Researchers identify genes associated with asthma

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(PhysOrg.com) -- Yale University researchers have identified three genes containing genetic variations that appear to increase a child's risk of developing asthma. The findings will be published in three separate journals: the *Journal of Allergy and Clinical Immunology*, *Human Heredity* and *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*.

Scientists at the Yale School of Public Health's Center for Perinatal, Pediatric and Environmental Epidemiology used different techniques to identify each of the genes in question. One approach scanned the human genome and identified a genetic change in the PDE11A gene that is found more frequently in asthmatic children than their non-asthmatic peers. When scanning other asthma datasets, the researchers found that

most asthmatics were likely to have at least one genetic change in the PDE11A gene.

The findings come from the Perinatal Risk of Asthma in Infants of Asthmatic Mothers (PRAM) study, led by Michael B. Bracken, the Susan Dwight Bliss Professor of Epidemiology. The study assessed the extent to which the well-documented increased risk of asthma to children of asthmatic mothers is due to genetic factors and how much is due to factors occurring in the intrauterine and perinatal period, specifically related to the mother's own asthma status.

"We now believe that increased susceptibility to asthma and other complex human diseases is caused by very large numbers of quite rare genetic changes," Bracken said. "Each variant only increases risk slightly and many variants are likely needed in an individual to induce clinical disease."

In a second study, the researchers used a novel approach to rank candidate genes for asthma. They systematically reviewed the published literature and identified genes previously reported to be associated with asthma — finding 251 altogether. The top 50 genes were further tested for mutations in the PRAM study subjects. One of these genes—RAD50—contained a mutation that was associated with an increased risk of asthma. This gene is believed to help control inflammatory responses, suggesting that mutations to it alter immune system functioning that may lead to a predisposition toward asthma.

Finally, the group replicated an association between asthma and missing genetic material in the T-cell receptor gamma gene. They were able to demonstrate that this deletion was present in only a small proportion of the cells collected for DNA extraction. This is potentially significant because it suggests that this type of mutation is not inherited and therefore may be caused by environmental factors.

Taken together, these three genes highlight the complex nature of asthma and support the hypothesis that numerous factors play a role in determining whether or not a child will develop the disease, Bracken said.

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