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2005 Program

Team Science Project
(2-year project)

Project Title: Reactive Oxygen Species and Tobacco Smoke-Induced Airway Disease

Project Summary: The long-term objective of this program entitled "Reactive Oxygen Species and Tobacco Smoke-Induced Airway Disease" is to understand how tobacco smoke leads to changes in the lungs of smokers that result in chronic bronchitis and why chronic bronchitis does not disappear in all ex-smokers. Chronic bronchitis, the most common adverse effect of smoking occurring in up to 50% of all smokers, is a condition with productive cough due to increased phlegm production caused by an abnormally high production and reduced natural clearing of phlegm from the airways. Chronic bronchitis has detrimental effects on lung health and is associated with an increased rate of being sick and in some studies even with an increased risk of death. Understanding how tobacco smoke-induced changes occur and lead to chronic bronchitis will provide new ideas about how to treat chronic bronchitis in smokers and ex-smokers and perhaps how to prevent chronic bronchitis. One important feature of tobacco smoke believed to contribute to the development of chronic bronchitis is the presence of reactive molecules that can oxidize components of the bronchi. These reactive molecules typically contain oxygen and are therefore called "reactive oxygen species" or ROS. ROS are not only contained in smoke itself but tobacco smoke can also induce an increased production of ROS by the airways themselves. The three projects making up this program will examine how ROS, like those found in tobacco smoke and produced by the airway cells themselves, cause changes that are associated with chronic bronchitis. Thus, these projects may perhaps point to the reason why chronic bronchitis does not disappear in all ex-smokers.

The specific aims of the projects are to study: a) exactly how the high concentration of ROS contained in smoke causes a slowing of mucus movement up and out of the bronchi; b) the function of small amounts of ROS normally made by and found in non-smokers' bronchi, and how those functions are disrupted by increased ROS produced by the airway cells in smokers; and c) how ROS cause the increased number of cells that make and secrete mucus seen in smokers and ex-smokers in the airway. All of the projects will use human bronchial lining cells that are obtained from organ donors whose lungs could not be transplanted and whose families consented to using the organs for research. These cells will be grown in a unique specialized system that exposes the top of cells to sterile air, and the bottom to nutrients, thus resembling the bronchial lining and its functions in humans. Modern, highly sophisticated, microscopic imaging, state-of-the-art molecular genetics, and standard biochemical methods will be used to carry out the proposed research on these cells. These projects might be able to identify new therapeutic targets, thereby provide some relief from a significant social and financial burden on society caused by smoking.