Acquired Resistance and Immune Responses of Eight Strains of Inbred Rats to Infection with *Angiostrongylus cantonensis*

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Abstract. The occurrence of acquired resistance and the kinetics of humoral immune responses to *Angiostrongylus cantonensis* infection were studied in eight inbred rat strains. Consequently, it was found that both BUF and ACI strains acquired less protective immunity than other strains and, conversely, Tokyo and NIG strains yielded higher resistance. The remaining strains showed various intermediate degrees of acquired resistance. Striking strain differences in pattern of reagin production were found; Tokyo was a high responder while ACI was a low responder. In contrast, the kinetics of indirect hemagglutination (IHA) antibody response was essentially the same in all the strains examined. The IHA antibody titers were generally high in both Tokyo and NIG. Histopathologically, ACI was distinct from NIG in that fibrotic reactions around the nodules of developing eggs in the lung parenchyma were almost undiscernible. These data suggest that genetic factors would be involved in acquired resistance and reaginic antibody responses to *A. cantonensis* infection in rats.

Strain-dependent differences in susceptibility to a wide variety of parasitic infections have been found in various experimental animal models, as reviewed by Yoshimura [16]. And these differences are thought to be possibly determined by host genetic factors among which immune responsiveness would be one of the most important components. However, only limited information is available on a possible association between the host susceptibility and immune responsiveness; such an attempt has been made in *Leishmania donovani* [3], *Toxoplasma gondii* [14], *Trypanosoma congolense* [6], *Trichuris muris* [13],

Trichinella spiralis [9] and *Echinococcus multilocularis* [2] infections in mice and *Trichostrongylus colubriformis* infection in guinea pigs [10].

Up to the present, however, no specific data are available on not only differences in susceptibility to *Angiostrongylus cantonensis* of different inbred rat strains but also the functional relationship between the host immune responses and susceptibility. As a prelude to such an exploration, the present study was attempted to compare the susceptibility and immune responses of eight inbred strains of rats to infection with *A. cantonensis*. The main criteria used were

worm recovery from a primary infection and protective immunity against a challenge infection. Besides, a particular emphasis was placed on detection of a possible correlation between acquired resistance and reagenic and IHA antibody responses of the infected rats.

Materials and Methods

All of eight inbred rat strains used came from our breeding colony. The breeding nuclei for the ACI/N (ACI) (F102), Buffalo (BUF) (F66), NIG III (NIG) (F33), Wistar-King-A (WKA) (F202), Wistar-King-S (WKS) (F14), Wistar/Mishima (W/Ms) (F71) were obtained from the National Institute of Genetics, Mishima, Japan. Similar breeding nuclei for the Lewis (LEW) (F17) and Tokyo (F50) strains were obtained from the Institute of Medical Science, University of Tokyo and from the Faculty of Science, Hokkaido University, respectively.

Rat infections with the Hawaiian strain of *A. cantonensis* were performed as previously described [20]. Challenge infection was made 10 weeks following a primary infection and all animals were necropsied 5 weeks later. The methods for worm recovery and stool examination have been described previously [18]. Differentiation between primary worms and secondary worms could be made by assessing worm sizes.

At appropriate times after primary infection, the rats were bled and the serum was separated as previously described [20]. A small and equal aliquot of each individual serum was pooled within each strain, and the pools were stored at -20°C until use. The techniques of 48-hr passive cutaneous anaphylaxis (PCA) and of IHA test with or without prior 2-mercaptoethanol (2-ME) treatment have been described elsewhere [18].

For histopathological examinations, the lungs were fixed with alcohol-formol-acetic fixative, embedded in paraffin, and sectioned at 5–7 μm . Some slides were stained with hematoxylin and eosin (H-E) and others with elastic-Van Gieson's stain.

Worm recovery assays were performed on only the animals which survived the course of the experiments. The percent worm recovery rate was calculated first for each rat since the number of infective larvae fed was slightly variable in individual animals. The mean recovery rates for both primary and challenge infections were then determined for each strain. For convenience, the following formula was taken as a measure of each strain's protective immunity:

Percentage of protection

$$= \frac{\text{Recovery rate for primary infection} - \text{Recovery rate for challenge infection}}{\text{Recovery rate for primary infection}} \times 100$$

Statistical analysis on differences in worm recovery rate and percentage of protection between strains was performed by using Student's t-test. The Chi-square test was also used to analyze differences in worm sex ratio and the ratio of number of worms from the brain to the total number of worms recovered.

Results

Experiment I

Four strains of inbred rats (2 males and 3 females each), i.e., ACI, BUF, NIG and WKS were infected at 5.1 to 6.3 weeks of age with 15 to 16 (mean = 15.3) larvae and later challenged with 16 larvae. Two ACI rats (male and female each) and one female WKS rat died during the course of the experiment.

Worm recovery data (Table 1) indicate that in primary infection, the worm recovery rate was high in BUF (77%) and those for the remaining three strains were quite similar to each other, ranging from 62 to 66%. The recovery rate for a challenging infection was also high in BUF. Percentage of protection (22%) in BUF strain was thus significantly lower than that (82%) in WKS but did not differ from those in ACI (62%) and NIG (70%).

The kinetics of reagenic antibody responses (Fig. 1) demonstrated that reagin production was extremely delayed in ACI which first became positive for PCA at week 9 following primary infection and exhibited a reincrease in titer 4 weeks after challenge infection. Three other strains showed a transient reagenic antibody response. In NIG, reagin appeared one week earlier (at week 4) than in BUF and WKS, although the titer was extremely low in NIG, as was seen in BUF. No secondary response was observed in all strains except for ACI.

Table 1. Worm recovery from 4 inbred rat strains infected with 15 third-stage larvae of *A. cantonensis* and 10 weeks later challenged with 16 larvae

Strain	No. of rats exam-ined	Total No. of larvae infected	Worm burden				Mean % worm recovery ± SD	Significance of difference in worm recovery	Mean % pro-tection* ± SD	Significance of difference in protection
			Male	Female	Sex ratio (♀/♂)	Total				
Primary infection										
ACI	3	45	13	15	1.15	28	62.2±13.85			
BUF	5	75	28	30	1.07	58	77.3±17.39			
NIG	5	78	22	28	1.27	50	63.5±24.65			
WKS	4	62	23	18	0.78	41	66.1±11.02			
Challenge infection										
ACI	3	48	5	7	1.40	12	25.0±16.55		61.7±18.66	
BUF	5	80	20	24	1.20	44	55.0±20.92 ^a		21.6±45.56 ^d	
NIG	5	80	7	8	1.14	15	18.8±8.82 ^b	a vs b p<0.01	70.3±10.48	
WKS	4	64	5	3	0.60	8	12.6±7.22 ^c	a vs c p<0.01	81.8±8.80 ^e	d vs e p<0.05

Remarks.

SD: Standard deviation.

* See text for computing the percentage of protection.

Fig. 1. Reaginic antibody titers in 4 inbred rat strains after an initial infection with 15 third-stage larvae of *A. cantonensis*, followed by a challenge infection with 16 larvae

Remarks.

Arrow indicates infection.

Experiment II

Six inbred rat strains of BUF (♂6, ♀2), LEW (♂5, ♀4), NIG (♂4, ♀3), Tokyo (♂5, ♀2), WKA (♂5, ♀4) and W/Ms (♂4, ♀6) were initially exposed at 7.1 to 7.7 weeks of age to 28 to 31 (mean = 29.5) infective larvae and later challenged with 35 to 45 (mean = 39.5) larvae. A single male rat of BUF, two Tokyo rats (♂1, ♀1), and three W/Ms rats

(♂1, ♀2) died during the course of the experiment.

As shown in Table 2, worm recovery data on primary infection indicate that the recovery rate was high in both BUF and NIG (61%), followed by LEW (59%), Tokyo (54%), WKA (51%) and W/Ms (44%). In primary infection, the male worms recovered from BUF strain outnumbered the females

Table 2. Worm recovery from 6 inbred rat strains infected with 30 third-stage larvae of *A. cantonensis* and 10 weeks later challenged with 40 larvae

Strain	No. of rats examined	Total No. of larvae infected	Worm burden				Mean % worm recovery $\pm$ SD	Significance of difference in worm recovery	Mean % protection* $\pm$ SD
			Male	Female	Sex ratio (♀/♂)	Total			
Primary infection									
BUF	7	207	72	55	0.76**	127	61.4 $\pm$ 18.35		
LEW	9	270	74	84	1.14	158	58.5 $\pm$ 14.83		
NIG	7	204	58	67	1.16	125	61.2 $\pm$ 6.71		
Tokyo	5	149	40	41	1.03	81	54.3 $\pm$ 14.83		
WKA	9	267	66	70	1.06	136	50.9 $\pm$ 11.89		
W/Ms	7	203	38	52	1.37**	90	43.7 $\pm$ 25.13		
Challenge infection									
BUF	7	270	50	60	1.20	110	41.1 $\pm$ 11.36 ^a		24.9 $\pm$ 36.50
LEW	9	366	48	55	1.15	103	28.4 $\pm$ 11.72 ^b	a vs b p<0.05	47.7 $\pm$ 27.07
NIG	7	275	43	29 (2) ***	0.72	74	27.1 $\pm$ 10.94 ^c	a vs c p<0.05	54.6 $\pm$ 20.67
Tokyo	5	188	20	21	1.05	41	22.1 $\pm$ 9.80 ^d	a vs d p<0.02	56.0 $\pm$ 20.90
WKA	9	359	45	45 (1)	1.02	91	25.4 $\pm$ 12.60 ^e	a vs e p<0.05	47.1 $\pm$ 29.42
W/Ms	7	282	39	34	0.87	73	26.1 $\pm$ 19.39		-24.7 $\pm$ 176.08

Remarks.

SD: Standard deviation.

* See text for computing the percentage of protection. No statistically significant difference in protection was found between any combinations of the strains.

** Difference between these ratios was statistically significant ($p<0.05$).

*** Figures outside parentheses mean the number of worms recovered from the lungs whereas those in parentheses represent worms from the brain.

Fig. 2. Reaginic antibody titers in 6 inbred rat strains after an initial infection with 30 third-stage larvae of *A. cantonensis*, followed by a challenge infection with 40 larvae

Remarks. Arrow indicates infection.

Fig. 3. IHA antibody titers in 6 inbred rat strains after an initial infection with 30 third-stage larvae of *A. cantonensis*, followed by a challenge infection with 40 larvae

Remarks.

●—●: Titer prior to 2-mercaptoethanol treatment.

○—○: Titer after 2-mercaptoethanol treatment.

Arrow indicates infection.

and vice versa, in W/Ms (Table 2).

On the other hand, worm recovery from a challenging infection was also high in BUF whose recovery rate (41%) was significantly higher than those (22–28%) of LEW, NIG, Tokyo and WKA (Table 2). However, no significant differences in percentage of protection could be observed between any combination of these strains. The worm recovery rates for both primary and chal-

lenge infections were extremely variable in W/Ms and thus, the most pronounced variation in percentage of protection ensued.

Each of BUF, LEW and NIG strains showed a transient reagin response with a peak PCA titer at week 5 (Fig. 2). To the contrary, the remaining three strains (Tokyo, W/Ms and WKA) exhibited comparable reaginic antibody response throughout the time of weeks 5 to 9 (Fig. 2). Only W/Ms

Table 3. Worm recovery from 4 inbred rat strains infected with 55 third-stage larvae of *A. cantonensis* and 10 weeks later challenged with 38 larvae

Strain	No. of rats exam-ined	Total No. of larvae infected	Worm burden			Mean % worm recovery $\pm$ SD	Significance of difference between strains	Mean % pro-tection* $\pm$ SD	Significance of difference in protection
			Male	Female	Sex ratio (♀/♂)				
Primary infection									
ACI	8	439	90	84	0.93	39.6 $\pm$ 10.31 ^a	a vs b p<0.001		
NIG	8	439	138	146	1.06	64.7 $\pm$ 4.85 ^b	b vs c p<0.05		
Tokyo	5	272	73	76	1.04 [†]	54.7 $\pm$ 20.30			
WKS	5	272	70	84	1.20	56.6 $\pm$ 6.47 ^c	a vs c p<0.01		
Challenge infection									
ACI	8	304	40 (1)**	51 (1)	1.27***	30.5 $\pm$ 9.13	d vs f p<0.001	21.9 $\pm$ 20.68 ^h	
NIG	8	303	35 (1)	50 (3)	1.47	29.5 $\pm$ 10.46	e vs f p<0.05	54.8 $\pm$ 14.93 ⁱ	h vs i p<0.01
Tokyo	5	187	8 (3)	26 (5)	2.82***, [†]	22.4 $\pm$ 10.71	f vs g p<0.02	56.8 $\pm$ 21.39 ^j	h vs j p<0.02
WKS	5	190	24 (1)	40 (1)	1.64	34.7 $\pm$ 12.73		38.0 $\pm$ 23.93	

Remarks.

SD: Standard deviation.

* See text for computing the percentage of protection.

** Figures outside parentheses mean the number of worms recovered from the lungs whereas those in parentheses represent worms from the brain.

*** Difference between these ratios was statistically significant (p < 0.05).

† Difference between these ratios was statistically significant (p < 0.01).

Fig. 4. Reaginic antibody titers in 4 inbred rat strains after an initial infection with 55 third-stage larvae of *A. cantonensis*, followed by a challenge infection with 38 larvae

Remarks.

Arrow indicates infection.

Fig. 5. IHA antibody titers in 4 inbred rat strains after an initial infection with 55 third-stage larvae of *A. cantonensis*, followed by a challenge infection with 38 larvae

Remarks.

●: Titer prior to 2-mercaptoethanol treatment.

○: Titer after 2-mercaptoethanol treatment.

Arrow indicates infection.

and Tokyo strains evoked the slowly developing secondary reagin response following challenge infection (Fig. 2).

All strains examined showed similar patterns of IHA antibody responses (Fig. 3). However, it was noted that the IHA titer was generally higher in Tokyo, NIG and W/Ms while low in three other strains, especially at later stages of infection in BUF. When the sera first became positive for IHA, the 2-ME resistant IHA antibody (IgG) had been already detectable (Figs. 3 and 5).

Experiment III

Four strains of rats, i.e., ACI (δ 3, η 5), NIG (δ 4, η 4), Tokyo (δ 5, η 3) and WKS (δ 5, η 3) were infected at 10.1–13.4 weeks of age with 54–56 (mean = 54.7) infective larvae and challenged with 37–39 (mean = 37.8) larvae. Three rats of Tokyo and WKS (one male and 2 females each) died before the end of the experiment.

Stool examinations revealed that all strains were negative for the 1st stage larvae until day 36. On day 38, however, 25% (2/8) of ACI rats, 50% (4/8) of NIG and 57% (4/7) of WKS became positive for the larvae, although all individuals of Tokyo strain were still negative. Subsequently, it was found that all individuals of 4 strains became positive up to 41 days postinfection. Since then, the number of larvae shed rapidly increased until about 50 days postinfection.

Worm recovery data on a primary infection (Table 3) showed that the highest recovery rate was obtained from NIG (65%), followed by WKS (57%), Tokyo (55%) and ACI (40%). Statistical analyses indicated that the worm recovery from ACI was lower than those from NIG or WKS and also that there exists a significant difference between WKS and NIG (Table 3).

On the other hand, it was found that the protective immunity induced in Tokyo

(57%) and NIG (55%) was significantly higher than that (22%) in ACI strain.

In Tokyo strain, it was noticeable that the sex ratio of the worms derived from challenge infection was strongly biased in favor of the female worms and in addition to this, more worms were found still remained in the brain at necropsy (Table 3).

The kinetics of reaginic antibody responses in 4 strains of inbred rats (Fig. 4) indicated that ACI was negative for PCA until week 9 following primary infection and became positive 3 weeks postchallenge, showing a slight elevation in PCA titer at later stages. Conversely, Tokyo became positive for reaginic antibody 3 weeks after a primary infection, having a peak PCA titer (1:64) at weeks 5 and 7. In this strain, furthermore, rather high titers lasted until week 9 and a distinct booster effect was observed following a challenge infection (Fig. 4). In NIG and WKS, reagin production occurred 5 weeks postinfection, persisting until week 9 but disappearing at week 11. Although both strains exhibited a peak PCA titer at week 5, the titer was much higher in WKS (1:256) than in NIG. A challenge infection provided a distinct but transient secondary reagin response in NIG 3 weeks postchallenge but not in WKS (Fig. 4).

The IHA antibody was detectable in NIG, WKS and Tokyo strains 5 weeks after primary infection while ACI became positive at week 7 (Fig. 5). Additionally, the IHA antibody titer appeared to be generally higher in both Tokyo and NIG than in two other strains (Fig. 5).

The ACI and NIG rats (two females each) were infected, at 11.7 and 13.4 weeks of age respectively, with 54–56 larvae and 29 weeks later all necropsied for the histopathological examinations of the lungs. At necropsy, the ACI and NIG weighed 203–210 g and 194–218 g, respectively. The weight of the lung

(10.6–17.2 g) in NIG, however, was about fivefold over that (2.1–3.5 g) in ACI. Moreover, the former lung was extremely hard as compared with the latter and, indeed, gross appearance suggested carnification.

Histopathological observations on the NIG lungs revealed that the intima of the pulmonary artery was extremely hypertrophic due to the intensive proliferation of fibrous tissues and a distinct parietal thrombus could be seen inside the artery (Fig. 6). Moreover, the adventitia and its adjacent areas were intensively infiltrated with masses of neutrophils, and with some eosinophils, plasma cells and histiocytes (Fig. 6). In ACI, the intimal surface of the pulmonary artery was irregularly protruded due to the proliferation of the endothelial cells. However, no detectable levels of fibrous hypertrophy could be seen at the intima. And only slight inflammatory infiltration of plasma cells and lymphocytes was observed at the adventitia (Fig. 7). In both strains, a tremendous number of nodules of developing eggs were found in the lung parenchyma. In ACI, a marked congestion or hemorrhage was noticeable around the masses of developing eggs, though fibrotic reactions around them were almost undiscernible (Fig. 9 and cf. Fig. 8). In contrast, the egg granulomas in the lungs of NIG strain were devoid of such congestion or hemorrhage, but accompanied with the extensive proliferation of fibrous tissues where infiltration of some eosinophils and neutrophils could be seen (Fig. 3). The lung parenchyma between these nodular lesions was usually atelectatic and accompanied by the proliferation of fibroblasts, together with inflammatory infiltration of eosinophils, plasma cells and histiocytes.

Discussion

Strictly speaking, the protective immunity

described in this study is a sum of acquired resistance, induced by a primary infection, plus so-called "age resistance" [1]. Nevertheless, it is conceivable that our equation used for determining the percentage of protection would serve as a parameter to compare strain differences in development of acquired resistance, since the age of each rat strain was quite similar at the onset of the individual experiments.

The results of the present study clearly indicate that marked differences in development of protective immunity to *A. cantonensis* infection are found between different rat strains, suggesting that this trait would be genetically determined. Among eight strains examined, four (BUF, ACI, Tokyo and NIG) of them are thought to be of interest. Regardless of dose of the 3rd stage larvae employed, the BUF strain always developed the lowest acquired resistance within each experimental group (Tables 1 and 2). These data plus generally high worm recovery rate for primary infection (Tables 1 and 2) are indicative that among 8 strains of rats, at least, BUF is most susceptible to *A. cantonensis*. It is also of interest to note that the ACI strain yielded the lowest recovery rate for primary infection in each experimental group (Tables 1 and 3), and acquired poor resistance (Table 3). In contrast, the development of *A. cantonensis*, especially in challenge infection, seems to be poor in Tokyo strain, when one considers the facts that this strain yielded a slightly longer prepatent period for a primary infection (Exp. III), the highest protective immunity within each experimental group (Tables 2 and 3), and the delayed migration of intracranial young adult worms into the lungs (Table 3). Likewise, the NIG strain acquired considerably high resistance following primary infection (Tables 1–3).

A transient IgE production, with a peak PCA titer at 5 weeks postinfection, has been well documented in *A. cantonensis* infected rats [20, 22] but no typical anamnestic responses have been found in these rats [22]. However, the present study established that inbred rat strains differ markedly in their patterns of IgE production following primary infection whereas the kinetics of IHA antibody response is essentially the same in all strains. Some strains such as Tokyo, W/Ms and NIG, indeed, are capable of inducing a secondary immune response following challenge infection as well. In Tokyo strain exposed to 55 infective larvae, reagin became detectable in early stages of infection (3 weeks postinfection) and high PCA titers lasted for a long period of time (Fig. 4). In similarly exposed ACI, however, reagin antibody was absent throughout the course of the primary infection (Fig. 4). Even when reagin was produced in ACI following a primary infection, it occurred only at later stages of infection (9 weeks postinfection) (Fig. 1). The remaining strains showed various intermediate patterns of reagin antibody responses. In BUF, for example, only a transient and low titer reagin production occurred (Figs. 1 and 2). All of these data are suggestive that genetic factors would possibly be involved in reagin antibody production in rats infected with *A. cantonensis*. Similar strain differences in reagin production have also been found in inbred rats experimentally immunized with ovalbumin or hapten-protein conjugates [7, 8, 12, 15, 19]. In helminthic infections, furthermore, such differences have been documented in inbred mouse strains infected with *T. spiralis* [9]. To the contrary, Rousseaux-Prevost et al. [11] have reported that no differences in pattern of IgE production, as measured by radioimmunoassay, were found in four

strains of inbred rats infected with *Schistosoma mansoni*, though there were significant differences in basal serum IgE levels between these strains of rats.

The present data demonstrate that, in general, low levels of reagin responses and low titers of IHA antibody were found in both BUF and ACI strains whose levels of acquired resistance were also low. Conversely, a persistent reagin production and high titers of IHA antibody were observed in Tokyo strain in which level of acquired resistance was high. These observations may be suggestive of a possible association between humoral immune responses and host resistance to challenge infection, although Yoshimura et al. [18] have recently reported that the acquired resistance induced in outbred Wistar rats by infection with *A. cantonensis* or by such an infection intermitted with anthelmintic treatment could not be explained simply by the difference in appearance of reagin, IHA or precipitating antibodies. Recently, it has been found that in guinea pig, an abnormal host for the parasite, delayed hypersensitivity (DH) to *A. cantonensis* infection could be induced more readily than circulating antibodies [17, 21]. Therefore, it might be necessary to assess not only humoral immune but DH responses for better understanding the acquired resistance in BUF, ACI and Tokyo strains.

The ACI and NIG strains differed in their pulmonary pathology to *A. cantonensis* infection. A marked fibrotic reaction was found around the pulmonary egg granulomas (Fig. 8) in NIG strains which yielded high titers of IHA antibody. Contrarily, no discernible fibrosis could be noted in similar lesions of ACI strain (Fig. 9) in whom reagin and IHA antibody responses were rather low. It is still unknown whether differences in pathological changes are closely

associated with host immune responsiveness, including DH or cell-mediated immunity. Nevertheless, both strains would serve as useful models for understanding a possible relationship between pathological reactions and host immune responses.

Only in Tokyo strain, the sex ratio of worms from challenge infection was strongly biased in favor of female worms (Table 3). The reason for this is still not known. It seems unlikely, however, that the bias of the sex ratio occurred owing to the unbalance of the ratio in the population of the infective larvae used, since such a great bias was not observable in other strains. Alternatively, it may be considered that in challenge infection, the male worms died due to unknown reason and thus, more females remained. Jenkins and Phillipson [4, 5] have reported that a low-level trickle infection of rats with *Nippostrongylus brasiliensis* resulted in bias of the worm sex ratio in favor of the female worms, and suggested that the female worms would possibly be suited to life in an immune host. Similar adaptation of the female worms to the host immune response may occur in Tokyo strain, since immune responsiveness was rather high in this strain. It must be stressed, however, that such a bias of the worm sex ratio was not observable in Experiment II where the rats had been primarily exposed to a smaller dose of the 3rd stage larvae. Further experimentation, using more animal individuals and a variety of immune conditions, is therefore required to draw a definite conclusion as to the unbalance of worm sex ratio in Tokyo strain.

In conclusion, the present study provided a base line data on immunogenetic studies of *A. cantonensis* infection in rats. Hence, the subsequent examinations on F_1 , F_2 hybrids of BUF, ACI and Tokyo strains as well as on their backcross progeny would

serve to gain insight into the genetic control of host resistance and immune responsiveness in *A. cantonensis* infected rats.

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要 約

8 系統の近交系ラットにおける広東住血線虫に対する獲得免疫産生と免疫応答の比較：吉村堅太郎・合場広子（順天堂大学医学部寄生虫学教室），平山中巳（麻布獣医科大学寄生虫学教室），吉田俊秀（国立遺伝学研究所細胞遺伝部）——8 系統（ACI/N, Buffalo, Lewis, NIG III, Tokyo, Wistar-King-A, Wistar-King-S, Wistar/Mishima）の近交系ラットに広東住血線虫（*Angiostrongylus cantonensis*）を感染させ，10週後に攻撃感染を行ない，攻撃感染防御能，ならびにレアギン抗体と間接血球凝集（IHA）抗体の産生能を比較した．その結果，Buffalo と ACI/N では他の系統より攻撃感染防御能が低く，これに対して Tokyo と NIG III では防御能の高いことがわかった．残りの4 系統も多かれ少かれ獲得免疫を産生したが，その程度は前述の4 系統の中間的なものであった．本虫の感染に対するレアギン抗体の産生パターンには系統間で著しい差異が認められた．すなわち，Tokyo はレアギン抗体の high responder であり，ACI/N は low responder であった．一方，IHA 抗体の産生パターンは系統間で酷似していた．しかし，Tokyo や NIG III では一般に他の系統より IHA 抗体価が高かった．ACI/N と NIG III について肺の病変を比較したところ，ACI/N では肺の虫卵結節周囲に線維化がほとんど認められず，このことは NIG III との著しい相違点であった．以上の成績は，広東住血線虫感染に対するラットの攻撃感染防御能やレアギン抗体産生能は遺伝的支配を受けていることを示唆するものと思われる．

Explanation of Figures

Fig. 6. Lung of NIG rat, showing the adult worms in the pulmonary artery. Note the hypertrophic intima and the parietal thrombus inside the artery. The adventitia and its adjacent areas are intensively infiltrated with masses of neutrophils, and with some eosinophils, plasma cells and histiocytes. H-E. $\times 67$.

Fig. 7. Lung of ACI rat. Note the proliferation of endothelial cells of the pulmonary artery and slight infiltration of plasma cells and lympho-

cytes at the adventitia. H-E. $\times 67$.

Fig. 8. Lung of NIG rat, showing egg granulomas in the lung parenchyma. Note the extensive proliferation of fibrous tissues around the masses of developing eggs (cf. Fig. 9). H-E. $\times 168$.

Fig. 9. Lung of ACI rat, showing nodules of developing eggs in the lung parenchyma. Note the marked congestion or hemorrhage around the masses of eggs (cf. Fig. 8). H-E. $\times 168$.