Medical Xpress

Allergy study on 'dirty' mice challenges the hygiene hypothesis

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The notion that some level of microbial exposure might reduce our risk of developing allergies has arisen over the last few decades and has been termed the hygiene hypothesis.

Now, an article published in *Science Immunology* by researchers from Karolinska Institutet challenges this hypothesis by showing that mice with high infectious exposures from birth have the same, if not an even greater ability to develop allergic immune responses than "clean" laboratory mice.

How microbes may prevent allergy has been a topic of great interest in recent times. Studies have suggested that certain infections might reduce the production of inflammatory antibodies to allergens and alter the behavior of T cells involved in allergies. It has also been suggested that good bacteria in our intestines may be able to switch off inflammation in other parts of our body.

Robust allergic responses

Researchers have now compared the allergic immune response in "dirty" wildling mice to those of typical clean laboratory mice. They found very little evidence that the antibody response was altered or that the function of T cells changed in a meaningful way. Nor did anti-inflammatory responses evoked by good gut bacteria appear to be capable of switching off the allergic immune response. On the contrary, wildling mice developed robust signs of pathological inflammation and allergic responses when exposed to allergens.

"This was a little unexpected but suggests that it's not as simple as saying, 'dirty lifestyles will stop allergies while clean lifestyles may set them off.' There are probably very specific contexts where this is true, but it is perhaps not a general rule," says Jonathan Coquet, co-author of the study and Associate Professor at the Department of Microbiology, Tumor and Cell Biology at Karolinska Institutet in Sweden.

More like the human immune system

The wildling mice are genetically identical to clean laboratory mice but are housed under seminatural conditions and have rich microbial exposures from birth.

"The immune systems of wildling mice better represent the human immune system and so we hope that they can bring us closer to the truth of how microbes act upon the body," says Jonathan Coquet.

The findings contribute to our general understanding of how allergies may arise and may also have clinical implications. In clinical trial settings, researchers and clinicians have recently made attempts to treat patients suffering from inflammatory diseases with experimental infections.

For example, infecting people with worms or performing fecal transplantations has been proposed as a tool to combat inflammatory diseases. Newborns delivered through C-section, have had maternal fecal transplantation and bacterial supplementation with the aim of promoting good bacteria in the baby's gut and the child's future health.

Can provide important insights

"This field of research can provide important insights into how infections and microbes can be used to facilitate health, but it is still in its infancy. Our study is a reminder that general and broad exposures to microbes may not have the clear beneficial effects that we wish them to have," says Susanne Nylén, co-author of the study and Associate Professor at the Department of Microbiology, Tumor and Cell Biology at Karolinska Institutet.

The work was led by Junjie Ma and Egon Urgard, researchers in Jonathan Coquet's group, and done in close collaboration with Professor Stephan Rosshart at University Medical Center Freiburg in Germany and

Susanne Nylén (MTC).

Several other research groups at Karolinska Institutet and elsewhere also contributed to this work, including the teams of Assistant professors Itziar Martinez Gonzalez and Juan Du (both at the Department of Microbiology, Tumor and Cell Biology, MTC).

More information: Junjie ma et al, Laboratory mice with a wild microbiota generate strong allergic immune responses, *Science Immunology* (2023). DOI: 10.1126/sciimmunol.adf7702. www.science.org/doi/10.1126/sciimmunol.adf7702

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