Basophil and lymphocyte functional assays with *Aspergillus* molecules: the case for ABPA

Moïse Michel¹, Youssouf Sereme¹, Farid Mankouri¹, Marion Gouitaa², Clarisse Gautier³, Jean-Louis Mege⁴, Carole Cassagne⁵, Stéphane Ranque⁵, Martine Reynaud-Gaubert¹, and Joana Vitte⁶

¹Aix-Marseille Universite

²Hopital Nord

³IHU Mediterranee Infection

⁴Assistance Publique Hopitaux de Marseille

⁵Aix-Marseille Univ, APHM

⁶Aix-Marseille Universite Faculte de Medecine

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Abstract

Background. Allergic bronchopulmonary aspergillosis (ABPA) is an underestimated allergic disease due to *Aspergillus fumigatus* (AF). The main diagnostic criteria for ABPA rely on the evaluation of immunoglobulin (Ig) E and IgG responses to AF extracts, although these cannot discriminate AF-sensitization from ABPA. **Objectives.** To evaluate the performance of cellular functional assays with extract and molecular AF allergens in ABPA. **Methods.** A prospective cohort of 67 patients (6 ABPA) was investigated with basophil activation test (BAT) and lymphocyte stimulation test (LST) with AF extract. Nine patients were further investigated for BAT responses to molecular AF components: Asp f 1, Asp f 2, Asp f 3, Asp f 4 and Asp f 6. BAT supernatant was assessed for cytokine production. **Results.** BAT with AF extract with an optimized cutoff displayed 100% sensitivity and 77.6 % specificity for ABPA diagnosis. Among patients with positive BAT to AF, BAT with Asp f 4 was significantly higher in ABPA patients at 10 ng/mL (mean basophil stimulation index 10.56 in ABPA vs 1.24 in non-ABPA patients, $p = 0.0002$). High LST with AF extract was associated with ABPA occurrence three months after the test. No significant ex vivo cytokine release was observed in BAT supernatants. **Conclusion.** BAT with AF is a promising diagnostic biomarker in the context of suspected ABPA, which can be further improved with AF molecular allergens, especially Asp f 4. LST with detection of AF-induced activation of peripheral T cells suggests an underlying pathophysiological process and may predict ABPA occurrence.

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