

Preface

There are many patients who are suffering from various types of vascular diseases. Atherosclerosis results in luminal narrowing and insufficient blood perfusion, leading to organ damage such as myocardial infarction, cerebral infarction, and amputation of lower extremities. Atherosclerotic diseases are a leading cause of death in industrialized countries. Obstructive atherosclerotic diseases are treated by percutaneous catheter intervention or bypass surgery, which requires subsequent re-vascularization procedures due to re-stenosis of the target lesion or a bypass graft in many cases. Aortic aneurysm and cerebral aneurysm may cause sudden death by unanticipated rupture. Graft vasculopathy—diffuse intimal hyperplasia in arteries of the transplanted organs—causes graft failure. Moreover, coronary aneurysm is the major sequel of Kawasaki's disease, a mucocutaneous lymph node syndrome in children. Unfortunately, exact pathogenesis of most of the vascular diseases remains to be clarified. Subsequently, there are no established methods to diagnose and prevent those vascular diseases accurately.

Genetically modified mice are a very powerful tool for studying the pathogenesis of various diseases, including immunology, oncology, the central nervous system, autoimmune disease, and congenital diseases. Genetically modified mice also provide good tools to track the origin and the fate of the cells that play a key role in the disease process. However, mice had always been thought to be too small to be used for research in the field of vascular diseases. Most of the models of vascular diseases, which have been used for larger animals, could not be applied to mice.

I have been working as an interventional cardiologist. I treated many patients with coronary artery diseases by performing percutaneous coronary intervention (PCI). However, re-stenosis at the site of PCI limited the long-term prognosis of the treatment in many patients. Therefore, I started research on gene therapy to prevent post-PCI re-stenosis. However, no gene therapy has been shown to be effective enough to be used in clinical practice. When I became an independent researcher in Japan in 1999, I realized that we should clarify the exact pathogenesis of re-stenosis using genetically modified mice. I had a hard time developing a mouse model of post-angioplasty re-stenosis. After many efforts and failures, I finally succeeded in

establishing a mouse model of vascular injury that induces rapid onset of medial cell apoptosis followed by reproducible neointimal hyperplasia like a rat model of balloon-induced arterial injury. With this useful model, I published numerous papers by taking advantage of genetically modified mice to investigate the cell cycle, apoptosis, and origin of neointimal cells. I welcomed all visitors who wanted to learn the method to my laboratory. Moreover, I sent a videotape or CD of the tutorial videos of the procedure. Now, the tutorial videos (Ver. 1 and Ver. 2) can be viewed on the Internet. The method has been adopted successfully in many laboratories in the world and used to elucidate the pathogenesis of post-PCI re-stenosis. The methodological paper published in the *Journal of Molecular and Cellular Cardiology* in 2000 has been cited in 229 papers.

Besides my wire-mediated endovascular injury, other mouse models of vascular diseases have been reported and have substantially contributed to basic research on cardiovascular and metabolic disorders. However, like my wire-mediated vascular injury model, those models are technically very difficult to reproduce in other laboratories, even when researchers carefully read the literature in which the model has been used to analyze genetically modified mice. Many investigators in the vascular disease area have wanted a detailed methodological source to learn how to treat mice to get reproducible vascular lesions in mice.

Under these conditions, I had a chance to edit a book with Springer. I had no hesitation to edit a methodological sourcebook on mouse models of vascular diseases. Covering various areas, each chapter is written by a pioneering researcher who has developed an original vascular disease model. Notoriously difficult to reproduce, each model is described in detail and numerous photographs are provided, with links to videos. There are detailed descriptions about the knacks and pitfalls for each procedure. I hope that this book can be used as a bible in many laboratories that are working on cardiovascular diseases. Finally, I acknowledge all authors for their generosity in providing detailed descriptions of the methods that they had spent tremendous efforts and time to establish.

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