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Selection Experiment for Immune Response to Enhance Disease Resistance in Mice

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Abstract

Selection for peripheral immune traits was done in mice to investigate the possibility of breeding for disease resistance. Selections for high phagocyte activity (PA), high antibody production (ABP), and high PA, and high ABP (aggregate breeding value weighted by standard deviation of each breeding value) were produced. They were respectively named N line, A line, and NA line. Furthermore, a control line without selection was named C line. Selective breeding has continued: data for 14 generations are now available. Immune traits of about 5500 mice from each line were measured. Moreover, to ensure the disease resistance of these mice, they were infected by i.v. route with Shiga-like toxin at 11 generations of selection. We compared weight loss and some immune traits such as leukocyte number, phagocyte activity, and antibody production between each selection line and the control line.

The heritabilities estimate for PA in N line was 0.35±0.03. That for ABP in A line was 0.34±0.07; PA and ABP in NA line were 0.57±0.05 and 0.33±0.06. The phenotypic values of immune traits varied greatly, but the breeding values showed a substantial increase with selection. In an exposure experiment with Shiga-like toxin, immune responses of the selection line were significantly higher than that of the control line. Line differences were also found among three selection lines.

These results suggest that establishment of a selection line related to the immune traits is possible: selection for peripheral immune traits is effective to enhance disease resistance.

Introduction

Recently, the selection breeding of animals with genetically high resistance to disease has been requested. But, it was difficult because generally, it was reported that the heritabilities of immune traits were low. However, Biozzi succeeded in the selection experiment concerning immune traits in the mice.

The mouse is the best animal due to the short generation interval and easy handling. From this reason, we tried and examined effectiveness of the selection for peripheral immune traits in

mice to investigate the possibility of breeding for disease resistance.

The immunity is classified into the two aspects, natural immunity and acquired immunity. We have established three mice closed colonies, which were selectively bred based on the natural immunity (line N), the acquired immunity (line A), both of the natural and acquired immunities (line NA) and no selection colony (line C).

Selection experiment

Material and Method

The base population was established from four-way line crossing of two inbred lines (C57BL/6, BALB/C) and two selected lines (selected for high aggression and low aggression) that were selected over 20th generations (Kawamoto et al., 1993). The selection traits were phagocyte activity (PA), and antibody production (ABP), and both (PA, ABP), which were designated respectively as the line N, A and NA. A control line without selection was named line C.

In each of the 14th generations, three selection lines were measured for each immune trait with 90 animals, and 25 males and 25 females were selected.

PA was measured at 5 weeks of age using chemil-uminescence method. ABP was measured at 9 weeks of age with ELISA method using peripheral blood. For ABP measurement, SRBC were intraperitoneally vaccinated at 5 and 7 weeks of age as the antigen. (BCG and PPD were used as an antigen until the 5th generation.)

Table 1. The selected lines, selection traits and number of animals.

Lines	**Selection traits**	***N***
High natural immunity (line N)	Phagocyte activity (PA)	1,829
High acquired immunity (line A)	Antibody production (ABP)	1,820
Both high immunity (line NA)	PA and ABP	1,835
Control line (Without selection) (line C)	Nothing	1,292

Statistical Method

Genetic parameters and breeding values were estimated by the VCE4.2.5 program and the PEST program. The following model was used to estimate genetic parameters and breeding values:

$$Yijklm = \mu i + Sij + Gik + ail + eijklm$$

Results and Discussion

Table 2. Estimates of heritabilities (*h*2) and genetic correlations for the PA and ABP.

	N line		A line	
	PA	ABP	PA	ABP
PA	.35±.03	.07±.22		
ABP		.25±.10		.34±.06

	NA line		C line	
	PA	ABP	PA	ABP
PA	.57±.05	.50±.14	.46±.06	.59±.34
ABP		.33±.06		.32±.12

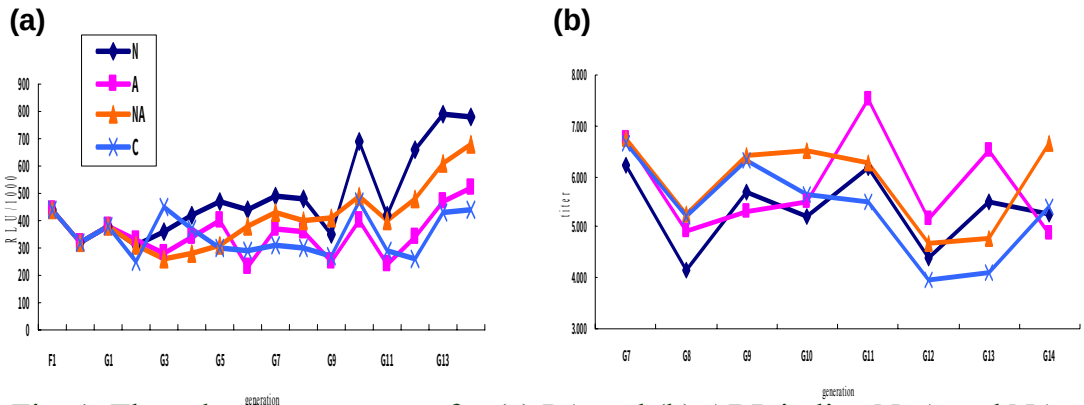

Fig. 1. The selection responses for (a) PA and (b) ABP in line N, A and NA.

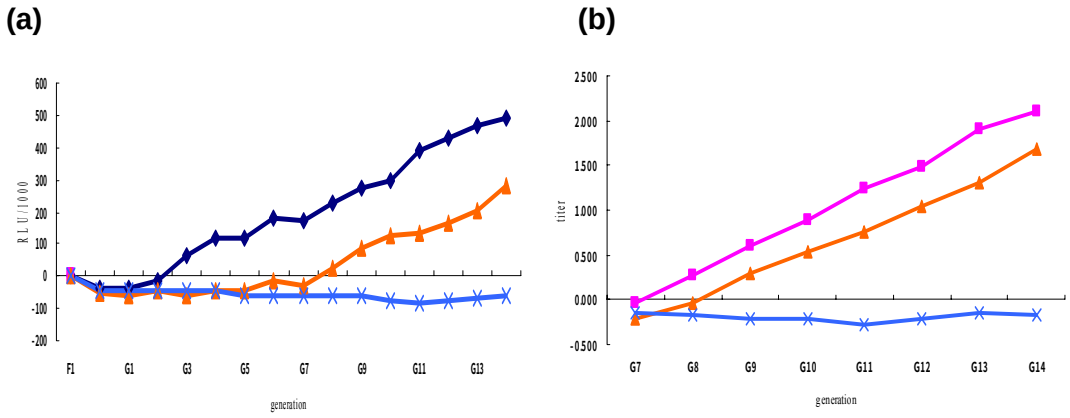

Fig. 2. The genetic responses for (a) PA and (b) ABP in line N, A and NA.

Moderate or high heritabilities were estimated for PA and ABP, and genetic correlation was high in line NA (Table 1). Generally, it has reported that the heritabilities of immune traits were low. But the result of this study was different from it, and it might be advantageous for the selection. However, there was a possibility that a common environmental effect influenced at this heritabilities.

The phenotypic values of immune traits varied greatly, especially in ABP. But the breeding values showed a substantial increase with selection (Figure 1 and Figure 2).

Exposure experiment

Material and Method

To ensure the disease resistant phenotype of the established mice groups, they were administrated with the Shiga-like toxin through the i.v. injection at the 11th generation. The total number of the mice was 250.

The body weight, and immune traits, including the number of white blood cells, phagocyte activity, antibody production, and TNF-α production of selectively bred mice lines were measured, and compared with that of non-selected control. Data were analyzed by PROC GLM of SAS.

Results and Discussion

There was no significant difference of the body weight loss among the selectively bred lines and the control line.

However, the immune responses of the selected lines were significantly higher than that of the control line ($p<0.05$). Moreover, the each selected lines had the different biological characteristics, when they are compared with the control groups (data not shown in this poster)

These results suggested the possibility that the animal breeding based on the immune traits is effective and useful for the establishment of the disease resistant animals.

Conclusion

First, the heritabilities for PA and ABP were moderate or high, and it was advantageous for the selection. Secondly, Selection for peripheral immune traits is effective to enhance disease resistance.