Gene Transfer Therapy in Vascular Diseases

Mandi J. McKay and Mohamed A. Gaballa

Department of Internal Medicine, University of Arizona Sarver Heart Center and Southern Arizona VA Health Care System, Tucson, AZ, USA

Key Words: Angiogenesis—Atherosclerosis—Gene therapy—Ischemia—Peripheral vascular disease—Restonosis—Thrombosis.

ABSTRACT

Somatic gene therapy of vascular diseases is a promising new field in modern medicine. Recent advancements in gene transfer technology have greatly evolved our understanding of the pathophysiologic role of candidate disease genes. With this knowledge, the expression of selective gene products provides the means to test the therapeutic use of gene therapy in a multitude of medical conditions. In addition, with the completion of genome sequencing programs, gene transfer can be used also to study the biologic function of novel genes in vivo.

Novel genes are delivered to targeted tissue via several different vehicles. These vectors include adenoviruses, retroviruses, plasmids, plasmid/liposomes, and oligonucleotides. However, each one of these vectors has inherent limitations. Further investigations into developing delivery systems that not only allow for efficient, targeted gene transfer, but also are stable and nonimmunogenic, will optimize the clinical application of gene therapy in vascular diseases. This review further discusses the available mode of gene delivery and examines six major areas in vascular gene therapy, namely prevention of restenosis, thrombosis, hypertension, atherosclerosis, peripheral vascular disease in congestive heart failure, and ischemia. Although we highlight some of the recent advances in the use of gene therapy in treating vascular disease discovered primarily during the past two years, many excellent studies published during that period are not included in this review due to space limitations.

The following is a selective review of practical uses of gene transfer therapy in vascular diseases. This review primarily covers work performed in the last 2 years. For earlier work, the reader may refer to several excellent review articles. For instance, Belalcazer et al. (6) reviewed general aspects of somatic gene therapy and the different vehicles used for the delivery of therapeutic genes. Gene therapy in restenosis and stimulation of angiogenesis in the cardiac muscle are discussed in reviews by several investigators (13,26,57,74,83). In another review, Meyerson et al. (43) discuss advances in gene therapy for vascular proliferative disorders and chronic peripheral and cardiac ischemia.