

# Basophil activation test in allergic rhinitis

**To the Editor** In a paper published in the July–August issue of this journal, Leśniak et al<sup>1</sup> investigated a correlation between a nasal provocation test (NPT) and a basophil activation test (BAT) in patients with allergic rhinitis (AR). The authors concluded that the NPT is still the gold standard in AR, while the BAT may be used as an alternative.<sup>1</sup> The use of the BAT to replace subsequent diagnostic tests exemplifies one of the many attempts to improve diagnosis of allergy. These attempts have been made to prevent misleading interpretations potentially occurring in the diagnosis of AR.

As a matter of fact, a recent paper by Gomez et al<sup>2</sup> has raised the issue of a possible diagnostic misinterpretation of local allergic rhinitis (LAR) with nonallergic rhinitis (NAR) by using the simple NPT.<sup>2</sup> They found a close correlation between the BAT and NPT in a group of patients with AR ( $r = 0.78$ ;  $P < 0.0001$ ).<sup>2</sup> Leśniak et al<sup>1</sup> found a correlation ranging from 0.50 to 0.74, and their observations were quite similar to those reported by Gomez et al.<sup>1,2</sup> According to Gomez et al,<sup>2</sup> the BAT was able to attribute at least 50% of cases of LAR to *Dermatophagoides pteronyssius*, while Leśniak et al<sup>1</sup> suggested the BAT for assessing patients' eligibility to undergo serum immunotherapy for AR.<sup>1</sup> The question of whether the BAT may replace the NPT for diagnosing LAR is still a matter of debate and should involve a further search for the new approaches to differentiating LAR from NAR. Gomez et al<sup>2</sup> reported that a much more complex allergy scenario might be described, actually. In the study by Leśniak et al,<sup>1</sup> this distinction has not been completely addressed.<sup>1</sup> The introduction of the atopy patch test, for example, should improve the diagnostic sensitivity of noncellular diagnostic tests, namely, the skin prick test and measurement of serum immunoglobulin E (IgE) levels.<sup>3</sup> According to Leśniak et al,<sup>1</sup> the presence of NAR could be easily detected by a CD63-based BAT; actually, these authors reported that a proportion of [BAT+]/[NPT–] subjects would be indicated as false positives, which they attributed to such individuals globally defined as atopic. In these patients, there is a significant probability that a practitioner will misinterpret LAR as NAR.<sup>1</sup>

However, despite the evaluation reported by Leśniak et al,<sup>1</sup> a BAT based only on a CD63 percentage or the stimulation index cannot provide

a different perception on rhinitis, be it caused by an IgE- or a non-IgE-mediated challenge, because CD63 is easily activated by nonallergic stimulation.<sup>4</sup> Furthermore, the ability to perform an accurate BAT depends also on the gating strategy used by the test to catch basophils in the flow cytometry electronic capture.<sup>5</sup> The Flow2CAST™ (BÜHLMANN, Schönenbuch, Switzerland) used by Leśniak et al<sup>1</sup> should improve the use of the previous commercial Flow-CAST, but gating basophils with CCR3 may create analytical bias. The best way to address this problem is to initially use 2 different BATs in order to gain a more reliable insight into the ability of the test to prevent a diagnostic misinterpretation whereby NAR is diagnosed instead of LAR. Leśniak et al<sup>1</sup> replicated an experience similar to the latest one recently published by using a CD63-CD203c markers-endowed BAT<sup>6</sup>, and in this sense, their paper does not seem to add truly novel findings to the field. BATs should provide further insight into the ability of a diagnostic test to achieve a better analytical performance respect to further assays, such as NPT. However, the complex immunology of rhinitis may raise further concerns about patients' eligibility for immunotherapy, particularly in the case of asthma and AR when immunotherapy is accomplished with a sublingual approach, the efficacy of which depends on the feature of the allergic pathology. This might be foreseeing also for serum immunotherapy. This would mean that, as it occurred in the study by Leśniak et al,<sup>1</sup> if one applies clinical instead of objective NPT evaluation, the number of truly LAR-positive subjects assessed with the BAT may decrease significantly.<sup>2</sup>

The study published by Leśniak et al<sup>1</sup> suggests that the BAT may be successfully used in the diagnosis of allergy once the clinical scenario of the allergy onset has been thoroughly elucidated.

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**Authors' reply** We are grateful to Dr. Chirumbolo for the comment on our paper describing the correlation between a nasal provocation test (NPT) and a basophil activation test (BAT) in patients with allergic rhinitis (AR).<sup>1</sup> We agree with most of the issues raised by Dr. Chirumbolo, but some points need to be addressed. Differentiation of AR, nonallergic AR (NAR), and local AR (LAR) requires further studies, and the use of the atopic patch test seems to be an interesting complement to diagnostic workup, but only in the case of the reaction occurring in type IV hypersensitivity.<sup>2</sup>

Our paper is part of a larger project encompassing studies on the usefulness of the BAT in type I hypersensitivity reactions, which have been conducted for several years by our research team, especially in patient selection for and monitoring of specific immunotherapy (SIT). As noted by Heffler,<sup>3</sup> the need for biomarkers assessing the probability of response to SIT before it is initiated, as well as biomarkers predicting the safety, long-term efficacy, and time to symptom relapse when SIT is stopped, is crucial and is still a hot topic in allergy and clinical immunology research.<sup>3</sup>

Our study<sup>1</sup> focuses on the possibility of replacing the NPT by BAT during patient selection for SIT.<sup>1,4,5</sup> We knew the paper by Gomez et al<sup>6</sup> and cited it in our paper. Owing to different aims, we used other inclusion criteria: our patients had a suspicion of AR based on history and the results of SPT or the measurement of serum immunoglobulin E (sIgE) levels, and caused by an allergy to birch or house dust mites. In the second step, all patients underwent the NPT and BAT at the same time, with 2 allergens successively: birch and house dust mites. Gomez et al,<sup>5</sup> referred patients for AR, NAR, LAR, and healthy controls on the basis of medical history and SPT, sIgE, and NPT results at baseline. In the second step, they performed only the BAT.<sup>6</sup>

As rightly pointed out by Dr. Chirumbolo, we applied a different method of performing the BAT

(ie, Flow2CAST), although we are aware of its limitations. There is no doubt that the BAT can provide a valuable complementary tool in the diagnosis of allergy and in patient selection for SIT. It is likely that in order to further refine treatment choice and, consequently, its effectiveness, it will be necessary to combine the BAT with other tools in the panels of biomarkers.<sup>3</sup> For technical reasons, research on the BAT is conducted on groups of a few dozen patients, so it is necessary to repeat similar experiments in larger populations and using optimized protocols.

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