

Investigating mutations of a crucial gene might assist treatment and prevention of asthma and other allergies

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Mutations in a specific gene are linked with human susceptibility to allergic asthma according to new research. These findings suggest novel ways in which immune responses could be modulated in allergic diseases, says Maria Curotto de Lafaille of the A*STAR Singapore

Immunology Network.

The study led by Curotto de Lafaille and Fook Tim Chew of the National University of Singapore included members from three A*STAR institutes and research groups from across three continents. The international collaboration allowed the authors to analyze different populations from Singapore, the Netherlands, North America and Korea.

They focused on mutations in the gene that codes for a protein called inducible costimulator (ICOS), which has previously been linked to allergies. The ICOS protein is found in activated cells of the [immune system](#) known as T cells. This protein helps the T cells to assist other immune cells—the B cells—to produce antibodies that can bind to invading microbes and also to allergens.

Curotto de Lafaille notes there is a 'a yin-yang' aspect to ICOS's function, "while ICOS is very important for normal and beneficial immune responses – it is also necessary for the function of regulatory T cells that work to suppress the [immune response](#)." In suppressing the immune response, regulatory T cells protect against excessive inflammation, autoimmunity and allergy, Curotto de Lafaille explains.

The researchers speculated that mutations in the gene that codes for the ICOS protein might be involved in the overproduction of a class of antibodies known as immunoglobulin E. Such antibodies are already known to be involved in various allergic conditions, including eczemas, rhinitis and asthma.

The scientists analyzed the effect of mutations at single points in the ICOS gene, known as [single nucleotide polymorphisms](#), which alter just one of the nucleotide building blocks of DNA. They identified one specific mutation that led to an increase in ICOS production but surprisingly lowered the risk of allergy. This led them to conclude that,

in this case, more ICOS is better than less ICOS as it is expected that increased ICOS expression in regulatory T [cells](#) will lead to protection from allergies.

The subtleties in the effects of the ICOS gene mutations were thought to result from the dual function of ICOS as both a promoter of the immune response and an immune-suppressing regulator, explains Curotto de Lafaille.

These findings could allow drugs to be developed that can promote the helpful regulatory functions of ICOS. "Such therapies may prevent young children from becoming allergic and suppress disease in those already allergic," says Curotto de Lafaille.

More information: Andiappan, A. K., Narayanan, S., Myers, R. A., Lee, B., Nieuwenhuis, M. A. et al. "Genetic variants of inducible costimulator are associated with allergic asthma susceptibility." *The Journal of Allergy and Clinical Immunology* 135, 556-558 (2015). [dx.doi.org/10.1016/j.jaci.2014.06.028](https://doi.org/10.1016/j.jaci.2014.06.028)

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