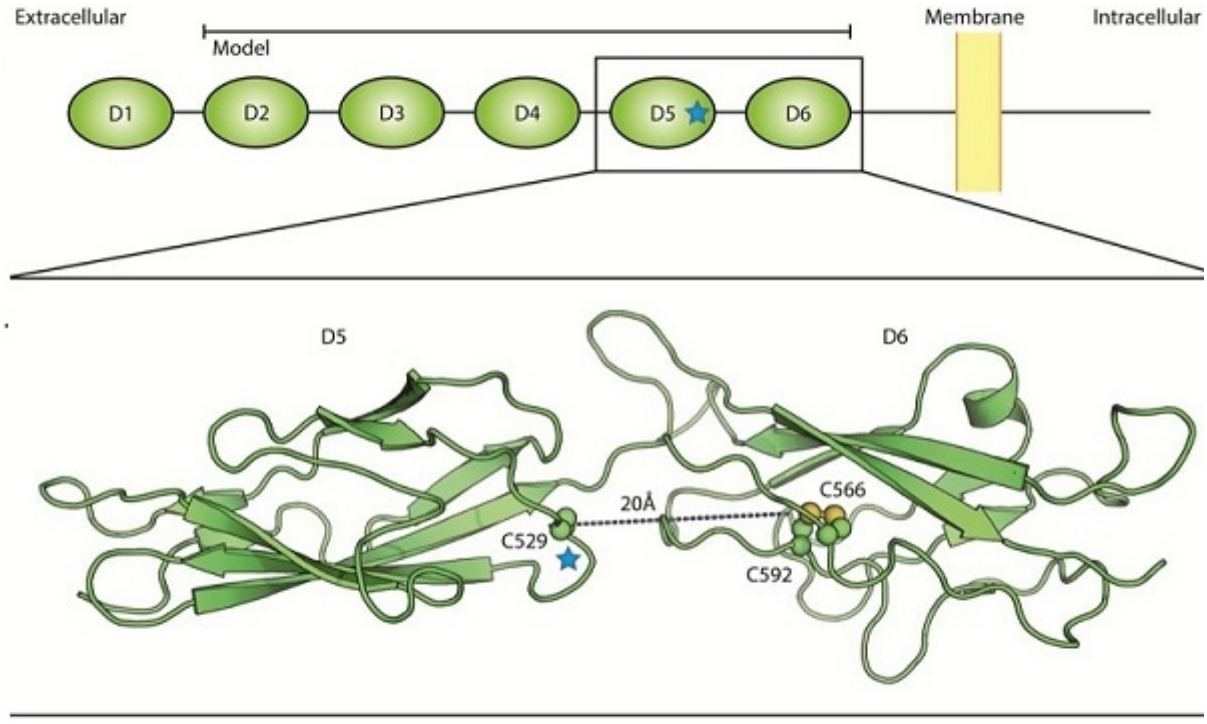
Researchers identify main genes responsible for asthma attacks in children

The results have been published in the prestigious scientific journal Nature Genetics.



Overview of the CDHR3 protein model

An international team involving researchers from the joint programme between Barcelona Supercomputing Center (BSC) and Institute for Research in Biomedicine (IRB Barcelona) including Silvia Bonàs, Josep Maria Mercader and David Torrents, had identified the genes that put some children at particularly high risk of serious asthma attacks, including one which was 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. 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 involving Barcelona Supercomputing Center researchers and spearheaded by researchers from the University of Copenhagen have 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**.

The 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 the research has 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. The study supports the theory that asthma is not just a single disease, but a complex of several subtypes that should be genetically mapped and understood individually if we are to prevent and treat the disease properly in future.

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

The study was headed by Klaus Bønnelykke, MD, PhD from Copenhagen Studies of Asthma in Childhood (COPSAC), the Danish Pediatric Asthma Center, and Copenhagen University Hospital, 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.

Today doctors use the same medication to treat different types and degrees of asthma, but the researchers hope that an 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 Bønnelykke.

The Computational Genomics group at the BSC has contributed to a better characterization of the genomic regions that influence the risk of asthma in children using highly demanding statistical and computational techniques. This methodology enables the computational prediction of genetic variants that were not originally experimentally analysed, based on other available genetic resources, making possible a better characterization of the genetic profile of each individual without the need of performing new experiments, and therefore, at a much lower cost. However, this task, like most of the analyses related to genetics and genomics, required managing large volumes of data and computation, for which the supercomputer resources available at BSC were essential.

"The characterization of these genomic regions related to asthma in children means a step forward towards the basis of personalized medicine, which is one of the central aims of our group and of our center. After the positive results of our new methodology for genetic variants imputation in GWAS analysis, we are now expanding the same type of analysis to other complex diseases", says David Torrents, head of the Computational Genomics group at the BSC .

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, Lyngby, 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).

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About asthma:

Asthma means shortness of breath. It is a respiratory disorder that can affect people of all ages – children, adults and the elderly. The symptoms often manifest as bouts of coughing, breathlessness and wheezing. You can be genetically disposed to the disease, but beyond that the reasons some people get asthma are unknown. For most sufferers, asthma is a chronic condition lasting many years. Some people grow out of the disease while others find themselves symptom-free and needing no medication for a period, after which their asthma returns. The new research findings indicate that more disease sub-type mapping is needed in order to improve future treatment and prevention options. (*Source: Astma-Allergi Danmark and Klaus Bønnelykke, PhD, Danish Paediatric Asthma Center, University of Copenhagen*)

About the CDHR3 gene

CDHR3 impacts the lungs directly, and the new research results indicate that it plays a particularly important role in the lungs of young children with severe asthma. Over time the researchers hope to be able to map the precise mechanisms involving the gene as well as the environmental factors that trigger activation of the gene in some children. The goal is to be able to prevent and treat the disease with customised medication.

About BSC

Barcelona Supercomputing Center (BSC) is the national supercomputing centre in Spain. BSC specialises in high performance computing (HPC) and its mission is two-fold: to provide infrastructure and supercomputing services to European scientists, and to generate knowledge and technology to transfer to business and society.
BSC is a Severo Ochoa Center of Excellence and a first level hosting member of the European research infrastructure PRACE (Partnership for Advanced Computing in Europe). BSC also manages the Spanish Supercomputing Network (RES).
BSC joins experts in genomics, genetics of complex disease, systems biology, and has direct access to supercomputing resources, as it hosts and manages the MareNostrum supercomputer, with a total capacity of 1 Petaflop, ranking among the top 36 supercomputers in the world. The Life Sciences department of the BSC has a joint program with Institute for Research in Biomedicine (IRB-BSC), which gives access to all

the laboratories and facilities of this institution.

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