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Editorial

Gene Therapy in the Cardiovascular System

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Cardiovascular disease is the leading cause of mortality in the Western world, and although major progress has been made in the prevention and management of cardiovascular diseases, currently available interventions are often insufficiently efficacious or associated with various adverse effects. Also, most therapies are directed at the consequences (e.g. ischemia) rather than the causes (e.g. atherosclerosis) of the disease. Novel therapies that much more specifically interfere in pathogenetic processes might be of great benefit for prevention and treatment of cardiovascular disorders and the underlying causes.

The transfer of genes into the somatic cells of patients (or: ''gene therapy'') to interfere with pathogenetic processes contributing to cardiovascular disease may provide such a novel approach for better prevention and treatment of cardiovascular disorders [1,2]. Two major developments have importantly contributed to the intense investigation of the potential of gene therapy in cardiovascular medicine: First, the tremendous increment in knowledge on specific pathways and mediators that appear to play pivotal roles in the pathogenesis of cardiovascular disease has provided several therapeutic targets for specific intervention. Second, the amazing advances in molecular biology have provided a dramatic improvement of the technology that is necessary to clinically apply gene therapy.

Gene therapy for cardiovascular disorders is now fast developing and a considerable number of succesful reports on the effects of gene transfer in various animal models are being published. Also, initial clinical studies are being developed or in progress. However, a large number of issues need to be resolved before this approach can further expand, and much research is currently devoted to solve these issues. Hence, the editorial team of *Cardiovascular Research* thought that it might be timely to devote a spotlight issue to the subject of ''Gene Therapy in the Cardiovascular System''. Many thanks should be directed to the guest editors of this spotlight issue, Christophe Bauters, Peter Carmeliet and Hans Pannekoek, who were extremely helpful in soliciting contributions from various outstanding researchers in the field for this special issue and in reviewing the various manuscripts.

This spotlight issue of *Cardiovascular Research* contains several reviews and original articles dealing with the potential and limitations of gene therapy, the identification of ideal genes to interfere with, optimal techniques for gene transfer and transduction of vascular cells and cardiomyocytes, application of gene therapy in different animal models, and potential clinical applications.

Optimal techniques for gene delivery in arteries and local drug delivery systems are being reviewed by Feldman and Steg [3] and by Brieger and Topol [4], and several original articles deal with various viral vectors for gene transfer [5–7]. One of the important limitations of viral gene transfer may be the immunological response to the viral vector. Yap et al. [8] describe how immunosuppression may partly overcome this response. Gene transfer may be helpful for inherited or acquired diseases of the heart, as reviewed in this issue [9,10], and further illustrated by two original contributions [11,12]. A major point of impact for gene therapy is represented by atherothrombotic vascular diseases: Subsequently, the potential of gene therapy for treatment of hypercholesterolemia, arterial thrombosis, and restenosis are reviewed [13–15]. In addition, reports of original studies on transfection of endothelial cells [16], and transfer of the nitric oxide synthase gene, the vascular endothelial growth factor gene, or the GAX gene [17–19], are included. Finally, the subject of gene transfer-induced therapeutic angiogenesis is highlighted in two review articles [20,21].

In summary, this issue of *Cardiovascular Research* reflects the exciting development of gene therapy for a broad spectrum of disorders in the cardiovascular system. Whether these novel therapeutic approaches will be as successful as they promise to be remains to be seen in appropriate clinical trials. However, the exploration of gene transfer in various areas of cardiovascular research will certainly yield an enormous enhancement of the insights in pathogenesis and therapeutic targets in cardio-

vascular disease and the possibilities of molecular genetic technologies in cardiovascular medicine.

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