

Correspondence

Reply

To the Editor:

We appreciate the comments of Guéant et al.¹ We agree that our study supports the *IL4* pathway as playing a mechanistic role in β -lactam allergy.² We thank you for drawing attention to your study that, like the one we referenced, found an association with an *IL4R* single nucleotide polymorphism, although we did not.³ We agree that there might be several reasons why our relatively small study did not find an association, including small sample size and different allele frequencies of the control subjects between countries. Therefore additional research is needed before a definitive conclusion can be made about the generalizability of Guéant et al.'s results to non-Italian populations.

Our limited resources did not allow us to include *IL13* polymorphisms, and our emphasis was a little different: identifying both clinical and genetic risk factors and examining the importance of genetic risk factors relative to those clinical risk factors. We agree it would be informative to study *IL4* and *IL13* gene pathway interactions. The products of these 2 genes, closely located on chromosome 5, both use the IL-4 receptor α . Thus an interaction between *IL4* or *IL13* and *IL4RA* would support the role of IgE in drug allergy. Nonetheless, for gene-gene interaction studies, a very large sample size is needed to obtain reliable results. We also call attention to the marginal association of a single nucleotide polymorphism from another gene: the β -lactamase gene (*LACTB*) was marginally associated, lending support to the other aspect of our theory that penicillin is multifactorial with contributions from

several genes (the *IL4* pathway but also others) and the environment (exposure to antibiotics).

Andrea J. Apter, MD, MSc^{a,b,c}

Hedi Schelleman, PhD^b

Timothy Rebbeck, PhD^b

From ^athe Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine; ^bthe Center for Clinical Epidemiology and Biostatistics and the Center for Education and Research on Therapeutics; and ^cthe Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, Pa. E-mail: apter@mail.med.upenn.edu.

Supported by the Agency for Healthcare Research and Quality Centers for Education and Research on Therapeutics Cooperative Agreement (HS10399); the National Heart, Lung, and Blood Institute (HL K23 04337-01, to A.J.A.); and the National Institutes of Health (P20RR02074).

Disclosure of potential conflict of interest: T. Rebbeck has received research funding from and served in an advisory capacity for the National Institutes of Health and has served in an editorial capacity for the American Association for Cancer Research. The rest of the authors have declared that they have no conflict of interest.

REFERENCES

1. Gueant JL, Gueant-Rodriguez R-M, Cornejo-Garcia J-A, Viola M, Blanca M, Romano A. Gene variants of *IL13* and *IL4RA* are predictors of β -lactam allergy. *J Allergy Clin Immunol* ■■■;■■■:■■■.
2. Apter AJ, Schelleman H, Walker A, Addya K, Rebbeck TR. Clinical and genetic risk factors of self-reported penicillin allergy. *J Allergy Clin Immunol* 2008;122:152-8.
3. Guglielmi L, Fontaine C, Gougat C, Avinens O, Eliaou JF, Guglielmi P, et al. IL-10 promoter and IL4-Ralpha gene SNPs are associated with immediate beta-lactam allergy in atopic women. *Allergy* 2006;61:921-7.

Available online ■■■,
doi:10.1016/j.jaci.2008.10.059