



MICROBIOME

Wildling mice put the hygiene hypothesis to the test

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The hygiene hypothesis states that early-life exposure to microbes protects against the development of allergies. A new study published in *Science Immunology* challenges this concept by showing that ‘wildling mice’ — mice that have been exposed to diverse microbes and pathogens from early life — develop similar, if not greater, allergic immune responses compared with specific pathogen-free (SPF) mice.

“Most of the evidence for this concept comes from association studies in humans. I wanted to test this principle in another way. Having done a lot of research on mice, I thought we could use mouse models to address this concept,” comments senior author Jonathan Coquet.

Today, most laboratory mouse colonies are housed under SPF conditions in abnormally clean facilities, which are not reflective of the human environment. Mice housed under SPF conditions fail

to faithfully replicate human immune responses, thereby limiting their translational value. Eager to work with more exposed mice to carry on their allergy experiments, Coquet and co-author Susanne Nylén decided to strike a collaboration with Stephan Rosshart, the creator of wildling mice. These mice, which were created by transferring B6 embryos into wild mouse mothers, acquire the microbes and pathogens of wild mice and therefore better resemble a mouse you’d find in the wild. “Because wildlings had a stable microbiota from birth and were genetically identical to normal lab mice, we thought this would be a great model to test the hygiene hypothesis,” says Coquet.

When comparing wildlings with SPF mice, the researchers showed that wildlings accumulated large populations of immune cells, including high levels of T_H2 cells, that participated in subsequent allergic

responses. Thus, wildling mice were not protected from developing pathological allergic immune responses. “The conclusion we draw from this is that an overall increase in microbial exposure, as the hygiene hypothesis suggests, is not enough to protect against allergic inflammation and could possibly even make it worse,” explains Nylén.

Rosshart adds that the explanation must be more complicated, likely multifactorial. “Thus, our study may help to recalibrate scientists’ views on the hygiene hypothesis, prompting the field to have a closer look at other factors such as indoor living, physical activity, pollutants and chemical compounds present in the modern world,” he concludes.

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