



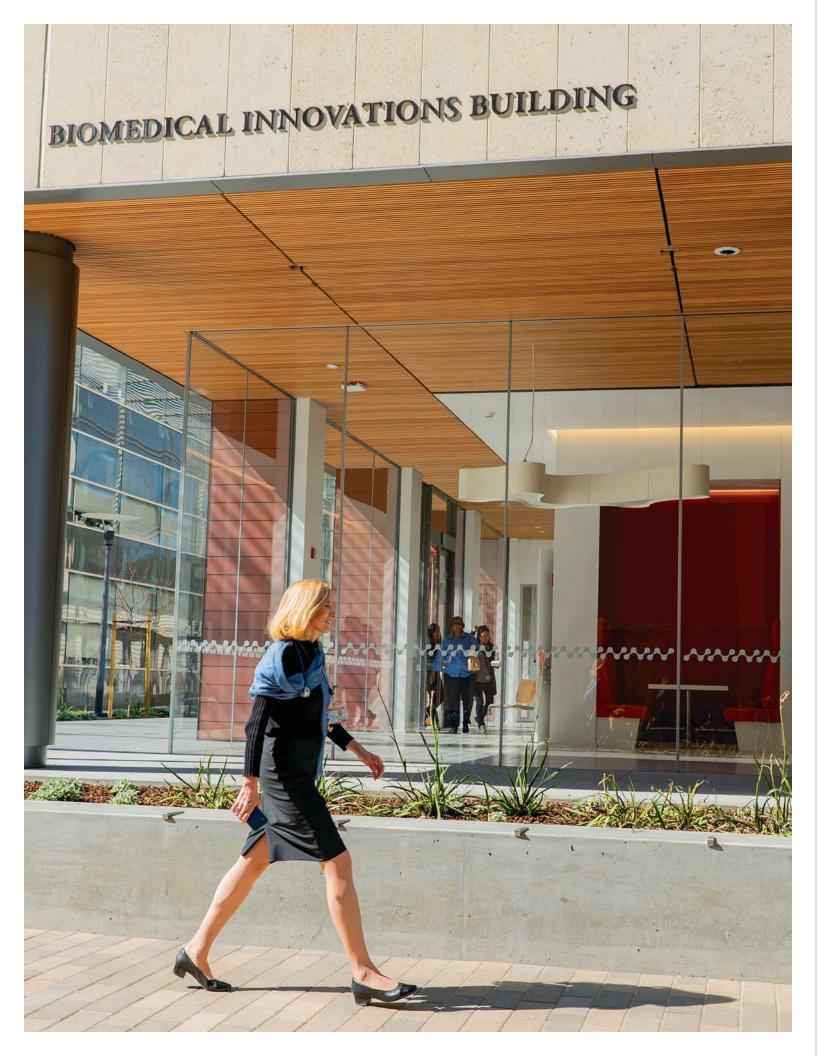
Together, We Are Fulfilling Our Promise

Thanks to our generous philanthropic community and brave patients, we are discovering new treatments and diagnostics for allergy and asthma, treating more people than ever, and shaping policies around climate change.



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All Thanks to You, We Are Delivering on Our Promise



Thank you. None of the work we have done this year would be possible without you—our donors, our friends, our patients.

And what a year it has been! In January 2020, the Food and Drug Administration approved the first oral immunotherapy medication for peanut allergy—thanks in great part to research at the Sean N. Parker Center for Allergy & Asthma Research. We performed the first two vaccine studies in food allergy. We received national attention in the media and the scientific community for studies on oral immunotherapy maintenance dosing and

the effects of wildfires on health. We opened a new clinic on the Stanford campus and secured laboratory space in the Biomedical Innovations Building, which will allow us to expand our research and patient care.



While we do receive support from the National Institutes of Health and other non-profit organizations, the vast majority of our funding comes from philanthropy, often from families affected by allergies and asthma. Your generosity and leadership have allowed us to advance the science, improve care, and expand our outreach to underserved, low-income communities to get them access to information and treatment for allergies and asthma.

Just six years after our Center was founded, we are delivering on the promise we made then to improve the health of children and adults with allergies and asthma. All thanks to you.

I hope you enjoy reading about the many achievements you have made possible at our Center in 2019. And I hope you take pride in all you are making possible for years to come as we continue to create innovative science and deliver compassionate care for all people living with allergies and asthma. We can't do it without you.

All the best,

Kari C Madeau

Kari C. Nadeau, MD, PhD, FAAAAI

Director, Sean N. Parker Center for Allergy & Asthma Research at Stanford University Naddisy Foundation Professor of Pediatric Food Allergy, Immunology, and Asthma Professor of Medicine and Pediatrics and, by courtesy, Otolaryngology at Stanford Section Chief, Asthma and Allergy
Division of Pulmonary & Critical Care
Division of Allergy, Immunology, & Rheumatology
Member, Institute for Immunity, Transplantation and Infection at Stanford
Fellow, Stanford Center for Innovation in Global Health
Faculty, Stanford Woods Institute for the Environment

Scientific Advances and Program Achievements

The Sean N. Parker Center for Allergy & Asthma Research is bringing innovative, life-changing progress and hope to people with allergies and asthma worldwide.



In 2019, our Center made tremendous progress in identifying and understanding the molecular pathways underlying allergic disease, enabling us to get closer to causes and cures for allergy, asthma, and inflammation. More than 400 patients addressed their sensitivity to peanuts and other foods through oral immunotherapy trials we conducted. Food allergy immunotherapy involves having patients ingest tiny doses of an allergen, such as a peanut protein, to desensitize their immune system to the food. A milestone was reached in January 2020 when the Food and Drug Administration (FDA) approved the first oral immunotherapy medication for peanut allergy—Palforzia from Aimmune Therapeutics. The FDA gave it a green light because of Palforzia's effectiveness in reducing allergic reactions and the high unmet need for treating peanut allergy. Our Center was one of the sites that evaluated this drug in patients. Having the first immunotherapy drug for food allergy approved by the FDA is a monumental achievement, heralding a new era of safe and effective treatments. None of this important work could have been done without our generous donors and brave patients.

We look forward to using rigorous science and compassionate care to develop life-changing treatments and find preventions and cures for allergy and asthma.

Here are Some Highlights from the Past Year:

Advancing Clinical Trials

In 2019, we continued to expand clinical research, conducting more than 25 trials. We launched seven new studies and continued working on more than 20 ongoing studies. Research topics included allergic rhinitis, atopic dermatitis, asthma, eosinophilic esophagitis (EoE, or allergic inflammation of the esophagus), and allergies to peanuts, milk, cashew, shrimp, and multiple foods. We had 1,744 clinical visits, including visits with 191 patients tested for allergy for the first time, and 40 adults and children enrolled in new studies. Our biobank of specimens, which are used in our research, increased from about 72,000 to nearly 75,000.

It was exciting to start a Phase 2 trial for peanut allergy with dupilumab, a promising biologic drug (meaning it is produced from or contains components of living organisms) that was previously approved for eczema and asthma. We also began a Phase 2 trial for multi-food allergies that combined dupilumab with another drug, omalizumab.

In addition, we started a Phase 1 trial of a novel vaccine, ASP0892 (formerly ARA-LAMP-Vax). It contains DNA that produces peanut proteins when injected into the body. The vaccine is designed to desensitize a patient to three major allergenic proteins in peanuts. Other new trials started in 2019 included oral immunotherapy for shrimp or cashew and a study of omalizumab as the principal therapy and as an adjunct therapy in people with multiple allergies.

In addition to food allergy, we continue to work on other allergic diseases. Allergic diseases often show up first as atopic dermatitis, or eczema, and then progress to food allergy, allergic rhinitis that affects the nose, and, subsequently, asthma. This is known as the "atopic march," which can start with defects in the skin barrier. We evaluated the effectiveness of two types of emollients, or moisturizers, one that is paraffinor petroleum-based and the other a trilipid cream mimicking the skin's natural lipid composition and pH. Based on trans-epidermal water loss, a measure of skin barrier integrity, the trilipid cream was superior to paraffinor petroleum-based emollients at restoring the skin barrier.

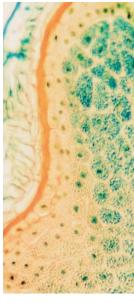
For a list of clinical trials, see pages 34–37 in the Clinical Impact section of this update.

Making Progress with Food Allergies

In 2019, we completed a large Phase 2 trial of peanut immunotherapy, called POISED. This study shed light on important questions about life after peanut immunotherapy. Current research suggests that patients need to continue a maintenance dose to stay desensitized, but there is little information on how large that dose needs to be. This study found that although immunotherapy could desensitize individuals to up to four grams of peanut protein (about 16 peanuts), stopping the intake of peanut protein, or even decreasing it to 300 milligrams daily, could increase a person's risk of becoming sensitive to peanuts again.







The POISED study received a Top 10 Clinical Research Achievement Award for 2020 from the Clinical Research Forum, a nonprofit that promotes clinical research.

Dr. Sharon Chinthrajah, clinical associate professor, director of the Clinical Translational Research Unit of our Center, and a Carell Family Endowed Faculty Scholar for Food Allergy and Immunology Research, was honored at a virtual award event for leading the POISED research.

We have long studied B cells in blood, which produce immunoglobulin E (IgE), an antibody underlying food allergy. In one 2019 study, we obtained blood samples as well as biopsies from the stomach, duodenum, and esophagus from people with peanut allergy. Using DNA sequencing, we determined that IgE-producing B cells are found not only in the blood, but also in the gastrointestinal tract, a finding that may assist in discovering new ways to treat food allergy.

However, some individuals with peanut-specific IgE can eat peanuts without allergic reactions (known as sensitized tolerance). Using mass cytometry, in which antibodies are used to label proteins to determine a cell's properties, we found cellular and molecular indicators that may help us differentiate people who are allergic to peanuts and those who have peanut-specific IgE but do not have an allergic reaction.

In addition to peanut allergy, we continued developing immunotherapy for other allergies and multiple food allergies. We participated in a multicenter study on wheat oral immunotherapy and found that immunotherapy with high-protein wheat flour was safe and effective in desensitizing most participants within a year. More importantly, 13 percent of participants continued to be desensitized after two years, even if they discontinued immunotherapy for eight to 10 weeks.



Testing New Drugs

With our deep understanding of the molecular mechanisms underlying food allergy, our Center is well-positioned to test novel biologic drugs that have been developed. For example, we conducted trials of a peanut allergy drug called etokimab that inhibits interleukin-33, a key molecule that initiates a cascade of reactions leading to the symptoms of allergy. In a Phase 2 study, we evaluated the effectiveness of a single injection of etokimab in those with severe peanut allergy. We found that 15 and 45 days after treatment, 73 percent and 57 percent, respectively, could consume 375 milligrams of peanut protein (about one to 1½ peanuts). In contrast, all participants who received the placebo had an allergic reaction upon eating peanut protein. The drug was also found to be safe, and none of the participants experienced severe side effects.

Current therapies for peanut allergy require daily intake of peanut allergens, making it difficult to follow the regimen. Etokimab could be used as a single therapy and would not require that patients consume the allergen regularly for desensitization.

Assisting the Underserved

We are working toward ensuring proper and timely diagnosis for the poor and the uninsured. Often, the medically underserved must go to the emergency room for treatment, where they might be undertreated. For example, only 33 percent receive epinephrine at some point in their care, just 10 percent are seen by an allergist, and a mere 30 percent get referred to an allergist for further treatment.

Our Center is in discussions with the pediatric and adult emergency rooms at Stanford Hospital and Lucile Packard Children's Hospital Stanford to create a process where people with allergic reactions who do not get evaluated by an allergist are directed to our Center for free food allergy testing. This will assist with proper diagnosis and care.

Shaping Policy

We rely on robust scientific data as we help advance treatments toward FDA approval. Our research has shown that the long-term benefits of desensitization with peanut oral immunotherapy outweigh the short-term risks of allergic reactions during immunotherapy. However, on July 10, 2019, the Institute for Clinical and Economic Review (ICER) reported that the clinical evidence for peanut oral immunotherapy is insufficient and that current evidence does not yet demonstrate that long-term benefits outweigh short-term risks.

ICER's conclusion contrasted with compelling data from our Center and other research institutions. Many patients undergoing immunotherapy for food allergies report major improvements in their quality of life. We believe that the risks of allergic reaction are minimal if immunotherapy is conducted at sites that are trained and equipped to immediately treat upon the first signs of an allergic reaction. Risks also are minimized when patients are educated on how to recognize an allergic reaction, when to get medical help, and when and how to use epinephrine auto-injectors.

Dr. Nadeau led more than two dozen researchers in the U.S., Canada, and Europe to write an article voicing strong support for oral immunotherapy for peanut allergy, which appeared in November in the Journal of Allergy and Clinical Immunology. This advocacy assisted with getting support from the FDA's Allergenic Products Advisory Committee and approval from the FDA for Palforzia to treat peanut allergy.

Advancing New Technologies

Increasingly, bioinformatics—the computerized analysis of large volumes of biological data—is playing a central role in allergy research. Bioinformatics is becoming more important in our investigation of immune changes in people undergoing peanut immunotherapy. For example, we are using RNA sequencing on gastrointestinal samples from patients in immunotherapy to investigate the genetic makeup of those who benefit from immunotherapy. We are also evaluating biomolecules that can help predict who can maintain desensitization to peanut allergens after successful immunotherapy.

Our Center is also continuing to innovate in making food allergy and aeroallergen diagnosis more accurate, specific, and easy. Our patents include two diagnostic tests for allergy. Both detect certain proteins on basophils, white blood cells in the immune system, which are activated when stimulated by allergens. One uses a technique called flow cytometry, which uses a laser beam to separate cells based on associated biomarkers. The other is a microfluidic device, which we have developed in collaboration with Dr. Sindy Tang, associate professor of mechanical engineering at Stanford. The device uses only a tiny drop of blood to detect proteins present on basophils during activation. The device can quickly and easily diagnose multiple allergies simultaneously. One of our other patents is for a mixture of allergens that is designed to promote and support the immune system and a healthy gut microbiome.

Investigating Wildfires and Pollution

In recent years, California has seen increases in the frequency, length, and magnitude of wildfires. Our Center is investigating the long-term health effects of these fires on the heart, lungs, and immune system. For example, Mary Prunicki, MD, PhD, Barakett Endowed Faculty Scholar for Expanded Access, has been studying the molecular changes associated with prolonged exposure to wildfires. In addition to changes in immune cells, she has found that wildfire leads to increased expression of the PDL2 protein, which has been associated with airway inflammation and cancer. Our work on wildfires has been cited in the Washington Post, the New York Times, and Nature.



In one study, we compared people who were and were not exposed to smoke from the 2014 El Portal wildfire near Yosemite National Park and found that exposed individuals had significant increases in IL-beta and c-reactive proteins, both indicators of inflammation. As the people tested lived 62 miles away from the fire, the findings indicate that wildfire impact may affect the health of even those living at a distance.

Dr. Prunicki has also started a study on the effect of wildfire exposure in firefighters by examining their blood biomarkers associated with smoke exposure. In another study conducted near Fresno, California, a region with high levels of air pollution, she has completed a study on adolescents that looked at the effect of pollutants on inflammatory markers and blood pressure. She has also completed research in young children to evaluate the effect of air pollution on monocytes, immune cells that are predominant in plaque, which can build up and clog arteries.

Much of our research is done through partnerships that make us stronger. The Center has formed collaborations with the Woods Institute for the Environment and The Bill Lane Center for the American West, both at Stanford, to conduct wildfire research. In 2019, Dr. Nadeau was appointed a senior fellow at the Woods Institute and is part of the FIRE team there, which aims to deliver comprehensive recommendations based on sound science to support local, state, and federal agencies. We are also developing curriculum on pollution, climate change, and human health to foster education and awareness of these issues.

We could not have accomplished all that we did without you!

Planting Seeds for Discovery

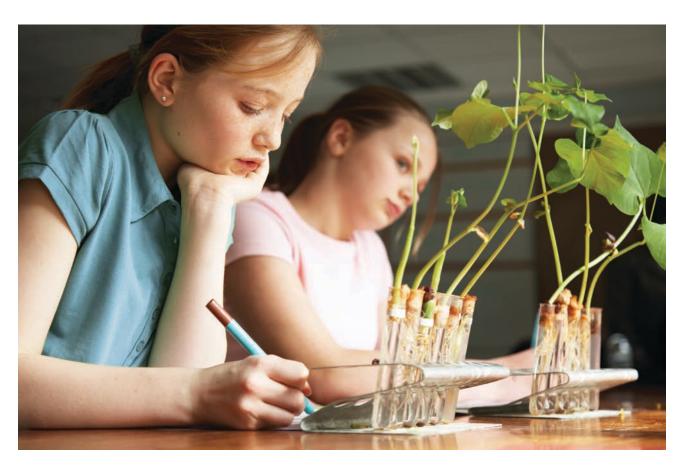
Seed grants fund the exploration of ideas that can benefit scientific knowledge and medical treatment of patients with allergies, asthma, and respiratory problems. This research lets physicians and scientists plant the seeds for medical breakthroughs and develop new technologies and methods. Your philanthropy is important in supporting this innovative research.

Our Center Awarded Seed Grants to the Following Researchers in 2019:

Michele Barry, MD, FACP, professor of medicine, Susanne Sokolow, PhD, DVM, senior research scientist, and Giulio De Leo, PhD, professor of biology, all at Stanford. They lead a group that is assessing a 10-year program for people living near tropical rainforests in West Kalimantan, Borneo, from Health in Harmony, a nonprofit. Health in Harmony developed a health clinic and provided medical services, while also offering incentives for reducing illegal logging and providing sustainable agriculture training. The group led by the Stanford researchers will examine data on child

mortality, infectious diseases, and economic measures while looking at data on vegetation coverage in forests and carbon storage of trees. The review will test the hypothesis that providing affordable healthcare to poor communities improves well-being and reduces practices that harm the environment.

Stephanie Eisenbarth, MD, PhD, associate professor of laboratory medicine at Yale University School of Medicine. She will test whether the presence and level of food-specific immunoglobulin A (IgA), an antibody of the immune system, in human stool is a good marker for tolerance of specific foods. Using stool samples and clinical data from patients in peanut oral immunotherapy trials at Stanford, she will look at whether peanut-specific IgA increased in patients who were successfully desensitized to peanuts. She developed a test that quantifies peanut-specific IgA and plans to create tests for eggs and milk. Eventually, she will examine how levels of IgA correspond to how tolerant people are of peanuts, eggs, and milk. Food-specific IgA potentially could be used to stratify people by degree of risk for anaphylaxis.



Expanding Our Scientific Talent

The Center continues to expand by bringing in new talent to work alongside the best and the brightest minds dedicated to allergy research. In 2019, our team grew to include the following people:



Shu Cao, MS, biostatistician. She performs statistical analysis to explore the clinical and molecular risks associated with severe allergic symptoms. She obtained a dual bachelor's degree in biological

engineering and international economics and business at Shandong University of Science and Technology, and a master's degree in statistics at West Virginia University.



Maya Kasowski, MD, PhD, clinical instructor of pathology and *Sean Parker Faculty Scholar*. Her research focuses on how noncoding genetic variation influences gene regulation and disease risk. Her lab will dissect

the genetics that underlie allergy. She obtained her MD/PhD from Yale University, completed her residency in pathology, and served as a postdoctoral fellow in genetics at Stanford University.



Meng Chen, MD, clinical assistant professor of allergy and immunology. Dr. Chen is an active investigator in food allergy trials. She also evaluates the impact of climate change on pollen patterns. She received her medical

degree from the University of California, San Francisco, and completed her internal medicine residency at the University of California, Los Angeles. She completed a fellowship in allergy and immunology at the University of California, San Diego, and Rady Children's Hospital.



Rachel Moericke, MA, director of clinical trial operations & regulatory affairs. She oversees clinical trial operations and regulatory matters for our clinical research team and our team working with Stanford's Good

Manufacturing Practices facility. She received her master's degree in clinical and research health psychology and studied the impact of biopsychosocial factors on patients receiving medical care.



William J. Collins, MD, clinical assistant professor of internal medicine and faculty fellow. He works as a hospitalist at Stanford Hospital and does clinical research at our Center. In addition to work in

food allergy, he also has research interests in asthma and drug allergies. He completed his residency at the University of California, San Diego, and received his medical training at the University of California, San Francisco.



Lisa Patel, MD, clinical assistant professor of pediatrics. She is the advocacy and policy lead at our Center, where she is focusing on a strategy to address climate change. She earned her bachelor's degree in biological

sciences at Stanford University, obtained her master's degree in environmental sciences at the Yale School of Forestry, and was a Presidential Management Fellow at the Environmental Protection Agency. She obtained her medical degree from Johns Hopkins University and completed her residency in pediatrics at the University of California, San Francisco.

Our 2019 Scientific Advisors

Our Center's Scientific
Advisory Committee brings
together the best minds in
allergy and asthma science.
These scientists and
physicians from different
specialties contribute
their insights to improve
diagnostics, prognostics,
and therapies.

Kari Nadeau, MD, PhD, director of the Sean N. Parker Center for Allergy & Asthma Research, Stanford

Sean Parker, philanthropist, entrepreneur, founder and president of the Parker Foundation

Cezmi Akdis, MD, PhD,

director, Swiss Institute of Allergy and Asthma Research

Mübeccel Akdis, MD, PhD, head of dermatology, Swiss Institute of Allergy and Asthma Research

Michele Barry, MD, senior associate dean, global health; director, Center for Innovation in Global Health, Stanford

Scott Boyd, MD, PhD, associate professor of pathology, Stanford

Carlos Carmago, Jr., MD, DrPH, Conn Chair in Emergency Medicine,

Conn Chair in Emergency Medicine, Massachusetts General Hospital

Howard Chang, MD, PhD, director, Center for Personal Dynamic Regulomes, Stanford

Yueh-hsiu Chien, PhD, professor of microbiology and immunology, Stanford

R. Sharon Chinthrajah, MD, director, Clinical Translational Research Unit of the Sean N. Parker Center for Allergy & Asthma Research, Stanford

Mark Davis, PhD, director, Stanford Institute for Immunity, Transplantation, and Infection

Manisha Desai, PhD, director, Quantitative Sciences Unit, Stanford

Andrew Fire, PhD, George D. Smith Professor in Molecular and Genetic Medicine, Stanford

Stephen Galli, MD, *Mary Hewitt Loveless, MD, Professor* and professor of pathology, Stanford

Christopher Gardner, PhD, *Rehnborg Farquhar Professor* of medicine,
Stanford Prevention Research Center

Ruchi Gupta, MD, MPH, director of Science and Outcomes of Allergy and Asthma Research, Northwestern University and Ann & Robert H. Lurie Children's Hospital of Chicago

Theodore Jardetsky, PhD, professor of structural biology, Stanford

Purvesh Khatri, PhD, associate professor, Stanford Institute for Immunity, Transplantation, and Infection

Chaitin Khosla, PhD, director of Stanford Chemistry, Engineering, and Medicine for Human Health (ChEM-H) and Wells H. Rauser and Harold M. Petiprin Professor, Stanford Engineering

Gideon Lack, MD, professor of pediatric allergy, King's College London

Donald Leung, MD, PhD, head of pediatric allergy and immunology, National Jewish Health, Denver

David Lewis, MD, chief of pediatric allergy, immunology, and rheumatology, Stanford

Holden Maecker, PhD, director, Human Immune Monitoring Center, Stanford

Lloyd Minor, MD, Carl and Elizabeth Naumann Dean, Stanford Medicine

Cathryn Nagler, PhD, *Bunning Food Allergy Professor*, University of Chicago

Mark Nicolls, MD, chief of pulmonary and critical care medicine, Stanford

Garry Nolan, PhD, Rachford and Carlota A. Harris Professor of microbiology and immunology, Stanford

Julie Parsonnet, MD, George
DeForest Barnett Professor in Medicine
and professor of health research
and policy, Stanford

Bali Pulendran, PhD, *Violetta L. Horton Professor* of pathology, and professor of microbiology and immunology, Stanford

Stephen Quake, MS, PhD,

Lee Otterson Professor, Stanford Engineering, and professor of bioengineering, Stanford Medicine

Michael Snyder, PhD, chair of genetics and director of the Center for Genomics and Personalized Medicine, Stanford

Justin Sonnenburg, PhD, associate professor of microbiology and immunology, Stanford

Sindy Tang, PhD, associate professor of mechanical engineering, Stanford

Steven Ziegler, PhD, director of immunology research, Benaroya Research Institute



2019 JOURNAL PUBLICATIONS

Our Center's contribution to allergy and asthma research in 2019 included nearly 40 articles related to asthma, allergies, and immunology published in peer-reviewed journals.

Development of multiple features of antigen-induced asthma pathology in a new strain of mast cell deficient BALB/c-Kit (W-sh/W-sh) mice.

Hernandez JD, Yu M, Sibilano R, Tsai M, Galli SJ. LABORATORY INVESTIGATION.

2019 Dec 19. [Epub ahead of print].

Sustained successful peanut oral immunotherapy associated with low basophil activation and peanut-specific IgE.

Tsai M, Mukai K, Chinthrajah RS, Nadeau KC, Galli SJ.
THE JOURNAL OF ALLERGY AND CLINICAL
IMMUNOLOGY.

2019 Dec 2. [Epub ahead of print].

The future of omics for clinical practice.

Long A, Bunning B, Borro M, Sampath V, Nadeau, KC.

ANNALS OF ALLERGY, ASTHMA & IMMUNOLOGY. 2019 Dec; 123(6): 535-536.

Transcriptomic and methylomic features in asthmatic and non-asthmatic twins.

Dhondalay GKR, Bunning B, Bauer RN, Barnathan ES, Maniscalco C, Baribaud F, Nadeau KC, Andorf S. ALLERGY.

2019 Nov 22. [Epub ahead of print].

Global metabolic profiling to model biological processes of aging in twins.

Bunning BJ, Contrepois K, Lee-McMullen B, Dhondalay GKR, Zhang W, Tupa D, Raeber O, Desai M, Nadeau KC, Snyder MP, Andorf S. AGING CELL.

2019 Nov 19: e13073.

Can food allergy be cured? What are the future prospects?

Sampath V, Sindher SB, Alvarez Pinzon AM, Nadeau KC.

ALLERGY.

2019 Nov 16. [Epub ahead of print].

Phase 2a randomized, placebo-controlled study of anti-IL-33 in peanut allergy.

Chinthrajah S, Cao S, Liu C, Lyu SC, Sindher SB, Long A, Sampath V, Petroni D, Londei M, Nadeau KC. JCI INSIGHT.

2019 Nov 14; 4(22).

Trends in egg specific immunoglobulin levels during natural tolerance and oral immunotherapy.

Andorf S, Bunning B, Tupa D, Cao S, Long A, Borres MP, Galli SJ, Chinthrajah RS, Nadeau KC.

Accepted November 14, 2019. [Epub ahead of print].

Blockade of TIM-1 on the donor graft ameliorates graft-versus-host disease following hematopoietic cell transplantation.

Iliopoulou BP, Hsu K, Pérez-Cruz M, Tang SW, Pang WW, Erkers T, Kambham N, Freeman GJ, Dekruyff RH, Meyer EH.

BLOOD ADVANCES.

2019 Nov 12; 3(21): 3419-3431.

Conflicting verdicts on peanut OIT from the ICER and FDA Advisory Committee; where do we go from here?

Eiwegger T, Anagnostou K, Arasi S, Bégin P, Ben-Shoshan M, Beyer K, Blumchen K, Brough H, Caubet JC, Chan ES, Chen M, Chinthrajah S, Davis CM, Roches AD, Du Toit G, Elizur A, Galli SJ, Håland G, Hoffmann-Sommergruber K, Kim H, Leung DYM, Long A, Muraro A, Nurmatov UB, Pajno GB, Sampath V, Saxena J, Sindher S, Upton J, Worm M, Nadeau K. THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY.

2019 Nov 1. [Epub ahead of print].

Genetic and environmental susceptibility to food allergy in a registry of twins.

Kivistö JE, Clarke A, Dery A, De Schryver S, Shand G, Huhtala H, Mäkelä MJ, Asai Y, Nadeau K, Harada L, Chan ES, Ben-Shoshan M.

THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY: IN PRACTICE.

2019 Nov - Dec; 7(8): 2916-2918.

Cow's milk and vitamin D supplementation in infants—timing is everything.

Du Toit G, Elizur A, Nadeau KC.

JAMA PEDIATRICS.

2019 Oct 21. [Epub ahead of print].

Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study.

Chinthrajah RS, Purington N, Andorf S, Long A, O'Laughlin KL, Lyu SC, Manohar M, Boyd SD, Tibshirani R, Maecker H, Plaut M, Mukai K, Tsai M, Desai M, Galli SJ, Nadeau KC.

THE LANCET.

2019 Oct 19; 394(10207): 1437-1449.

Epithelial RABGEF1 deficiency promotes intestinal inflammation by dysregulating intrinsic MYD88-dependent innate signaling.

El Abbas S, Radermecker C, Bai Q, Beguin C, Schyns J, Meunier M, Pirottin D, Desmet CJ, Meuwis MA, Art T, Louis E, Tam SY, Tsai M, Bureau F, Galli SJ, Marichal T. MUCOSAL IMMUNOLOGY.

2019 Oct 18. [Epub ahead of print].

Natural Tr1-like cells do not confer long-term tolerogenic memory.

Yadava K, Medina CO, Ishak H, Gurevich I, Kuipers H, Shamskhou EA, Koliesnik IO, Moon JJ, Weaver C, Nadeau KC, Bollyky PL.

ELIFE.

2019 Oct 11; 8.

House dust mites activate nociceptor-mast cell clusters to drive type 2 skin inflammation.

Serhan N, Basso L, Sibilano R, Petitfils C, Meixiong J, Bonnart C, Reber LL, Marichal T, Starkl P, Cenac N, Dong X, Tsai M, Galli SJ, Gaudenzio N.

NATURE IMMUNOLOGY.

2019 Oct 7. [Epub ahead of print].

The impact of prescribed fire versus wildfire on the immune and cardiovascular systems of children.

Prunicki M, Kelsey R, Lee J, Zhou X, Smith E, Haddad F, Wu J, Nadeau K. ALLERGY.

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(continued from page 11)

ICER report for peanut OIT comes up short.

Eiwegger T, Anagnostou K, Arasi S, Bégin P, Ben-Shoshan M, Beyer K, Blumchen K, Brough H, Caubet JC, Chan ES, Chinthrajah S, Davis CM, Roches AD, Du Toit G, Elizur A, Galli SJ, Håland G, Hoffmann-Sommergruber K, Kim H, Leung DYM, Muraro A, Nurmatov UB, Pajno GB, Sindher S, Szepfalusi Z, Torres MJ, Upton J, Worm M, Nadeau K. ANNALS OF ALLERGY, ASTHMA & IMMUNOLOGY. 2019 Sep 9.

Almond (prunus dulcis) allergen pru du 8, the first member of a new family of food allergens. Che H, Zhang Y, Jiang S, Jin T, Lyu SC, Nadeau KC, McHugh T.

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. 2019 Aug 7; 67(31): 8626-8631.

Recent progress in the analysis of $\alpha\beta T$ cell and B cell receptor repertoires.

Davis MM, Boyd SD.

CURRENT OPINION IN IMMUNOLOGY.
2019 Jul 17; 59: 109-114.

Blockade of repulsive guidance molecule b (RGMb) inhibits allergen-induced airways disease.

Yu S, Leung KM, Kim HY, Umetsu SE, Xiao Y, Albacker LA, Lee HJ, Umetsu DT, Freeman GJ, DeKruyff RH. THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY.

2019 Jul; 144(1): 94-108.e11.

Proteasome-dependent regulation of distinct metabolic states during long-term culture of human iPSC-derived cardiomyocytes.

Ebert A, Joshi AU, Andorf S, Dai Y, Sampathkumar S, Chen H, Li Y, Garg P, Toischer K, Hasenfuss G, Mochly-Rosen D, Wu JC. CIRCULATION RESEARCH.

2019 Jun 21; 125(1): 90-103.

Modeling cardiovascular risks of e-cigarettes with human induced pluripotent stem cell-derived endothelial cells.

Lee WH, Ong SG, Zhou Y, Tian L, Bae HR, Baker N, Whitlatch A, Mohammadi L, Guo H, Nadeau KC, Springer ML, Schick SF, Bhatnagar A, Wu JC.
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY.

2019 Jun 4; 73(21): 2722-2737.

A perspective on the pediatric death from oral food challenge reported from the Allergy Vigilance Network.

Upton J, Montserrat A, Nadeau K. ALLERGY. 2019 Jun; 74(6): 1035-1036.

Changing patient mindsets about non-life-threatening symptoms during oral immunotherapy: A randomized clinical trial.

Howe LC, Leibowitz KA, Perry MA, Block W, Kaptchuk TJ, Nadeau KC, Alia J. Crum AJ. THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY: IN PRACTICE. 2019 May - Jun; 7(5): 1550-1559.

Genetic and environmental susceptibility to food allergy in a registry of twins.

Kivistö JE, Clarke A, Dery A, De Schryver S, Shand G, Huhtala H, Mäkelä MJ, Asai Y, Nadeau K, Harada L, Chan ES, Ben-Shoshan M.

THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY: IN PRACTICE.

2019 May 23. [Epub ahead of print].

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(continued from previous page

Future trends in mechanisms and patient care in allergic diseases.

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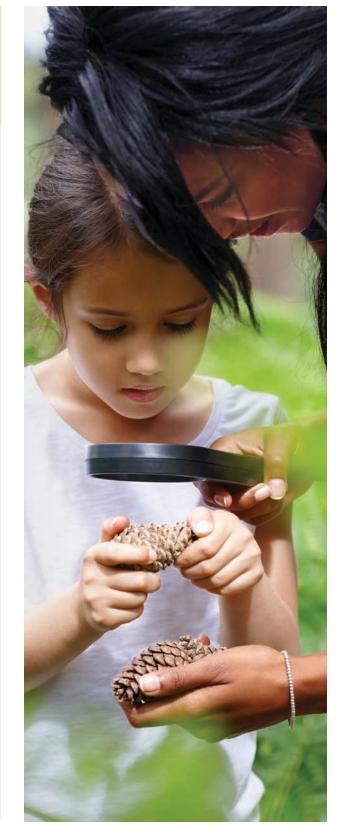
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Philanthropic Impact

Your dedication to our Center's compassionate care and innovative science drives us together toward a cure for allergies and asthma.





Our Center runs on philanthropic support. The vision and leadership of donors like you have allowed us to prove the effectiveness of immunotherapy, create a device to diagnose allergies, and bring new tools and education to families in underserved areas. Fueled by your commitment, we expect to make many more discoveries, develop better treatments, and help more people around the world. Thank you!





These philanthropic partners played a leading role in new research and expanded care in 2019:

The Friend family provided a gift to study wheat epitopes to determine the best ways to block the molecular pathways involved in wheat allergies.

The Barakett family and an anonymous donor are making possible the next phase of a trial of a new vaccine for peanut allergies and a study of skin lubricants for children with eczema. (See pages 2 and 3 for more information.) Also, thanks to the Barakett family, we are able to offer Saturday hours at our research clinic, allowing more families to participate in our clinical trials. (See page 25.)

Very generous gifts from two anonymous donors have made possible two important research projects. One is a collaboration with Mayo Clinic, Arizona, on a study of whether the drug dupilumab will improve the safety and effectiveness of oral immunotherapy for milk allergies. The other is for the development of a prognostic device that will indicate how well immunotherapy will work for food allergy patients and tell whether they need to keep taking a maintenance dose of the allergen.

We also thank The Safe + Fair Food Company, End Allergies Together (EAT), Food Allergy Research and Education (FARE), and the National Institutes of Health (NIH) for their important contributions to our research and care.

PHILANTHROPIC IMPACT

Helping Others Find Peace of Mind

Inspiring stories from some of our courageous and generous donor families, in their own words.



From left, Carter, David, Gavin, Kori, and Keegan

Shaw Family

Our daughter Keegan was a toddler when we first discovered she had a severe peanut allergy. As we moved from Maryland to California, we saw doctor after doctor. They all told us the same thing: our only option was food avoidance. During this process, we also discovered our 6-month-old son Carter was allergic to nuts and eggs.

When we moved to Palo Alto, a friend told us about Dr. Nadeau and her food allergy oral immunotherapy clinical trials at Stanford University. We were able to get both Keegan and Carter enrolled in the first multiple food allergy trial using omalizumab (Xolair), which tested oral immunotherapy for up to five allergens at once.

After that trial, we saw our children's lives change. Today, Keegan and Carter are thriving and playing sports as active teenagers. Keegan can eat up to 16 peanuts—at the start of the trial even trace amounts caused her to have an allergic reaction—and Carter can eat many more foods without fear of a serious reaction. Our children's participation in the trial has been life-changing for our family. Now we can travel freely and live without fear.

As a "founding family," our kids were the research. We were one of the first to try the protocols to help other families dealing with food allergies.

We're thankful that we've been able to work closely with Dr. Nadeau, from planning community events to donating and fundraising for trials to spreading awareness in schools and groups. Together we are letting the world know that food allergies are very scary and a real health crisis. And that food avoidance is not the only option.

"We are working to find a cure for allergies and asthma, increase choices of therapy, and fight this global epidemic with prevention, early detection, and best care. We do this because of patients and families who inspire us to improve lives throughout the world." — Kari Nadeau, MD, PhD



Back, from left: Ken, Andrew, and Pansy; front, from left: Audrey, Alex, and Luke

Andrew Yang

When I was 6 months old, my face turned bright red after I ate some walnut crumbs. I was diagnosed with a nut allergy. Since that time, most of my life has been one of infinite caution. Because I had anaphylactic reactions to all nuts, eating in restaurants was a risk. Traveling and eating in foreign countries was dangerous. Even at home and school we had to be extremely careful about everything I ate.

Then, several years ago, my mom read an article in the New York Times about Dr. Nadeau and her amazing work. My mom knew immediately that participating in one of Dr. Nadeau's trials would be a life-altering experience for me and my family. We were able to be part of a study using omalizumab, or Xolair, which helps speed up the desensitization process.

In the beginning, it was definitely hard. After the Xolair shot, my reaction to nuts was non-lethal but still very uncomfortable and painful. But as time went on and my dosage increased, nuts became easier to tolerate. All the discomfort was worth it!

I owe my life to this program! I never thought I would be able to do what I can now, which is eat 12 nuts a day. I know I am safe from accidental ingestion of nuts, and that I won't have to go to the emergency room as I did before. I can enjoy eating out with my family and travel without fear. I feel safer in any environment.

My family and I support Dr. Nadeau and her team at the Center because we want other kids to have the same opportunity I had—the chance to live without a sword hanging by a thread over their heads. I think allergy research is one of the worthiest causes to support.



Ariella Nelson

When I was 4 years old, I bit into a chocolate chip cookie at my grandmother's house. Later that night, I started coughing, felt nauseous, and vomited. My parents took me to an allergist who diagnosed my allergy to tree nuts.

My life changed dramatically. As I got older, I quizzed servers in restaurants, parents at friends' homes, and even relatives who knew about my allergy but didn't understand the seriousness of it. At school, I sat at the "no nut" table, which I called the "no fun" table. There were never a lot of kids there and I felt like an outsider. People meant well but mistakes were made, and occasionally I had to use my EpiPen and ended up in the ER.

Three years ago, a friend told me about a clinical study at Stanford. My friend connected me with Dr. Nadeau and I began oral immunotherapy. Eating real nuts—even in powder form—was scary. But I knew that if this worked even a little, it would be worth it. Today, I am on a maintenance dose of

four nuts a day. Though I still carry EpiPens, I no longer worry if a lone pistachio makes its way into my vanilla ice cream, or if my cinnamon roll was keeping company with an almond croissant.

My family and I are strong supporters of the Sean N. Parker Center because the groundbreaking research being done there is already having a positive impact on kids throughout the country, if not the world.

I will be going off to college next year. Thanks to oral immunotherapy, I no longer live in a constant state of anxiety and fear. While I still won't be getting the takeout cashew chicken to eat with my dormmates, I will be able to enjoy a more typical college life. And that means everything.

Gifts that Last a Lifetime and Beyond

By endowing our brightest researchers and providing continued support for our programs and research, you are enriching so many lives. Thank you for your commitment and leadership.



Bringing the Best Care to the Most Vulnerable

The generosity of the Canfield, Barakett, Freidheim, and Giorgi families is making it possible for people in underserved areas of Chicago, New York, and San Francisco to get support in dealing with the often-overwhelming challenges of allergies and asthma. (Read about this amazing work on page 26.)

Driving the Science that Drives the Care

The Bunning family has generously supported our research into the molecular causes of allergies and asthma.

A gift from the Hill family is providing computational work for our clinical trials, allowing us to sort through and categorize huge amounts of data necessary for breakthrough discoveries.

Generous donations from the Lubetzky and Hartman families laid the groundwork for our peanut allergy vaccine trial. Many dedicated families in Southern California supported a collaboration with the University of California, Los Angeles, on a peanut oral immunotherapy dosing trial. The Orzak, Kepner, and Englander families joined an anonymous donor to fund development of a diagnostic microchip to more accurately and safely diagnose allergies.

Providing Wings for Top Talent to Soar

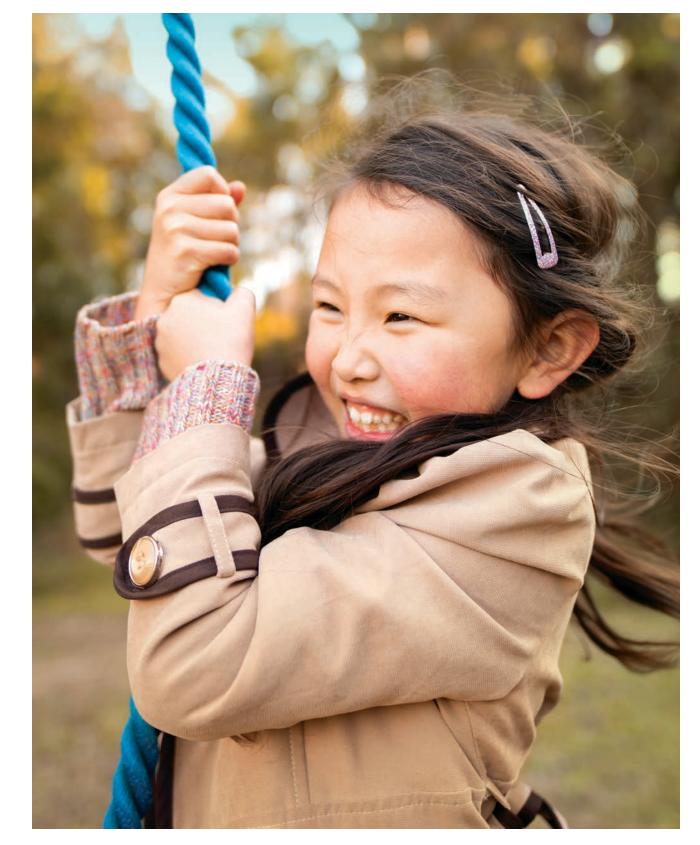
Faculty endowments guaranteeing support for our talented Center scientists provide the backbone for our research. The Gies family has endowed Sayantani (Tina) Sindher, MD, one of our top clinicians. With support from the Barakett family, Mary Prunicki, MD, PhD, and her team have made national headlines with their findings on the adverse health effects of wildfire exposure. (For details on this important research, see page 5.) The Carell family's endowment for Dr. Chinthrajah, our clinical director, has been instrumental in making her one of the leading allergy and asthma clinical researchers in the world.

Philanthropy also supports our basic scientists, including Bali Pulendran, PhD, endowed by the Soffer family; and Scott Boyd, MD, PhD, who is endowed by an anonymous donor.

Dr. Pulendran is studying how the immune system responds to allergens and infections. Dr. Boyd's work examines the role of B cells in allergic reactions.

Research in the "wet" lab—where tissue samples are studied using powerful microscopes and advanced cell-sorting technology—requires the powerful computing of the "dry" lab to create discoveries. The Li family supports Manisha Desai, PhD, our Center's new computational director. Computer scientist Bibek Paudel, PhD, who is using machine learning to study the impact of environmental and lifestyle changes on the health of vulnerable people, is supported by the Bravo family.

Dr. Nadeau's professorship, which gives her the freedom to design and share new research and create exciting collaborations, is supported by the Lainovic family and many others, including the Li, Carell, Sandberg, Orzak, Kepner, Staggs, Bates, Limaye, Arrillaga, and Yun families.



Space to Grow

Thanks to the generosity of the Koch family, we have a new clinic on the Stanford campus—the David and Julia Koch Clinic. It is located steps away from our new laboratory in the Biomedical Innovations Building, made possible by Sean N. Parker and an anonymous donor. These exciting new spaces are allowing us to bring our innovative science and compassionate care to more people with allergies and asthma, and we look forward to moving ahead with our philanthropic community toward finding cures for these diseases.







Photos by Matthew Anderson Photography







From top: Sharon Chinthrajah, MD, in the David and Julia Koch Clinic on the Stanford campus; Jamie Saxena, MS, FNP-C, research nurse practitioner, checks the vital signs of Ayden Chou, a clinical trial participant, during his visit to the Koch Clinic; Medical equipment cabinet in the clinic.

Community Connections

Outreach programs, events, and a book! These are just some of the ways our Center brought education and compassionate care to people with allergies and asthma this year.





Thanks to the generosity of our wonderful donors, we have been able to partner with other organizations and sponsor projects around the country that aim to improve the health of children in underserved communities.

Opening Doors

A busy schedule shouldn't be an obstacle to getting a person's food allergy under control. Thanks to the incredible support of our donor community, our Center added early and late hours on weekdays and started opening its doors one Saturday a month.

Extended clinic hours have been particularly helpful to Robin Fletcher, a high school student from San Francisco, and her mother, Jacqueline Lisa Fletcher. Robin is enrolled in our COMBINE study for treating multiple allergies, and she needs to come in every two weeks. "Our main goal of coming to Saturday clinic is to make sure she misses school as little as possible," says Jacqueline.

Jamie Saxena, MS, FNP-C, a research nurse practitioner who coordinates staffing at the clinic, has seen a real uptick in enrollment as a result of the expanded time. "These are long studies that require patients to come in for two or three hours every two weeks. The missed school can really add up," she says. The extra hours also help working parents fit their children's appointments into their schedules.

Donor funds make it possible to underwrite the cost of staffing a nurse practitioner or doctor and lab specialist during these added hours.

Toxic Stress

Children who have experienced toxic stress due to physical and emotional abuse or neglect have a higher risk of developing allergies and asthma. To address this issue, our Center has been working with the Center for Youth Wellness, a San Francisco non-profit dedicated to improving the health of children exposed to toxic stressors.

With the help of donor funds, we have built a select committee of pediatric nurses, doctors, asthma and allergy experts, psychiatrists, psychologists, and other scientists. The team has gathered evidence that demonstrates the link between toxic stress and disease. They are now working on a set of guidelines that health workers can use to help them recognize the signs of toxic stress in patients and better manage their care.

Next, we are involving nurses, social workers, and community members in the committee, ensuring the guidelines work for the people on the front lines. Once the guidelines are finished, we'll develop a pilot study to measure their effectiveness, collect feedback from health workers, and optimize them so they can be adopted by national health agencies.





Left, Sayantani (Tina) Sindher, MD, works with our Center's clinical research coordinator, Debjani Ghoshal, to treat patient Robin Fletcher at her Saturday oral immunotherapy appointment. Right, Dr. Sindher works closely with Andrew Long, PharmD, a pharmacist who manages the many medications for the Center's clinical trials.

COMMUNITY CONNECTIONS

Allergies and Socioeconomic Status

Donor support enabled our Center to sponsor a study based in the Chicago Public Schools system on allergies and income. Our Center advised the research team, which included physicians and psychologists. Researchers from local universities found that lower-income Black and Latinx students with allergies were less likely to have a care management plan in place compared to higher-income white students. The study identified specific barriers to proper allergy management, such as caregivers' confusion about the severity of allergies and difficulty communicating with other caregivers and teachers about their children's needs.

The result was two booklets: an easy-to-use "passport" booklet filled with colorful graphics, which caregivers can fill out and then use

to communicate with others about their children's needs, and a patient-information booklet that helps caregivers navigate their children's allergies after diagnosis.

Next the team would like to test the materials with families to measure the impact of these tools.

Caring for Homeless Families

Based in New York, the Dare2B program performs outreach to homeless families in underserved areas, such as the Bronx and Harlem, to educate them on maintaining proper nutrition and caring for a child's allergies and asthma, even in the most unstable circumstances.

Our Center's Dr. Chinthrajah led a workshop to inform children and their families about what an allergy is, when to get tested, and how to recognize the signs of an allergic reaction. Families of children with asthma learned about lifestyle changes that could help keep a child's asthma under control. Parents reported feeling much more comfortable with managing their children's health thanks to Dr. Chinthrajah's easy-to-understand instructions and genuinely caring approach.

Donor support underwrote the cost of running the event and allowed the outreach team to offer incentive prizes to program participants, which greatly increased turnout.

Workshops in East Palo Alto

Contributions from our valued donors also allowed us to lead workshops in East Palo Alto, California, where representatives from our Center taught young teenagers with allergies how to properly use an epinephrine auto-injector and talked to them about nutrition and their bodies.









Thank you, too, for helping our Center spread hope and celebrate resilience in the following ways:

2019 Summer Scamper

Our amazing community came together last summer to champion children's health and run their hearts out. The annual 5k and 10k races, plus a fun run for the little kids, raises money for Lucile Packard Children's Hospital Stanford. Our 2019 patient hero, Keegan, is an active 11-yearold who loves and enjoys all kinds of foods. Once one of the most peanutsensitive kids to join a clinical trial at our Center, Keegan (photo on opposite page, bottom right) reached her goal in June 2018 of eating a peanut every day. She is an inspiration to everyone who wants to overcome their fears and live life to the fullest.

Dr. Nadeau's New Book on Food Allergy

Many families are still hearing that the only hope for their child with a severe food allergy is avoiding the problem food. That's why Dr. Nadeau decided to write a book with Sloan Barnett—a lawyer, journalist, and mom of two children with food allergies who were successfully treated at our Center. Dr. Nadeau wanted parents to hear from someone who knows what they are going through and who can explain in easy-to-understand terms how children can train their immune systems to overcome a food allergy. To be released in October, The End of Food Allergy: The First Program to Prevent and Reverse a 21st Century Epidemic walks families through different treatment options and explains how to manage their children's allergies and put a plan of action into place.

Ambassadors Coffee Talk

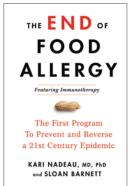
Last year, the Ambassadors, a group of 230 local philanthropists and volunteers committed to Packard Children's, invited Drs.
Nadeau and Chinthrajah to talk about the latest discoveries from our Center. At the event, they presented their extraordinary work in discovering the causes of, and new treatments for, pediatric food allergies. (Photo below, top center.)

Our patients are an inspiration to everyone who wants to overcome their fears and live life to the fullest.













Clinical Impact

Thanks to your amazing support, more and more patients are getting the most advanced treatments in our clinical trials—and living life to the fullest!







We are excited to report that we opened the David and Julia Koch Clinic at Stanford in 2019. This new clinic allows us to see more patients with allergies and asthma and enroll them in our trials. The location on the Stanford campus means we are close to our laboratory team and other departments on campus, and better able to coordinate research and care.

Off-campus clinics and collaborations are expanding, too. We are reaching more patients through our partnership with the Allergy, Asthma, and Immunology Clinic in Atherton, California, a clinic for adults. We now have an allergy clinic in San Francisco through the California Pacific Medical Center—Sutter Health California Pacific Medical Center. Dr. Nadeau and other providers from our clinic see patients there, which has been a great way for us to recruit patients into our allergy trials from across the San Francisco Bay Area.

For our patients with eosinophilic esophagitis (EoE), Dr. Sindher has joined a clinic that combines EoE and gastroenterology specialists. By bringing together gastroenterologists, allergists, and dieticians under one roof, they can treat patients holistically for a full range of symptoms. The clinic is so popular it has increased its hours from every other week to once a week to meet patient demand.

What makes working at the Center so special? Let's hear from three of our clinicians. (Featured, right.)



Rachel Moericke, MA

Director, Clinical Trial Operations & Regulatory Affairs

I oversee clinical trial operations and regulatory affairs for our clinical research team and good manufacturing practice (GMP) facility, including our team's work with the National Institutes of Health and industry sponsors. I help ensure research is conducted within regulatory guidelines and good clinical practices.

One of the greatest things about working at our Center is the team. We have an incredibly dedicated group of research and GMP staff dedicated to making a difference in the field and with patients and their families.

Personally, I know many people struggling with food allergy and asthma. There are often many fears and restrictions placed on the child, parent, family, and community. Working together we can help build a brighter future.



Clinical Life Science Research Scientist





Jamie Saxena, MS, FNP-C

Research Nurse Practitioner

As a nurse practitioner at our Center, I assess the health of the patients who participate in our trials, as well as take steps to ensure their safety.

I love the relationships that we build with our participants. Since they come into our Center frequently, we get to know them and their families well, and it is fun to be part of their journey. I also love that we are involved with groundbreaking scientific discoveries. It is thrilling to be part of a team that has such a positive impact on the world!

Giving Patients Freedom and Peace of Mind

Through clinical trials, our patients improve their own allergies and contribute to the pursuit of better treatments and diagnostics for all. Here are some of their stories.



8 years old

When Ayden was 4, he was at an outdoor festival with his aunt and ate peanut butter crackers. With one bite Ayden immediately knew something was wrong. He was so young, he didn't know how to tell others what was going on, which was scary. From that incident, we found out he had a peanut allergy.

This changed our lives. A lot of Ayden's favorite Asian cuisines are cooked with nuts and we started carefully reading the ingredient lists on foods and becoming more cautious. I found the Center's clinical trials online and we were lucky enough to be admitted into a peanut desensitizing trial. Eventually, as part of the program, Ayden was also able to participate in a food challenge and eat peanuts without any negative symptoms. We were amazed with the outcome and feel so blessed we were able to be a part of a program that we hope will one day be available to all children. — David (Ayden's dad)



12 years old

When Dylan was a year old, he took a small bite of a peanut butter and jelly sandwich and his lips immediately blistered up. A visit to the emergency room was followed by blood tests to confirm a severe allergy to peanuts (in addition to cashews and pistachios).

Since March 2019, we have been traveling to the Center for appointments—we live three hours away. The treatment has given Dylan and our family a certain level of comfort because if an accidental exposure occurs, his body will be able to tolerate it. That peace of mind is priceless. We are in the final stretch of the program and it has been so worth it. — Andrea (Dylan's mom)





Samantha

15 and 13 years old

We are both allergic to eggs, peanuts, and cashews, while Samantha is also allergic to dairy and Nicholas has walnut and sesame allergies. We spent a lot of time at the clinic during the study and became very familiar with the staff, who made our experiences as comfortable as possible. We always felt we were being very well taken care of. While some of the experiences we had at the clinic were new and unfamiliar, the staff always thoroughly explained what was happening and made sure we felt safe.

Now we have more freedom when we go out to eat. We don't have to ask questions. We can just order something. It's been fun trying new foods...and we both really like eggs! — Samantha and Nicholas



Aneesh

17 years old

When I was around 3 years old, my parents noticed I had an allergic reaction and took me to the doctor's office for testing. The results showed I had a peanut allergy. There were no treatments for peanut allergy back then. All I did was avoid peanuts. Then I participated in a clinical trial and now I am a lot less anxious!

Melanie Shojinaga and Jamie Saxena from the clinic are great and helpful to me. They care about me as a person. They offered me a patient support number so that I can call the clinicians at any time with any food allergy questions. After getting into the clinical trial, everything has gone smoothly. — Aneesh





13 years old

When I was a baby, my parents found out I had allergies to milk, nuts, and peanuts. In 2014, I participated in the Phase 2 multi-allergen Xolair oral immunotherapy food allergy trial at the Center. Before that, it was really hard. I couldn't eat out at all, and I couldn't hang out with my friends as much as I would have liked. Also, if we went on a trip, we had to stay close to a hospital, and we had to bring pots and pans to cook in our hotel room.

Now I feel like I don't have food allergies. I can eat foods that my friends can eat—I just can't eat as much as they can. I can go camping with my friends even when it's not close to a hospital. It's a lot of fun just being outdoors because I never got to be away in the middle of the wilderness before. Participating in this study has changed my life by giving me the freedom to travel and live without fear. My new freedom led me to discover my love of bass fishing.

I wanted to do something to give back to the Center because it changed my life. So I decided to do a bass fishing tournament because it's a way that I can help people get into fishing, and it's also a way to support the Center. I was planning to hold the tournament in May at Lake Berryessa, which is close to Sacramento, but I will have to wait until it is safe to hold a large community event—hopefully by next spring! I'm going to charge an entry fee and ask companies to donate products so I can raffle them off. I will donate the proceeds to the Center so that other kids with food allergies also have the same opportunity to live freely and discover their passions.

Thank you for helping so many people by donating to the Center. You're helping more than just the people who are there now. You're helping people in the future who have food allergies, and you're making a big difference. — Dean

TESTING FOR BETTER WAYS TO TREAT PATIENTS

Our Center participated in or sponsored more than 25 clinical trials in 2019, including the following:

STUDY TOPIC	Date Started/Status	Purpose
PEANUT ALLERGY		
Omalizumab (Xolair), a biologic drug approved for treating asthma	2013, ongoing	Study efficacy of omalizumab at four centers to safely and rapidly desensitize patients with severe peanut allergy. Determine if pretreatment with anti-IgE mAb (omalizumab) can greatly reduce allergic reactions and allow for faster and safer desensitization.
OIT with peanut flour follow-up	2016, completed	Demonstrate the safety, tolerability, and efficacy of AR101 peanut flour through a characterized oral desensitization immunotherapy (CODIT) in peanut-allergic children and adults who have completed a previous AR101 OIT study.
Skin patch	2016, ongoing	Evaluate the safety of Viaskin Peanut, a skin patch, to induce desensitization to peanuts in children 4 to 11 years old.
OIT with peanut flour follow-up	2017, completed	Study the long-term safety, tolerability, and efficacy of AR101 peanut flour in children who have completed a previous AR101 OIT study.
Skin patch follow-up	2017, ongoing	Follow patients who completed a Viaskin Peanut skin patch study for two to three more years.
Skin patch	2017, ongoing	Assess the safety and efficacy of Viaskin Peanut skin patch to induce desensitization to peanuts in peanut-allergic children 1 to 3 years old.
OIT with peanut flour, long-term study	2017, ongoing	Assess AR101 peanut flour's safety and tolerability over an extended dosing period.
Skin patch, long-term assessment	2018, ongoing	Assess the long-term safety and therapeutic benefit of Viaskin Peanut skin patch in peanut-allergic children.
OIT with peanut flour in young children	2018, ongoing	Study the efficacy and safety of AR101 peanut flour in a characterized desensitization OIT regimen in peanut-allergic children 1 to 4 years old, using escalating doses over six months.

STUDY TOPIC	Date Started/Status	Purpose
PEANUT ALLERGY (CONT.)		
OIT with dupilumab added to peanut flour	2018, ongoing	Study the safety of combining dupilumab, a monoclonal antibody approved for treatment of eczema, with AR101 peanut flour and assess improvement of desensitization to peanuts over 28 weeks.
Sublingual (under the tongue) therapy with SAR439794, which combines a synthetic TLR4 agonist (a drug that targets a transmembrane protein involved in inflammation and immune response) with a peanut extract	2018, ongoing	Investigate the safety, tolerability, and effects of repeated daily sublingual doses of SAR439794 in peanut-allergic adolescents and adults.
OIT with dupilumab monotherapy	2019, ongoing	Assess tolerability in a peanut protein food challenge in children 6 to 17 years old after being treated only with dupilumab over 24 weeks.
Vaccine	2019, ongoing	Evaluate safety, tolerability, and immune respons in peanut-allergic adolescents receiving a protein DNA plasmid injection.
Skin patch follow-up	2019, ongoing	Study the long-term benefits and safety of Viaskir Peanut skin patch in children 1 to 3 years old.
OIT with peanut flour	2019, ongoing	To determine the safety, efficacy, and tolerability of the drug AR101 in peanut allergic children 1 to 4 years old.
EOSINOPHILIC ESOPHAGITIS (EO	E)	
Fluticasone propionate, a corticosteroid used in nasal sprays	2017, ongoing	Compare the efficacy and safety of fluticasone propionate in a tablet form with placebo in adults with EoE.
Injectable dupilumab, a biologic medication used to treat allergic diseases such as eczema	2018, ongoing	Investigate the efficacy and safety of injectable dupilumab in adult and adolescent patients with EoE.

TESTING FOR BETTER WAYS TO TREAT PATIENTS

(continued from previous page)

STUDY TOPIC	Date Started/Status	Purpose
		1
ASTHMA		
Fevipiprant, a drug that blocks CRTh2 (a protein associated with certain allergic responses), combined with standard therapy	2017, completed	Assess the efficacy and safety of QAW039 (Fevipiprant) oral medication when added to standard-of-care asthma therapy in patients with uncontrolled asthma.
GRASS ALLERGY		
Injectable dupilumab	2018, completed	Evaluate the efficacy of injectable dupilumab as a therapy added to subcutaneous grass immunotherapy to reduce allergic hay fever symptoms.
COW'S MILK ALLERGY		
Skin patch	2014, ongoing	Evaluate the safety and efficacy of Viaskin Milk skin patch immunotherapy after 12 months, and assess long-term effects after 48 months in children with cow's milk allergies.
SHRIMP OR CASHEW ALLERGY		
OIT	2019, ongoing	Study safety and efficacy in up-dosing regimen of OIT in shrimp- or cashew-allergic adolescents and adults over 28 weeks, followed by maintenance therapy over an additional 24 weeks.
MULTIPLE FOOD ALLERGIES		
OIT with omalizumab, a monoclonal antibody approved for treating asthma	2017, completed	Determine whether omalizumab improves safety and tolerance for patients receiving OIT for multiple food allergens and whether it lowers the maintenance dose of each food allergen.
OIT with dupilumab, omalizumab, or both	2019, ongoing	Compare safety and efficacy of OIT combined with dosing of dupilumab, omalizumab, or both in children and young adults who have multiple food allergies, one of which must be peanut.
Omalizumab monotherapy compared with omalizumab with OIT	2019, ongoing	Study efficacy of injectable omalizumab in children and adults with multiple food allergies compared to treatment combining omalizumab and OIT of multiple allergens.

STUDY TOPIC	Date Started/Status	Purpose
ECZEMA (SKIN ALLERGY)		
Skin cream pilot	2018, ongoing	Compare two different skin creams (EpiCeram and Aveeno) and their effect on water loss throug the skin in children and adults with eczema.
OTHER		
Twin study	2010, ongoing	Provide a better understanding of how the immure system works in twins with and without allergic disease by comparing genetic differences.
Prescreening protocol to enroll in clinical studies at Sean N. Parker Center	2018, ongoing	Perform skin tests and oral food challenges to diagnose food allergies in children and adults wh want to participate in clinical trials.
Sean N. Parker Center Registry	2018, ongoing	Create an electronic database with information on healthy, asthmatic, and allergic individuals.



Training the Next Generation

Your philanthropy has allowed our Center to provide a pathway for future leaders to continue our important work.



Through mentorships, research opportunities, and networking, we provide our trainees opportunities in the field of allergy and asthma that they can't get anywhere else. We engage with young researchers at every level: Our trainees include undergraduates, graduate students, and post-doctoral scholars. Our goal is to strengthen the community of allergy and asthma researchers and physicians committed to helping patients. We are confident that our cultivation of these young researchers will bring us that much closer to finding better treatments and cures.



Cade Cannedy

Cade is an undergraduate research assistant who joined our Center in the summer of 2019. He is working on studies on the effectiveness of

home air purifiers and the health consequences of wildfires in California. Cade has a deep interest in social and environmental justice and the economic conditions that exacerbate health problems. He graduated from Stanford in June 2020, after majoring in political science and writing a senior thesis on air quality, regulation, and local governance in California's Central Valley. He hopes to pursue a career in environmental law or public health.



Ziyuan He, PhD

Dr. He joined the Nadeau Lab at our Center in the summer of 2019. His research focuses on using computational and bioinformatic

methods to analyze immunology-related data. His current work includes analyzing gut microbiota of patients in the oral immunotherapy clinical trials. He received his PhD in microbiology and immunology from Tulane University. Before joining the Nadeau lab, he studied white blood cells and aging in Rhesus macaque monkeys at UC Davis and the Tulane University Primate Center.

"Food should nourish and unify, not sicken and distress. Our research lays a foundation of knowledge, upon which a future free of food allergies is being built." — Christopher Warren, PhD



Christopher Warren, PhD

Dr. Warren is a postdoctoral scholar who joined our Center's clinical research team in the fall of 2019 after receiving his PhD from

the University of Southern California's Department of Preventive Medicine. In recent years, his epidemiological studies have characterized the prevalence, distribution, and causes of food allergies in the United States. By elucidating the burden of allergic disease—both physical and psychosocial—his work informs ongoing efforts to understand disease origins as well as evaluate the effectiveness of emerging immunotherapies and prevention strategies. In addition to this population-level epidemiological work, his research also focuses on developing and validating ways to measure patient-reported changes in health in hopes of advancing food allergy surveillance efforts in the U.S. and beyond.



Emily O'Neal, MA

Emily is a virtual reality (VR) experience designer particularly interested in medical and educational applications of the

technology. For her master's thesis with Stanford's Virtual Human Interaction Lab, Emily partnered with our Center to design and develop a VR application to reduce patient anxiety during the food challenge procedure. The application immerses patients in a fantastical forest and each bite they take fuels magic powers. Emily's work is motivated by a passion for user-centered design and improving patient experience. Emily graduated from Stanford University in March of 2020 with a bachelor's degree in human biology and a master's degree in communications and media studies.



Hesam Movassagh, PhD

Dr. Movassagh is a postdoctoral scholar at our Center. He obtained his PhD in immunology from the University of Manitoba, Canada.

During his PhD program, Dr. Movassagh discovered a novel immune regulatory axis, Semaphorin 3E-PlexinD1, which may lead to new diagnosis and treatment options for asthma. His current project focuses on the impact of exposure to air pollution on dysregulation of the immune system in children and its consequence on pediatric asthma. Dr. Movassagh believes understanding the mechanisms underlying this dysregulation is the key step to developing innovative strategies to control illness and death associated with air pollution.



Andrea Nadosy Bunt, MBA

Andrea joined our Center as a graduate student intern in the fall of 2019. She holds an undergraduate degree from Harvard College and an

MBA from Harvard Business School. After business school, she ran a company that designed and produced stylish tech accessories that were sold online and in Apple stores. In 2011, after the birth of her first child, her focus shifted entirely to the importance of prenatal and childhood health. She is currently a master's student in the Community Health and Prevention Research Program at Stanford Medical School and is interested in the "why" of disease, particularly the epigenetic mechanisms that could be at the root of certain diseases.



Tomorrow's Leaders Searching for Answers Today

Every year, in the lab and in the clinic, our Center's interns and postdocs—the next generation of researchers—focus on finding ways to improve the lives of allergy and asthma patients everywhere.





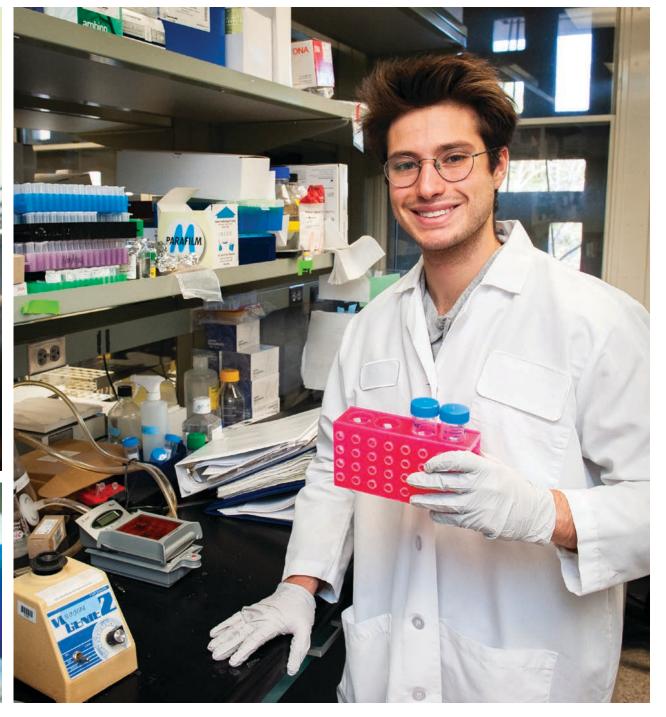












From Top Clockwise:

A wildfire study participant gets a blood pressure check.

Emily O'Neal, VR/AR experience designer, demonstrates how VR technology helps ease fear in clinical trial participants.

Shifaa Alkotob, MD, postdoctoral to collect biological specimens of a wildfire study participant during

Eric Smith, one of our undergraduate interns, works in the lab.

An experiment testing a white blood cell sample is conducted under a biofume hood.

Biological specimens from clinical trial participants are preserved and stored for food allergy research.

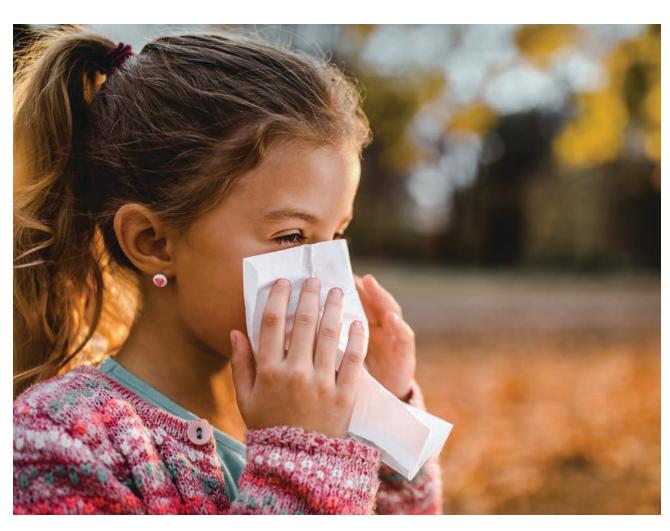
Christopher Warren, PhD, a postdoctoral research fellow at



Global Vision

Our dedicated donors enable our Center to connect with organizations around the world to solve allergy- and asthma-related health challenges.





Leading the Charge to Prevent Disease

Due to climate change, wildfires are expected to increase 50 percent by 2050. Meanwhile, fires caused by agricultural practices are on the rise. The increased level of smoke can lead to cardiovascular and chronic lung diseases as well as cancer and diabetes. Last year, these noncommunicable diseases accounted for 71 percent of deaths worldwide and this number is expected to increase to 80 percent by 2045. The economic impact is predicted to be in the trillions of dollars.

Using its expertise in allergic diseases, our Center team is leading the charge to improve the air we breathe and mitigate the effects of pollution.

Building Coalitions

To address this widescale problem, Dr. Nadeau organized a wildfire-specific section of panelists at the Planetary Health Alliance Annual Meeting held last September at Stanford in partnership with the Stanford Center for Innovation in Global Health, Stanford Woods Institute for the Environment, and the Wellcome Trust. The event brought together leading experts from around the world and across all disciplines—from scientists to policy makers and community groups—to form connections and propose solutions.

Speaking at a panel discussion exploring the impact of fire pollution on human health, Dr. Nadeau made an urgent call to action: "We need to act together to preserve forest ecology and protect our health."



Panelists spoke about the direct correlation between smoke from wildfires or fires caused by agricultural practices and the dramatic increase in respiratory disease and even premature death. Proposed solutions included changing slash-and-burn agricultural practices and developing digital mapping tools to track which populations will be hit hardest by air pollution caused by fires.

Last year, a global health fellow at Stanford, Herb Riband, launched a new Stanford Global Non-Communicable Disease Innovation Initiative, with support from our Center, Stanford faculty across multiple departments, as well as external partners. He now works for the World Health Organization in Geneva, Switzerland, where he continues to work with Stanford to improve outcomes for people with cardiovascular, respiratory, and other chronic diseases.

Finding Solutions Through Science

Better air quality is crucial to preventing not only severe asthma attacks and strokes but also changes to the immune system that could be irreversible. In a first-of-its-kind study currently underway, Dr. Nadeau and Mary Prunicki, MD, PhD, director of air pollution and wildfire research in the Nadeau laboratory, have been looking at the long-term health effects of wildfire smoke on the immune system.

During last year's rampage of infernos in Northern California, Drs. Nadeau and Prunicki, with a team of students and postdocs, raced to begin collecting samples from hundreds of people in the Bay Area who had already signed up to participate in a study on the long-lasting effects of wildfire smoke. Their team will conduct tests on blood samples to assess subjects' circulatory, respiratory, and immune systems through 2037. Our Center hopes to enroll as many as 2,000 participants. According to an article in the top British scientific journal *Nature*, it will be the most diverse group of people enrolled in a wildfire pollution study occurring over a long period of time. Results could potentially lead to guidelines on ways to reduce health risks through prediction, mitigation, and air filtering.



Their work so far in a small group of children shows that the immune system and DNA of children exposed to wildfire are changed. Noting that the fires will only get bigger and become more frequent, Dr. Prunicki told the Washington Post earlier this year: "The work is urgent. They are not going to go away."

To counter the harm that poor air quality causes, Dr. Prunicki is running another study on college students in Fresno, an area in California's Central Valley with elevated air pollution. She has already recorded the pollution levels that these students are exposed to with a monitor they can clip to their backpacks. Next the participating students will turn on air purifiers placed in their dorms. Dr. Prunicki will measure the differences between students who have filtered air in their rooms with those who don't. If revealed to be beneficial, the purifiers could be used as an intervention against wildfire pollution.

Our Center would not be able to respond so quickly to this urgent problem and launch studies that will help identify solutions to global health challenges without the compassion and generosity of our donor community.

International Collaborations

We continue to work with international partners to make new discoveries and change lives on a global scale. Following is an update on key collaborations last year:

- We have completed preparation for a clinical trial that will be run with King's College London in England and National Jewish Health in Denver, Colorado, to study the potential benefits of applying a combination of skin moisturizer and mild anti-inflammatory cream on infants less than 10 weeks old who have had an incident of atopic dermatitis (eczema). The study is set to begin later this year and could potentially show that twice daily use of these creams prevents future outbreaks and allergic reactions. Positive results could also support the hypothesis that sensitization to allergens occurs through the skin.
- Our study with the Swiss **Institute of Allergy and Asthma Research** on the role of laundry detergent in the development of allergy was published in the Journal of Allergy and Clinical *Immunology* in May 2019. Results showed that some detergents can damage cells in the lungs.

- We are working closely with the Pediatric Pulmonology and Allergy Department at Lille University **Hospital** in France to understand the genetics behind food allergy and asthma. This study will look at children's age at their first allergic and asthmatic reactions, severity of the reactions, and type of food allergy. Next, investigators will look for biomarkers of disease that cause allergen-triggered asthma.
- We are working with colleagues in Australia on two studies. One is looking at how wildfire pollution affects the immune system. The other is studying the causes of food allergy in a cohort of participants who are all similar in age.
- In a collaboration with Canadian institutions McMaster University and the **University of British** Columbia, we are investigating blood samples from a group of participants similar in age to see what might be leading to allergy and asthma.
- At the **University of Utrecht** in the Netherlands, we are trying to understand seed allergies and milk allergies, including the role of baby formulas and soy proteins.

Industry Partner Projects

We are grateful to have the opportunity to work with our prominent industry partners, AllerGenis (New York City), ThermoFisher (Sweden), and Ukko (Israel), on developing tests that could improve diagnostics and replace oral food challenges. We are also making strides with Regeneron/Sanofi (international) on developing therapies that can mitigate abdominal and other allergic symptoms in people participating in food allergy trials.

Center Academic and Research **Accomplishments** in 2019 — What Your **Gift Made Possible:**

peer-reviewed research publications, sharing our knowledge and strengthening our position



new global collaborations, including with the Swiss

seed grants from

supporting the exciting research of students,

post-doctoral scholars,

and junior investigators.

different institutions

Institute of Allergy and Asthma Research (SIAF) and University of Utrecht in the Netherlands.

new clinical trials, and asthma.



all with the goal of furthering our understanding of allergies



laboratory research collaborations on a wide range of issues including aging metabolomics, wildfires, vaping,

allergies.

and microbiome in food



shared trainees with other departments



and institutions, building on interdisciplinary resources to improve treatments for people with allergies and asthma.

projects for the underserved, including in the South Side of Chicago and Harlem in New York City.



Funding Needs

Your generosity is the engine that fuels our Center. It allows us to conduct the research that is having a direct impact on how we diagnose and treat allergies and asthma.





Please consider funding the following projects—we need philanthropic support to launch and grow these exciting areas of research:

Disrupting the Field

We have the researchers, tools, and technology in place to create highly personalized treatments for food allergy, including determining who can and cannot be cured through oral immunotherapy. This work involves improving diagnostics; finding new biomarkers to predict when allergic reactions will happen and when an allergy disappears; and creating the ideal dosing strategy for each patient—including when, if ever, the patient can stop oral immunotherapy. We are looking for medications that can do in a single pill what would take weeks of oral immunotherapy. We are looking for ways to predict and measure allergic reaction that are so accurate they may eventually replace stressful and burdensome food challenges. This research is happening, but slowly and in pieces as we look to fund each stage separately through philanthropy or grants.

Your support would accelerate this research and bring it to the hands of doctors who could help more children.

Innovating for Tomorrow

In keeping with the innovation that Stanford and Silicon Valley are known for, we are quickly bringing potentially life-changing laboratory discoveries directly to patients through clinical trials. This type of research—with the potential to produce breakthroughs that will change the field—is almost impossible to fund through government grants or industry sponsors. We need philanthropic investment to start key projects and keep others progressing. Funds for clinical trials go toward recruiting participants, collecting biospecimens and other information for laboratory studies, and mechanistic studies in the laboratory to identify and isolate allergen-specific cells for further study. We have a pipeline of exciting new clinical trials designed and ready to go once funds are in place. These include a first-of-its-kind study to desensitize people allergic to shrimp and look at immune cells involved in those allergies; an oral immunotherapy trial using a new combination of drugs we believe will desensitize people to food allergies faster and without some of the side effects of basic oral immunotherapy; a trial of a singledose pill to successfully and safely stop peanut allergies in adults; and a study to determine whether air filters in homes will protect children from the detrimental health effects of wildfire smoke.

Addressing Climate Change

The impact of pollution and global warming on human health is one of the biggest and most complex problems for medical science. It requires creative and far-reaching solutions. Our Center is up for the challenge. We are working with partners at Stanford and around the world to document how pollution and wildfires damage the immune system at the molecular level and develop and test strategies to limit damage, as well as advocating for policies to halt root causes of climate change. An endowed research fund—a fund that continues to pay out in perpetuity—would give us leeway to greatly expand our studies related to global climate change, planetary health, and wildfires, and help provide evidence to shape public health policies with a solid basis in science.



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Building Our Data Capabilities

The bottleneck for new discoveries is no longer the generation of biological and clinical data, but managing, analyzing, and interpreting large and complex data sets. This work, so key to developing algorithms or identifying trends that lead to important treatments, is extremely labor intensive. To tackle the challenges of Big Data in biology and medicine, we need computational scientists who not only have deep data analysis knowledge but also a working understanding of the underlying biological and medical questions—and the ability to bridge the two. We need biostatisticians and data scientists to help analyze the data we receive continuously and put this into a form we can use for our studies. Your support would allow us to hire and retain biostatisticians who can expand our ability to extrapolate and interpret the enormous amounts of information we generate from our studies, allowing researchers to more accurately predict response to treatment, determine the most promising treatments, and design future studies.



Attracting World-Class Talent

Senior Faculty Scholars

Whether they are investigating a link between air pollution and asthma or using data from clinical trials to determine the best treatment for food allergy, our Center's senior faculty scholars are paving the road to breakthrough discoveries and better therapies. Philanthropic support makes it possible for these academic stars to perform the groundbreaking research that leads to national funding, clinical trials, and cures.

Junior Faculty Scholars

Junior faculty scholars at our Center run the engine of our research by gathering and analyzing the data that reveal the underlying mechanisms of disease. In our clinics, they provide compassionate care and outreach to all patients, including those from underserved areas. With your funding, we can inspire promising scientists to start and continue their careers at Stanford.

Internship Fund

It is crucial to nurture young talent at the high school and college levels. Our Center's summer interns have made important contributions to investigations and are inspired to pursue careers in scientific research. Support of this program will allow students from underserved communities to receive a stipend for their participation, which will help them compete for admission to top universities and medical schools.

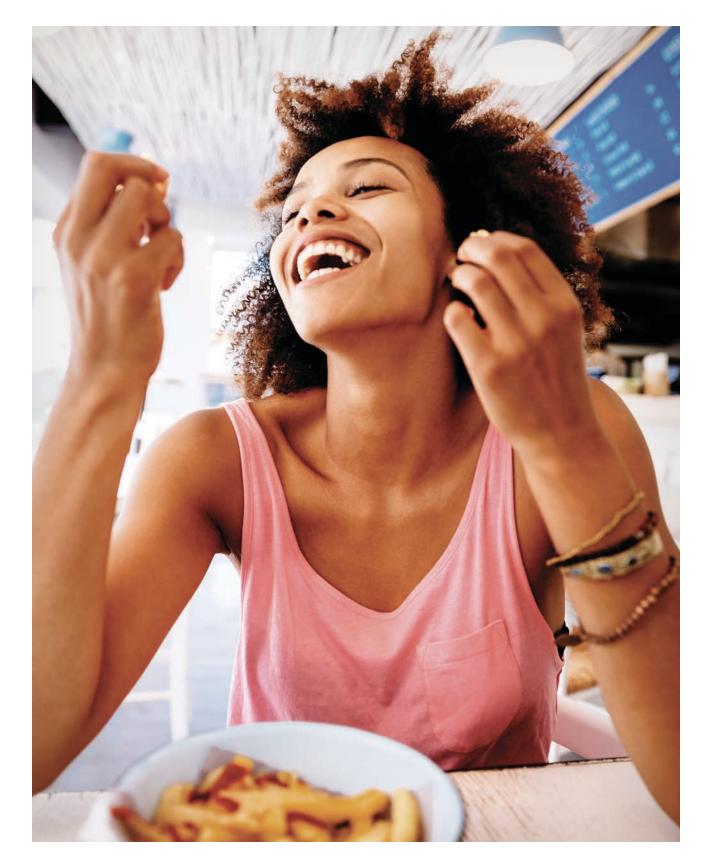
Software Development: The Promise of Technology

Telehealth

Using our location in Silicon Valley as a springboard, we aim to organize a Health Hackathon, in which we challenge Stanford students to create a mobile app that puts medical assistance at our patients' fingertips. Seed funding for this project will help bring the expertise and treatments of our Center to patients who live far away.

Virtual Reality

Virtual reality programs specific to food allergy can alleviate anxiety for children in our oral immunotherapy trials by distracting them during blood draws and encouraging them to eat food they've been conditioned to avoid. This fund would underwrite software development, cost of headsets and computer hardware, and administration of a study measuring the impact of virtual reality programming on allergy patients' quality of life.



Thankyou



From all of us at the Sean N. Parker Center for Allergy & Asthma Research at Stanford University, our patients, and people everywhere who benefit from your generosity, thank you. •

