Scientists have identified the ten main genes responsible for inherited allergies. The discovery may also reveal the cause of the rising incidence of type 1 diabetes.

Allergy is the most common chronic disease in Europe and the incidence has risen greatly in recent years.

Many years of family and twin studies have revealed that the risk of developing allergies is partly genetic.

Yet, scientists have not yet managed to pinpoint the exact genes that cause allergies, despite thousands of candidates having been suggested in a long series of large and small studies.

Now a Danish-led international study points to ten genes as the main culprits in the development of allergies.

The conclusions of the study, which is based on genome sequencing of DNA from 30,000 people, represent a breakthrough in allergy research.

“Environmental factors are important in the development of allergies, but our genes are crucial for our vulnerability to allergic reactions. We have known this for more than 50 years, but only now can we say with certainty which genes are involved, says Klaus Bønnelykke, MD, PhD, who headed the study together with colleagues Professor Hans Bisgaard and Eskil Kreiner-Møller, MD, of the Copenhagen Studies of Asthma in Childhood (COPSAC) at the Copenhagen University Hospital, Denmark.

The study has just been published in the scientific journal Nature Genetics.

Allergies caused by gene mutations

In the study, the researchers compared the genomes of about 10,000 allergy patients with the genomes of 20,000 people without allergies. The study was carried out as part of the international consortium the Early Genetics and Lifecourse Epidemiology research cohort (EAGLE), and includes data from 16 different studies.

In the comparison, the researchers discovered that people with allergies often exhibit tiny changes in ten specific sites in the genome, where one of the DNA building blocks has been replaced by another. These changes in the genome did not occur to the same extent in the group of people without allergies.

The results allow the scientists to conclude two things:

“We now know that these ten changes in the genome are closely linked to the development of allergies,” says Bønnelykke.

“At the same time, our participants had a wide variety of allergies, which confirms the theory that we primarily inherit the tendency to become allergic to one particular substance and not a specific allergy in
itself.”

Genes associated with immune system

In addition to locating these changes in the genome, the researchers also discovered which genes are affected by these small changes.

Not surprisingly, they found that most of the changes in the genome are located in genes that are closely associated with the immune system.

This makes good sense, as allergy is an immune-related disease.

"There are, however, also some genes that we had not previously believed to play a role in the development of allergies,” says the researcher. “Once we have studied these genes in depth, we will probably reach a greater understanding of some of the mechanisms behind allergies that we have not focused on before.”

Allergy genes cause other diseases too

Out of the ten genes that the researchers link to the development of allergy, three are particularly interesting. These three are also associated with the development of autoimmune diseases such as inflammatory bowel disease, type 1 diabetes and sclerosis.

This may help explain the recent surge in the number of people with allergies and autoimmune diseases.

"It has been difficult to explain why the number of people with both types of diseases has increased at the same time when it’s usually said that allergies reduce the risk of autoimmune diseases and vice versa,” says Bønnelykke.

“The discovery of genes that play a part in both types of diseases may help explain this simultaneous increase. This discovery is very interesting in its own right.”

Study sharpens focus

The new findings do not, however, present an immediate revolution in the treatment and diagnostics of allergies.

According to Bønnelykke, the study should primarily be regarded as a tool that researchers can use to sharpen their focus in their future research.

"Now we can focus on ten genes rather than 100,” he says. “We will now start looking at which substances in the body are affected by the genes and how these substances interact with environmental factors. This will hopefully provide us with the knowledge required to treat and prevent allergies in the future.”

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Fact box

The genome is the entirety of an organism’s hereditary information and is encoded either in DNA or RNA. The genome contains thousands of genes, each of which has its own effect on various processes in the body.

In the new study, researchers have identified the sites in the genome where the small changes occur and in which genes they occur.

These genes are: TLR6, C11/f30, STAT6, SLC25A46, HLA-DQB1, IL1RL1, LPP, MYC, IL2 and HLA-B.

Since some genes are common to both asthma and allergies, the study also sheds new light on the link between the two diseases.

Fact box

The latest issue of *Nature Genetics* also includes a related genetic study of allergy symptoms in 53,000 people, carried out by US and British researchers.

The Danish researchers collaborated with the US/British team and together they have now presented the hitherto most complete insight into the link between genes and allergies.

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