody-forming cells (AFC) in the recipients' spleen was determined by the local active [8] or passive [3] hemolysis in gel test.

To study the comparative immunoreactivity of animals of different lines (without cell transplantation), 5 x 10^6 SRBC or 10 μg Vi-antigen was injected intravenously into them and the number of AFC was determined 4 days later.

**EXPERIMENTAL RESULTS**

In the experiments of series I the ability of spleen cells of F1 hybrids of the various lines to give an immune response to SRBC was compared in lethally irradiated syngeneic and semisyngeneic (parental line) recipients. As Fig. 1 shows, (CBA x C57BL/6)F1 and (A x CBA)F1 lymphocytes gave an equal immune response in syngeneic and semisyngeneic recipients. The same result was obtained when the immune response of (A x A.CA)F1 cells was tested in A or (A x A.CA)F1 mice (not shown in Fig. 1). Conversely, spleen cells of (CBA x M523)F1 and (A x M523)F1 mice produced only 1/100-1/1000 the number of AFC in lethally irradiated CBA or A mice respectively as in syngeneic recipients. Transplantation of the same cells into lethally irradiated M523 mice, as Fig. 1 shows, gave an intermediate result.

In the experiments of series II, instead of SRBC a different test antigen was used, namely S. typhi Vi-antigen. As Fig. 2 shows, in this case also the (CBA x M523)F1 spleen cells produced only 1/100 the number of AFC in the irradiated CBA mice as during syngeneic adoptive transplantation. Special experiments also showed that CBA, M523, and (CBA x M523)F1 mice formed equal numbers of AFC in response to injection of SRBC. The pattern observed was thus unconnected with any special features of the test antigen or the genetic features of immunoreactivity of the mice and could be ascribed to the weakened ability of lymphocytes of hybrid mice to proliferate and differentiate in recipients of the parental line.

Does the pattern discovered extend also to F1 cells other than splenic lymphocytes? The writers showed previously [5] that a mixture of (CBA x M523)F1 thymus and bone-marrow lymphocytes also produces far fewer