Gene Therapy for Oxidative Stress

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Technology description

The inventors have disclosed a novel gene therapy approach for protection against pathogenic extracellular oxidative stress.

Technology Overview

Oxidative stress is a common cause of tissue damage along with concomitant initiation or acceleration of disease, and a known risk factor for numerous diseases including cancer, diabetes and pulmonary, neurological and cardiovascular disorders.

Oxidative stress is mediated by free radicals such as hydroxyl and superoxides, which in turn lead to reactive species such as hydrogen peroxide. Together these are referred to as reactive oxygen species (ROS). They have been known to damage lipids, proteins and DNA which produce numerous pathogenic outcomes.

Antioxidant enzymes catalase and superoxide dismutase (SOD) catalyze the neutralization of hydrogen peroxide and superoxide, respectively. These enzymes are sufficient for tackling oxidative stress from normal cellular processes, such as respiratory bursts from neutrophils and monocytes, but cannot effectively neutralize ROS derived from environmental or hyper-disease states.

For example, both enzymes are not found in the sera or mucosal surfaces where they can at as a first line of defense to exogenous ROS. One of the 3 isoforms of SOD, called SOD3, is secreted, but has a heparin binging domain, that attaches to cell surfaces, and hence not enough enzyme can perfuse across the epithelial surface to reach mucosal surfaces.

The inventors have devised a strategy to address this issue. This technology involves the use of a cDNA that encodes a novel monomeric secreted functional catalase and a modified extracellular SOD. The genetic codes of modified catalase and SOD3 are incorporated (alone or together) into an adeno-associated virus (AAV) vector to provide persistent and consistent expression of these anti-oxidant enzymes in a treated region, in the sera, and across epithelial and mucosal surfaces to protect against ROS' detrimental effects. Both the modified enzymes were found to be released into the sera and maintain function. Other vectors may also be used, such as adenovirus (for short term 2-3 week expression) or retrovirus and lentivirus (for proliferating cell populations).

Application area

Enhanced expression of catalase and SOD3 can provide much needed protection against chronic oxidant stress from environmental pollution and other causes.

Advantages

This technology allows for persistent and consistent expression of antioxidant enzymes.

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