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A novel painless and reliable allergy test

Although allergies are widespread, their diagnosis is complex and, depending on the type of allergy, the prospects of success with therapy are not always clear. Skin tests so far have been unpleasant, time-consuming and associated with a certain risk of triggering an allergic overreaction. Researchers at the University of Bern and Inselspital, Bern University Hospital, have now developed a novel test that massively simplifies the diagnosis of allergies and can reliably predict the success of a therapy.

Approximately one third of the world's population suffers from one or more allergies, with the trend increasing every year. By far the most widespread form of allergy is the so-called type I allergy, also known as immediate-type allergy. This includes, for example, allergic rhinitis (hay fever), allergic asthma, food allergies, or allergies against insect venoms, pollen, grasses or house dust mites. It is an overreaction of the immune system to actually harmless foreign components (allergens), which typically occurs within seconds or minutes of contact with the allergen. Allergic symptoms can range from redness and swelling of the skin, itching or shortness of breath to anaphylactic shock and death.

Diagnosing an allergy is complex: In addition to the medical history (anamnesis), test parameters of often unclear diagnostic value are taken into account and patients undergo skin tests. Such skin tests are unpleasant, at times painful, time-consuming and associated with a certain risk of triggering an allergic overreaction. Allergies are treated with symptom control, in severe cases also with immunotherapy. This involves injecting doses of an allergen in increasing concentrations under the patient's skin over a period of up to five years, with the aim of desensitizing the patient to the allergen. Immunotherapy is not always successful: At present, there is no reliable method for predicting the chances of success before concluding such therapy.

A research group led by Alexander Eggel from the Department for BioMedical Research (DBMR) at the University of Bern and the Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, together with Thomas Kaufmann from the Institute of Pharmacology at the University of Bern, has now developed an allergy test that, on the one hand, greatly simplifies diagnosis and, on the other hand, can reliably predict the success of immunotherapy. The test was recently presented in a publication of the *Journal of Allergy and Clinical Immunology*.

In vitro mast cells provide unprecedented reliability

Type I allergy occurs when the body produces immunoglobulin E (IgE) class antibodies in response to allergens. The IgE antibodies are bound by IgE receptors on the surface of specialized immune cells in the body called mast cells. Subsequent contact with the same allergens then leads to activation of the mast cells and therefore to the release of inflammatory mediators such as histamine or leukotrienes, which are responsible for the allergic symptoms.

For their novel allergy test, the researchers led by Alexander Eggel and Thomas Kaufmann have developed a new in vitro cell culture which, with the help of a few molecular biological techniques, can generate almost any desired number of mature mast cells – and this within a few days. These mast cells contain IgE receptors on their surface and behave very similarly to mast cells in the human body when they are exposed to IgE and allergens. In the test, these mast cells are brought into contact with blood serum from allergic individuals – thereby binding the IgE antibodies from the serum to the cells – and then stimulated with the allergens to be tested. At this point, the activation of the cells can be quantified very easily and quickly using so-called flow cytometry. “We were surprised and delighted to see that our mast cells could be activated at almost 100 percent. To our knowledge, there are no comparable cell lines that can be activated so well,” explains Alexander Eggel. He adds: “Another important advantage is that the test works with serum, which is very stable and can be stored frozen for a long time, which also allows retrospective tests and studies. In contrast, other comparable tests use whole blood, which cannot be stored and must be processed within hours.”

High-throughput approach enables application on a larger scale

In order to be able to perform a large number of tests, the researchers have developed a high-throughput approach in which up to 36 conditions can be measured in a single test tube. This makes possible the testing of either multiple allergens with one blood serum or multiple sera together for the same allergen. “A trained person can already perform about 200 tests per day using this procedure, and the process will be further optimized,” clarifies DBMR’s Noemi Zbären, lead author of the study.

Great potential for various applications

In addition to the initial diagnosis of allergies, the researchers hope the test will have other major applications. “We are confident that with our test we will be able to measure within a few months after the start of an immunotherapy whether the therapy is effective and to what extent,” says Thomas Kaufmann. “This would be an important aid in the decision-making process for the allergologist treating the patient, whether it makes sense to continue the therapy or not.” According to the researchers, the test also has great potential for monitoring therapeutic success and the duration of action for new allergy medications in clinical trials, as well as for determining possible allergic reactions and for quality control of food products.

And academic research should not be neglected either. “The new cell line – and already planned modifications to the same – will enable us to address many of the still unanswered questions in allergy research,” explains Alexander Eggel.

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Please see the following page for more information.

Publication:

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Contact persons:

Assoc. Prof. Dr. Alexander Eggel

Department for BioMedical Research (DBMR), University of Bern, and Department of

Rheumatology, Immunology and Allergology, Inselspital Bern

Tel. +41 31 632 22 87 / alexander.eggel@dbmr.unibe.ch

Assoc. Prof. Dr. Thomas Kaufmann

Institute of Pharmacology, University of Bern

Tel. +41 31 632 32 89 / thomas.kaufmann@pki.unibe.ch

Department for BioMedical Research (DBMR)

The Department for BioMedical Research (DBMR) of the Faculty of Medicine at the University of Bern, led by Prof. Dr. med. Mark A. Rubin, was established in 1994 by the University of Bern and Inselspital, Bern University Hospital. The DBMR is comprised of 13 research programs with approximately 100 participating individual labs and several independent research labs whose research spans across all biomedical fields. In order to bridge the gap between bench and bedside, the DBMR promotes an integrative perspective to clinical research with a strong emphasis in the development of translational approaches, the use of omics and other cutting-edge technologies, as well as extensive interaction and collaboration between laboratory-based and patient-oriented clinical research. The DBMR is also committed to fostering the careers of young academics.

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