International Journal of
Clinical & Medical Microbiology

Commentary Open Access

[*Pasteurella*] *pneumotropica* as a Potential Mouse Infection Model for Assessment of Substantial Opportunistic Bacterial Infections

Hiraku Sasaki[1*], Hidehiro Ueshiba[2], Eiichi Kawamoto[3] and Ron Boot[4]

[1]*Laboratory of Microbiology and Hygiene, Department of Health Science, School of Health and Sports Science, Juntendo University, Inzai, Chiba 270-1695, Japan*

[2]*Institute of Laboratory Animals, Tokyo Women's Medical University, Shinjuku, Tokyo 162-8666, Japan*

[3]*Animal Research Center, Tokyo Medical University, Shinjuku, Tokyo 160-8402, Japan*

[4]*National Institute of Public Health and the Environment, Antonie van Leeuwenhoeklaan 9, 3721 MA Bilthoven, the Netherlands*

[*Pasteurella*] *pneumotropica* (Pp) is a gram-negative respiratory pathogen that commonly colonizes laboratory rodent species. Infected immunocompetent animals exhibit no clinical signs; however, this bacterium can cause a broad range of infections in immunodeficient and immunosuppressed rodents, from relatively mild diseases to life-threatening pneumonia [1]. Thus, infections caused by Pp are an issue in the management of laboratory rodents.

Recently, the draft genome sequences of Jawetz and Heyl biotypes of Pp has been reported [2,3]. With respect to putative virulence-associated genes possibly involved in pathogenicity, hemagglutinins, adhesins, hemolysins, type VI secretion proteins, RTX exoproteins [4,5], and outer membrane components were identified in both biotypes of Pp. Almost all of these factors have been biologically and molecularly characterized in human or animal pathogens.

In immunocompetent mice, Pp colonizes the oral cavity, upper respiratory tract, conjunctiva, intestines, and vagina without typical clinical signs. According to Patten et al. [6], chronic infection caused by Pp induced upregulation of selected inflammatory cytokines in C57BL/6 mice. Against that background, Pp infection might be considered a robust model to study bacterial infections in mice. Co-infection of severe acute respiratory syndrome coronavirus and Pp induced exacerbated pneumonia in mice, resembling that found in humans [7]. Further, there are no endodontic pathogens specific for laboratory rodents, and therefore oral Pp infection is used as a mouse endodontic model [8]. Similarly, the oral infection caused by the bacterium that is genetically related to Pp is suggested to be a potential periodontitis in a murine ligature-induced disease model [9].

Immunological studies showed that recombinant outer membrane proteins (OMPs) homologous to the OMPs of *Haemophilus influenzae* protected mice from pneumonia [10]. Multiple intranasal immunizations with recombinant PnxIIIA protein successfully elicited PnxIIIA-specific secretory IgA and defended mice against opportunistic infection by Pp [11]. These studies not only focused on prevention of Pp infection in mice but also on a broad perspective of vaccination strategies as a countermeasure against important human opportunistic pathogens.

The Pp infection model has become a substantial infection model for assessment of responsible infectious agents in mice, even though there are still issues to be addressed. For instance, diversified genetic and biochemical properties of Pp in wild-type strains, and in particular, the significant differences in various characteristics between mouse and rat isolates [12-14] might make this model unsuitable for studies, depending on experimental conditions. Furthermore, some virulence factors associated with the host pathophysiology are not exhaustively identified. These relationships involving strain diversity and bacterial virulence need to be clarified in future studies.

Publication History:

Received: November 24, 2016
Accepted: December 17, 2016
Published: December 19, 2016

Keywords:

[*Pasteurella*] *pneumotropica*, Mouse infection model, Opportunistic infection

In general, Pp is the causative agent of rodent pasteurellosis; however, Pp infections have been reported in various hosts, including humans and non-rodent organisms. Either of these cases were thought to be based on misclassification due to the commercial systems for identification. In any cases,the isolates were assumed to be identified as Pp or closely related species in *Pasteurellaceae*. Cases of systemic or local infection caused by Pp or Pp-like pathogens in humans with underlying diseases, who have contact with household pets, have been described [15,16]. Even though Pp is usually considered an exceptional human pathogen, reported cases suggest that its ability to infect humans should not be underestimated.

Competing Interests

The authors declare that there is no competing interest.

References

1. Kawamoto E, Sasaki H, Okiyama E, Kanai T, Ueshiba H, et al. (2011) Pathogenicity of Pasteurella pneumotropica in immunodeficient NOD/ShiJic-scid/Jcl and immunocompetent Crlj:CD1 (ICR) mice. Exp Anim 60: 463-470.
2. Sasaki H, Ishikawa H, Asano R, Ueshiba H, Matsumoto T, et al. (2014) Draft Genome Sequence of the Rodent Opportunistic Pathogen Pasteurella pneumotropica ATCC 35149T. Genome Announc 2: e00771-14.
3. Sasaki H, Ishikawa H, Terayama H, Asano R, Kawamoto E, et al. (2016) Identification of a virulence determinant that is conserved in the Jawetz and Heyl biotypes in [Pasteurella] pneumotropica. Pathog Dis 74: ftw066.
4. Sasaki H, Ishikawa H, Sato T, Sekiguchi S, Amao H, et al. (2011) Molecular and virulence characteristics of an outer membrane-associated RTX exoprotein in Pasteurella pneumotropica. BMC Microbiol 11: 55.

[*]**Corresponding Author:** Dr. Hiraku Sasaki, Laboratory of Microbiology and Hygiene, Department of Health Science, School of Health and Sports Science, Juntendo University, 1-1, Hiragagakuendai, Inzai, Chiba 270-1695, Japan, Tel: +81-476-98-1001; E-mail: hirakus@juntendo.ac.jp

Citation: Sasaki H, Ueshiba H, Kawamoto E, Boot R (2016) [*Pasteurella*] *pneumotropica* as a Potential Mouse Infection Model for Assessment of Substantial Opportunistic Bacterial Infections. Int J Clin Med Microbiol 1: 115. doi: https://doi.org/10.15344/2456-4028/2016/115

5. Sasaki H, Kawamoto E, Tanaka Y, Sawada T, Kunita S, et al. (2009) Identification and characterization of hemolysin-like proteins similar to RTX toxin in Pasteurella pneumotropica. J Bacteriol 191: 3698-3705.

6. Patten CC Jr, Myles MH, Franklin CL, Livingston RS (2010) Perturbations in cytokine gene expression after inoculation of C57BL/6 mice with Pasteurella pneumotropica. Comp Med 60: 18-24.

7. Ami Y, Nagata N, Shirato K, Watanabe R, Iwata N, et al. (2008) Co-infection of respiratory bacterium with severe acute respiratory syndrome coronavirus induces an exacerbated pneumonia in mice. Microbiol Immunol 52: 118-127.

8. Silva MJ, Kajiya M, AlShwaimi E, Sasaki H, Hong J, et al. (2012) Bacteria-reactive immune response may induce RANKL-expressing T cells in the mouse periapical bone loss lesion. J Endod 38: 346-350.

9. Darzi Y, Jiao Y, Hasegawa M, Moon H, Núñez G, et al. (2016) The Genomic Sequence of the Oral Pathobiont Strain NI1060 Reveals Unique Strategies for Bacterial Competition and Pathogenicity. PLoS One 11: e0158866.

10. See SB, Thomas WR (2013) Protective anti-outer membrane protein immunity against Pasteurella pneumotropica infection of mice. Microbes Infect 15: 470-479.

11. Sasaki H, Ishikawa H, Kojima K, Itoh M, Matsumoto T, et al. (2013) Intranasal immunization with a non-adjuvanted adhesive protein descended from Pasteurella pneumotropica and its preventive efficacy against opportunistic infection in mice. Vaccine 31: 5729-5735.

12. Boot R (2010) A Pasteurella pneumotropica strain of mouse origin colonizes rats but is out competed by a P. pneumotropica strain of rat origin. Scand J Lab Anim Sci 37: 261-265.

13. Sasaki H, Kawamoto E, Okiyama E, Ueshiba H, Mikazuki K, et al. (2006) Molecular typing of Pasteurella pneumotropica isolated from rodents by amplified 16S ribosomal DNA restriction analysis and pulsed-field gel electrophoresis. Microbiol Immunol 50: 265-272.

14. Sasaki H, Kawamoto E, Tanaka Y, Sawada T, Kunita S, et al. (2009) Comparative analysis of Pasteurella pneumotropica isolates from laboratory mice and rats. Antonie Van Leeuwenhoek 95: 311-317.

15. Rimoldi SG, Pagani C, Di Gregorio A, Palazzin A, Romano P, et al. (2016) Pasteurella spp. in knee mega prosthesis infection: a case report. Int J Clin Med Microbiol 1: 105.

16. Tirmizi A, Butt S, Molitorisz S (2012) First reported case of Pasteurella pneumotropica tricuspid valve endocarditis. Int J Cardiol 161: e44-45.