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REPLACEMENT OF ALLERGEN CHALLENGE:
SAFELY SCORING PREVALENCE & SEVERITY OF ALLEGIES

Keywords: basophil activation test (BAT), flow cytometry, sensitized, (non-) allergic, scoring system, oral food challenge (OFC), skin prick test (SPT)

INVENTION NOVELTY

Allergies have become the most common chronic disease in Western countries, afflicting about 30% of the population. Although symptomatic treatments are available, many patients are not diagnosed correctly, as common skin prick (SPT) and serological tests only prove the presence of IgEs, but not their clinical relevance. Because IgE detection alone is not sufficient for diagnosing allergies, many patients must undergo time-consuming, lengthy, and potentially life-threatening provocation tests (e.g., oral food challenges, OFC), which still represent the current gold standard. The present invention provides a safe BAT-based alternative to reliably determine and score the prevalence and severity of allergies *in vitro*.

VALUE PROPOSITION

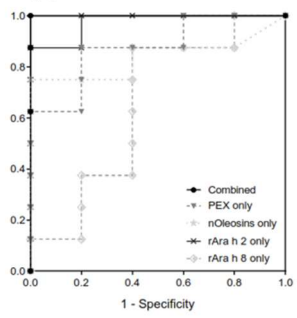
The innovation exploits a well-balanced set of stimuli derived from an allergy-triggering source to individually determine basophil activation and change in expression of certain activation markers. All these data are combined in an algorithm, which allows to reliably determine the presence and severity of an allergy against said source. Combined with a recently introduced improved BAT assay, the method provides the accuracy to replace costly and potentially dangerous allergen challenges and facilitate clinical treatment decisions. In addition to its unprecedented performance, the entire procedure can be performed in a fully automated, high-throughput workflow suitable for e.g., routine/service labs, medical care units and hospitals.

TECHNOLOGY DESCRIPTION

The BAT mimics an allergic reaction *in vitro*. For this, a blood sample is incubated with a potential allergen, which finds a matching, basophil coupled IgE only in case of an existing allergy. However, only the IgE/allergen complex mediates cross-linking with the IgE receptor, resulting in the release of histamine, and eventually the surface-exposure of activation markers like CD63 or CD203c, which can be readily detected e.g., by flow cytometry. Considering its simplicity and accuracy, attempts have been made in the past to exploit this system for determining the presence and severity of allergies. To this end, prior-art tests either used an extract of the allergy-triggering source, or one or two specific allergens present therein, which allowed to discriminate between allergic and non-allergic individuals, but not to determine the actual allergy severity and to guide clinical treatment decisions.

The present invention overcomes these shortcomings by individually determining basophil activation and change of activation markers for at least three different stimuli of the allergy-triggering source, i.e., an extract, a major allergen, and a lipid-associated allergen. The resulting data are then used to calculate a combined symptom and tolerance class (CSTC), on which basis patients can be categorized into individuals with high tolerance and no allergy (CSTC 0), mild allergy and substantial tolerance (CSTC 1), moderate allergy and moderate tolerance (CSTC 2), and severe allergy and low to no tolerance (CSTC 3). In combination with an improved BAT system, the whole method and evaluation can be conducted in high-throughput and in a fully automated fashion.

(A)



(B)

Analysis	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Performance
Combined	1.0 (1.0 – 1.0)	1.0 (0.63 – 1.0)	1.0 (0.48 – 1.0)	perfect
PEX-only	0.88 (0.68 – 1.0)	0.88 (0.47 – 0.99)	0.80 (0.28 – 0.99)	good
nOleosins-only	0.84 (0.61 – 1.0)	0.75 (0.41 – 0.96)	0.80 (0.38 – 0.99)	good
rAra h 2-only	0.98 (0.90 – 1.0)	1.0 (0.63 – 1.0)	0.80 (0.28 – 0.99)	excellent
rAra h 8-only	0.65 (0.31 – 0.99)	0.88 (0.53 – 0.99)	0.60 (0.23 – 0.93)	poor

(C)

CSTC	n	Positive predictive value (95% CI)	Negative predictive value (95 % CI)
0	5	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)
1	1	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)
2	2	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)
3	5	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)

***Performance of combined method and individual stimuli in determining and scoring allergies**. (A) ROC curves, (B) Prediction of allergy prevelance, (C) Prediction of allergy severity/scoring using the combined method (Walsemann et al., unpublished).*

DEVELOPMENT STATUS

The method was validated in a cohort of children (n=15) with suspected peanut allergy, which were also scheduled for OFC. Cross evaluation showed that all individuals that were responsive in BAT (ca. 87%) were classified correctly (AUC: 1). Hence, the BAT-based system can replace allergen challenges and guide clinical therapy decisions.

COMMERCIAL OPPORTUNITY

The innovative BAT-based algorithm and scoring system is available for in-licensing.

PATENT SITUATION

Priority-establishing EP patent application EP23182051.5 has been filed in June 2023.

FURTHER READING

Behrends, *et al.* (2021) Allergy 76: 3776-3788.

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