

Limitations of Animal Models of Infection

While the utility of the animal models described above, as well as hundreds of other, has been made clear by the identification of numerous therapeutic agents, there are some important limitations that should be kept in mind. First, many infectious diseases are host limited. Species-specific interactions between microbial ligands and host receptors are a significant part of the disease process that is often not replicated in an animal model of human infectious disease. Transgenic science is capable of “humanizing” animals to improve their correlation with the human condition, but they are still only an approximation of a human host. In a similar manner, there may be differences between the clinical and laboratory strains of an infectious agent. Although laboratory strains generally originate from primary clinical isolates, careful growth, enrichment, and selection are required to produce biological samples suitable for laboratory experiments. This process may evoke changes in gene expression and causes the infectious agent to adapt to growth in an artificial media. Laboratory monocultures can be significantly different from the clinical isolates that grow in a complex and dynamic environment (the human body).

Finally, while transmission pathways can play an important role in disease progression, very few animal models take this into account. Unique pathogenic phenotypes may result from the residence of an infectious agent in a particular microenvironment. Naturally occurring infectious diseases begin with an initial introduction of an infectious organism (via ingestion, inhalation, etc.), continue with a period of replication establishing the infection in the host, and then an exit from the host for transmission to the next host. In contrast, most animal models of infectious disease introduce an infectious agent at a high dose with a needle and syringe. Clearly, this method of introduction is very different from the natural life cycle of infectious organisms and could have a significant impact on the validity of the data acquired in an animal study.⁴⁹

ANIMAL MODELS OF ONCOLOGY

According to the International Agency for Research on Cancer (IARC), there were 12.7 million new cancer cases and 7.6 million cancer-related deaths in 2008 worldwide. These figures are expected to grow to 21.4 million new cases and 13.2 million cancer-related deaths by 2030 as the population grows and ages.⁵⁰ The treatment and prevention of cancer has been and will likely continue to be an important component of the pharmaceutical industry’s pipeline of products and research efforts. Much like infectious diseases, however, cancer is not a single disease, but rather a multitude of related diseases that share some common feature. As a result,