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Researchers identify main genes responsible for asthma attacks in children

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An international team spearheaded by researchers from the University of Copenhagen has identified the genes that put some children at particularly high risk of serious asthma attacks, including one not previously suspected of being implicated in the disease. In the long term, these new findings are expected to help improve treatment options for the disease, which represents a high cost for families and society alike.

Asthma is the most frequent chronic disease in children and also the most common reason for Danish children being admitted to hospital. Very young children are at especially high risk of severe asthma attacks requiring hospitalisation. This is hard on both child and family and severely strains society's resources. Nonetheless, doctors still have insufficient knowledge about asthma attacks in infants, making the condition difficult to prevent and treat. It is hoped that the recent research findings will help change this. An international team spearheaded by researchers from the University of Copenhagen have now identified the genes that put some children at risk of experiencing severe asthma attacks. The results have been published in the prestigious scientific journal *Nature Genetics*.

"Our results show that asthma attacks requiring young children to be hospitalised are usually genetically related. Genes play a far greater role in children with asthma than in adults. By screening children's DNA we've discovered that a gene called CDHR3, which was previously unassociated with the disease, plays a key role for the development of asthma, particularly in the very early years of life. Our study supports the

theory that asthma is not just a single disease, but a complex of several sub-types that should be genetically mapped and understood individually if we are to prevent and treat the disease properly in future," says Klaus Bønnelykke, MD, PhD. He works for the Copenhagen Studies of Asthma in Childhood (COPSAC), the Danish Pediatric Asthma Center, Copenhagen University Hospital.

The researchers have studied the genes of 1,200 young children aged between two and six who had been hospitalised several times because of severe asthma attacks, and compared them with 2,500 healthy people.

Individualised treatment

Today doctors use the same medication to treat different types and degrees of asthma, but the researchers hope that improved understanding of the sub-types of the disease will pave the way for individualised treatment in future.

"Although good asthma medication is available today, it doesn't work for everyone. Specifically we need effective medicine to prevent very young children from being hospitalised and to treat them once they have been admitted. That's why we started looking at this particular group. Because asthma symptoms are fairly similar in all children, doctors tend to approach the condition in the same way. However, in reality asthma has many different underlying mechanisms, which need to be individually mapped," says Klaus Bønnelykke. He explains that to date researchers have focused on various theories about asthma attack prevention in young children, for example, recommending breastfeeding and avoiding pets and dust mites in the home.

"We know that children exposed to smoking have a higher risk of asthma attacks, but beyond that, none of our advice has really helped, and we won't make any progress until we understand the individual sub-

types of asthma and their underlying mechanisms. In this respect knowledge about risk genes is an important step in the right direction," he points out.

Large volume of data

The study was headed by Klaus Bønnelykke and his colleague Hans Bisgaard, Professor of Paediatrics at the University of Copenhagen, chief physician of the Copenhagen Studies of Asthma in Childhood (COPSAC) and head of the Danish Paediatric Asthma Center. The study was conducted in collaboration with various research groups, including the Danish Centre for Neonatal Screening, Statens Serum Institut, Copenhagen, and Center for Biological Sequence Analysis (CBS), Technical University of Denmark,, as well as research teams in the USA, Spain, the UK and the Netherlands.

The study was based on examinations of 1,200 Danish children hospitalised for asthma and 2,500 healthy individuals. Two- to six-year-old children who had been hospitalised at least twice were identified in the hospital records. Their DNA was then screened for risk genes, and subsequent studies of children from Denmark and abroad confirmed the discovery of a new risk gene (CDHR3).

More information: *Nature Genetics* DOI: 10.1038/ng.2830

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