

Animal models in cardiovascular diseases

Editorial

The use of animal models, which can range from mice to even fruit flies,¹ has added to increasing our Understanding and providing new methodologies focused to advance the diagnostic and treatment of certain pathologies. A number of models have been shaped to address cardiovascular complications, however factors such as genetics and environment, play a role in cardiovascular pathophysiology and have made it quite difficult to match a particular disease, with just a single experimental model. The development of animal models of cardiovascular diseases (CVD), including cardiac and atherothrombotic diseases, has provided us today with important insights into the pathophysiology, and they were found to be essential tools to evaluate new therapeutic strategies to predict and to prevent these complications.² Coronary artery ligation is a commonly used model of myocardial infarction for assessing intramyocardial therapeutic delivery of genes, cells or proteins. In this procedure, Zaragoza et al.³ explained that first a thoracotomy is performed on the anesthetized animal, and the heart is rapidly exteriorized by gentle pressure on the right side of the thorax. The coronary artery is either ligated or heat cauterized between the pulmonary artery outflow tract and the left atrium. The heart is then returned to its normal position and the thorax immediately closed.³ There are two main ligation models, permanent left main descending coronary artery (LCA) occlusion to induce a myocardial infarction (MI) and a temporary coronary artery occlusion to induce ischemia/reperfusion injury (IR).⁴ Of course one obvious drawback is that animals have different physiologies than humans,⁵ so as researchers we must take this into consideration. However there are some benefits to this model procedure such as undamaged pectoral muscles, which is significant because these muscles are essential to cover the opening once the heart has been returned to the thoracic space and excludes the stitching of the muscle. In junction with the coronary ligation model, administration of the drug isoproterenol is used since in certain dosages, the drug can cause heart lesions similar to myocardial infarction.⁶

In low dosage, Isoproterenol is used primarily for the treatment of cardiovascular problems such as bradycardia (slow heart rate) or heart block (condition that causes a fault with the SA node due to an obstruction). By the activation of β_1 and β_2 -receptors in the heart, it can induce a chronotropic, dromotropic, and inotropic effect. However, associated with the drug are its negative cardiovascular side effects such as tachycardia or cardiac dysrhythmias. Isoproterenol has been observed to produce certain biochemical, electrophysiological and histological alterations in the heart. In a study done by Jaehnig et al.⁷ and Zhengrong et al.⁸ showed that in rabbits with electrical storm (recurrent multiple ventricular fibrillation episodes associated with myocardial infarction) and ventricular arrhythmia, Isoproterenol was able to prolong action potential duration and increased type calcium current. Thus showing the important role of isoproterenol in the mechanism of cardio electrophysiology. The genetic and physiological similarities between animals, like mice, and humans have focused considerable attention on potential models of human health and diseases.⁹ In the last few decades, there has been generation of genetic animal models to observe disease conditions. Specifically, researchers are now able to use gene alterations which can control

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expression of an animal model used. Using site-specific recombinase (SSR) systems, we can knock out the target gene within a particular cell type at certain developmental phases (conditional knockout).¹⁰ The Cre-lox recombination system is widely used to carry out deletions, insertions, translocations and inversions at specific sites in the DNA. Another successful method used for conditional gene expression is the tetracycline (Tet)-inducible system, which is responsible for the reversibly turning on or off of genes in the presence of the antibiotic tetracycline or its derivatives.¹¹ This system is similar to the Cre-lox systems except for the fact that the Tet- inducible system is reversible (which makes this system an advantage to the Cre-lox system). Gene knockout animal models are proven to be an important component in conjunction with transgenic lines of mice as a means of generating “humanized” mouse models as part of drug discovery strategies.^{9,12-17}

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Conflict of interest

Author declares that there is no conflict of interest.

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