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Mycobacterial Diseases

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Perspective

Mouse Models of Experimental Tuberculosis in ABSL-3 Conditions and Assessment of Animal Welfare

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DESCRIPTION

Mycobacterium tuberculosis (Mtb) is the causative agent of human tuberculosis, a disease that is estimated to cause 1.5 million deaths a year. Although tuberculosis is primarily a pulmonary disease, the bacterium can infect and cause disease in almost all organs and tissues. In our understanding of tuberculosis, animal models provide many advantages including the pathogenesis, pathology, and immunology of this disease. The complex spectrum of disease caused by Mtb in humans, makes modeling tuberculosis accurately in animals a challenge. In general, most experimental animals are susceptible to infection with Mtb such as mouse, rabbits, guinea pigs, monkeys and fish. However, modeling the human infection and disease in animals can be difficult, and interpreting the data from animal models must be done carefully, because every animal model has limitations and advantages. Besides, animal models of tuberculosis which should be studied under biosafety level (BSL) 3 measures, do not only require due diligence in the establishment of an ideal animal model but also due care in regard to laboratory workers' health and environmental health. The mouse model is the most commonly used animal model in tuberculosis research. The ease of manipulation and housing conditions, inbred strains, microbiologically and genetically altered strains has made it the most advantageous animal that is used in infectious disease models. Compared to other animal models, mouse is relatively inexpensive and easy to house, especially under Animal Biosafety Level (ABSL) 3 conditions. Besides, reagents available for immunologic analyses such as flow cytometry, cytokine measurement, and immunohistochemistry as well as for in vivo manipulation of the host (e.g., antibodies for depleting cells) are easily provided. A range of inbred mouse strains, Mtb strains, bacterial doses, and routes of infection have an effect on experimental design in the murine model. Granulomas in resistant mice are well organized, consisting of aggregated lymphocytes and macrophages.

Aerosol infections are the most common route for introducing Mtb into mice. Intravenous (I.V.), intratracheal (I.T.), intranasal (I.N.) and intraperitoneal (I.P.) administration are other routes. There are major differences between these routes. Specifically, delivering Mtb to the lungs directly is more physiologically appropriate, as most humans are infected via the respiratory route. An added complication of i.v. infection is the systemic administration of bacteria that causes priming of T cells in numerous lymphoid tissues. There is a dissemination of bacteria to the mediastinal lymph nodes, probably within dendritic cells, Mtb-specific CD4 and CD8 T cells infiltrate the lungs in response to infection, beginning at about 2 weeks.

CONCLUSION

The mouse model of tuberculosis, basic elements of quality assurance in animal experiments which are appropriate animal model, laboratory workers' health and animal welfare concepts are discussed together in this article. It is essential to practice good microbiological techniques and adapt the study principles of ABSL-3 laboratories at every step of experimental study. Accurate interpretation of research results can only be possible by an effective experimental design, compliant with the disease pathogenesis. Furthermore, as it is the case in all the experimental animal studies, it is the responsibility of the researcher to act within ethical principles and give priority to animal welfare. It should never be ignored that animals are sensitive living creatures with intrinsic values.

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