Immune Reactions in Different Mouse Strains

N. V. Masnaya, A. A. Churin, O. S. Borsuk, and E. Yu. Sherstoboev

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 10, pp. 437-439, October, 2002
Original article submitted July 8, 2002

The responses of immunocompetent cells to thymus-dependent antigen differ in mice of different strains. Immunization stimulated phagocytic activity of peritoneal macrophages in CBA/CaLac, DBA/2, and BALB/c mice and suppressed it in CC57W mice. By the formation of antibody-producing cells in the spleen in response to thymus-dependent antigen DBA/2 and CBA/CaLac mice can be classified as high responders, BALB/c mice as medium-responders, and C57Bl/6 and CC57W mice as low responders.

Key Words: *mouse strains; thymus-dependent antigen; immunocompetent cells; antibody-producing cells; peritoneal macrophages*

Inbred animals with different genotypes are used in experimental medicine as the models of various human diseases [1,5]. The reactivity of these animals to exo- and endogenous stimuli is intensively studied [1,2,5-7]. It was found that the response to the same antigen can differ in inbred (genetically identical) animals [1-3]. We investigated the reactions of the immune system in CBA/CaLac, DBA/2, C57Bl/6, CC57W, and BALB/c mice to thymus-dependent antigen (sheep erythrocytes, SE).

MATERIALS AND METHODS

Experiments were carried out on 125 mice of 5 strains (25 animals per strain, 5 control animals per group): 3-month-old CBA/CaLac, DBA/2, C57Bl/6, CC57W, and BALB/c mice (18-20 g) obtained from Laboratory of Biomedical Modeling, Institute of Pharmacology, Tomsk Research Center.

The animals were immunized with SE (0.2 ml 15% suspension intraperitoneally). Intact mice of the same strains served as controls.

Material for analysis was collected on days 4, 7, 14, and 21 after immunization. The mice were decapitated. Phagocytic activity of peritoneal macrophages (PAPM) [11], number of antibody-producing cells (APC) in the spleen [10], and production of specific IgM and IgG hemagglutinins [4] were evaluated.

The results were processed using Statistica for Windows software.

RESULTS

In CBA/CaLac mice PAPM increased after immunization with SE and then gradually decreased to the control level. The maximum APC count in the spleen was observed on day 4, and by the end of the experiment this value returned to the control level; the content of IgM antibodies peaked on day 4, transition from IgM to IgG production occurred by day 14.

In DBA/2 mice high PAPM was observed on days 4 and 7. On day 14 PAPM in experimental animals virtually did not differ from the control. The count of APC in the spleen of experimental animals peaked on day 4 and then decreased to the control level. The peak of IgM antibodies was observed on day 4 and the peak of IgG on day 14 of the experiment.

In C57Bl/6 mice injected with the antigen PAPM slightly increased by day 7 and then returned to the control level. APC count in the spleen of experimental mice practically did not differ from the control. The maximum content of IgM antibodies in experimental mice was observed on day 4 and that of IgG hemagglutinins on day 14.

In CC57W mice PAPM notably decreased on day 4 after immunization with SE. At later terms this para-

Institute of Pharmacology, Tomsk Research Center, Siberian Branch of Russian Academy of Medical Sciences

0007-4888/02/1344-0376$27.00

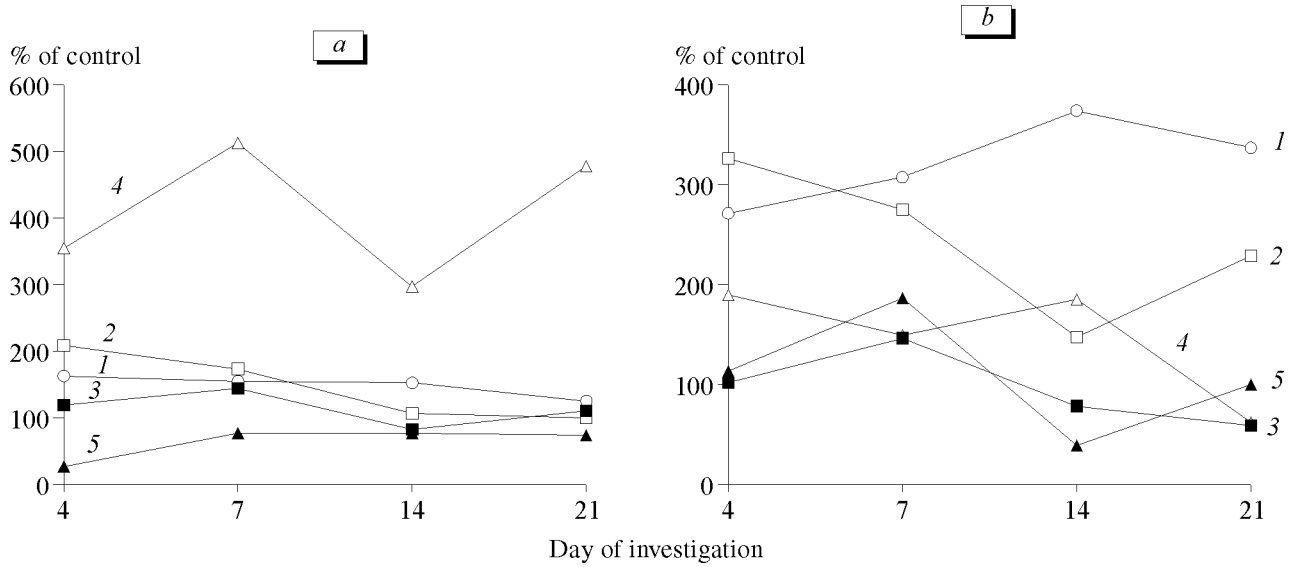

Fig. 1. Dynamics of phagocytic activity of peritoneal macrophages (*a*) and absolute counts of APC in the spleen (*b*) in CBA/CaLac (*1*), DBA (*2*), C57Bl/6 (*3*), BALB/c (*4*), and CC57W (*5*) mice immunized with thymus-dependent antigen.

meter did not significantly differ from the control. The content of APC in the spleen of immunized CC57W mice peaked on day 7, while on day 14 this parameter decreased below the control. The maximum titer of IgM antibodies in the serum was observed on day 4, and the content of IgG hemagglutinins remained high throughout the observation period.

In BALB/c mice PAPM surpassed the control throughout the observation period. The number of APC in the spleen of immunized mice was notably higher than in the control on days 4 and 14; high titers of IgM and IgG hemagglutinins were observed on days 4 and 14, respectively.

Thus, we revealed some differences in the response of immunocompetent cells in different mouse strains to thymus-dependent antigen. In order to compare these reactions, we presented the data in percents (Fig. 1). These data suggest that the most pronounced stimulation of PAPM after immunization was observed in BALB/c mice, medium stimulation in DBA/2 and CBA/CaLac animals, C57Bl/6 mice virtually did not respond to SE immunization, while in CC57W mice PAPM was suppressed (Fig. 1, *a*). By their response (APC formation in the spleen) to thymus-dependent antigen, DBA/2 and CBA/CaLac mice are high responders, BALB/c mice were medium responders, and C57Bl/6 and CC57W mice were low responders (Fig. 1, *b*).

Differences in the reactions of various systems in inbred animals are genetically determined [2,6-8]. Experiments demonstrated differences in activities of antigen-presenting cells (macrophages, dendritic cells) in animals of different strains [3,8,9]. High activity of macrophages eliminating antigen material can be responsible for decreased percentage of presented antigens [3,9]. We believe that in our experiments high PAPM (which persisted until the end of the experiment) was responsible for less intense primary immune response in BALB/c mice in comparison with DBA/2 and CBA/CaLac mice.

If the antigen concentration is high, the presenting cells do not "cope" with the processing of the material and the immune response is delayed. In our experiments, CC57W mice had low PAPM at the initial stages after immunization. This probably explains the shift of the peak of splenic APC formation in this mouse strain.

Class II histocompatibility antigen (HLAII) plays an important role in cooperation of different types of immunocompetent cells in the immune response [2, 7,8]. Animals of different strains possess genetically determined differences in the content of HLAII (Ia-a) [2,7,8]. For example, presentation of the antigen Ia-a complex by macrophages (dendritic cells) can be disturbed in low responders in case of low Ia-R concentration on presenting cells [8]. Presumably, this factor determines low immune response to the antigen in CC57W and C57Bl/6 mice. Impaired antigen presentation on macrophages (dendritic cells) can be responsible for the absence (low level) of T lymphocyte proliferation, which is triggered by Ia-a and interleukin-1. Recognition of Ia-a by T cells induced interleukin production and activates T cell proliferation and subsequent stages of the immune response leading to production of specific antibodies [8]. Mice of different strains differ by spontaneous and stimulated proliferation capacity of splenic (T and B) cells [6]: this parameter is high in CBA mice and low in C57Bl/

6J and BALB/c mice. Low proliferative activity can be the cause of low level of APC formation (in our case in C57Bl/6, CC57W, and BALB/c mice).

Hence, individual sensitivity of the immune system to the antigen in mice of different strains can be explained, among other things, by their genetic characteristics.

REFERENCES

1. Z. K. Blandova, V. A. Dushkin, V. P. Kryshkina, *et al.*, *Immunologiya*, No. 1, 77-81 (1982).
2. B. D. Brondz and O. V. Rokhlin, *Molecular and Cellular Bases of Immunological Recognition* [in Russian], Moscow (1978).
3. V. G. Galaktionov, *Immunology* [in Russian], Moscow (1998).
4. N. R. Ling and D. Catty, *Hemagglutination and Antibody-Dependent Hemolysis Reaction. Antibodies. Methods* [in Russian], ed. by D. Catty, Moscow (1991), Book 1.
5. V. M. Man'ko, T. B. Rudneva, and N. A. Razvalyaeva, *Immunologiya*, No. 6, 41-46 (1995).
6. V. M. Man'ko, M. A. Chizhevskaya, T. B. Masternak, *et al.*, *Ibid.*, No. 4, 17-21 (1994).
7. N. V. Medunitsyn, *Ibid.*, No. 5, 85-87 (1988).
8. N. V. Medunitsyn and L. P. Alekseev, *Ia-Antigen System: Genetics, Structure, Function* [in Russian], Moscow (1987).
9. M. V. Pashchenkov and B. V. Pinegin, *Immunologiya*, No. 2, 7-16 (2001).
10. A. J. Cunningham, *Nature*, **207**, 1106 (1965).
11. B. Vrav, J. Hoebeke, M. Saint-Guillain, *et al.*, *Scand. J. Immunol.*, **11**, 147-153 (1980).