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学位論文内容の要旨
Abstract of the dissertation

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学位論文題名
The title of the doctoral dissertation

Profiling of cellular immune responses to *Mycoplasma pulmonis* infection in C57BL/6 and DBA/2 mice
(C57BL/6 マウスと DBA/2 マウスにおける *Mycoplasma pulmonis* 感染に対する細胞免疫反応のプロファイリング)

Mycoplasma infections cause respiratory tract damages and atypical pneumonia, resulting in serious problems in humans and animals worldwide. *Mycoplasma* species, particularly *Mycoplasma pulmonis (M. pulmonis)* is an important pathogen involved in microbiological test items of specific pathogen-free rodents, because it causes pneumonia after infection in rodents. As a result, *M. pulmonis* has significant impact on research using rodents. Previous studies with different inbred mouse strains showed various susceptibilities to this bacterial infection. For instance, infected C57BL/6 (B6) mice have bacterial load in their lungs 100,000 times lower than DBA/2 (D2) mice as well as lower gross lung lesions and lung histopathological lesions. However, the profiling of cellular immune responses and the genetic loci or genes responsible for the resistance/susceptibility to the infection are still little known.

In Chapter 1, the cellular immune response was examined by using two inbred mouse strains, B6 (resistant) and D2 (susceptible), to exhibit the profiling of the infection by observing disease-associated phenotypes such as lung histopathological lesions, propagation of bacteria in lung, lung cytological change, cytokine levels in BALF, and areas of lymphoid clusters (LCs) in mediastinal fat tissues (MFTs). D2 mice constantly had

much greater number of colony-forming unit (CFU) of *M. pulmonis* in their lung, greater severity of lung lesions, higher pulmonary infiltration of immune cells, and higher levels of cytokines in BALF. This study first examined and complied the cellular immune responses from *M. pulmonis* infection in B6 and D2 mice. These results suggest that D2 mice are more susceptible than B6 mice to *M. pulmonis* infection due to a hyper-immune inflammatory response.

In Chapter 2, quantitative trait locus (QTL) analysis was performed using the infected phenotypes (in Chapter 1) that showed the difference between infected B6 and D2 mice as quantitative traits (QTs) to dissect genetic factors regulating the difference between these two inbred strains. Detected QTLs were different each other depending on QTs used. These data suggest that the difference in each phenotype between infected B6 and D2 is attributed to different genetic factors. However, only when body weight change was used as a QT, a significant QTL was detected on chromosome (Chr) 4. The peak signal for this QTL was at *D4Mit42* located at 151.6 Mbp with 3.6 LOD score, which mapped to the distal region of Chr 4, residing within 17.1 Mbp between *D4Mit54* and *D4Mit256*. This region included some candidate genes that might be involved in *M. pulmonis* infection. Further study of this locus may provide insights into therapeutic strategy for murine respiratory mycoplasmosis.

In conclusion, from this study, the profiling of cellular immune response to *M. pulmonis* infection in B6 and D2 mice was established. These data provided the better understanding of immune systems that response to the infection and would benefit to the identification of genetic loci and genes responsible for the host defense to the *M. pulmonis* infection. Moreover, the result may be extrapolated to mycoplasmosis in other animals including human.