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REVIEW ARTICLE

Model Systems for Pulmonary Infectious Diseases: Paradigms of Anthrax and Tuberculosis

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Abstract: Robert Koch utilized animal model systems to put forward his postulates while discovering the etiological agents of anthrax and tuberculosis, *Bacillus anthracis* and *Mycobacterium tuberculosis*, respectively. After more than 130 years, we have achieved limited success towards understanding these two pestilences, which have propagated as scourge against humans. *B. anthracis* and *M. tuberculosis* are diverse organisms, which share a common evolutionary path in tropics. They adapt unique strategies to overcome unfavorable conditions and surpass the host defense mechanisms. *B. anthracis* is an endospore forming bacteria that primarily acts by releasing toxins in the host cells.. *M. tuberculosis* is an intracellular bacteria that resides within the host macrophages by blocking phagosome-lysosome fusion events and ensuring its own survival. The bacterium can remain dormant for long periods, and when activated, it spreads in lungs and other extrapulmonary sites leading to formation of necrotic granulomas. The two diseases are immunologically distinct examples of inducing primarily either humoral or cell mediated immunity. Natural immune response to the two diseases probably explains early success achieved with the anthrax vaccine, while the hunt for successful tuberculosis prevention is still on. For comprehensive understanding of these diseases, model systems are of utmost importance that can alleviate detailed assessment of disease etiology and introductory treatment regimes. In this review, we discuss the various *in vitro* and *in vivo* model systems used to study these two diseases, discussing their contributions and recent themes.

Keywords: *Bacillus anthracis*, *Mycobacterium tuberculosis*, cell lines, zebrafish, mice, guinea pig, rabbit, non-human primates, human subjects.

1. INTRODUCTION

Globalization and changing demographic trends have acted as catalysts for rapid spread of various infectious diseases. In most of the cases, the infected individuals are too vulnerable to provide the samples for clinical research purposes, during the course of infection. To elaborate our understanding of underlying detailed mechanisms various model systems are used that mimic the disease etiology. In this era of big data driven science, model systems need to simulate the course of disease, but must be easy to manage and give results that closely replicate the natural infection in primary host. They are important for understanding the mechanism of disease spread and the associated phenotype as well as to explore the effects of new vaccines and antimicrobial compounds. Practically, no model is perfect and can substitute the information obtained from studying human samples. Nevertheless, the essentiality of developing various model systems has been reiterated over the years. The models used for research purposes are the cell lines, either the secondary cancer cell lines or the primary cells extracted from animal tissues. Among the lower animal group, mice, guinea pigs and rabbits are the most commonly used models, mainly because of the close genetic homology with humans, easy handling and availability of reagents. Non-human primates (NHPs) are the superior models that replicate etiology of the human disease very closely. Choice of model system in a study is based on a list of selection criteria which includes relatedness of disease etiology [1], number of required replicates, infrastructure, ease of vaccine administration and follow-up feasibility [2], and anti-microbial drug efficacy [3,4]. So, the purpose to get results as closer as possible to natural response in humans often requires use of multiple models for one study (Fig. **1**).

Model systems are of great importance for the contagious diseases that spread readily within the population. Anthrax and tuberculosis are two such diseases that target pulmonary system causing fatal airborne infections and spread in the human and animal populations. Both these infectious diseases have been studied extensively from last century and a

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