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Correspondence

Reply to Cunha et al

To the Editor—In a previous study, Cunha et al showed that polymorphisms in long pentraxin 3 (*PTX3*) influenced susceptibility to invasive aspergillosis among hematopoietic stem cell transplant recipients [1]. A similar association is now reported in 2 studies of solid organ transplant recipients, the Swiss Transplant Cohort Study [2], and a cohort of lung transplant recipients, as described in the current letter by Cunha et al [3]. The risk allele arises, respectively, from the donor of hematopoietic stem cells and from the recipient of solid organ transplant, which is consistent with the different origin of immune cells in these patients. The functional role of PTX3 in fungal immunity has been demonstrated both in vitro and in vivo [4–6], and there is evidence that the polymorphisms influence the genes' expression [1]. Altogether, these observations make PTX3 polymorphisms a promising host genetic marker of infection in transplant recipients.

Polymorphisms in >20 genes have been reported to influence susceptibility to invasive aspergillosis in oncohematological patients [7]. After initial studies, the concept rapidly emerged that aspergillosis risk could be stratified according to a combination of genetic and nongenetic factors, and that patient management could be personalized, for instance by using specific surveillance and/or prophylactic regimens in the higher-risk patients [8].Yet, such strategies have not been implemented so far. Some of the polymorphisms initially associated with susceptibility to invasive aspergillosis had low minor allele frequencies [9, 10], thereby limiting the ability to obtain replication, as very large confirmatory cohorts would be needed to reach a sufficient statistical power. Other studies were limited by methodological issues or by a lack of a definite role for the reported genes and/or polymorphism(s) in antifungal immunity [7]. In addition, prophylactic regimens have been used increasingly, especially among hematopoietic stem cell transplant recipients, making it more difficult to replicate associations observed without prophylaxis.

Because the association of *PTX3* polymorphisms seems robust, it might be considered as a key factor for risk stratification. Yet, many questions remain open, such as in which population it would be most beneficial, and to which extent it would impact individual management. Thoracic organ recipients may constitute a potential group for further studies, because those patients have a relatively high risk to develop the infection and they do not routinely receive antifungal prophylaxis in many centers. Yet, due to the small number of patients studied so far, the number of variables that can be implemented together within a potential score is limited, and makes it difficult to estimate risk and benefit. Large novel prospective studies or meta-analysis from several studies using systematically selected markers would be needed to address these questions before formal recommendations can be made.

Notes

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