

IV. ANIMAL MODELS

a. Introduction to Animal Models of Human Diseases

Animals are used for studying the biochemistry, molecular biology, and genetics of various diseases, that is, the disease mechanism. Once a suitable animal has been found where the mechanism is similar to that of a corresponding disease in humans, that particular animal may be used as an animal model for testing efficacy of candidate drugs. For oncology, animal models are typically injected with tumor cells. For immune disorders, animals are administered an agent that provokes inflammation. And for infections, animals are exposed to the relevant microorganism or virus.

For these reasons, animal models are described in this chapter. For the sake of continuity, what is also included are specialized topics on animals, such as validation, the Animal Rule, and use of animal data to arrive at doses for humans.

Regulatory approval for drugs requires data on safety and efficacy in animals. While data on safety can be acquired from studies on mice, rats, rabbits, dogs, and primates, with little or no need for correspondence of mechanisms of an

animal disease with mechanisms of a human disease, data on efficacy can only be acquired where there is an available animal model of the disorder in question. Where the goal of the drug is to enhance wound healing, it is easy to find a suitable animal model (all that is needed is to surgically remove a circle of skin from the animal). However, where the goal of the drug is to treat diseases such as cancer, immune diseases, or infections, there is a need to find an appropriate animal model. Brody (74) describes animal models for various diseases, and reveals the criteria needed for an animal model to predict the efficacy of a drug for the disease in humans.

While rodents spontaneously develop various cancers, it is not practical to acquire a group of rodents with the same type of cancer, and at the same stage of the cancer, at the same time. The variety of tumors that occurs spontaneously in rats has been exhaustively documented (75,76).

Separate animal models are available for various types of cancer. Marks (77) identified sources of various animal cancer models. Nandan and Yang (78), Kuperwasser et al. (79), Soda et al. (80), and Noonan et al. (81), discuss animal models for colorectal cancer, breast cancer, nonsmall-cell lung cancer, and melanoma, respectively.

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⁷⁷Marks C. Mouse Models of Human Cancers Consortium (MMHCC) from the NCI. Dis. Model Mech. 2009;2:111.

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⁸¹Noonan FP, Dudek J, Merlino G, De Fabo EC. Animal models of melanoma: an HGF/SF transgenic mouse model may facilitate experimental access to UV initiating events. Pigment Cell Res. 2003;16:16–25.