We performed a complementary study in a small, yet uniform cohort of 97 patients (median age, 54 years [range, 7–69 years]; 60% males) receiving lung transplant between 1999 and 2012. Main causes for transplantation were pulmonary fibrosis (41%), lung emphysema (29%), and bronchiectasis (14%). Single-lung transplant was performed in 71% of patients, whereas the remaining underwent bilateral transplantation. Most patients received triple-drug immunosuppression with a calcineurin inhibitor, prednisone, and either azathioprine or mycophenolate mofetil. Colonization with Aspergillus species was documented in 14 patients (14%), whereas 13 (13%) were diagnosed with proven/probable IA [4]. As shown in Table 1, the h2/h2 diplotype increased the risk of colonization in the lungs (hazard ratio [HR], 4.77; \( P = .01 \)) and IA (HR, 6.69; \( P = .01 \)). Of note, h2/h2 carriers also displayed increased susceptibility to cytomegalovirus infection (HR, 1.80; \( P = .02 \)). These findings highlight the pivotal role of PTX3 in binding these pathogens and conferring protection from experimental infection [5, 6].

Although PTX3 expression was not evaluated, alveolar levels discriminate microbiologically confirmed pneumonia in mechanically ventilated patients [7], and we previously established that the levels vary independently according to host genotypes [2]. Whether these are also genetically determined in SOT recipients in response to infection needs to be addressed. If confirmed, we can envisage the quantification of PTX3 in bronchoalveolar lavage fluids as a complementary surveillance measure in addition to the currently available diagnostic approaches.

The integration of genetic markers into clinically valid processes to stratify the risk and progression of fungal infection, and the efficacy of antifungal prophylaxis and therapy, holds the promise of a groundbreaking innovation for patients at risk [8]. Although the overall weight of the antifungal immune response clearly results from adding effects of single genetic factors and their complex interactions with clinical immune dysfunctions, PTX3 represents the most robust genetic marker identified to date. These consistent findings are expected to lay the foundations for well-designed prospective trials ultimately endorsing PTX3-based genetic testing in risk stratification approaches for aspergillosis.

Notes

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Potential conflicts of interest. A. M. has been a consultant to Sigma Tau Pharmaceuticals (Pomezia, Italy) and a board member of the Istituto di Ricerche in Biomedicina (Bellinzona, Switzerland) and Efranat Ltd (Rehovot, Israel). A. M. has received royalties from HyCult, BD Biosciences, and Santa Cruz Biotechnology. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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