Method of Treating Pneumoconiosis with Oligodeoxynucleotides

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Technology description

Summary

The inhalation of dust containing crystalline silica particles causes silicosis, an incurable lung disease that progresses even after dust exposure ceases. The World Health Organization estimates that over a million US workers are exposed to silica dust annually, and that thousands worldwide die each year from silicosis. The pulmonary inflammation caused by silica inhalation is characterized by a cellular infiltrate and the accumulation of chemokines, cytokines (including TNF-alpha, IL-1, and IL-6), and Reactive Oxygen Species (ROS) in bronchoalveolar lavage (BAL) fluid.
Macrophages are the predominant immune cell type present in alveolar spaces where they play an important role in the lung pathology associated with silica inhalation. The uptake of silica particles by macrophages triggers the production of ROS (including hydrogen peroxide) via the oxidative stress pathway, which in turn contributes to pulmonary damage and macrophage death.
One potential strategy for limiting the production of proinflammatory cytokines and ROS after silica exposure involves treatment with "suppressive" oligonucleotides (ODN). Suppressive ODN express motifs based on the repetitive TTAGGG hexamers present at high frequency in the telomeric ends of self DNA. Previous studies showed that these motifs (released by injured host cells) block Th1 and proinflammatory cytokine production in vitro and down-modulate over-exuberant/pathologic immune responses in vivo (such as those found in septic shock and autoimmune diseases).
This application claims methods for treating, preventing or reducing the risk of developing occupational lung diseases using. Preclinical in vivo studies show that pretreatment with suppressive (but not control) ODN reduces silica-dependent pulmonary inflammation. Preclinical in vivo studies also showed that treatment with suppressive ODN also reduced disease severity and improved the survival of mice exposed to silica.

Application area

Development of ODN-based therapeutics for the treatment of pneumoconiosis.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com