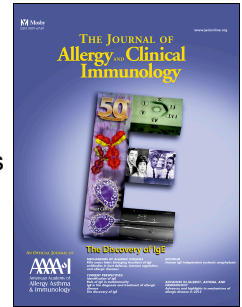


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Investigating innate immune mechanisms in the early-life development and outcomes of food allergy

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1 **TITLE:** Investigating innate immune mechanisms in the early-life development and outcomes of
2 food allergy

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11 The U.S. Centers for Disease Control and Prevention has reported an approximately 50%
12 increase from 1997 to 2011 in the prevalence of reported food allergies in children ¹, with
13 estimates of up to 6 million American children with food allergies at an economic cost of ~\$25
14 billion per year^{1, 2}. Notably, a good proportion of these individuals will develop immunologic
15 tolerance and resolution of the food allergy ³. For example, food allergy resolution can be
16 observed in 43–57% of children with milk allergy in early to late childhood (2–10 years) ³; 47–
17 50% of children with egg allergy in early to late childhood (2–9 years) and 22% of infants with
18 peanut allergy by 4 years of age^{4, 5}. The underlying immunologic mechanisms leading to initial
19 food sensitization, subsequent development of food allergies and natural resolution versus
20 persistent food allergy are poorly understood.

21 Studies of recent, prospective birth cohorts suggest a role for altered early innate immunity in
22 the development of CD4⁺ Th₂ responses and predisposition to allergic diseases⁶. Functional
23 characterization of the ontogeny of microbial pattern-recognition responsiveness of peripheral
24 blood mononuclear cells (PBMCs) and CD4⁺ T cells over the first 5 years of life has revealed a

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