VALIDITY OF ANIMAL MODELS

Although it is possible to argue the merits and drawbacks of each method of model development, from the standpoint of drug discovery, the source of a model is not nearly as important how well the model recapitulates the human condition. An animal model that does not correlate with a human disease or condition is of little value for the development of novel therapies. In general, animal models can be divided into three categories based on how well they reproduce the human disease or condition, homologous, isomorphic, and predictive.[13] Homologous animal models are the most desirable, as they have the same causes, symptoms, and treatment options available for humans. They are the rarest type, as they are difficult to achieve, but unlike other models they have construct validity. Typical examples include the non-obese diabetic mouse model of type 1 diabetes[5] and numerous bacterial infection models.[14] The majority of animal models are not homologous models.

Isomorphic animal models, on the other hand, are far more common. This type of animal model has the same symptomology as the human conditions and treatment options are generally the same. However, the root cause of the disease or condition in the animal model is not the same as that observed in humans. Consider, for example, animal models of stroke. The ischemic damage caused by a stroke can be experimentally created in an animal model by interfering with brain blood flow.[9] The impact of this interference will certainly be similar to an occlusive event caused by a blood clot in a blood vessel of the human brain, and treatment options will be similar, but the root cause of the stroke is not the same. Similarly, the degenerative damage associated with osteoarthritis can be mimicked by injecting sodium iodoacetate into the joints of an animal. Osteoarthritis begins to develop in 2–4 months, and this model can be used to study the antidegenerative properties of test compounds.[15] This is clearly not how this condition develops in humans, but the symptoms and disease progression make it a suitable model of the human condition. Isomorphic models are considered to have "face validity." In other words, the models have the same overall appearance of the disease state that they are modeling, but are not actually the same.

When homologous and isomorphic models are not available, predictive animal models are employed instead. This class of animal models is most often used when the disease or condition is poorly understood or simply does not occur in animals. In some cases, the animal model itself may have little or no obvious resemblance to the human condition, but there are facets of the model that allow researchers to use it as a predictive tool. The impact of potential therapeutic intervention in the model can be correlated to how humans will respond to the same compound. The model displays the treatment characteristics of the disease or condition