Genetics Play Role in Response to Asthma Drug
Genes affect how people with asthma respond to albuterol, the most commonly used drug for quick relief of asthma attacks, according to a new study of adults with mild asthma. Asthma causes the airways to be inflamed or swollen and the surrounding muscles to tighten.

A study funded by the National Heart, Lung, and Blood Institute (NHLBI) found that, over time, participants responded differently to daily doses of inhaled albuterol depending on which form of a specific gene they had inherited. While a few weeks of regular albuterol use improved asthma control in people with one form of the gene, stopping albuterol use eventually improved asthma control in those with another form of the gene.

The Beta-Adrenergic Response by Genotype (BARGE) trial is a study of an asthma drug in people selected according to their genotype—the specific genes that they have. Asthma drugs are known to vary widely in their effects in different patients, and research suggests that genetics may play a role in these differences.

This study provides important insight as to why albuterol may benefit some people with asthma more than others. The findings, published in the Oct. 23, 2004, issue of The Lancet, could lead to better ways to individualize asthma therapy based on patients' genetic patterns.

Albuterol, along with other common bronchodilator drugs for asthma, targets the beta-2 adrenergic receptor molecules, which are located in the smooth muscles in the airways in lungs. By targeting these molecules, the beta-2 bronchodilators relax the muscles in the airways and open up the air passages.

The BARGE study examined the effects of two forms of the beta-2 adrenergic receptor gene in people with mild asthma. The trial paired 78 participants with matching levels of airway function but with different forms of the receptor gene. Researchers compared participants who have arginine versions of the gene (the arginine genotype) to those with glycine versions of the gene (the glycine genotype). Albuterol was used daily—in a few research settings.

"More work is needed to determine how to integrate these findings into clinical practice," says Elliot Israel, M.D., of Brigham and Women's Hospital in Boston, lead author of the study. "In the future, patients with the arginine genotype might even be advised to use an alternate reliever medication."

Barbara Alving, M.D., acting director of the NHLBI, says, "If we can pinpoint which individuals will do better with a certain type of therapy, we can improve their lives more quickly and save them—and the health care system—the expense and risk of trying drugs that are less effective for them. This study helps put asthma at the forefront of pharmacogenetics."

Pharmacogenetics is an emerging science that links variations in genotypes to variations in drug responsiveness. Scientists have long known that genes can play a role in how people respond to disease and to medications. As drugs move through the body, they interact with thousands of molecules or proteins. Because genes direct how proteins behave, variations in the structure of a gene can affect how the protein responds to a medication.