Medical Xpress

Exposure to farmyard bugs reduces immune overreaction found in childhood asthma

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Exposure to farmyard microbes was already known to protect children from developing asthma, with studies of Amish families in the United States showing a link. The Imperial team has shown a mechanism by which these bugs may protect us from developing abnormal lung function in early life. Credit: Wikicommons / Ernest Mettendorf

Treating new born mice with farmyard microbes reduces wheezing and inflammation in the airways, by 'taming' their immune systems.

The findings, from a study recently published in the journal *Science Immunology*, reveal more about the mechanisms underlying hyperresponsiveness in the airways of the lungs – which causes wheezing and is a core component of childhood asthma.

According to researchers, the work could lead to targeted treatments for young children which could ultimately help to curb childhood respiratory conditions, including asthma, and impaired lung function in adulthood.

The findings further highlight a 'window of opportunity' in early life in which the immature immune system can be shaped by the environment through exposure to allergens, such as dust and certain types of beneficial microbes.

Sejal Saglani, Professor of paediatric respiratory medicine at Imperial's National Heart & Lung Institute (NHLI), said: "Exposure to farmyard microbes was already known to protect children from developing asthma in epidemiological studies. While these studies showed a link, we have shown a mechanism by which they may protect us from developing abnormal lung function in early life.

Professor Saglani added: "Our study looked at mice, but if we can find a way to replicate the effect in humans, we could potentially stop the immune system from 'overreacting' early on in life, catching the root cause of childhood asthma before it can gain a foothold."

Burden of asthma

Asthma affects an estimated 10 per cent of children in UK, causing breathlessness and can in severe cases disrupt work and leisure activities.

When symptoms are triggered, attacks lead to the airways constricting, causing difficulty breathing and which, if untreated, can lead to hospitalisation.

One of the key features which develops in early childhood is wheezing. This is caused by airway hyperresponsiveness, where the small airways of the lungs become more sensitive to elements like dust, or allergen particles from animal hair or mites.

However, exactly why this process occurs is not well understood, and there are currently no treatments to prevent wheeze from developing.

In the latest study, researchers from Imperial College London looked to mice to try and uncover what was going on.

Animals were exposed to low levels of allergens from dust mites, similar to levels found in the average home, measuring the immune responses in the animals' airways.

The researchers also exposed new-born mice to a strain of common bacteria found on farmyards, Acinetobacter Iwoffii, for three weeks along with the dust mite allergen. Previous studies have found a link between reduced rates of asthma and exposure to farmyard microbes in humans, but how they have an effect on the lungs was unclear.

The team discovered that mice treated with the bacteria had reduced levels of an inflammatory marker called IL-13, produced by their T cells, and were completely protected from airway hyperresponsiveness, showing the microbes dampen down a key inflammatory pathway.

They also found that compared to adults, younger mice had greater activity in their T cells, which were more likely to cause an overreaction, resulting in inflammation and wheezing.

When exposed to the dust mite allergens, these cells pumped out IL-13, which kicked off the immune response. But in knockout mice where these T cells were unable to produce IL-13, they found a greatly reduced immune response.

Other types of immune cells, more prevalent in adults and which produce the same marker, were unable to generate the same response in the airways, pointing to the T cells as the culprits for driving hyperresponsiveness in new-borns and infants.

Targeting T-cells

According to the group, the findings highlight the need to focus specifically on reducing the effect of T cells in infants to tackle the underlying mechanisms that lead to wheezing.

Professor Saglani said: "Wheezing disorders are common in children, particularly following viral infections, or colds, but some children go onto develop asthma by school age, and we can't predict which children, and why.

"Our findings show that there are key differences in the immune responses to allergens in young compared to adult mice, reinforcing the importance of age as an influence on immune pathways."

Professor Clare Lloyd, Vice-Dean (institutional affairs) of Imperial's National Heart & Lung Institute, who led the study, added: "A key clinical aspect of asthma in childhood is wheezing, which is caused by the narrowing of the small airways in the lungs, a process called bronchoconstriction.

"In order to develop new treatments for childhood wheezing we need to understand the underlying molecular mechanisms of this process and

how it changes airway hyperresponsiveness."

"We now need to translate our findings and examine similar pathways in children with preschool wheeze," explained Professor Lloyd. "Ultimately, we would hope to be able to treat patients with a drug similar to the farmyard microbes to protect from wheezing and asthma."

More information: Sejal Saglani et al. Inception of early-life allergen–induced airway hyperresponsiveness is reliant on IL-13+CD4+ T cells, *Science Immunology* (2018). DOI: 10.1126/sciimmunol.aan4128

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