

Children's Memorial Food Allergy Study: Addressing major questions about food allergies in children

XIAOBIN WANG, MD, MPH, SCD, JACQUELINE A. PONGRACIC, MD

In the U.S., the prevalence of food allergies (FA) in children increased 18% percent in the past decade, affecting approximately 3 million children.¹ While this life-threatening condition in children is on the rise, effective means to treat and prevent FA are lacking. We launched the ongoing Children's Memorial Food Allergy Study in 2005 to discover the causes of FA by studying 3 different populations enrolled in Chicago, Boston and China. This multi-center design allows us to study variation in the prevalence and types of FA across diverse populations and geographic regions with different environment exposures and lifestyles.

This study will greatly enhance our understanding of environmental and genetic contributions to FA and its underlying biological mechanisms. Such information will help develop strategies to identify individuals highly susceptible to FA, strategies for early and targeted prevention, and novel targets for developing effective therapies.

Our team has recruited over 5000 newborns in Boston and approximately 2000 twin pairs in China. In Chicago, we have recruited over 500 FA affected families and need to enroll an additional 500 FA affected families to reach the goal of 1000. The large sample size is necessary in order to have sufficient statistical power to study over 1 million genetic markers and hundreds of prenatal and postnatal environmental exposures.

Data gathered from these populations already have resulted in important discoveries about the development of allergy and related conditions. We will review our major findings to-date that are beginning to shed light on some of the most salient questions about FA in children.

Is food allergy genetically determined?

Like asthma and other allergic diseases, FA is believed to be a complex trait determined by both environmental and genetic factors. In the Chicago cohort, we found positive associations between mother and offspring and between the index child and other siblings for any FA and specifically allergy to egg whites, cow milk, and peanut.² Such familial aggregation suggests that shared environmental or genetic factors play an important role in FA.

In another study using the Chinese twin cohort, we demonstrated that sensitization to common foods and aeroallergens was influenced by both genetic and environmental factors.³ We also observed high phenotypic correlations between sensitization to aeroallergens (cockroach and dust mite) and food allergens (peanut and shellfish), suggesting that co-sensitization to multiple allergens might share some common sets of genetic and environmental factors.³

Is obesity associated with sensitization to food allergens?

While obesity has been associated with asthma, associations with allergic sensitization have been inconsistent. Our team sought to examine the association of adiposity and lipid profiles with allergic sensitization in a large sample of rural Chinese twins.⁴ This study suggests a gender-specific link between adiposity, serum lipids and allergic sensitization. In this relatively lean Chinese population, higher percent of body fat, lower HDL and higher LDL were associated with greater risk of allergic sensitization in males. Serum lipids and allergic sensitization also may have some common genetic influences.

There also may be prenatal links between the obesity/metabolic syndrome epidemic and the allergy epidemic, as suggested by our novel findings using the inner city Boston birth cohort.⁵ Maternal obesity has been previously associated with gestational diabetes. Our data demonstrated that in term births, gestational diabetes significantly increased the risk of atopic dermatitis and early childhood allergen sensitization to common foods and aeroallergens, independent of maternal pre-pregnancy body mass index and fetal growth.

Is there geographic or population difference in food allergy?

Our team also found an apparent dissociation between high allergic sensitization and low allergic disease in a rural Chinese population. This is not the case in our Chicago and Boston study populations.⁶ We are still searching for answers to this disparity, trying to understand whether it might be due to urban vs. rural exposures, diet and lifestyle differences, or genetic susceptibility.

500 families still needed to help researchers unlock causes of food allergies and propel cures

Children suffering with food allergies need your help to make this a landmark study of food allergy.

Contact: If you would like to promote the study in your office with posters and flyers, please call a toll free number 888.573.1833 or email allergystudy@childrensmemorial.org.

Who is eligible: This is a family-based study. An eligible family includes both biological parents and at least 1 food allergy affected child (age 0-21 years). Both parents and affected children must be willing to participate.

What is involved: Participants undergo routine clinical measurements (height, weight, blood pressure), a lung function test, allergy skin test, blood draw (10 ml or 2 tsp for allergy test and genotyping) and a questionnaire interview. Visits are conducted in Chicago and suburban locations by trained research staff. The study team will make every effort to accommodate the study family's schedule and preferred location.

Sponsors: The study is supported by the National Institutes of Health (NIH), the Chicago Community Trust, Food Allergy Initiative, David and Denise Bunning and the Sunshine Charitable Foundation, the Sacks Family Foundation, and other generous donors.

Please visit <http://www.childrensmrc.org/allergy> for more information about this study.

Searching for genetic clues to food allergy

In an ongoing effort, our team is conducting a large-scale candidate-gene association study in the Boston birth cohort. We are focusing on promising yet unproven candidate genes involved in various immune pathways of FA.

We are also conducting the first genome-wide association (GWA) study of FA. We plan to genotype 1000 trios (mother, father, and food allergy affected child) enrolled in the Chicago cohort using Illumina Infinium 1M Omini Beadchip with more than 1 million genetic markers. This research may lead to identification of novel genetic loci of FA.

REFERENCES

- [1.] *Branum AM, Lukacs SL. Food allergy among U.S. children: Trends in prevalence and hospitalizations. NCHS data brief, no 10. Hyattsville, MD: National Center for Health Statistics. 2008.*
- [2.] *Tsai HJ, Kumar R, Pongratic J, Liu X, Story R, Yu Y, Deanna C, Costello J, Schroeder A, Fang Y, O'Gorman M, Wang X. Familial aggregation of food allergy and sensitization to food allergens: A family-based study. Clinical and Experimental Allergy 2009 Jan;39(1):101-109.*
- [3.] *Liu X, Zhang SC, Tsai HJ, Hong XM, Wang BY, Fang YP, Liu X, Pongratic J, Wang X. Genetic and environmental contributions to allergen sensitization in a Chinese Twin Study. Clinical and Experimental Allergy 2009;39(7),991-998.*
- [4.] *Ouyang F, Kumar R, Pongratic J, Story RE, Liu X, Wang B, Xing H, Liu X, Li Z, Zhang W, Fang Y, Zhang S, Xu X, Wang X. Adiposity, serum lipid levels, and allergic sensitization in Chinese men and women. Journal of Allergy & Clinical Immunology 2009;123(4):940-948,e10.*

[5.] *Kumar R, Ouyang F, Story RF, Pongratic JA, Hong X, Wang G, Pearson C, Ortiz K, Bauchner H, Wang X. Gestational diabetes, atopic dermatitis and allergen sensitization in early childhood. Journal of Allergy & Clinical Immunology. In press; available online September 6, 2009. doi:10.1016/j.jaci.2009.06.052.*

[6.] *Kim JS, Ouyang F, Pongratic JA, Fang Y, Wang B, Liu X, Xing H, Caruso D, Liu X, Zhang S, Xu X, Wang X. Dissociation between the prevalence of atopy and allergic disease in rural China among children and adults. Journal of Allergy & Clinical Immunology 2008;122:929-935,e4.*



XIAOBIN WANG, MD, MPH, SCD

Co-leader, Children's Memorial Food Allergy Study; director, Mary Ann & J. Milburn Smith Child Health Research Program, Smith Research Professor, Children's Memorial Research Center; professor of pediatrics, Northwestern University's Feinberg School of Medicine; Chicago, Illinois
xbwang@childrensmemorial.org



JACQUELINE A. PONGRATIC, MD

Co-leader, Children's Memorial Food Allergy Study, division head, Allergy and Immunology, Children's Memorial Hospital; associate professor of pediatrics and medicine, Northwestern University's Feinberg School of Medicine; Chicago, Illinois
jponggratic@childrensmemorial.org