Study finds honeybee venom triggers immune response

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Credit: AI-generated image (disclaimer)

Allergy-like immune reactions could represent a mechanism of the body that protects it against toxins. This surprising conclusion has been reached by scientists at Stanford University, USA, working on a research project co-financed by the FWF. The recently published findings prove that honeybee venom triggers an immune response in mice associated

with the formation of IgE antibodies, which are also typical for allergic responses. These IgEs then confer protection against higher amounts of the venom subsequently administered to the mice. Thus, for the first time, IgEs were observed as having a direct protective function against a venom – a finding that substantiates a controversial hypothesis on the emergence of allergies formulated in the 1990s.

Allergies are quite unnecessary: instead of fighting microbes that pose a threat to health, the immune system targets harmless pollens, hairs or dust particles. The question as to why the body puts up such a fight against harmless substances is one that preoccupies scientists all over the world. A study by an Erwin Schrödinger Fellow of the Austrian Science Fund FWF, which has been currently published in the journal *Immunity*, gives new impetus to a controversial hypothesis for the explanation of such allergic reactions.

Toxin Protects Against More Toxin

Dr. Philipp Starkl, who is using his fellowship to collaborate with Prof. Stephen J. Galli and his team at the Department of Pathology at Stanford University School of Medicine, summarises the results of the joint study as follows: "Mice, to whom we had previously administered small amounts of honeybee venom, subsequently displayed astonishing resistance to larger volumes of the toxin. As in the case with a vaccination, the body appeared to build a kind of immune protection against the bee venom." Interestingly, however, completely different responses in humans are also known – in some unfortunate people repeated contact with bee venom causes allergic reactions or even an anaphylactic shock. IgE-type antibodies are mainly responsible for this response.

Dr. Starkl and his colleagues investigated the question as to whether these antibodies are also involved in the reactions observed in mice. To

establish this, honeybee venom was administered to three different mouse strains, in which the functioning of an immune reaction based on IgE was prevented in different ways. The results showed that, unlike the previously examined "normal" mice strains, these mice were unable to form any protection against honeybee venom. Therefore, IgEs seem to have a positive function in mice. This finding patently contradicts what was already known from humans, in who IgE antibodies are mainly seen as causing allergic reactions. It had been suspected that a positive function existed beyond this (for example in the immune response to parasites); however, it had not been possible to demonstrate it directly up to now.

Evolution Follows Function

The Stanford team though was not very surprised to discover this positive function of IgE. Dr. Starkl, who, together with his Belgian colleague Dr. Thomas Marichal, is co-first author of the current publication, explains: "In our view, the assumption that the function of IgE antibodies is limited to triggering allergic reactions always fell short of the mark. Otherwise, IgEs would surely have been eliminated in the course of evolution, a consideration that also underlies the so-called toxin hypothesis."

According to this hypothesis, the body can build protection against toxic substances using IgE antibodies and allergic reactions. Thus, IgEs would have fulfilled a very important role in human evolution – which only relinquished its significance with the development of increasingly protected lifestyles of humans. Furthermore, according to the hypothesis, allergic reactions are extreme or uncontrolled forms of the protection mechanism. The "underemployment" of this response in modern times could then actually contribute to its tendency to malfunction or overreact.

The toxin hypothesis, which was proposed by Margie Profet in 1991, has been hotly contested up to now – but never been refuted. The research carried out by the FWF Erwin Schrödinger Fellow now provides the first experimental finding that substantiates it – and demonstrates, once again, the importance of keeping an open mind in science.

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