[Jpn. J. Parasitol., Vol. 34, No. 5, 423-425, October, 1985]

Research Note

H-2-Independent Decrease of Nucleated Cell Density of Spleen by *Toxoplasma* Infection in Mice

YASUHIRO SUZUKI AND AKIO KOBAYASHI

(Received for publication; June 18, 1985)

Key words: splenomegaly, *Toxoplasma* infection, mice

Toxoplasma infection induces an enlargement of the spleen in mice. However, the regulation of the splenomegaly is not clear. In the present study, we found that a decrease of nucleated cell density in the spleen occurred together with an enlargement of the spleen during the course of *Toxoplasma* infection, and the decrease appeared to be genetically controlled.

Inbred female C57BL/6, C57BL/10 (B 10), B 10.D 2 and BALB/c mice were purchased from Shizuoka Agricultural Cooperative Association for Laboratory Animals (Hamamatsu).

C57BL/6 mice were inoculated intraperitoneally with 5×10^3 bradyzoites of the avirulent Fukaya strain of *T. gondii* as described previously (Suzuki *et al.*, 1981 a). At various days after infection, mice were sacrificed, and both the spleen weight and cell number were measured. Spleen weight increased markedly during the acute phase of infection (Fig. 1). The enlargement of the spleen was most remarkable during the first and second week of infection. Coupled with the enlargement of the spleen, the nucleated cell density decreased (Fig. 1). The decrease was already detected by the 3 rd day of infection, however, the most remarkable decrease occurred between the first and second week of infection. Table 1 shows the weight and cell number of the spleen on the 7 th day of the infection. The spleen weight increased to four times the size of an unifected control. On the other hand, the number of nucleated cells was only twice as many as the uninfected control. Therefore, the nucleated cell density of the spleen was less than half that of normal mice on day 7 of the infection. The number of red blood cells increased to more than seven times the amount of the uninfected mice, indicating that one cause of the decrease of the nucleated cell density of the spleen is an increase in the number of red blood cells. On the 4 th week of infection, the decrease of cell density was still detectable, however, on the 8 th week, the cell density increased to a normal level.

Department of Parasitology, Jikei University School of Medicine, 3-25-8 Nishi-shinbashi, Minato-ku, Tokyo 105, Japan.

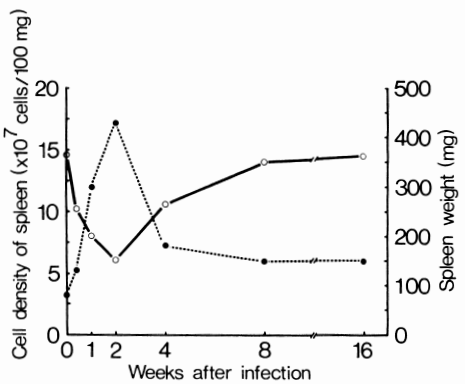

Fig. 1 Change in spleen weight and nucleated cell density during the course of *Toxoplasma* infection in C 57 BL/6 mice. Mice were inoculated intraperitoneally with 5×10^3 bradyzoites of *T. gondii*. Each point represents the mean value on 5 mice. Symbols: ●, spleen weight; ○, nucleated cell density of spleen.

Table 1 Change in weight and cell numbers of spleen in acute phase of *Toxoplasma* infection in C 57 BL/6 mice

Mice	Weight (mg)	Number of nucleated cells ($\times 10^7$)	Number of red blood cells ($\times 10^7$)	Cell density*
Normal (N)	74.1±3.62	10.8±0.43	2.67±0.29	14.7±0.54
Infected (I)†	305.4±8.81‡	21.0±1.35‡	19.7±1.63‡	6.87±0.32‡
Ratio (I/N)	4.12	1.94	7.38	0.47

* Number of nucleated cells ($\times 10^7$)/100mg weight.
† On day 7 of *Toxoplasma* infection.
‡ Significantly different from normal control mice at $p<0.001$.

Table 2 H-2-independent change in cell density of spleen by *Toxoplasma* infection in mice

Strain of mice		Number of nucleated cell ($\times 10^7$)/100mg weight			
		Nomal		Infected†	
B10	(H-2^b)	14.0±0.36	N. S.‡	7.39±0.24	N. S.
B10.D2	(H-2^d)	14.9±0.29	$p<0.001$	6.74±0.25	$p<0.001$
BALB/c	(H-2^d)	12.9±0.38		8.59±0.45	

* Mean ± S.E. of 10 mice.
† On day 7 of *Toxoplasma* infection.
‡ Not significant.

This pattern of a decrease in nucleated cell density of the spleen during the course of infection correlates well with that of the depression of antibody responses in mice by *Toxoplasma* infection (Suzuki *et al.*, 1981 a, b). Although an activation of suppressor macrophages appears to be a major cause of the suppressed antibody responses in the infected mice (Suzuki *et al.*, 1981 a, b, Suzuki and Kobayashi, 1983, 1984), the decrease of spleen cell density by infection may be an additional factor among the causes of the depression of antibody responses *in vivo*. Pelster (1980) also reported in a histological examination that a loss of lymphocytes in the spleen occurs in an acute phase of *Toxoplasma* infection in mice.

We have found that the induction of suppressed antibody responses by *Toxoplasma* infection in mice is regulated by both H-2-linked and-nonlinked genes (Suzuki and Kobayashi, 1985). Therefore, we examined whether or not a genetic control is present in an induction of the decrease of spleen cell density by *Toxoplasma* infection. The mice used in this experiment were B 10 mice, which shows the most severe suppression of antibody responses in *Toxoplasma* infection, BALB/c mice, in which the suppressive effect of infection is very weak, and B 10.D 2 mice, which have the B 10 background and the same H-2 haplotype as BALB/c mice.

The three strains of mice were inoculated intraperitoneally with 5×10^3 bradyzoites of *T. gondii*, and 1 week later, the spleen weight and spleen cell numbers were measured. Table 2 shows the nucleated spleen cell densities of the mice. A decrease in the cell density was observed in all strains of mice in *Toxoplasma* infection. However, the infected BALB/c mice showed a significantly higher cell density than the infected B 10 and B 10.D 2 mice, while there was no difference in cell density between B 10 and B 10.D 2 mice.

By contrast, in uninfected control mice,

the nucleated cell density was higher in B 10 and B 10.D 2 mice than in BALB/c mice. This indicates that the change in spleen cell density by *Toxoplasma* infection was significantly smaller in BALB/c mice than in B 10 and B 10.D 2 mice. Between B 10 and B 10.D 2 mice, no significant difference in this change was observed. These results demonstrate that a change of spleen cell density with a splenomegaly by *Toxoplasma* infection was regulated by H-2-nonlinked genes. Allen *et al.* (1977) reported that an enlargement of spleen by an injection of *Mycobacterium bovis* (BCG) appears to be controlled by H-2-nonlinked genes.

The decrease in the nucleated cell density of the spleen by *Toxoplasma* infection might play a role in the depression of antibody responses in the infected mice as an H-2-nonlinked factor, in addition to an activation of suppressor macrophages.

References

1) Allen, E. M., Moore, V. L. and Stevens, J. O. (1977): Strain variation in BCG-induced chronic pulmonary inflammation in mice. I. Basic model and possible genetic control by non-H-2 genens. J. Immunol., 119, 343–347.
2) Pelster, B. (1980): Dynamics of lymphocytes and immunosuppression in *Toxoplasma* infected mice. Z. Parasitenkd., 63, 177–189.
3) Suzuki, Y. and Kobayashi, A. (1983): Suppression of unprimed T and B cells in antibody responses by irradiation-resistant and plastic-adherent suppressor cells in *Toxoplasma gondii*-infected mice. Infect. Immun., 40, 1–7.
4) Suzuki, Y. and Kobayashi, A. (1984): Macrophage-mediated suppression of immune responses in *Toxoplasma*-infected mice. I. Inhibition of proliferation of lymphocytes in primary antibody responses. Cell. Immunol., 85, 417–427.
5) Suzuki, Y. and Kobayashi, A. (1985): Macrophage-mediated suppression of immune responses in *Toxoplasma*-infected mice. II. Both H-2-linked and-nonlinked control of induction of suppressor marcophages. Cell. Immunol., 91, 375–384.
6) Suzuki, Y., Watanabe, N. and Kobayashi, A. (1981 a): Nonspecific suppression of primary antibody responses and presence of plastic-adherent suppressor cells in *Toxoplasma gondii*-infected mice. Infect. Immun., 34, 30–35.
7) Suzuki, Y., Watanabe, N. and Kobayashi, A. (1981 b): Nonspecific suppression of initiation of memory cells in *Toxoplasma gondii*-infected mice. Infect. Immun., 34, 36–42.

短　報

H-2遺伝子と相関なく起こるトキソプラズマ感染マウスの脾有核細胞密度低下について

鈴木康弘　小林昭夫

(東京慈恵会医科大学寄生虫学教室)

トキソプラズマ感染急性期のマウスにおいて，脾腫に伴い脾の有核細胞密度が低下する事実が見い出された．その細胞密度低下の程度はマウス系統間で異なり，C57BL/6 および C57BL/10 (B 10) マウスでは BALB/C マウスより著明であった．また，遺伝子的に B10 background でかつ BALB/C と同じ H-2 ハプロタイプを持つコンジェニックマウスである B10.D 2 マウスは，感染時に B10 マウスと同様の脾細胞密度低下を示した．したがって，H-2 に連鎖していない遺伝子がこの細胞密度低下に関与していると考えられた．