Advantages of Transgenic Rabbit Models

Although the study of many human diseases has benefited significantly from the use of mouse models, *small rodents do not always accurately reflect human physiology*.

Take the cardiovascular system as an example. The length of the mouse's cardiac cycle is only one-tenth of that of the human. Indeed, murine and human hearts differ in several fundamental facets, and these differences are reflected at the molecular levels. For example, the cardiac sarcomere in the mouse consists of the "fast" myosin heavy chain (MHC) isoform a(a-MHC), whereas the "slow" b-MHC is the dominant isoform in the human ventricles. In addition, the high-density lipoproteins (HDL) are the predominant form of lipoproteins in the mouse plasma in contrast to the low-density lipoproteins (LDL) that are predominant in humans, conferring resistance to diet-induced atherosclerosis. Furthermore, mice are too small for any practical applications such as repeated surgeries, monitoring and/or measurements, which are essential for cardiovascular research and practice.

The rabbit would be an ideal choice (Table 1), considering the following: 1) Rabbit ventricles are similar to humans' and both a- and ß-MHC isoforms are expressed with ß-MHC being the predominant isoform in adults; 2) Rabbit lipoprotein metabolism is very similar to that of humans (e.g., LDL-mammals, same as humans), but very different from mice (HDL-mammals); 3) Cholesteryl ester transfer protein (CETP), which plays a central role in the atherosclerotic process, is abundant in both human and rabbit plasma but absent in the mouse; 4) Like humans, rabbits are very susceptible to diet-induced atherosclerosis.

Comparing to mice, rabbits are phylogenetically closer to human. Because of the anatomical, physiological, genetic and biochemical similarities between the rabbit and the human, this species is preferentially used in pulmonary, cardiovascular and metabolic studies, including airway obstructive disease, embolic stroke, arteriosclerosis, cholera, cystic fibrosis, neoplasia, diabetes, acute respiratory distress syndrome, malignant lymphoma, acquired immunodeficiency syndrome and hypercalcemia of malignancy.

As a classical experimental animal species, rabbit has several other advantages over some other animal species (e.g., monkey, pigs). It has a short gestation period (30-31 days), large litter size (4-12/litter) and can be housed conveniently in an indoor facility. In addition to the use as an animal model, rabbit is also used for drug screening, antibody production, and the production of therapeutic proteins (bioreactors). Some proteins can be properly synthesized in rabbit milk, but not in other animal systems (e.g. cattle or goats) due to the post translation processing.

Table 1. Selected Differences of Heart Physiology Between Mouse, Rabbit and Human

	Mouse	Rabbit	Human
Cardiac Sarcomere Composition	alpha-MHC	beta-MHC	beta-MHC
Lipoprotein Profile	HDL-rich	LDL-rich	LDL-rich
CETP	No	Yes	Yes
Dietary Cholesterol	Resistant	Sensitive	Sensitive
Atherosclerosis	Resistant	Susceptible	Susceptible

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