Non-pathogenic bacteria for the treatment and prevention of allergies

Researchers and physicians from the Department of Dermatology at Tübingen University Hospital are investigating huge numbers of non-pathogenic bacteria with the aim of shedding light on their potential for the prevention and treatment of allergies. The mode of action of highly promising candidates is being investigated in further detail.

"In principle we are putting the cart before the horse," said Prof. Dr. Tilo Biedermann, senior physician and head of the Department of Dermatology and Allergology at the University Hospital of Tübingen. Together with his team of researchers and physicians, Biedermann has investigated the effect of non-pathogenic and probiotic bacteria such as those found in yoghurt for example and which have been found to have a particularly positive effect on the intestinal flora. Using a mouse model, the team discovered a highly interesting effect: mice that were very susceptible to neurodermatitis developed the disease less frequently when a lysate of certain pathogens was applied onto the skin.

"The susceptibility of the lysate-treated mice to developing neurodermatitis was considerably lower than that of control mice. More detailed analyses showed that the animals had a higher concentration of immune-modulating interleukin 10 and a lower concentration of the proinflammatory mediator interferon γ," said Biedermann. Interferon γ is secreted when the immune system recognises foreign invaders and fine-tunes the immune system to effectively rid it of foreign intruders. The secretion of interferon γ causes inflammatory reactions that create a hostile environment for the intruders, thereby initiating their elimination. Non-pathogenic and probiotic bacteria do not cause an inflammation, but are nevertheless recognised by the human immune system. The elevated production of interleukin 10 in certain immune system cells leads to anti-inflammatory reactions, which in turn creates an active immunological tolerance. To put it more simply, this means that the human body is able to learn tolerate self peptides and harmless allergens when it is exposed to specific non-pathogenic microorganisms.

Bacteria can promote immunological tolerance
Prof. Dr. Biedermann is investigating the effect of probiotics and non-pathogenic bacteria for the prevention and treatment of hypersensitivity disorders of the skin.
However, there is one drawback: probiotic bacteria only seem to have a local effect in that they only "teach" immune system cells at the site where they exert their effect. This means that the oral administration of probiotic bacteria can have a positive effect in people with intestinal problems, but is largely ineffective for the treatment of inflammatory skin diseases. Therefore, the researchers decided to apply probiotic bacteria or lysates of non-pathogenic microorganisms directly to the skin. "Once the mode of action is deciphered, we will be able to apply specific isolates or synthetic drugs. However, we still have a long way to go," said Biedermann going on to add "however, initial evidence about the substances and signalling pathways that mediate the tolerance of the human immune system to certain pathogens is now available". "We are evaluating the profiles of a broad range of pathogens in terms of their potential effect in the human intestine as well as their effect on the skin. Since the immune functions of intestines and skin are very different, we hope that comparative investigations will provide us with insights into the interacting signalling pathways that lead to an immune response and enable us to develop strategies for the development of effective drugs," said Biedermann who attaches great importance to combinatorial thinking. "We want to find out when certain signalling pathways are initiated and where they interact in order to induce allergic reactions in some instances and inflammatory bowel diseases in others. We hope to use this knowledge to decide at which point in time and where in the signalling cascades we are able to interfere with the mechanisms." The group of researchers from Tübingen have already identified the first signalling cascades involved in these processes.

Components of non-pathogenic or probiotic bacteria are able to bind to the receptors of the natural immune system, for example dendritic cells. This triggers signals that induce regulatory T-cells (Treg) that have an anti-inflammatory effect on the skin.

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Preventing the recurrence of allergies

At present, Biedermann and his team are focusing on finding out whether treatment involving non-pathogenic bacteria is effective in preventing allergies and other disorders. "We are mainly focusing on children that present with childhood food allergies. These are children that run a high risk of developing allergic dermatoses, and the group includes children whose mothers and fathers suffer from severe atopic disorders". Biedermann is hoping that treatment involving specific probiotic microorganisms has a statistical effect in delaying the development of neurodermatitis in high-risk patients.

"We have seen that the use of lysates consisting of non-pathogenic microorganisms leads to a significant and permanent improvement in neurodermatitis patients," said Biedermann who also believes that this acute and severe disease should not be treated with lysates of non-pathogenic microorganisms. Other drugs such as topical glucocorticoids, have proven to have a more rapid and effective effect in treating neurodermatitis patients. Biedermann and his team believe that the application of non-pathogenic or probiotic bacteria to the skin is more effective in reducing the recurrence of diseases following the successful primary treatment of diseases such as neurodermatitis. "The bacteria lead to the permanent stabilisation of the immune system once glucocorticoid treatment has alleviated the acute reaction. Our goal is to establish an immunological barrier in order to prevent the onset of subsequent allergic skin reactions."

Future projects will also focus on the natural microflora of the skin. However, the effect and function of the microflora are rather complex, which is why many details are still missing. And the issue does not get any simpler when additional probiotic or non-pathogenic bacteria are used for the investigations. However, Biedermann is confident that he will be able to make a considerable contribution to the elucidation of mechanisms to prevent allergic skin reactions from developing and recurring. "This requires close collaboration between microbiologists, geneticists, physicians and scientists," said Biedermann.

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