develop two different molecules: the clinical test pharmaceutical agent, and a preclinical test pharmaceutical agent to be used in the preclinical studies on animal species, which has target specificity corresponding to the clinical pharmaceutical agent, and of which safety and such must be examined. The great disadvantage of such a surrogate approach is that the surrogate antibody for the preclinical studies is a modified product of the clinical test antibody pharmaceutical. Therefore, data obtained in preclinical studies using a surrogate antibody may not often be directly applicable to humans. Therefore, the predictability of clinical study results based on preclinical study results using these approaches may decrease.

The above-mentioned approach adapts the test pharmaceutical agent so that it is suitable for the animal used in preclinical studies. On the other hand, other known approaches adapt animals used in the preclinical studies to the candidate pharmaceutical agent to be administered to humans.

An example of adapting a test animal to a test antibody pharmaceutical intended for administration to humans is producing a transgenic animal that expresses the human molecule to which the test antibody pharmaceutical specifically binds instead of the non-human molecule intrinsic to the test animal species. In this method, the test antibody pharmaceutical administered in preclinical studies is expected to bind to a human antigen in the transgenic test animal. For example, in a study conducted by Bugelski *et al.*, preclinical safety evaluation was performed on the monoclonal antibody keliximab using human CD4 transgenic mice to predict long-term treatment of rheumatoid arthritis in human patients. Keliximab is a monoclonal antibody that has specificity to CD4 of humans and chimpanzees. Bugelski *et al.* conclude that the use of a human protein-expressing transgenic mouse provides a useful alternative method to studies conducted in chimpanzees using biological pharmaceuticals that have limited cross-species specificity. However, production of transgenic animals for test purposes is time consuming and costly since it demands a lot of work.

Prior Art Documents

[Patent Documents]

[Patent Document 1] WO2008/047723

[Non-patent Documents]

[Non-patent Document 1] J. Med. Primatol. (1986) 15, 441-451

[Non-patent Document 2] J. Med. Primatol. (2001) 40, 141-147

[Non-patent Document 3] Cancer Immunol. Immunother. ~~(2005) 20, 1-12~~ 2006 May; 55(5): 503-14

[Non-patent Document 4] Hum. Exp. Toxicol. (2000) 19, 230-243