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C1qa deficiency in mice increases susceptibility to mouse hepatitis virus A59 infection

Han-Woong Kim [1,2], **Sun-Min Seo** [1], **Jun-Young Kim** [1,3], **Jae Hoon Lee** [4], **Han-Woong Lee** [4], **Yang-Kyu Choi** [1,*]

[1]Department of Laboratory Animal Medicine, College of Veterinary Medicine, Konkuk University, Seoul 05029, Korea
[2]Regenerative Dental Medicine Institute, Hysensbio, Gwacheon 13814, Korea
[3]Green Cross Corporation, Yongin 16924, Korea
[4]Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University, Seoul 03722, Korea

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***Corresponding author:**
Yang-Kyu Choi
Department of Laboratory Animal Medicine, College of Veterinary Medicine, Konkuk University, 120 Neungdong-ro, Gwangjin-gu, Seoul 05029, Korea.
E-mail: yangkyuc@konkuk.ac.kr

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ORCID iDs
Han-Woong Kim
https://orcid.org/0000-0001-7542-3575
Sun-Min Seo
https://orcid.org/0000-0001-7543-846X
Jun-Young Kim
https://orcid.org/0000-0002-4948-6860
Jae Hoon Lee
https://orcid.org/0000-0001-9777-5918
Han-Woong Lee
https://orcid.org/0000-0001-9515-3605
Yang-Kyu Choi
https://orcid.org/0000-0002-4969-5443

ABSTRACT

Background: Mouse hepatitis virus (MHV) A59 is a highly infectious pathogen and starts in the respiratory tract and progresses to systemic infection in laboratory mice. The complement system is an important part of the host immune response to viral infection. It is not clear the role of the classical complement pathway in MHV infection.
Objectives: The purpose of this study was to determine the importance of the classical pathway in coronavirus pathogenesis by comparing *C1qa* KO mice and wild-type mice.
Methods: We generated a *C1qa* KO mouse using CRISPR/Cas9 technology and compared the susceptibility to MHV A59 infection between *C1qa* KO and wild-type mice. Histopathological and immunohistochemical changes, viral loads, and chemokine expressions in both mice were measured.
Results: MHV A59-infected *C1qa* KO mice showed severe histopathological changes, such as hepatocellular necrosis and interstitial pneumonia, compared to MHV A59-infected wild-type mice. Virus copy numbers in the olfactory bulb, liver, and lungs of *C1qa* KO mice were significantly higher than those of wild-type mice. The increase in viral copy numbers in *C1qa* KO mice was consistent with the histopathologic changes in organs. These results indicate that *C1qa* deficiency enhances susceptibility to MHV A59 systemic infection in mice. In addition, this enhanced susceptibility effect is associated with dramatic elevations in spleen IFN-γ, MIP-1 α, and MCP-1 in *C1qa* KO mice.
Conclusions: These data suggest that *C1qa* deficiency enhances susceptibility to MHV A59 systemic infection, and activation of the classical complement pathway may be important for protecting the host against MHV A59 infection.

Keywords: Mouse hepatitis virus; classical complement pathway; knockout mouse; CRISP

INTRODUCTION

Mouse hepatitis virus (MHV) constitutes a group of betacoronaviruses and is commonly used as a model to study coronavirus entry, replication, and pathogenesis [1,2]. Many MHV strains can infect laboratory mice. MHV may be transmitted by aerosols, fomites, or direct contact

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