

Subset of immune cells linked to allergic rhinitis symptoms

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Have you ever suffered from asthma or know someone who does? It is excruciating to watch them suffer. An asthma attack makes something as simple as breathing, extremely difficult. I have seen this first hand with my mum, brother and sister, who are all asthmatic. Asthma is just one of the allergic diseases that grip our lives—rhinitis and eczema, that affect the nasal passages and skin, respectively, are also very common in Singapore. "How common?" you may ask?

In a study published in 2014 my colleagues and I found that almost half of the nearly 8,000 people surveyed had one of these three conditions. Allergic rhinitis (AR), known more commonly as 'hay fever' in the western world, affects nearly 40 per cent of the survey respondents, while [asthma](#) affects nearly 20 per cent. 15 per cent of volunteers said they had eczema or atopic dermatitis, often caused by allergens. There is also a worrying trend that the prevalence of allergies is increasing worldwide, and Singapore is not spared from this. Children's hospitals in Singapore report asthma prevalence in kids to be around 25 per cent and AR over 40 per cent. So what causes the allergies that lead to these conditions?

The culprit

We tested the blood of nearly 600 people for antibodies against common allergens. Antibodies are proteins specific to foreign substances that enter our body. The antibody 'IgE' is unique to allergens. About 80 per

cent of these individuals had antibodies against house dust mites. We verified this finding in a study of over 7,000 volunteers where we found the rates to be similarly high, nearly 75 per cent. This was a startling find; especially given we didn't find many antibodies for other common allergens such as pollen, molds and pet dander (hair and dead skin cells). People who had a history of asthma and AR had about ten times more IgE antibodies in their blood compared to those who didn't. So we hypothesize that the prevalence of asthma and AR could be associated with the house dust mite [allergy](#). But we still lack exact mechanisms to explain how this dust allergy leads to specific clinical manifestations. Interestingly, we had an exciting finding when we continued looking at the immune system. What did we find?

When we looked at one particular subset of immune cells called 'basophils' in the blood of nearly 500 of the participants of the study, we found something peculiar. Basophils are supposed to sense allergens and release molecules which lead to allergy symptoms. In nearly 10 per cent of these individuals, most basophils didn't seem to sense the allergen tested which was house dust mites in this case. Their IgE antibody levels were also reduced. This reduced response called 'basophil anergy' was naturally occurring in some individuals, who also had reduced or no nasal allergies. So basophil anergy appears to reduce the risk for AR. Why is this important?

We are very excited with the above finding because, we can use this naturally occurring phenomenon to understand how we could potentially treat patients with nasal allergies. One of the treatments for AR is 'allergen-specific immunotherapy'. Here the patient is given small doses of the allergen over a longer period of time to help train the immune system to tolerate the [allergen](#). Could it be that our phenomenon of basophil anergy is one of the mechanisms that controls this training? We don't know yet, but we can find out! For this, we need to work with the clinicians who actually see the allergy patients day in and day out. We

are currently working together with local clinicians and pharmaceutical companies to try to understand the cause of allergies, develop drugs and help better treat patients.

Currently there is no cure for allergies, although effective treatments are available. Asthma control, however, is still a concern. While most patients respond to treatment, about 510 per cent of asthmatics unfortunately don't and have frequent attacks and are hospitalized as a consequence. Some studies have shown that this could be due to mutations in genes which could cause the treatment to fail. We have now initiated a global partnership to understand why it's difficult to control asthma in some asthmatic children. This effort is called Pharmacogenomics in Childhood Asthma (PiCA). With genetic data from nearly 15,000 children from 12 countries with asthma status and medication usage, we aim to develop personalized treatments for every asthmatic.

We know that allergies are inherited. Children with parents who have had allergies are at a higher risk to develop allergies themselves. However, we don't exactly know what the causes are for the manifestation of [allergic diseases](#) like asthma and [allergic rhinitis](#). Is it mutations (genetic changes) we inherit from our parents? Or the environment we live in?

The answer could lie somewhere in between, in a new and exciting field of research called "epigenetics", which I will explain at length in the second installment of this two-part series.

More information: Kia Joo Puan et al. Systematic characterization of basophil anergy, *Allergy* (2016). [DOI: 10.1111/all.12952](https://doi.org/10.1111/all.12952)

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