COPD? Eat your veggies

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You know it's good for you in other ways, but could eating your broccoli also help patients with chronic lung disease? It just might.

According to recent research from Johns Hopkins Medical School, a decrease in lung concentrations of NRF2-dependent antioxidants, key components of the lung's defense system against inflammatory injury, is linked to the severity of chronic obstructive pulmonary disease (COPD) in smokers. Broccoli is known to contain a compound that prevents the degradation of NFRP.

The findings were published in the second issue for September of the *American Journal of Respiratory and Critical Care Medicine*, published by the American Thoracic Society.

COPD is the fourth-leading cause of death in the U.S. and affects more than 16 million Americans.

In this study, researchers examined tissue samples from the lungs of smokers with and without COPD to determine if there were differences in measured levels of NRF2 expression and the level of its biochemical regulators, including KEAP1, which inhibits NRF2, and DJ-1, which stabilizes it. Dr. Biswal had previously shown that disruption in NRF2 expression in mice exposed to cigarette smoke caused early onset of severe emphysema.

When compared to non-COPD lungs, the lungs of patients with COPD showed markedly decreased levels of NRF2-dependent antioxidants,

increased oxidative stress markers, a significant decrease in NRF2 protein with no change in NRF2 mRNA levels (indicating that it was expressed, but subsequently degraded), and similar KEAP1 levels, but a marked decrease in the level of DJ-1.

"NRF2-dependent antioxidants and DJ-1 expression was negatively associated with severity of COPD," wrote principle investigator, Shyam Biswal, Ph.D., an associate professor in the Bloomberg School's Department of Environmental Health Sciences and Division of Pulmonary and Critical Care at the Johns Hopkins School of Medicine. "Therapy directed toward enhancing NRF2-regulated antioxidants may be a novel strategy for attenuating the effects of oxidative stress in the pathogenesis of COPD."

While clinical trials to date of antioxidants have been disappointing in improving the clinical course of patients with COPD, this study points to a possibility of benefit from restoring NRF2 levels in damaged lungs by reducing the action of KEAP1, which is an inhibitor of NRF2. "*ncreasing NRF2 may also restore important detoxifying enzymes to counteract other effects of tobacco smoke," wrote Peter Barnes, D.M., of the National Heart and Lung Institute in London, in the accompanying editorial. "This has been achieved in vitro and in vivo by isothiocynate compounds, such as sulforaphane, which occurs naturally in broccoli and [wasabi]."*

Sulforapane has been shown to be able to restore antioxidant gene expression in human epithelial tissue in which DJ-1 has been reduced. Isothicyanate compounds such as that found in broccoli inhibit KEAP1, and thus prevent it from degrading NRF2, according to Dr. Barnes.

"Future studies should target NRF2 as a novel strategy to increase antioxidant protection in the lungs and test its ability to decrease exacerbations and improve lung function in patients with COPD,"

concluded Dr. Biswal.

John Heffner, MD, past president of the ATS, commented that "mounting evidence over several decades underscores the importance of oxidant-mediated damage for the development of COPD in addition to other lung diseases. This study adds greater precision to our understanding of the specific antioxidants that may protect the lung against emphysema to allow clinical trials based on valid pathophysiologic principles."

Source: American Thoracic Society