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Mouse Models in Vaccinology: Advancements and Applications

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ABSTRACT

Testing drugs in humans before they are proven safe is ethically prohibited. Immunologists face these barriers to bring vaccines and other treatments from labs to humans, thus using disease models to prove the safety and efficiency of vaccines is considered. Animal models used to develop vaccines must be useful to observe the primary immune responses underlying natural and acquired immunity. Mice are well-studied species as they have been used in research for more than a century. Mice share mammalian characteristics with humans and are vulnerable to many of the same diseases that infect humans. Through genetic manipulation, mice can be used to mimic any particular human infection or illness. Mice are easy to look after and economical to purchase.

Introduction

Although there are many types of animal models for various diseases, the mouse is considered more useful and validating. The information about immunogenicity, toxicity, and vaccine-induced protection. There is still a lot to be answered in terms of vaccine formulations of therapeutic importance. Animal models of infections are designed to predict the efficacy and safety of new candidate vaccines. We are now approaching an era where several vaccines are undergoing prolonged clinical evaluation, but there exists an urge to hurry to get these evaluations and trials done [1]. The role of T cells and mononuclear phagocytes was first demonstrated by the mouse model of *M. tuberculosis* infection [2]. The immune system of humans faced evolutions that were accompanied by pathogenic interactions. Recent research has studied the susceptibility of a disease which was enhanced by balancing selection. It is thought that exposure to pathogens influences the functional outcome of a gene. In this particular case, even mice models carrying human genes and tissues may still fail to mimic human disease. However certain measures like housing environment and bystander infections can lead to designing a model that can effectively mimic that phenotype seen in humans [3]. Studies on immunogenicity and safety based on animal models are the main drivers of vaccine discovery and development [12].

Human And Mouse Physiology:

The physiology of humans and mice is influenced by the microbiome. Changes in the microbiome are related to a wide range of disease states. For example, microbiome alterations are associated with bowel disease, cancer, and obesity etc [4]. It is an important consideration that all associated microorganisms in multiple tissues are referred to as microbiota. While, under predisposing conditions, some microbiota members are potentially pathogenic, and thus classed as pathobionts [5]. Human and mouse physiology is not only determined by genotype. However, there is still a need for more research on the impacts of infections which are bystanders on the disease conditions to study mechanisms. An understanding of the contribution of bystander infections to immune response can help to improve the mouse models of human diseases [6].

Use of Humanized Mice in Vaccine Development:

Murine models have been used in biomedical studies to develop vaccines and drugs [7]. Mouse models that integrate various humanized compartments give rise to questions that can be answered. For example, mice with the immune system of humans and lung tissue supplemented from humans could be used as a model for Tuberculosis or CMV (cytomegalovirus). Mice grafted with tissue effectively favoring various pathologies can be used to conduct a preclinical evaluation of vaccine potency, and the efficiency of pharmacological studies of therapeutics could be examined in a tissue. To further address the process of consistency of highly specialized pathogens, immune and tissue subsets are combined. HCV (Hepatitis C) is such distinct human liver-tropic virus with few treatments available. An HCV immune response can be evaluated by a humanized mouse model that helps in providing vast application in studying the relationship between HCV and host. With the successful integration of humanizing mouse techniques into vaccine and drug development, the technology must be vastly reachable and permit the generation of many animals at an economical cost. Designing mice models is demanding and it not only needs modern engineering skills but also an intricately designed setup. Wide-scale production of humanized mice can be a practical and economical solution [8].

Mouse Models in Novel Cancer Therapeutics:

The use of genetically modified cancer-prone mice in creating clinical applications is an unproven assumption. There is hope that a new generation of mouse models will provide great value in predictive utilization in the methods of vaccine and drug development [9]. Mouse models are a good substitute for conventional preclinical essays. They can address many complications of assays which are cell-based when designed properly. They provide a source of *in situ* tumor growth in an immune-potent animal setting. Not all models are good for conducting preclinic drug testing [Fig.1].

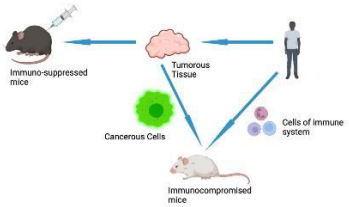

Figure 1. Immunotherapy Mouse Model for Cancer

There is hesitancy in the general acceptance of these models as tools to conduct preclinical tests due to non-uniform results obtained in the past. Viral and cellular oncogenes are ectopically expressed by transgenic mice, the first five types of genetically engineered mouse models created [10]. The most desired models for preclinical modelling are those that can alter endogenous genomes to impact the mutation that copies the condition of tumors. These belong to alleles in which genes are removed, also the genes are mutated, which favors subtle mutations in endogenous locus. Both alleles are important for modelling inherited tumors due to the loss of one copy of a tumor-suppressor gene [11].

Immuno-contraceptive Vaccines:

These vaccines may be a substitute for surgical sterilization. For the prevention of rabies, dual rabies vaccination and dog population control are helpful tools. The early accomplishment of immunocontraception in mice is promising, and vaccine development is currently being optimized using adjuvants and discovering new methods of administration to reduce dosage [13]. Proper management of animals is important to cut short zoonoses, like rabies. The effective elimination of canine rabies can be achieved by persistent strategic utilization of safe and potent vaccines. The efforts to vaccinate dogs against rabies could be made easier by adopting novel techniques [14]. Street dogs create concerns regarding their effects on wildlife, the public, and agriculture [15].

mRNA Vaccines:

mRNA vaccines are a promising substitute for traditional vaccine strategies because of their high potency. They can be developed rapidly and be administered safely. However, due to recent instability in the *in vivo* administration of mRNA, their use has been reduced. These issues have been resolved to a great extent by novel technological advancements, and many mRNA vaccine setups against infectious diseases and various forms of cancer have exhibited encouraging results in both animal models and humans [16].

Future Perspectives:

Significant future strategies of research will be to mimic the pathways of the human immune system through various mRNA vaccine setups, to enhance the present directions based on these mechanisms, and to start novel testing for

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multiple targeted diseases. Improvement of new production processes through therapeutic considerations and overcoming challenges to further document the increasing efficacy and safety. Dendritic cell vaccines and various directly administered mRNA are diverse approaches to vaccines against cancer. These approaches have been used in many trials and proved efficient and in some cases, long-term survival is observed [17].

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