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Reply to 08-1145: Gene variants of IL-13, IL-4, and IL-4R are predictors of beta-lactam allergy, by Guéant et al

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To the Editor:

We appreciate the comments of Guéant et al.¹ We agree our study supports the IL-4 pathway as playing a mechanistic role in beta-lactam allergy.² We thank you for drawing attention to your study that, like the one we referenced, found an association with an *IL4R* SNP while we did not.³ We agree there may be several reasons why our relatively small study did not find an association, including small sample size and different allele frequencies of the controls between countries. Therefore, additional research is needed before 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 clinical as well as 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 two genes, closely located on chromosome 5, both use the IL-4RA receptor. Thus, an interaction between *IL4* or *IL13* and the *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 SNP from another gene: *LACTB* was marginally associated lending support to the other aspect of our theory that penicillin is multi-factorial with contributions from several genes, IL-4 pathway but also others, and the environment (exposure to antibiotic).

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Abbreviations used

<i>IL4</i>	IL-4 gene
<i>IL4R</i>	IL-4 receptor gene
<i>IL13</i>	IL-13 gene
<i>LACTβ</i>	β-Lactamase gene