

Correspondence

Reply

To the Editor:

We have recently reported that mothers with elevated allergen-specific IgG levels close to birth could transmit allergen-specific IgG antibodies to their children and, when the allergen-specific IgG levels were above a certain threshold as shown in maternal blood samples close to birth and in cord blood samples, the children did not develop allergen-specific IgE sensitizations against these allergens up to the age of 5 years.¹ In a Correspondence, Aalberse et al² consider our assumption “that maternal allergen-specific IgG might protect the child against allergic sensitization” interesting but suggest that it needs more extensive studies for validation.² The authors propose to focus on few of the most frequently sensitizing airborne allergens and present own unpublished data that they obtained for the prevention and incidence of asthma and mite allergy (PIAMA) birth cohort for the major house-dust mite allergen Der p 1 and the major cat allergen Fel d 1. They present data for sera from 92 children from PIAMA without mentioning if and how these children were selected from the cohort and at which age serum samples were obtained from the children and analyzed. In their figures, the authors measured levels of maternal IgG antibodies against the major house-dust mite allergen Der p 1 and the major cat allergen Fel d 1, whereas IgE sensitizations in children are presented for house-dust mite and cat allergen extracts, which contain a variety of different allergens in addition to Der p 1 and Fel d 1, respectively. It is therefore not possible to relate maternal Der p 1- and Fel d 1-specific IgG antibodies to allergen-specific IgE in children. It is further unclear whether the maternal blood samples for which the authors analyzed Der p 1- and Fel d 1-specific IgG levels were obtained close to birth or at another time point because there is no mention that in the PIAMA birth cohort maternal or cord blood samples were obtained at all.³

In contrast, we have measured allergen-specific IgG levels in plasma obtained from 99 defined mother/child pairs, in particular plasma samples from mothers close to birth and cord blood samples to 164 different allergen molecules and analyzed IgE sensitizations to the very same 164 allergen molecules in children at age 5 years. Our results show for both, maternal blood samples and cord blood samples, cutoffs for allergen-specific IgG above which no IgE sensitization occurs in children at age 5 years. Another strength of our analysis is that we were able to measure maternal allergen-specific IgG and allergen-specific IgE in children against 164 allergen molecules because if one focuses the analysis on only a few allergen molecules, larger numbers of mother/child pairs would be needed to obtain meaningful results. If, as suggested by Aalberse et al, one focuses on only selected allergen molecules, the analyses can be easily confounded by the presence or absence of allergen exposure in early childhood because children can be born during or outside pollen seasons and in homes with or without exposure to house-dust mites or pets as the authors rightly suggest.

However, we agree with the authors that more extensive studies are needed. First of all, the protective effect of natural maternal IgG will depend not only on allergen-specific IgG levels but also on the epitope-specificity and avidity of the allergen-specific IgG antibodies because not all maternal allergen-specific IgG

antibodies will be able to block allergen-specific IgE reactivity and thus be able to prevent allergic sensitization. The authors' suggestion to study the effects of allergen-specific IgG induced in mothers by allergen-specific immunotherapy (AIT) is very useful. In fact, we have observed that AIT-induced IgG₁ and IgG₄ can cross the placenta⁴ and an earlier study indeed suggested that AIT of mothers may protect against allergic sensitization in children.⁵ However, to induce high levels of allergen-specific IgG antibodies that prevent IgE binding to allergens, subcutaneous forms of AIT (SCIT) instead of sublingual forms of AIT may be preferred because only SCIT induces high levels of allergen-specific IgG. Therefore, it may be also important to select new molecular forms of SCIT that induce IgG antibodies against the IgE-binding sites of defined allergens. One possible candidate vaccine is the recombinant grass pollen allergy vaccine BM32, which focuses IgG against the IgE-binding sites of the major grass pollen allergens without inducing IgE sensitizations.⁶ Another important aspect will be to demonstrate the safety of AIT also for nonsensitized subjects because it will be important to vaccinate not only allergic mothers but also nonallergic mothers. In this context, it has been shown recently that vaccination of nonallergic subjects with recombinant hypoallergenic allergen derivatives is safe, does not induce allergic sensitization, and gives rise to a sustained allergen-specific IgG response.⁷ Finally, proof-of-principle studies investigating whether allergic sensitization can be prevented by the induction of allergen-specific IgG in mothers by AIT may be preferentially conducted in populations with high exposure to certain defined environmental allergens. For example, a high percentage of subjects in Scandinavia and Russia are sensitized against the major birch pollen allergen Bet v 1 because of the high exposure to birch pollen in these countries.^{8,9} One must therefore consider our study indicating that maternal IgG may protect the offspring against allergic sensitization and the other recent study⁷ showing that AIT with defined hypoallergenic molecules is safe in nonallergic subjects as first steps toward prophylactic vaccination against allergy, which, as it seems, may be achieved by vaccination of mothers.

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