

Forum Editorial

Redox-Modulating Gene Therapies for Human Diseases

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ABSTRACT

Baseline levels of reactive oxygen species (ROS) are generated as an integral component of cellular function. Under certain conditions, *e.g.*, the presence of an elevated concentration of transition metal (Fe/Cu) ions, drug metabolism, or ischemia–reperfusion, ROS generation is exaggerated to an extent that overwhelms cellular antioxidant defenses and results in oxidative stress. Oxidative stress has been characterized by the assessment of oxidative damage to cellular components, *e.g.*, protein, lipid, and nucleic acid. More recent studies have determined that at a concentration much below that required for inflicting oxidative damage, ROS may serve as cellular second messengers through the regulation of numerous signal transduction pathways. For this reason, much of the current medical focus in this area has been directed toward the understanding of redox-driven physiological and pathophysiological processes in the cell. The goal of such research is to formulate effective strategies for manipulating the cellular redox environment in a manner that is beneficial for restoring normal cell functions in the setting of disease. *Antioxid. Redox Signal.* 3, 341–346.

GENE-BASED DRUG DELIVERY has prompted the development of novel approaches for the treatment of human diseases. Armed with the technical achievements of many years of research, gene therapy has provided new avenues for approaching molecular-based medicine in the new millennium. Despite the great promise of gene therapy-based molecular medicine, numerous hurdles remain in the development of effective and safe treatment paradigms. Recessively inherited genetic disorders will be among the first and easiest diseases to treat by using gene therapy. More complex multifactorial diseases, such as cancer and environmentally induced injuries, will require a more complete understanding of pathophysio-

logic mechanisms as the foundation for developing effective gene therapy interventions. Many diseases, including both inherited mitochondrial disorders and cancer, have large pathophysiological redox components. Furthermore, the cellular redox milieu has been increasingly recognized as a critical component of stress-induced cellular responses following environmental injury. At the foundation of therapeutic developments in this area is the directed understanding of how to manipulate signal transduction pathways that control cell fates and pathologic responses to the environment. The reviews and articles included in this issue will deal with areas of molecular medicine benefiting from redox-modulating gene

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