2016

Allergy + Asthma UPDATE

TRANSFORMING LIVES
with innovative science
and compassionate care

Stanford MEDICINE | Sean N. Parker Center for Allergy & Asthma Research

You Give Us the Strength to Provide the Hope

Allergies and asthma affect people everywhere, creating fear and disrupting lives. Thanks to the support of our generous and dedicated philanthropic community, we are making great progress in finding the root causes of these diseases that will enable us to prevent and treat them, bringing peace of mind to patients and their loved ones.

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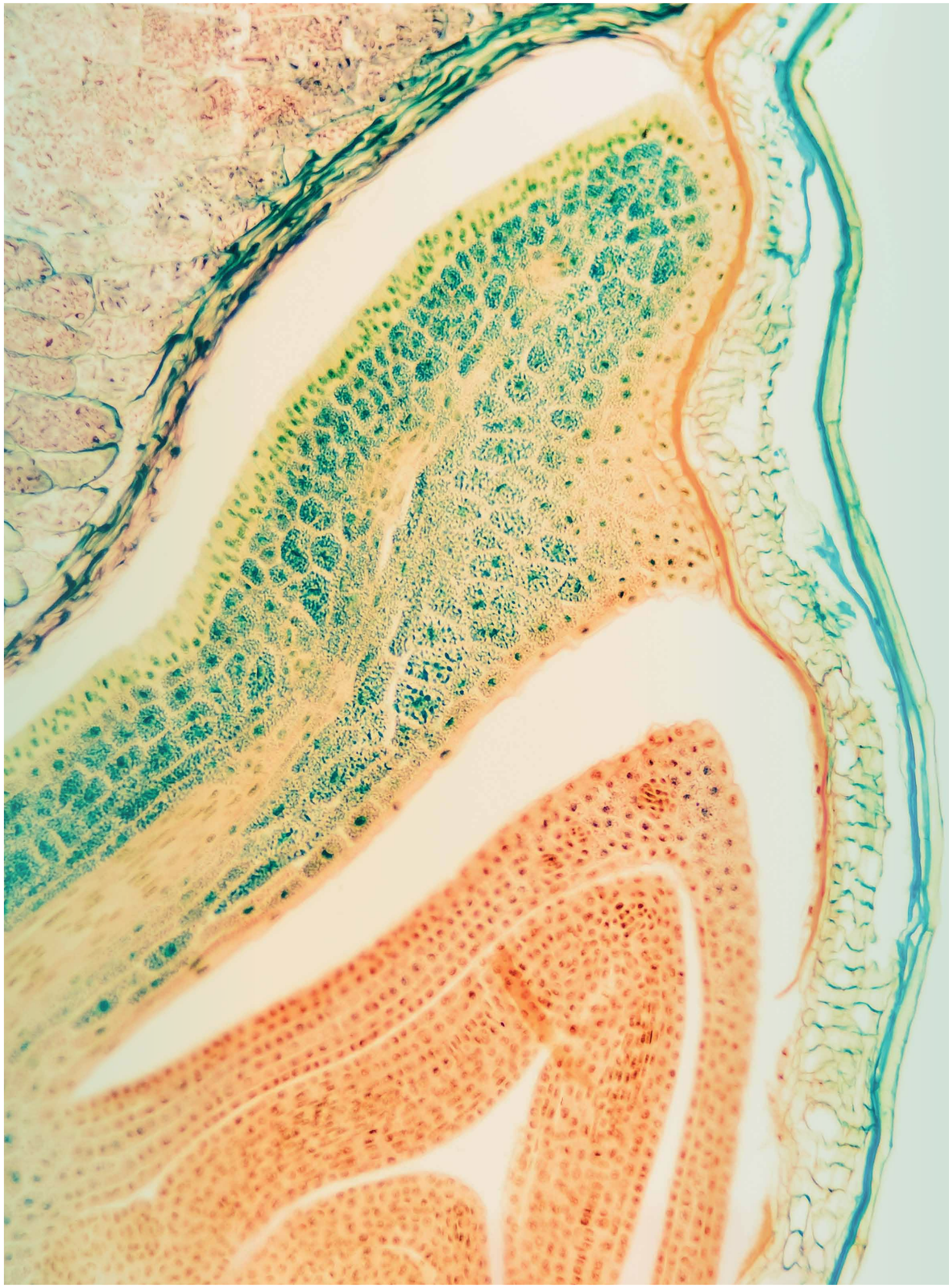


Bringing the Best to Those Who Need it Most

I am so grateful to you. For your foresight. Your generosity. Your dedication to ensuring every person with allergies or asthma receives the best possible care and treatment.

At the Sean N. Parker Center for Allergy & Asthma Research at Stanford University, we are doing great team science, as you will read in these pages. We are using the latest available technologies to make discoveries about molecular interactions in cells that can lead to allergies and asthma. We are caring for many patients in our clinical research center who begin their trials terrified of eating or breathing in the wrong thing and emerge feeling confident and safer. We are working on ways to prevent allergies as well as better and safer methods to diagnose them. In fact, this year marks the 10th anniversary of conducting these trials!

Thanks to you, we collaborate with scientists around the world and are involved in more than 100 research programs—searching for cures, diagnostics, and better prevention—in many countries, including South Africa, Australia, France, China, Japan, Switzerland, Norway, and Russia. This multiplies our impact across the globe as we try to answer remaining key questions about the international epidemics of allergy and asthma we currently face.

But all our wonderful breakthroughs and discoveries won't mean much if we can't get them to the most vulnerable populations. To children in homeless shelters and low-income neighborhoods facing economic disparities. To families who have so many stressors that a child with a food allergy, asthma, or other allergy can tip them into a place where they can't cope. To those breathing polluted air and smoke from wildfires that exacerbate allergies and asthma.

You, our amazing philanthropic community, have responded with incredible kindness. Because of your partnership, we are not only expanding our Center's innovative science and compassionate care, we are also able to bring our expertise to children and families in underserved communities. We have new projects to help educate and empower patients and their families and to inform public health policies that will help protect them. We plan to increase our work in this area, as we remain committed to curing allergies and asthma and improving the lives of all people everywhere who are affected by these diseases.

Thank you again for all you do. As always, I look forward to sharing our progress with you personally and hope to see you soon.

All the best,

Kari C Nadeau

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

1

The Sean N. Parker Center for Allergy & Asthma Research harnesses scientific ingenuity and innovation to help people with allergies and asthma worldwide.

By searching for causes, preventions, and cures for allergic disease, we assist patients—including the vulnerable, the underserved, and low-income individuals—through insightful science and compassionate care.

In 2018, our Center's clinical and basic science researchers continued to use state-of-the-art technology to illuminate our understanding of the immune pathways of allergic responses. With critical support from our generous donors, we tested the safety and efficacy of immunotherapy through clinical trials, using promising therapies that can block molecular reactions related to allergic inflammation.

Our Center's aims and approaches to trial design and patient care include:

- Ensuring the active phase of drug therapy in a clinical trial is less than a year for each patient, reducing time constraints and commitments for participants.
- Helping patients improve management of non-life-threatening allergic reactions.
- Moving participants quickly off the wait list and into clinical trials.
- Hastening development of diagnostic methods to replace food challenges, which can cause anxiety and be burdensome for patients.
- Collaborating with industry and nonprofit organizations in exciting new studies.
- Accelerating data-driven studies using genomics, proteomics, metabolomics, and other "omics" to reveal molecular mechanisms that can help predict outcomes of diagnosis and therapy.

Some key accomplishments in 2018 included:

Clinical Trials

We expanded our clinical trials, launching 11 new studies in 2018. There were more than 1,000 clinical visits in 2018, with 189 individuals newly screened, and 86 adults and children enrolled in new studies. Our biobank of specimens increased from 51,000 to nearly 72,000.

We conducted 14 clinical trials on peanut allergy, two on milk allergy, and one on multiple food allergies.

We started trials using the novel drug fevipiprant (QAW039) for uncontrolled asthma and completed trials of risankizumab (BI 655066), a monoclonal antibody targeting the IL-23A protein, for severe, persistent asthma. We are treating allergic rhinitis involving dust mites using sublingual (under the tongue) immunotherapy and involving grass with injectable dupilumab, an antibody that blocks chemical messengers that mediate inflammation. We are also using dupilumab to treat eosinophilic esophagitis (EoE), a chronic allergic inflammatory disease of the esophagus, which sometimes occurs in patients on oral immunotherapy (OIT).

For a list of clinical trials, see pages 30–33 in the Clinical Impact section of this update.

Environmental Effects on Asthma and Allergies

Worsening air quality related to climate change is having an impact on asthma and allergies. Recent devastating wildfires in western North America have brought this danger closer to home. We are looking at ways to offset the effects of wildfires and airborne pollutants on these diseases.

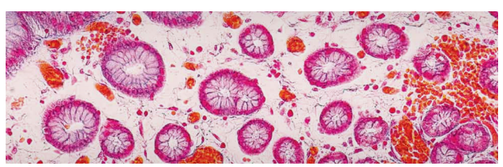
Using mass cytometry (CyTOF), a powerful imaging and sorting technology that measures dozens of unique molecular markers in single cells, we compared the immune effects of wildfires and prescribed burns that are often used to control wildfires. In blood samples from children exposed to prescribed burns and those exposed to wildfires, we found differences in immune markers between the two groups. The results were presented at the American Academy of Allergy, Asthma & Immunology (AAAAI) meeting in February 2019. Larger, controlled studies are needed to validate and fully understand these differences so that the Center can assess the effect of prescribed burns on immune function and help develop guidelines for management of wildfires.

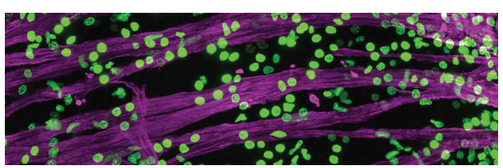
Our studies of teens exposed to high levels of air pollution in Fresno, CA, showed that increasing concentrations of fine particulates, carbon monoxide, and nitrogen dioxide change the expression levels of immune factors involved in allergy and asthma. We are expanding the number of pollutants under study and are looking at their effects on fetuses in the uterus and in children up to age 2, as they are more sensitive to pollutants because of their developing immune systems.

Diagnostics

We have continued our efforts to identify alternative diagnostic methods that eliminate or minimize the need for oral food challenges, currently considered the gold standard for diagnosing food allergies. We found that in some patients, readily obtainable biomarker values (such as levels of IgE, an antibody involved in allergic response, and the size of the irritated area after a skin prick) and patient demographics can accurately predict the presence of a food allergy. We also found that participants with a history of asthma and high allergen-specific IgE have a higher risk for severe reactions during food challenges.

Identifying those at risk of severe reaction can help improve the safety of food challenges. Knowing who is at risk allows us to give lower doses to these people. We developed a food challenge severity score that combines dose thresholds and allergic reactions to determine the risk of severe reaction in peanut oral food challenges.





Molecular and Cellular Characterization

Immune Monitoring

We improved our understanding of immune pathways by investigating the unique immune traits of different patient populations. We found differences in the levels of certain immune cell types in umbilical cord blood between two ethnically different study groups of people in India and the United States. Using CyTOF, we also found immune cell differences between those with food allergy, asthma, food allergy and asthma, and controls. Further investigations that build on this immune cell knowledge will assist in understanding the effect of these differences on health, which could lead to the development of new treatments.

T Cells and B Cells in Food Allergy

We are working to identify different types of T cells (white blood cells essential to the immune system) involved in food allergy to better understand what causes allergic symptoms, find markers that could lead to better diagnosis, and determine how to safely block cellular pathways that induce allergic reactions.

There are two major types of T cells, CD4+ and CD8+, which respond to peptides (short chains of amino acids) associated with allergens. It is well known that allergic reactions involve CD4+ T cells, but we are the first to demonstrate increases in CD8+ T cells in people with peanut allergies. We also showed that these cells recognize specific peanut-derived peptides that cause an allergic reaction. After detecting and isolating CD8+ T cells that arise in reaction to a particular allergen, we noted that these T cells responded differently to allergens in people with and without peanut allergy. This finding may enable better diagnoses and treatments.

A study of patients with peanut allergies found that decreases in the IgE antibody during OIT, in conjunction with the anti-IgE drug omalizumab, are accompanied by increases in IgG4, an antibody believed to reduce allergic reactions. These two antibodies are produced by B cells. We isolated these B cells from people with food allergies and used single-cell RNA sequencing to obtain insights into these cells and the antibodies they produce. These insights could lead to the development of drugs to enhance or block B-cell antibodies (IgG4 or IgE, respectively) to reduce or halt allergic reactions.

Immunotherapy

While OIT for food allergy has been proven effective, protocols have not been standardized. Our Center has worked with the European Academy of Allergy and Clinical Immunology Task Force on Allergen Immunotherapy for IgE-Mediated Food Allergy to develop evidence-based recommendations for immunotherapy protocols for food allergens.

Durability of Desensitization

With immunotherapy, most people need to continue to ingest allergens to maintain desensitization. We are evaluating biomarkers to help predict who can maintain desensitization without continued ingestion. In a study of wheat OIT, for example, we found that while half the patients were desensitized after one year on immunotherapy with wheat gluten, only 13 percent remained desensitized eight to 10 weeks after discontinuing wheat gluten consumption. We are looking at blood samples to see if there are molecular or genetic differences between those who remained desensitized and those who became resensitized.

In another study, we compared differences in desensitization rates in people consuming zero, 300, and 1,000 milligrams of peanut protein a day after successful desensitization with OIT. Rates of desensitization were greater in those taking a maintenance dose (300- or 1,000-mg) than those who discontinued their maintenance dose. Additionally, a 300-mg dose was equally as effective as a 1,000-mg dose in maintaining desensitization.

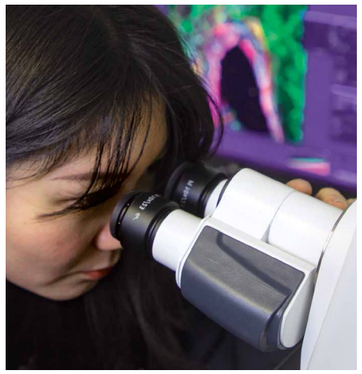
Technological Advances

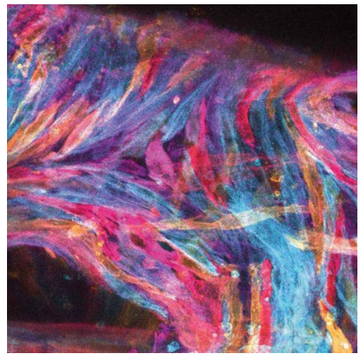
In 2018, our Center developed and used state-of-the-art technologies that advance our understanding of allergies and asthma. Here are examples:

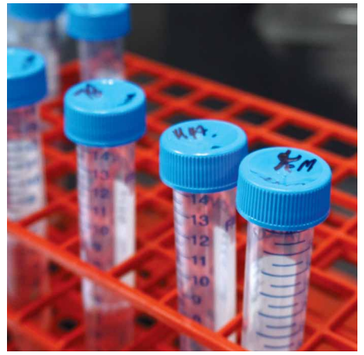
- **Software automating meta-analysis of CyTOF data.** We developed MetaCyto, a software that identifies commonly labeled cell subsets across studies, enabling combined or meta-analysis and increased statistical power. For example, we analyzed data from 10 different cytometry studies that looked at the characteristics of cells. Using nearly 2,900 samples, we detected cellular differences between different demographic groups of patients.
- **Single-nucleus RNA sequencing**. We are collaborating with the team of Aviv Regev, PhD, chair of the faculty and core member of the Broad Institute of MIT and Harvard, to eventually use this technique to evaluate transcriptional changes in DNA that occur in gastrointestinal cells in patients receiving OIT, potentially helping to improve gastrointestinal treatment during OIT.
- **CRISPR-Cas9 gene editing.** We are collaborating with Integrated DNA Technologies to use its CRISPR-Cas9 technology. By knocking out genes with CRISPR, we hope to determine the precise role of certain genes in T cells from patients with asthma.
- **AbSeq for detecting and quantifying proteins in single cells.** AbSeq detects and quantifies proteins and genome information in single cells at ultrahigh throughput, allowing us to analyze many more potential allergens at a time than we can with other cytometry methods. We used AbSeq to look for molecular differences in biomarkers of asthma in twins with and without asthma. Understanding why some people develop asthma and others do not can help us target specific molecular mechanisms with drugs or other therapies.
- **Agglutination polymerase chain reaction.** We have developed this more sensitive and specific method for measuring IgE antibodies against specific allergenic components in foods with very small sample volumes. This will help in identifying an allergen more accurately.
- **Triggered by Offset, Multiplexed, Accurate-Mass, High-Resolution, and Absolute Quantification (TOMAHAQ).** TOMAHAQ uses a synthetic peptide trigger to quantify rare critical peptides in a sample. We fine-tuned this method to identify biomarkers of atopic dermatitis (eczema) and to determine gastrointestinal leakage, helping to improve diagnoses.

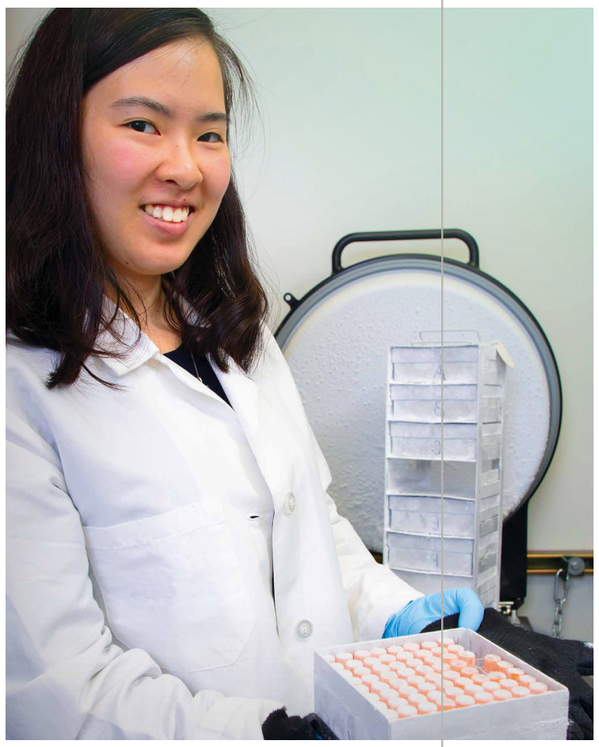
On the Path to Breakthroughs

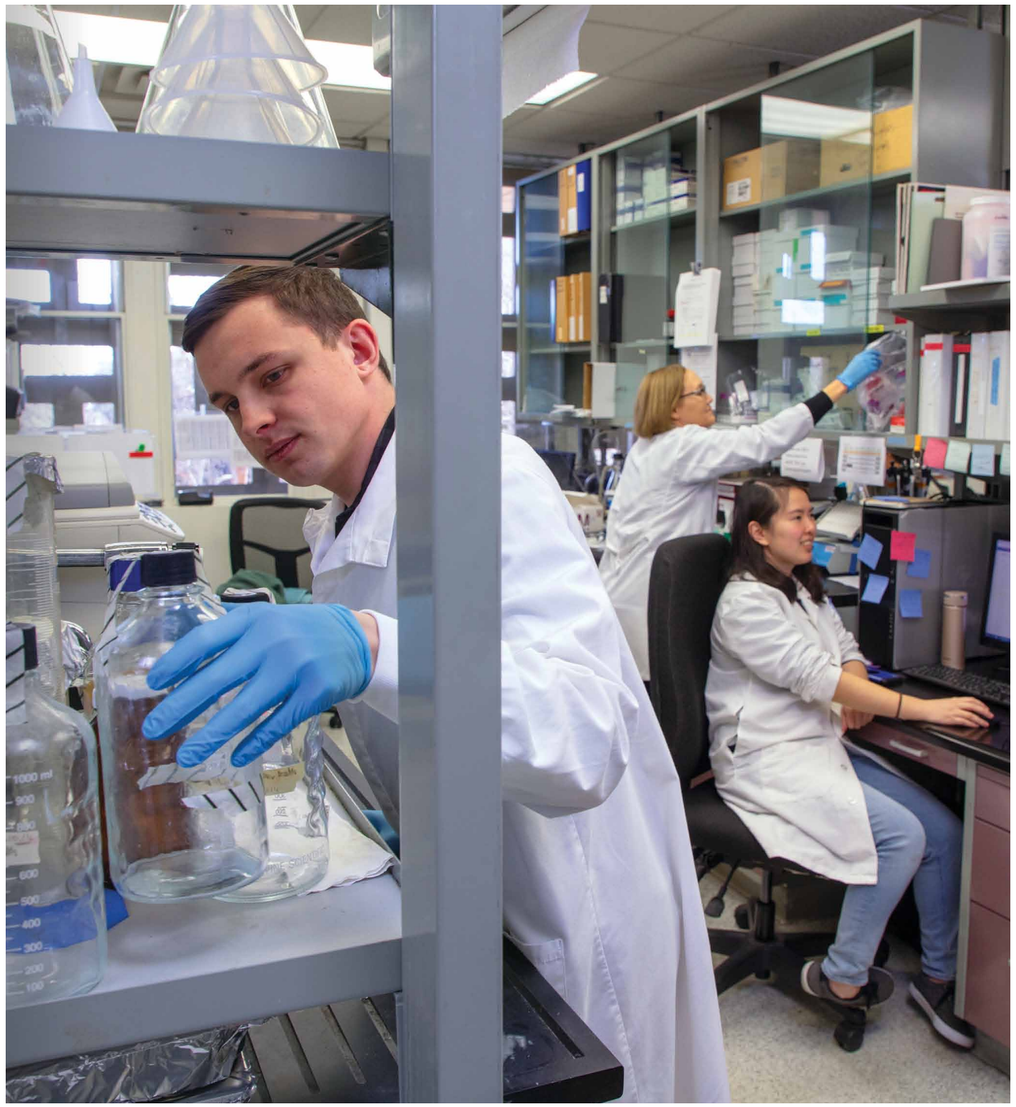
Our Center's laboratory team discovers and creates new ways to improve the lives of people with allergies and asthma.











From Top Clockwise:

Researcher Wenming Zhang, PhD, uses the confocal microscope to create high-resolution digital images of cells.

Diane Dunham, MS, researcher, with the mass cytometry (CyTOF) machine that determines and analyzes cell properties.

Iris Chang, a data aide, inspects vials of plasma and white blood cells kept frozen in liquid nitrogen.

Bryan Bunning, Diane Dunham, and Iris Chang work together to advance research.

Some of the lab team in front of the Biomedical Innovation Building under construction that will become our lab's new home in 2020.

Biological specimens from patients in clinical trials are preserved and stored for later research.

High-resolution microscope images of cells are key to scientific insights.

Disruptive Research

Seed grants support promising research that disrupts standard notions and improves care and treatment for allergies and asthma.

This research enables physicians and scientists to plant the seeds for medical breakthroughs. It expands the scientific and clinical understanding of allergies and asthma, while exploring new technologies and methods for treating these disorders.

Seed funding grows well in the fertile soil of scientific innovation at Stanford. Your gifts are critical in fostering emerging studies that would otherwise not happen.

Our Center has awarded seed grants to the following researchers:

2015

Mübeccel Akdis, MD, PhD, head of dermatology at the Swiss Institute of Allergy and Asthma Research. Dr. Akdis is looking at how respiratory viruses can interfere with immune pathways. She analyzed T cells and B cells of asthmatic and healthy people before and after experimental infection with rhinovirus, which causes the common cold. Infection created anti-viral responses in T cells and B cells of both groups, but responses were stronger in people with asthma. She showed how the molecular mechanisms behind anti-viral reactions differed in people with asthma and those without the disease.

Ruchi S. Gupta, MD, MPH, professor of pediatrics at Northwestern Medicine. Dr. Gupta analyzed data from a national survey to pinpoint the prevalence, severity, and distribution of food allergies. She found that 8 percent of U.S. children and 10.8 percent of U.S. adults have a food allergy, presenting a major public health issue. Forty-one percent of food-allergic children and 48 percent of food-allergic adults have multiple food allergies. She identified higher food allergy rates in black children and in racial and ethnic minority adults, compared with whites.

2016

Jayakar V. Nayak, MD, PhD, associate professor of otolaryngology at Stanford. Dr. Nayak is studying nasal and sinus disorders such as chronic rhinosinusitis (CRS). In one study, patients with nasal polyps received glucocorticoids, a type of steroid hormone. This led to an increase of T regulatory cells in the polyps, suggesting that T cells are critical to fighting inflammation and shrinking polyps. A second study found that some CRS patients' nasal tissue had a significantly greater population of B cells containing IgD antibodies, signaling proteins made by the immune system. This suggests IgD can help enhance mucosal immunity at mucus-producing sites in the body or, by contrast, create an inflammatory response.

Julie Parsonnet, MD, professor of health research and policy at Stanford. Dr. Parsonnet is studying how microbes affect childhood growth and immunity. She analyzed skin samples from young children in homes with and without detergents and other cleansers containing triclosan or triclocarban, two antimicrobial agents often found in cleaning products. The immune response in each group was different, providing molecular evidence that killing off microbes with triclosan or triclocarban is associated with higher prevalence of eczema and food allergies—also known as the "hygiene hypothesis."

2017

Stephen Luby, MD, professor of medicine at Stanford. Dr. Luby is investigating how air pollution from kilns in Bangladesh affects asthma and other respiratory and cardiovascular diseases. A field team is monitoring particulates in the air and interviewing individuals about their health, gathering demographic and socioeconomic information, and collecting health measurements. Kilns for brick manufacturing operate only in the dry winter months. Data will compare health outcomes in the "on" and "off" seasons and across households at varying distances from brick kilns. The results will provide much-needed evidence on the effects of air pollution on asthma, pulmonary disease, and hypertension in Bangladesh.

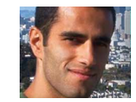
Justin L. Sonnenburg, PhD, associate professor of microbiology and immunology, and **Christopher Gardner, PhD,** professor of medicine, both at Stanford. In looking at how the gut microbiome affects the immune system, Drs. Gardner and Sonnenburg tested healthy adults with two dietary interventions—one involving high-fiber foods and the other fermented foods rich in microbes. Those eating fermented foods such as yogurt and cottage cheese experienced broad increases in microbial diversity and improved immune health, with fewer signs of inflammation. In those eating high-fiber foods, changes in the microbiome and immune system were more varied. More studies need to be done before diet-based treatments can be designed.

2018

Gary Darmstadt, MD, MS, associate dean for maternal and child health at Stanford. Dr. Darmstadt is studying the use of skin emollients (an ingredient in moisturizers) on infants in developing countries to prevent or limit eczema, asthma, and food allergies. He uses an emollient of low-cost ingredients that can be easily and reliably manufactured. He is overseeing its testing on newborns in Bangladesh as a skin barrier repair therapy that wards off eczema and the progression to asthma, food allergies, and allergic rhinitis. Successful results could lead to an affordable, effective way to reduce the toll of allergies in children worldwide.

Hans Oettgen, MD, PhD, associate chief of immunology at Boston Children's Hospital. Dr. Oettgen is looking at how the anti-inflammatory drug omalizumab, when used during oral immunotherapy (OIT), reduces allergic reactions and speeds up desensitization to an allergen. Among OIT patients allergic to peanuts, he found that those on omalizumab advanced more quickly on their increasing peanut doses and had fewer reactions than those in the placebo group. Patients receiving the drug had significant decreases in their peanut-specific IgE antibodies, while placebo subjects did not. The conclusion: OIT is enhanced by blocking either IgE function or the activation of inflammation-producing cells—called mast cells and basophils—triggered by IgE. This study is one of the first to show, from a molecular standpoint, why blocking IgE not only speeds up dose escalation for OIT but also may enhance immune tolerance of allergens.

Our Center collaborates with the Stanford Center for Innovation in Global Health in supporting cutting-edge research into global health problems in resource-poor settings. We support this seed grant:



Niaz Banaei, MD, associate professor of pathology and medicine at Stanford. Dr. Banaei, working with Juan Santiago, PhD, Stanford mechanical engineering professor, is developing a test using cell-free DNA (cfDNA) to detect tuberculosis (TB). CfDNA contains fragments of nucleic acids found in the non-cellular parts of blood and other fluids. Already used in prenatal testing, oncology, and transplantation, cfDNA is promising as an indicator of TB and other infectious diseases. The team is exploring its use as a non-invasive, affordable tool for TB diagnosis from readily available blood and urine samples, especially from adults and children in developing countries. The researchers have developed a microchip to purify cfDNA from a drop of plasma and are assessing the accuracy of their test.

Our 2018 Scientific Advisors

Our Scientific Advisory Committee brings together the best minds in allergy and asthma science. These world-renowned scientists and doctors with different specialties contribute their insights and expertise to create major advances in treatments 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, director, Center for Innovation in Global Health, Stanford

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

Bruce Cain, PhD, *Spence and Cleone Eccles Family Director,* Bill Lane Center for the American West, Stanford

Carlos Camargo Jr., MD, DrPH, *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 Cullen, MD, director, Center for Population Health Sciences, Stanford

Carla Davis, MD, chief of immunology, allergy, and rheumatology, Texas Children's Hospital

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

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

Noah Diffenbaugh, PhD, *Kara J. Foundation Professor* and *Kimmelman Family Senior Fellow*, Woods Institute for the Environment, Stanford

Chris Field, PhD, *Perry L. McCarty Director,* Woods Institute for the Environment, 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 S. Gupta, MD, MPH, director of Science and Outcomes of Allergy and Asthma Research (SOAAR), Northwestern University Feinberg School of Medicine and Ann & Robert H. Lurie Children's Hospital of Chicago

Robert Harrington, MD, *Arthur L. Bloomfield Professor of Medicine* and chair of medicine, Stanford

Lynn Hildemann, PhD, chair of civil & environmental engineering, Stanford Engineering

Robert Jackler, MD, *Edward C. and Amy H. Sewall Professor* and chair of otolaryngology, Stanford

Theodore Jardetzky, PhD, professor of structural biology, Stanford

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

Chaitan Khosla, PhD, director of chemistry, engineering, and medicine for human health and *Wells H. Rauser and Harold M. Petiprin Professor*, Stanford Engineering

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

Mary Leonard, MD, MSCE, chair of pediatrics, Stanford, and *Adalyn Jay Physician-in-Chief*, Lucile Packard Children's Hospital Stanford

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* and professor of microbiology and immunology, Stanford

Stephen Quake, MS, PhD, *Lee Otterson Professor*, Stanford Engineering, and professor of bioengineering, Stanford Medicine

Marc Rothenberg, MD, PhD, director of allergy and immunology, Cincinnati Children's Hospital Medical Center

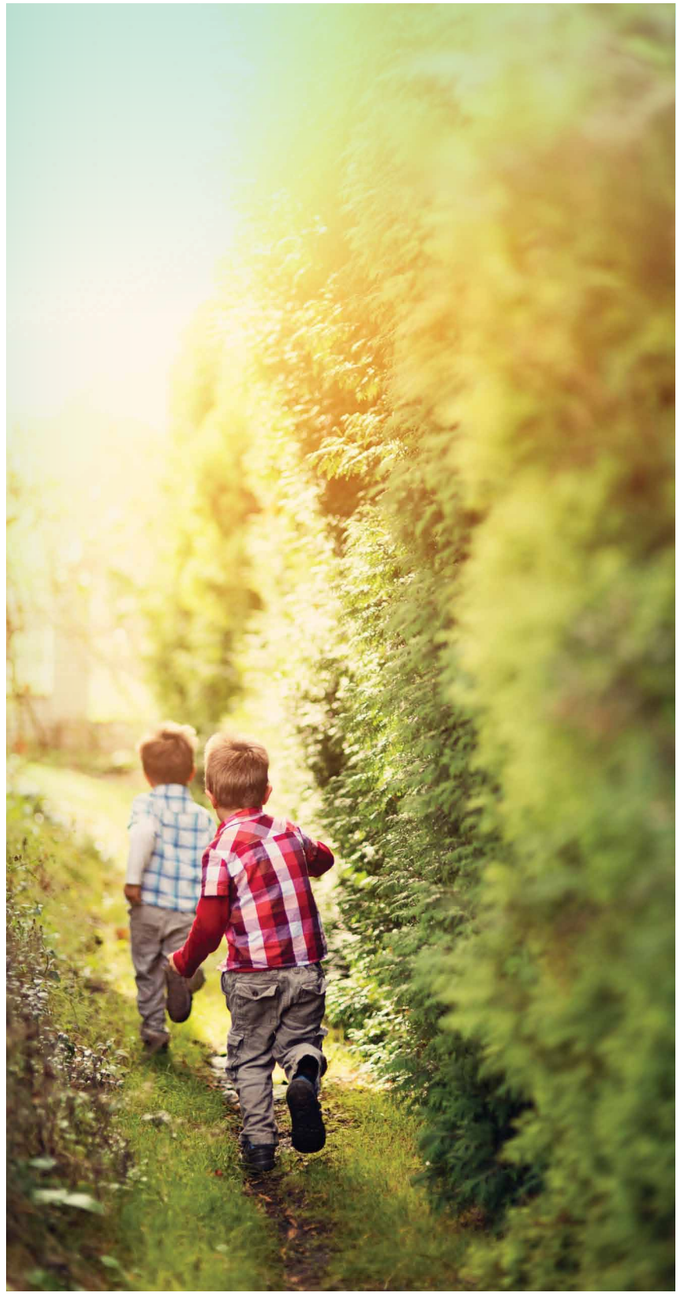
Lucy Shapiro, PhD, director, Beckman Center for Molecular & Genetic Medicine, Stanford

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

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

Dale Umetsu, MD, PhD, principal medical director, Genentech, and clinical professor of pediatrics, UCSF

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



PEER-REVIEWED JOURNAL ARTICLES

Our Center's contribution to allergy and asthma research in 2018 and early 2019 included 37 articles related to asthma, allergies, and immunology, published in peer-reviewed journals.

2018 Publications

High-affinity allergen-specific human antibodies cloned from single IgE B cell transcriptomes.
Croote D, Darmanis S, Nadeau KC, Quake SR.
SCIENCE.
2018 Dec 14;362(6420):1306-1309.

Predicting development of sustained unresponsiveness to milk oral immunotherapy using epitope-specific antibody binding profiles.
Suárez-Fariñas M, Suprun M, Chang HL, Gimenez G, Grishina G, Getts R, Nadeau KC, Wood RA, Sampson HA.
JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY.
2018 Dec 7. [Epub ahead of print].

Identification of almond (prunus dulcis) vicilin as a food allergen.
Huilian C, Zhang Y, Lyu SC, Nadeau KC, McHugh T.
JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY.
2018 Dec 4. [Epub ahead of print].

The public health impact of parent-reported childhood food allergies in the United States.
Gupta RS, Warren CM, Smith BM, Blumenstock JA, Jiang J, Davis MM, Nadeau KC.
PEDIATRICS.
2018 Dec;142(6).

Laundry detergents and detergent residue after rinse directly disrupt tight junction barrier integrity in human bronchial epithelial cells.
Wang M, Tan G, Eljaszewicz A, Meng Y, Wawrzyniak P, Acharya S, Altunbulakli C, Westermann P, Dreher A, Yan L, Wang C, Akdis M, Zhang L, Nadeau KC, Akdis CA.
JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY.
2018 Nov 27. [Epub ahead of print].

Analysis of a large standardized food challenge data set to determine predictors of positive outcome across multiple allergens.
Sindher S, Long AJ, Purington N, Chollet M, Slatkin S, Andorf S, Tupa D, Kumar D, Woch MA, O'Laughlin KL, Assaad A, Pongracic J, Spergel JM, Tam J, Tilles S, Wang J, Galli SJ, Nadeau KC, Chinthrajah RS.
FRONTIERS IN IMMUNOLOGY.
2018 Nov 27;9:2689.

Baseline gastrointestinal eosinophilia is common in oral immunotherapy subjects with IgE-mediated peanut allergy.
Wright BL, Fernandez-Becker NQ, Kambham N, Purington N, Tupa D, Zhang W, Rank MA, Kita H, Shim KP, Bunning B, Doyle AD, Jacobsen EA, Boyd SD, Tsai M, Maecker H, Manohar M, Galli SJ, Nadeau KC, Chinthrajah RS.
FRONTIERS IN IMMUNOLOGY.
2018 Nov 22;9:2624.

AR101 Oral Immunotherapy for Peanut Allergy.
PALISADE Group of Clinical Investigators, Vickery BP, Vereda A, Casale TB, Beyer K, du Toit G, Hourihane JO, Jones SM, Shreffler WG, Marcantonio A, Zawadzki R, Sher L, Carr WW, Fineman S, Greos L, Rachid R, Ibáñez MD, Tilles S, Assa'ad AH, Nilsson C, Rupp N, Welch MJ, Sussman G, Chinthrajah RS, et al.
NEW ENGLAND JOURNAL OF MEDICINE.
2018 Nov 22;379(21):1991-2001.

Differences in multiple immune parameters between Indian and U.S. infants.
Rathore DK, Holmes TH, Nadeau KC, Mittal P, Batra A, Rosenberg-Hasson Y, Sopory S, Gupta R, Chellani HK, Aggarwal KC, Bal V, Natchu UCM, Bhatnagar S, Tavassoli M, Lyell DJ, Rath S, Wadhwa N, Maecker HT.
PLOS ONE.
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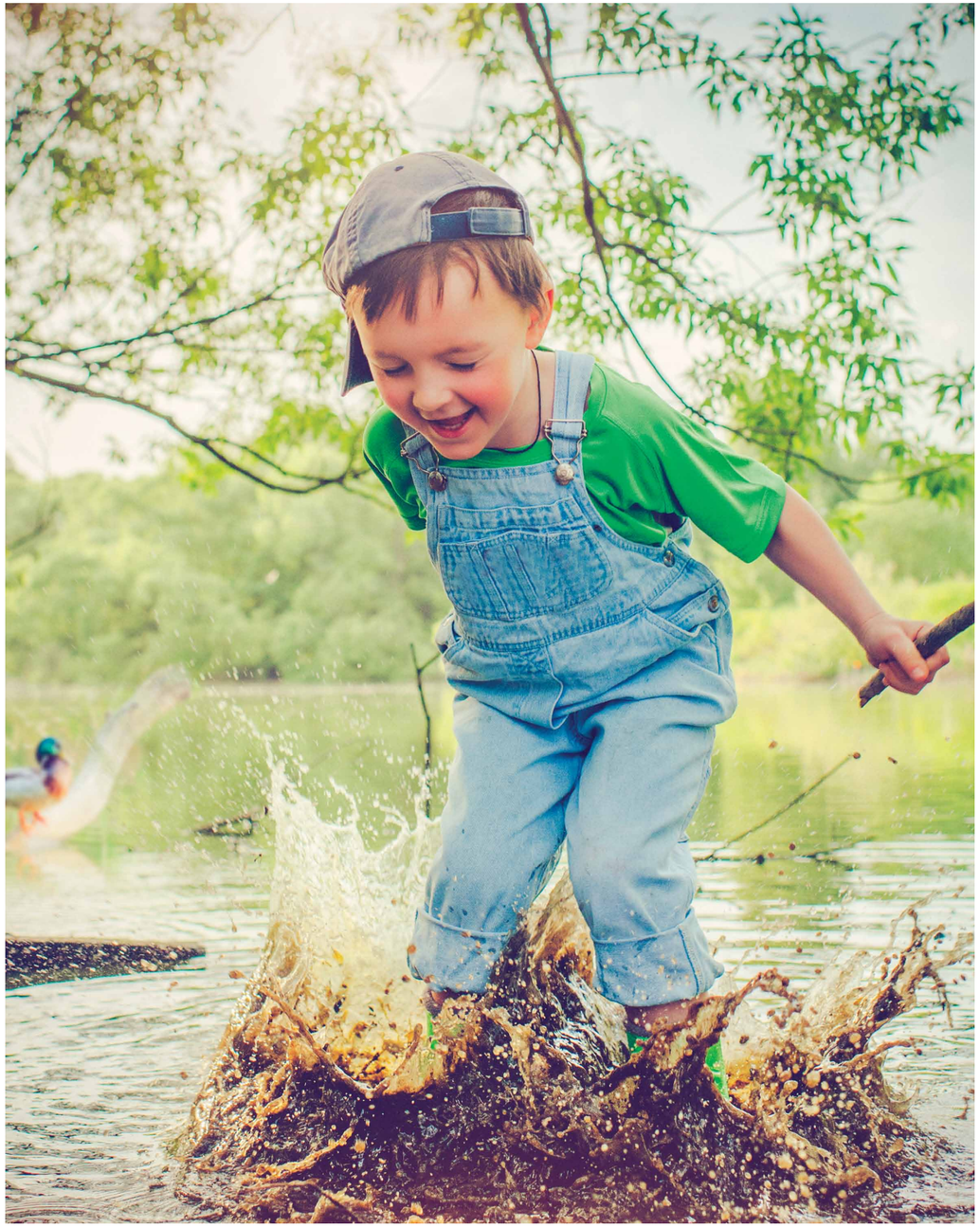


Philanthropic Impact

2

The loving arms of your generosity embrace and protect children and families in need.

Thanks to you, we can explore the tiniest changes in a cell. Use vaccines to try to cure food allergy. Treat children and empower families. Document the effects of pollution and climate change on children's health. Discover the best and fastest treatments for allergies and asthma. We are grateful for your leadership into an allergy- and asthma-free future.

Many Thanks!

Some of our most dedicated partners have made incredible contributions to new and continuing science and outreach projects in 2018.

Thanks to many generous supporters, we are moving into a new laboratory space in the Biomedical Innovation Building at Stanford soon after its scheduled completion in spring of 2020 (pictured top left).

The Friend family made a key gift for research into the molecular mechanisms in wheat allergy with the eventual goal of developing a vaccine for this disease. The Olsen-Small family supported a joint investigation with Boston Children's Hospital at Harvard Medical School to improve diagnosis of food allergies, and an anonymous donor made possible a clinical trial at Mayo Clinic Arizona to see if a biologic drug would help patients using OIT who develop severe stomach problems.

The Bunning family has established a new fund to address the flexible needs of food allergy and immunology research, and the Domansky family also made an important gift to support food allergy and asthma research at our Center. An investment in basic science and bioinformatics by the Hill family will be crucial to train new researchers and discover new therapies that can transform the lives of patients with allergies and asthma. A generous gift from the Freidheim family will help us continue treating children in underserved communities.

We express our continuing gratitude to Sean N. Parker, Julia and David Koch, Michele and Tim Barakett, Rebecca and Sacha Lainovic, The Safe + Fair Food Company, End Allergies Together (EAT), Food Allergy Research and Education (FARE), and the National Institutes of Health (NIH) for supporting our work in 2018.

Helping Others Find Peace of Mind

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

Karmely Family

Shahab, Eskander, Libby, Max

When we first met Dr. Nadeau at a coffee shop, she asked Eskander, then in second grade, "What do you want to be able to do after this study?" He looked at the display of treats. "I want to be able to eat one of those," he said. "Not anything with nuts. Just one that could have been near nuts."

For years, our son and our whole family had lived in constant fear. Eskander had multiple severe food allergies, including nuts, dairy, and egg. Until he was 2, we wouldn't let anyone touch him. We were afraid something someone had eaten and had on their hands might be absorbed through his skin and send him into anaphylactic shock. Many people told us Eskander was too allergic to be helped by treatment. We traveled to Israel seeking different options. Nothing worked. When we heard Dr. Nadeau speak at an event, we were in awe. When we received a call from Stanford saying we would be in a trial, it was the most exciting moment of my life.

Treatment was hard. Eskander was scared. But we are so grateful. Since he finished treatment, Eskander has completely blossomed. He's interested in science, he's outgoing. We can see a complete change in his personality and outlook on life. We recently took a family trip to Iceland that would have never been possible before the trial. Every child should live without fear of food. We believe in the research at Stanford that Dr. Nadeau is leading. We want to help.

Orsak Family

Nicole

Nicole was initially hesitant to start her oral immunotherapy trial. Diagnosed with multiple food allergies as a baby, she learned to read every ingredient on a food label and was very careful about what she ate, especially peanuts. But just before her trial, she'd had a serious allergic reaction after eating a piece of chocolate with trace amounts of peanut and cashew. She did not know if she could handle eating the food that made her so sick. Dr. Nadeau gently reassured Nicole she would be safe.

The treatment went slowly. Nicole often had severe stomach pain. At times she almost gave up. Each time, Dr. Nadeau worked with us to address Nicole's symptoms. After two years, Nicole was able to eat almost 16 peanuts without having a reaction. We were all ecstatic. For the first time in her life, our 13-year-old daughter walked into a bakery, selected a cupcake, and ate it with a big grin. The milestones continued: No more food labels. Trips without her parents. Her first football game. Most importantly, she applied to college without having to worry about needing fast access to medical care.

We believe in making a better world for people, especially children with food allergies. Food allergy is an invisible disease with life-threatening consequences. Now that Nicole is desensitized to peanuts, we want to support new ways of addressing food allergies that will help other families.

"We have a lot to look forward to because of the amazing research that's been done so far and because of the courage of those who come to our clinic. No one person can do this in a lifetime. We all need to work together." — Dr. Nadeau

Laaker Family

Micah, Ben

My family's lives changed dramatically when my youngest son, Ben, was diagnosed with tree nut allergies when he was 2. After accidentally eating a cashew, he immediately began struggling to breathe. At first, we thought he was choking. In fact, he was having a severe allergic reaction.

Fortunately, his mother recognized the signs of anaphylactic shock and called an ambulance. While waiting for the paramedics, Ben was covered in hives, struggling to remain alert as his airways constricted. It was terrifying. We do everything possible to keep a reaction from happening again. School potlucks, playdates, and birthday parties are a minefield. Ben is always accompanied by a parent or another adult trained to use an epinephrine auto-injector. Now almost 8, Ben is much more aware of and frustrated by the restrictions he has compared to those of his friends.

After Ben's allergic reaction, I shared his story with my colleagues at Google and Ben's mother learned about the Center's pioneering work. I set up fundraising efforts for the Center every year through our annual charitable giving drive. We support Dr. Nadeau because we want to give Ben and kids like him the best chance at happy, healthy, and more carefree lives. We fervently believe in a world where no one would have to experience a loved one struggling to hang on—as Ben did years ago—or worse. Ben is sharing his story because, he says, "If it helps other kids not have to live with allergic reactions, it's all worth it."

Friend Family

Matthew, Linda, Bill

Although we noticed warning signs such as "hives" when he teethed on a bagel, the reality of our son's wheat allergy did not hit us until Matthew had his first anaphylactic reaction at age 4. We didn't know that being allergic to wheat was serious or that wheat was in almost everything in our pantry. The emergency room doctor directed us to avoid any potential allergens—wheat, oat, barley, rye—always carry epinephrine auto-injectors, and stay within 20 minutes of a U.S.-based health center. The constraints suddenly became very real and very scary.

We did everything we could to keep Matthew from eating anything that might cause a reaction, but still we lived in fear for Matthew's life in case of accidental wheat ingestion. We learned from an acquaintance—now a good friend—about a researcher in California doing pioneering work in food allergies. Dr. Nadeau and her team changed Matthew's life forever. As a young adult, his daily maintenance dose of wheat continues to protect him. He now eats anywhere, with anyone, at any time.

We support Dr. Nadeau because she is not only a brilliant researcher and fearless pioneer. She is also a mom—someone who truly understands what it means to treat the whole person, work with the entire family, and remain tireless in search of more treatment options and, we hope, one day, a cure.

Ripples on a Pond

Endowed gifts and continuing support help improve the lives of children with allergies and asthma and their families for many years. Your kindness and commitment allow us to sustain successful programs and begin new ones.

Investigating Allergies and Asthma: from Basic Science to Treatments

Thanks to gifts from families committed to ending allergies and asthma, our Center is able to continue basic science research studies of the cellular changes involved in these illnesses and the best ways to circumvent those changes. Our work to create a microchip to more accurately and safely diagnose allergies has visionary support from the Orsak, Kepner, and Englander families. Our clinical trials, bringing the best therapies to patients, are made possible by philanthropic gifts from many generous leaders in the Stanford community and beyond.

Bringing Hope to Those in Need

Many families from across the nation, like the Canfield family, are generously supporting programs for underserved children in California, Chicago, and New York. Thanks to their kindness, staff from our Center have been able to offer health and wellness workshops focused on asthma and allergy prevention to homeless children with food allergies and their families in New York. In Chicago, we are working with allergy experts to create an educational toolkit with input from the families, who will also test it to make sure it meets their needs. In California, Barakett scholar Mary Prunicki, MD, PhD, is working with underserved children in Fresno who are exposed to air pollution and smoke. We are also continuing our advocacy work with the Center for Youth Wellness in San Francisco, looking for ways to translate the science on asthma and toxic stress into a plan of action for caregivers and families, a process we believe we will be able to apply to other areas of health care.

Supporting Leaders, Attracting Top Talent

An anonymous donor and the Barakett, Bravo, and Soffer families are supporting early and senior career researchers conducting basic science investigations in our lab, including Scott Boyd, MD, PhD, who is studying the role of B cells in immune reactions; Dr. Prunicki, who is documenting how smoke from air pollution and wildfires affects children at the molecular level; and Bali Pulendran, PhD, who is making discoveries in microbiology and immunology that will inform new treatments for allergies and asthma. The Carell and Gies families are supporting R. Sharon Chinthrajah, MD, our clinical director, and physician-researcher Sayantani (Tina) Sindher, MD. Dr. Nadeau is also grateful to those supporting her professorship, including the Lainovic, Carell, Li, Sandberg, Orsak, Kepner, Staggs, Bates, Limaye, and Arrillaga families, and many more.

Community Connections

3

Our Center family stays connected in many ways, including gala events, educational talks, and perhaps the most fun run in the Bay Area—Summer Scamper.

Substantial FARE

Leaders in our Center's philanthropic community from around the country came together in New York City to celebrate and contribute at the 21st Annual Food Allergy Ball, sponsored by Food Allergy Research & Education (FARE). As one of FARE's Centers of Excellence, our Center seeks to collaborate closely, linking arms on everything from research to education in support of our common goal to improve the quality of life and health of people with food allergies, and provide them hope through the promise of new treatment. Dr. Nadeau serves as FARE's chief innovation officer.

The evening honored Kim Yates (Grosso), a longtime member of our Center community, for her leadership and advocacy on behalf of families seeking life-changing therapies for food allergy. In 2012, Kim's daughter, Tessa, became the first person desensitized to five allergens at once through a trial at our Center.

"The clinical trial has so much more meaning than just my own safety," 15-year-old Tessa told FARE. "I've been able to connect with people who understand me, and I understand them."

We continued bringing our allergy and asthma community together in the following ways in 2018:

Community Events

2018 Summer Scamper: Our Center community, including 7-year-old Patient Hero Aaron, participated in this annual 5K, 10K, and kids' fun run benefiting Lucile Packard Children's Hospital Stanford and children's health. The event raised more than $3 million.

Day on the Bay: At the 2018 Day on the Bay in Santa Clara County, CA, our Center hosted a community booth and offered epinephrine auto-injector training, asthma peak flow testing, and education on asthma and food allergies. More than 10,000 people attended this community event.

Talks and Presentations

We started the year by gathering our scientific community at the inaugural Gordon Research Conference on Food Allergy in Ventura, CA. The conference provided an informal forum for researchers to present inspiring findings and spur further innovation in predicting, preventing, and curing food allergies.

Our Center hosted a series of guest lecturers, including biostatistician Henry T. Bahnson, MPH, from the Benaroya Research Institute in Seattle, a leader in developing statistical analysis plans to identify biomarkers for allergies, and Antoine Deschildre, MD, a French allergist who spoke about France's experience with omalizumab in treating asthma.

At our second annual State of the Center community forum in April, Dr. Nadeau and our Center staff gave in-depth presentations on allergy, asthma, and related gastrointestinal disorders, and answered questions from the audience of patients, families, and clinicians. Also in April, Dr. Nadeau spoke at TEDx Palo Alto on food allergy prevention.

Our Center's team took part in leading and speaking at the Global Climate Action Summit in San Francisco in September. The summit brought together thousands of leaders from nations, businesses, and nongovernmental organizations to address the threat of climate change. (Read more about our work at the summit in the Global Vision section of this update, page 39.)

Outreach and Support

Before, during, and after our trials, we continue to offer our patients a wide range of support services. These include: a patient registry to move patients into trials as soon as possible; the services of a child and family therapist in our clinic; a peer support team of trial graduate families; and graduate webinars with our clinical staff.

Expanding access to care: As we grow, making sure all children have access to the best care and education for allergies and asthma is becoming a larger part of our Center's work. We are excited about new programs we started in 2018 in San Francisco, Chicago, and New York that we plan to build on in the future.

Keeping All Informed

Through our e-newsletter, we continued to educate those in our community and beyond about our advancements in allergy and asthma research and our clinical trials. To learn about our work in 2019, sign up for the newsletter at our Center website, med.stanford.edu/allergyandasthma (click on News & Events). Or email us at snpcenterallergy.inquiry@stanford.edu.

Clinical Impact

4

Your generous support gives patients in our clinical trials access to cutting-edge treatments as we work to make the best and safest therapies available to all.

R. Sharon Chinthrajah, MD, medical director of clinical research, with a patient (above); Zachary Teixeira, RN, MS, and Lisa Lee, RN, MSN, clinical nurse practitioners (top right); Anny Uyehara, NP, research nurse practitioner, with a patient (center right); and Dr. Nadeau in the clinic (bottom right).

R. Sharon Chinthrajah, MD

Clinical Associate Professor and Medical Director of the Clinical Translational Research Unit

The best part of my job is seeing the patients as they embark on the journey of a clinical trial at our Center—they are so enthusiastic and grateful to be embraced by our team. They constantly comment on how much they learn from us, even after years of living with their allergies. And we learn from them—they inspire us to find better therapies. Our trials give them an opportunity to participate in groundbreaking treatments and to be part of the legacy of allergy research.

This is a great time to be in food allergy research. There is still so much more work to be done, and there is still a lot to learn. We're just beginning to make therapies safer and more effective. There are so many other discoveries to be made. **I love being part of that future.**

Sayantani (Tina) Sindher, MD

Clinical Assistant Professor

It's really nice to see the patients change from the beginning to the end of the studies. At the end, they're so much bigger and healthier. **My favorite part of the job is the peanut parties** we have at the end of some peanut trials. The patient will eat real peanuts and the staff joins them. It's such a celebratory moment—people take videos to share with their friends and families. **It's very moving to see these families who have gone through life avoiding social activities and being very scared of accidental ingestions to have such a sense of relief.**

Andres Alvarez Pinzon, MD, PhD, MHA

Director of Regulatory Affairs and Translational Medicine

My role is to make sure we follow all national and international regulatory affairs guidelines and ensure that we obtain clean data outcomes and use best research practices in translational medicine. **This has a direct impact on patient safety—our number one priority.** For all of us who work in clinical studies and behind the scenes, we know that **we play a key role in improving the quality of life for our patients. That's the gift we get from this work.** We make sure the new generations of clinicians have the opportunity to investigate new drugs and successfully treat conditions related to asthma, allergies, and immunology.

10 Years of 'Less Anxiety, More Laughter'

In 2018, we marked our 10th anniversary of running life-changing clinical trials, treating thousands of patients with your support. **Here are some of their stories:**

Andrew

15 years old

"When I was 8 years old, I took a bite of a sandwich that turned out to be peanut butter and jelly. My throat swelled up and I ended up in the ER after two EpiPen injections. Now that I've gone through Dr. Nadeau's trial, I know that I am safe against accidental exposure. It has changed my life."

Lena

12 years old

"Honestly, there are no words to describe how grateful I am to have experienced a trial at the Center. The doctors and staff were extremely supportive. I now know that my future will be filled with countless memories, less anxiety, and more laughter because of this amazing study."

Keegan

11 years old

"Now that I am desensitized to peanuts, I no longer live in constant fear of coming into contact with a peanut by accident. I am a serious foodie, and being a part of this program has opened up a whole new world of foods for me! I can be a regular kid."

Ryan

19 years old

"Before the trial, going to other kids' houses was a nightmare—no one wanted to have me over because they were scared they would kill me. After the trial, things are great. I'm away at college and don't worry as much about being exposed to peanuts accidentally."

Jordan

12 years old

"When I went to Asia in 2015, my mom wouldn't let me eat anything. When I went again in 2018 after eating a whole peanut in the trial, she was less worried and I could have the full experience. I am so thankful for this opportunity."

Mary

Adult patient

"I traveled from the Midwest to Stanford to participate in a clinical trial. Dr. Nadeau and her staff gifted me with an extra layer of protection from my allergies. With this gift comes freedom to comfortably eat at restaurants and the homes of friends, and to travel freely out of the country."

Matthew and Joshua

Twins, 17 years old: returning to help others

Our Center's omalizumab-assisted oral immunotherapy (OIT) trials have opened up the world of twin brothers Matthew and Joshua in more ways than one. Now they can enjoy meals with friends and family at restaurants without worrying. Before OIT, they never ate out. "I remember sadly watching my parents eat at restaurants," Joshua said. He was allergic to wheat. Now tempura, fortune cookies, and hamburgers are among his favorite foods. Traveling is easier because the family doesn't have to pack cooking utensils and foods to make sure there is no cross-contamination, Matthew added.

Both brothers have not only been patients of Dr. Nadeau—they have also worked in her lab. Over the course of an eight-week internship, Matthew saw firsthand how samples were analyzed at the lab. This was particularly exciting for him because during his time as a food allergy patient, Matthew had many blood samples taken. After this experience, Matthew is considering a career in research. "I really enjoyed working in a lab," he said. "The staff was very supportive and kind. They patiently explained the complex tools and concepts used in the lab to help me learn."

In the summer of 2018, Joshua also interned in Dr. Nadeau's lab. There, he learned how to analyze and mine data for a larger project. This was particularly fascinating as some of the information came from trials he had participated in. As it did for his brother, this experience has inspired Joshua to pursue a future in research.

More stories from students who have benefited from the Nadeau Lab internship program are featured in Training the Next Generation, pages 36–37.

OUR CLINICAL TRIALS: HELPING CURRENT AND FUTURE PATIENTS

We were involved in more than 25 clinical trials in 2018, including the following.

Study Topic	Date Started/Status	Purpose
Peanut Allergy		
Oral immunotherapy (OIT)	2013, completed	Compare peanut OIT to placebo in inducing tolerance and desensitization in peanut-allergic children for 134 weeks, followed by 26 weeks of peanut avoidance.
OIT maintenance	2014, completed	Determine whether desensitization to peanuts is maintained after avoiding them for three months, following successful completion of OIT.
OIT with AR101, a peanut flour containing major allergenic peanut proteins	2016, completed	Study the efficacy and safety of AR101 peanut flour in a characterized desensitization OIT regimen in peanut-allergic individuals.
Etokimab, an antibody that inhibits the activity of IL-33, a signaling protein that plays a role in immune and inflammatory response	2016, completed	Assess the safety and tolerability of etokimab in adult patients with peanut allergy.
Skin patch	2016, completed	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 in children	2017, completed	Assess the safety and tolerability of AR101 peanut flour for about six months in peanut-allergic children.
Vaccine	2016, ongoing	Evaluate safety, tolerability, and immune response in peanut-allergic adults receiving a protein DNA plasmid injection.
OIT with peanut flour follow-up study	2017, ongoing	Study the safety, tolerability, and efficacy of AR101 peanut flour in people who have completed a previous AR101 OIT study.
Skin patch	2017, ongoing	Assess the safety and efficacy of Viaskin Peanut skin patch treatment to induce desensitization to peanuts in peanut-allergic children 1 to 3 years old.

Study Topic	Date Started/Status	Purpose
Peanut Allergy (cont.)		
Skin patch follow-up	2017, ongoing	Follow patients who completed a previous Viaskin Peanut skin patch study for two to three more years.
OIT with peanut flour long-term study	2017, ongoing	Assess AR101 peanut flour's safety and tolerability over an extended dosing period.
OIT with peanut flour long-term study	2018, ongoing	Investigate AR101 peanut flour in peanut-allergic children in active treatment to gather information about safety and tolerability of the new drug in long-term, day-to-day use.
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 adult patients.
Skin patch	2018, ongoing	Test the long-term assessment of safety and therapeutic benefit of Viaskin Peanut skin patch in peanut-allergic children.
Eosinophilic Esophagitis (EoE)		
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.
Asthma		
Subcutaneous therapy	2016, completed	Test the safety and efficacy of subcutaneously administered (under the skin) BI 655066 as an add-on therapy over 24 weeks in patients with severe persistent asthma.

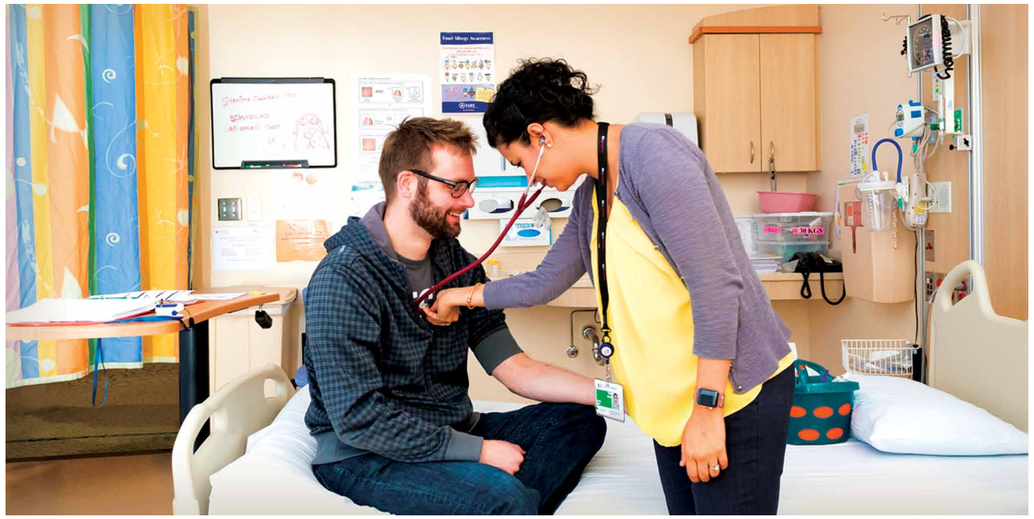
OUR CLINICAL TRIALS: HELPING CURRENT AND FUTURE PATIENTS

(continued from previous page)

Study Topic	Date Started/Status	Purpose
Asthma (cont.)		
Risankizumab, an anti-IL-23 antibody being investigated for the treatment of multiple inflammatory diseases	2017, ongoing	Assess the safety and efficacy of subcutaneously administered risankizumab as add-on therapy in patients with severe persistent asthma.
Fevipiprant, a drug that blocks CRTh2 (a protein associated with certain allergic responses), combined with standard therapy	2018, ongoing	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, ongoing	Evaluate the efficacy of injectable dupilumab as a therapy added to subcutaneous grass immunotherapy to reduce allergic hay fever symptoms.
Dust Mite Allergy		
Sublingual therapy with STG302, house dust mite allergen extracts	2017, ongoing	Study the efficacy and safety of house dust mite allergen extracts in adults and adolescents with house dust mite-associated allergic rhinitis.
Cow's Milk Allergy		
Skin patch	2015, completed	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.
Hydrolyzed formula (milk formula in which the proteins that trigger allergies have been broken down into very small parts)	2017, ongoing	Test the safety and efficacy of extensively hydrolyzed formulas in infants and children with cow's milk allergy.
Multiple Food Allergies		
OIT with omalizumab (Xolair), a monoclonal antibody approved for treating asthma	2017, ongoing	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.

Study Topic	Date Started/Status	Purpose
Eczema (Skin Allergy)		
Skin cream pilot study	2018, ongoing	Compare two different skin creams and their effect on water loss through the skin in pediatric and adult patients with eczema.
Other		
Twin study	2010, ongoing	Provide a better understanding of how the immune system works in twins with and without allergic disease.
Sean N. Parker Center Registry	2016, ongoing	Create an electronic database with information on healthy, asthmatic, and allergic individuals.

For more information on our trials or to join our registry and be considered for a trial, scan left or go to www.med.stanford.edu/allergyandasthma.



Training the Next Generation

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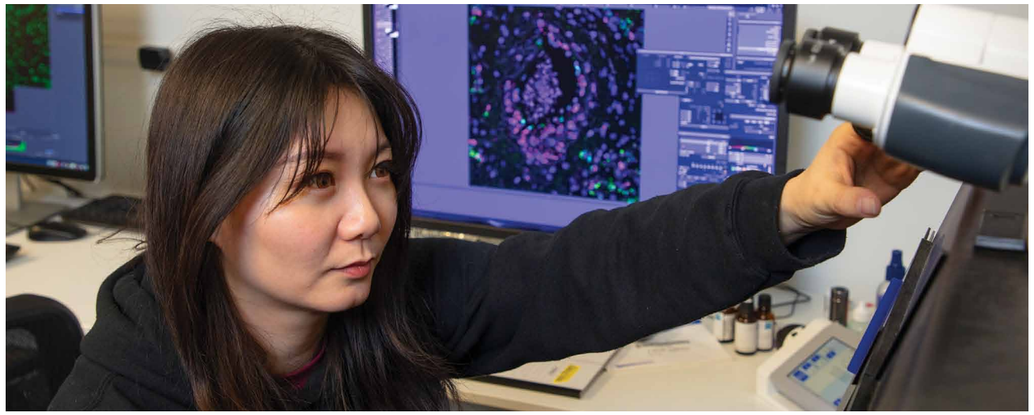
With your partnership, these young leaders are pursuing the root causes of allergies and asthma that will lead to treatments of the future.

Under the direction of Dr. Nadeau and other top researchers, our Center cultivates the next generation of scientists, researchers, and clinicians. A diverse pool of talent and the cross-pollination of specialties are essential to developing a robust multidisciplinary program.

By offering both mentorship and opportunities for independent work, our Center attracts the best and brightest scientists to its postdoctoral program. Postdoctoral researchers have access to sophisticated technology that allows them to look for the biomarkers of disease and develop new strategies to detect or treat asthma, allergies, and other immune-related illnesses.

College and high school students receive encouragement to pursue careers in allergy and asthma research by getting hands-on experience in diagnostic testing, bioinformatics, and basic science research. Some have grown up with allergies and asthma and are driven to make a difference for others struggling with these diseases. Some eventually return to our lab or clinic as staff.

The enriching experiences at our Center prepare these young scientists for the next step in their lives and careers, whether it's college, graduate or medical school, or a faculty position. Their passion represents our greatest hope for curing allergies and asthma.



Rising Stars

These six postdoctoral investigators joined our Center team from all over the world and stand poised to become leaders in the field of allergy and asthma research.

Abhinav Kaushik, PhD

Dr. Kaushik joined the Nadeau laboratory in July 2018. He received his PhD in bioinformatics from the International Centre for Genetic Engineering and Biotechnology in India in 2017. Before joining our Center, he worked as a visiting researcher in the Pathogen Genomics Laboratory at King Abdullah University of Science and Technology, Saudi Arabia. Dr. Kaushik's core area of research includes applications of systems biology and algorithm development for big-data analysis. He has developed and published a number of bioinformatics software and databases.

Dara Cohn, MD

Dr. Cohn is an allergy and immunology fellow at Rush University Medical Center in Chicago. She completed her pediatric residency in 2017 at the UPMC Children's Hospital of Pittsburgh. She is passionate about the challenges of managing food allergy and is excited to be working on the FAMILY study, which is identifying and addressing the barriers that low-income caregivers face while trying to manage their child's food allergy. The study is being done in collaboration with our Center. The process has involved talking directly to low-income families and devising a tool that will be helpful to them in daily life.

Xiaorui Han, PhD

Dr. Han received her doctorate in biotechnology from Peking University and joined the Nadeau laboratory in January 2018. She currently focuses on the underlying physiological processes of antigen-specific T cells and how they are involved with tolerance in allergic patients during immunotherapy. Dr. Han uses molecular biology techniques to study the effects of immune cells and their molecular signatures on tolerance in models of human allergy and immunological diseases.

Yu Wong, PhD, MD

Dr. Wong completed his MD at Weill Cornell Medical College and his clinical fellowship in allergy and immunology at Stanford University. His clinical interests include food allergies and human immunology. Dr. Wong has a long-standing research interest in the human immune system and is particularly interested in how the immune system avoids reacting to proteins found in foods. He believes a better understanding of these mechanisms may lead to improved ways to clinically manage food allergies.

Shifaa Alkotob, MD

Dr. Alkotob joined the Nadeau laboratory in September 2018 from the American University of Beirut in Lebanon. She screens patients for potential eligibility for current and future trials at our Center and is working on several studies with other team members. In one study, Dr. Alkotob is looking at the loss of water through the skin in peanut-allergic children who have eczema. She is also studying the effects of smoke from recent California wildfires on lung function and inflammation. In the future, Dr. Alkotob wants to pursue a specialty in pediatric allergy and immunology.

Bibek Paudel, PhD

Dr. Paudel is a postdoctoral research scholar at Stanford. He completed his PhD at the University of Zurich in Switzerland. His research focuses on applying machine learning and statistical methods to solve problems that are interdisciplinary in nature, including those from the biomedical, ecological, and socio-political sciences. He is keen on investigating the impact of environmental and lifestyle changes on human health, particularly asthma and other inflammatory conditions that now pose significant health challenges in both advanced and emerging economies.

Planting Seeds to Grow the Researchers of the Future

Our Center's internship program offers an opportunity for young scientists to discover, analyze, and apply what they learn in the classroom to the real world of allergies and asthma.

Cherie Liu
Senior
Henry M. Gunn High School
Palo Alto, CA

Because I've struggled with allergies and eczema since I was a little girl, I developed a strong interest in the internship at the Center. During my time in Dr. Nadeau's lab, I worked on a new diagnostic food allergy test, helped design a detection device, and analyzed data from an immunotherapy trial. The internship provided me an amazing opportunity to explore the immunology world and gain hands-on experience working in a professional lab.

Olivia Mendoza
Senior
Hillsdale High School
San Mateo, CA

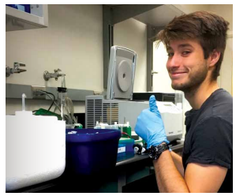
Working in Dr. Nadeau's lab was truly a life-changing experience. Mary Prunicki, MD, PhD, and Dr. Nadeau guided me through a project that investigated connections between exposure to air pollution and inflammatory response, and its possible impact on high blood pressure. I find it rewarding that our work could lead to medical advancements that would improve the health of children. I discovered my passion for conducting research through this opportunity, and I plan to pursue it in college.

Marcus Simmons
Doctor of Medicine
candidate 2021
Meharry Medical College
Nashville, TN

My research looked at which genes are suppressed during oral immunotherapy treatment for egg and milk allergy. Understanding how gene expression contributes to the underlying causes of allergy will lead to identifying a mechanism that can potentially reverse food allergy. I look forward to applying the knowledge and skill set I gained during my internship to directly serving children with health issues who do not receive equitable care.

Lucas Melo
Undergrad,
Biomedical Engineering
Columbia University
New York, NY

Under the mentorship of Gopal Krishna R. Dhondalay, PhD, I learned how to analyze data to compare gene expression in asthmatic and non-asthmatic patients. The internship taught me so much about the field of bioinformatics, and every day I felt like I was exploring a new, fascinating subject. I plan to pursue academic research and return to the lab this summer.

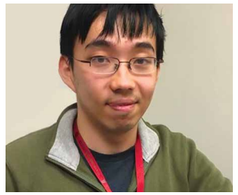


Eric Michael Smith
Junior, Biology
Stanford University
Palo Alto, CA

With my mentor, Swati Acharya, MS, PhD, and many other exceptional researchers, I embarked upon a project where we looked for biomarkers for allergies in plasma proteins using the new TOMAHAQ technique, which analyzes huge sets of data quickly and efficiently. Dr. Acharya had me draw from my prior undergraduate knowledge and inspired me to continue searching for answers to challenging questions. It was magical to see the lessons from my classes be applied to actual experiments. As I pursue a route in the field of medicine, I will always look back to this pivotal time.

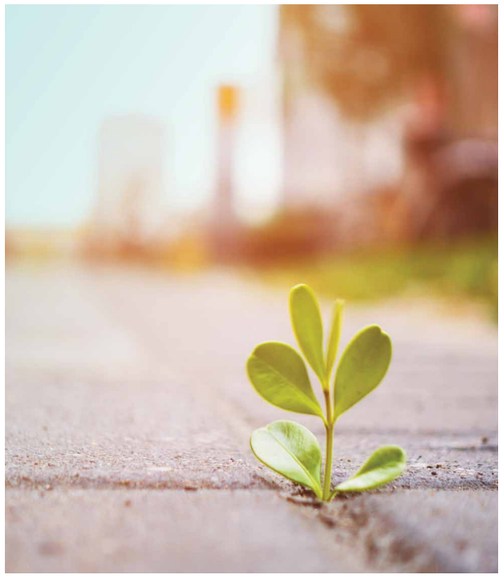
Alyssa Sweeney
Sophomore, Neuroscience
Baylor University
Waco, TX

Growing up with a brother who suffered from severe food allergies, my greatest challenge was keeping him safe. When my brother began oral immunotherapy, my fear slowly dissolved into relief. Having never forgotten the life-changing impact of immunotherapy, I decided to spend the last two summers researching in Dr. Nadeau's lab. Specifically, I identified unreported novel protein component allergens in tree nuts. Inspired by my experiences, I intend to pursue a Doctor of Medicine degree with a focus on immunological mechanisms in allergic diseases.



Zheng Yan
Junior, Computer Science
Stanford University
Palo Alto, CA

Dr. Nadeau's internship gave me the opportunity to develop an interest in bioinformatics through analyzing large data sets of cell types essential to the human immune system. Currently under peer review, my team's research looked at the influence of environmental and heritable factors on these cell types, which can be applied to predicting risk of immune disease or response of drug therapy. Now I have a better idea of the type of work I want to pursue in the future, and I am honored to continue working in the lab part time.



Global Vision

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Your support allows our Center to collaborate with partners worldwide to inform policy and develop ways to reduce harm from the environmental causes of allergies and asthma.

Air Pollution and Wildfires

In the summer of 2018, as wildfires raged across much of western North America and in Europe, our Center scientists were looking to answer two questions with implications for people with allergies and asthma around the world: Does smoke from wildfires increase the risk of these illnesses in people exposed to it, and is there a way to halt or at least reduce the harm from smoke inhalation?

"There is no safe distance away from a wildfire," Dr. Nadeau told participants in a multidisciplinary briefing in Sacramento, CA, organized by state lawmaker Bill Quirk. Our Center's research has shown that even in areas where smoke-related particulates aren't visible, they can still cause cancer, heart damage, immune dysfunction, and lung problems.

Mary Prunicki, MD, PhD, the *Barakett Endowed Faculty Scholar for Expanded Access*, is studying the effects of wildfire smoke and air pollution on children in underserved communities in California's Central Valley. She is looking for the best ways to protect the most vulnerable populations from the considerable threat these elements pose to developing circulatory and immune systems.

In a study of children and teens exposed to high levels of air pollution in Fresno, CA, Dr. Prunicki has found changes in the expression of genes involved in immune activity and inflammation. "We are currently trying to determine what level of exposure to wildfire smoke might result in similar immune changes," Dr. Prunicki said. In a more recent study of Fresno children and teens exposed to air pollution, she and her team have seen an increase in blood pressure levels as well as changes in two types of cells associated with heart failure. These findings suggest that exposure to poor-quality air could increase the risk for hypertension or heart disease in adults.

Researchers from our Center and others at the School of Medicine and the Stanford Woods Institute for the Environment have combined forces to find the most effective ways for people to protect themselves against air pollution, including wildfire smoke. Further studies will evaluate the effectiveness of respirator masks and home air filters for protecting children and adults from the harmful effects of wildfire smoke. These studies can help shape guidelines on the best ways to use these preventive measures and strengthen public health policy aimed at preventing wildfires and air pollution.

Dr. Nadeau, Dr. Chinthrajah, and others are speaking out about the need to address these issues. In November 2018, Dr. Chinthrajah told the *San Jose Mercury News*: "This is becoming something that we have to be more aware of and get the message out there to try to limit the exposure."

Speaking Out About Health and Climate Change

The evidence is clear: Climate change poses a threat to our future and our children's health. To address this looming issue and to look for solutions, Dr. Nadeau and our Center convened health experts from around the nation for a discussion at the Global Climate Action Summit in San Francisco in September 2018.

"Kids are the underserved and vulnerable population that is going to get hit by global climate change first," Dr. Nadeau said in her opening remarks. "We need to make sure we have their needs and their health as our centerpiece, and that we advocate for them."

Scientists from top universities around the country discussed research showing how fossil fuel emissions, malnutrition and hunger stress, water and soil contamination, and vector- and water-borne infectious diseases worsen or are predicted to worsen children's physical and mental health worldwide. They also offered hope, showing ways communities have reversed diseases related to climate change through activism that led to pollution reduction, changes in dietary and agricultural policies, and sanitation projects.

Panelist Yvonne (Bonnie) Maldonado, MD, division director of global child health and chief of pediatric infectious diseases at Stanford, noted that in 2016 fewer than 5 million children died worldwide—down from more than 12 million 25 years ago—thanks to a unified effort by the global community. "We've seen remarkable achievements in what we can do," she said, "if we have political and activist will to make changes."

National and International Action

Your generosity reaches children with allergies and asthma around the globe. These are some of the ways you are helping to transform awareness, prevention, and care for people with allergies and asthma everywhere.

- With donor support, our Center is collaborating with partners in San Francisco, Chicago, and New York to break down health barriers and create meaningful change for children with allergies and asthma in underserved areas. (You can read about this work in more detail in the Philanthropic Impact section of this update, page 22.)
- We continue to work with partners in England, Switzerland, India, Australia, and many other countries, as well as across the United States, on research collaborations to explore the molecular causes of allergies and asthma. Our researchers are looking at harmful cellular changes caused by detergents in South Africa, smoke from brick kilns in South Asia, and immunological differences in the cord blood of infants in the United States and India, among many other studies, to determine the role the environment plays in allergies and asthma.
- Dr. Nadeau spoke at TEDx Palo Alto on evidence-based food allergy prevention. She discussed the latest research showing how exposing babies to dirt, pets, and a variety of foods, and avoiding dry skin, seem to help protect against this disease.
- We work with global health agencies at the United Nations and the World Health Organization and have been designated a Center of Excellence by the World Allergy Organization, an international umbrella group of nearly 100 allergology and clinical immunology societies.
- We are collaborating with organizations across the United States to treat and educate patients and their families in underserved areas, train care providers who serve these patients, and advocate for children in poverty, who bear the brunt of environmentally caused diseases.
- We share our work with the scientific and patient communities through peer-reviewed studies in journals and talks at international conferences such as the Collegium Internationale Allergologicum symposium.

Center Academic and Research Accomplishments in 2018

Made Possible by Our Visionary Philanthropic Community

11 **new clinical trials with collaborators,** making us leaders in a community working toward the best possible treatments for allergies and asthma

11 **new high school, undergraduate, and graduate student internships and positions,** ensuring we have a pipeline of talented allergy and asthma scientists and care providers

3 **new programs for the underserved,** providing the best care for all children with allergies and asthma and their families

94 **percent of our funding** was raised from private philanthropy

3 **shared postdocs with other Stanford departments,** promoting collaborations across disciplines

7 **endowments at Stanford,** allowing us to attract and retain top experts in the field

34 **scientific papers,** sharing our expertise and breakthrough discoveries with the world

6 **new collaborations with research sites around the world,** sharing expertise in solving the puzzle of what causes allergies and asthma

32 **clinical studies,** exploring, developing, and improving treatments for people with allergies and asthma

3 **seed grants for interdisciplinary research,** supporting cutting-edge research and unprecedented discoveries

Funding Needs

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You are the oxygen that gives our Center life. Every stride we make in caring for people with allergies and asthma is thanks to you.

Your vision and generosity allow our Center to develop the most promising new research, talent, and treatments. Please consider helping make the next big discovery by supporting the following funds:

Basic Science Research: The Road to Curative Treatment

Omics Program

- Your support will bolster our focus on “omics”—the emerging field of identifying and analyzing pools of biological molecules involved in the immune responses resulting in allergies and asthma. With access to powerful technology that allows our scientists to conduct rapid analyses of thousands of samples, our Center is ready to launch several projects to pinpoint new targets for vaccines and therapeutics.

Endowment Opportunities: Luring 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. Your 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 allergy and asthma 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-ranked 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 (OIT) 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.

Worldwide Collaborations: Expanding Our Quest for Cures

The Swiss Institute of Allergy and Asthma Research (SIAF)

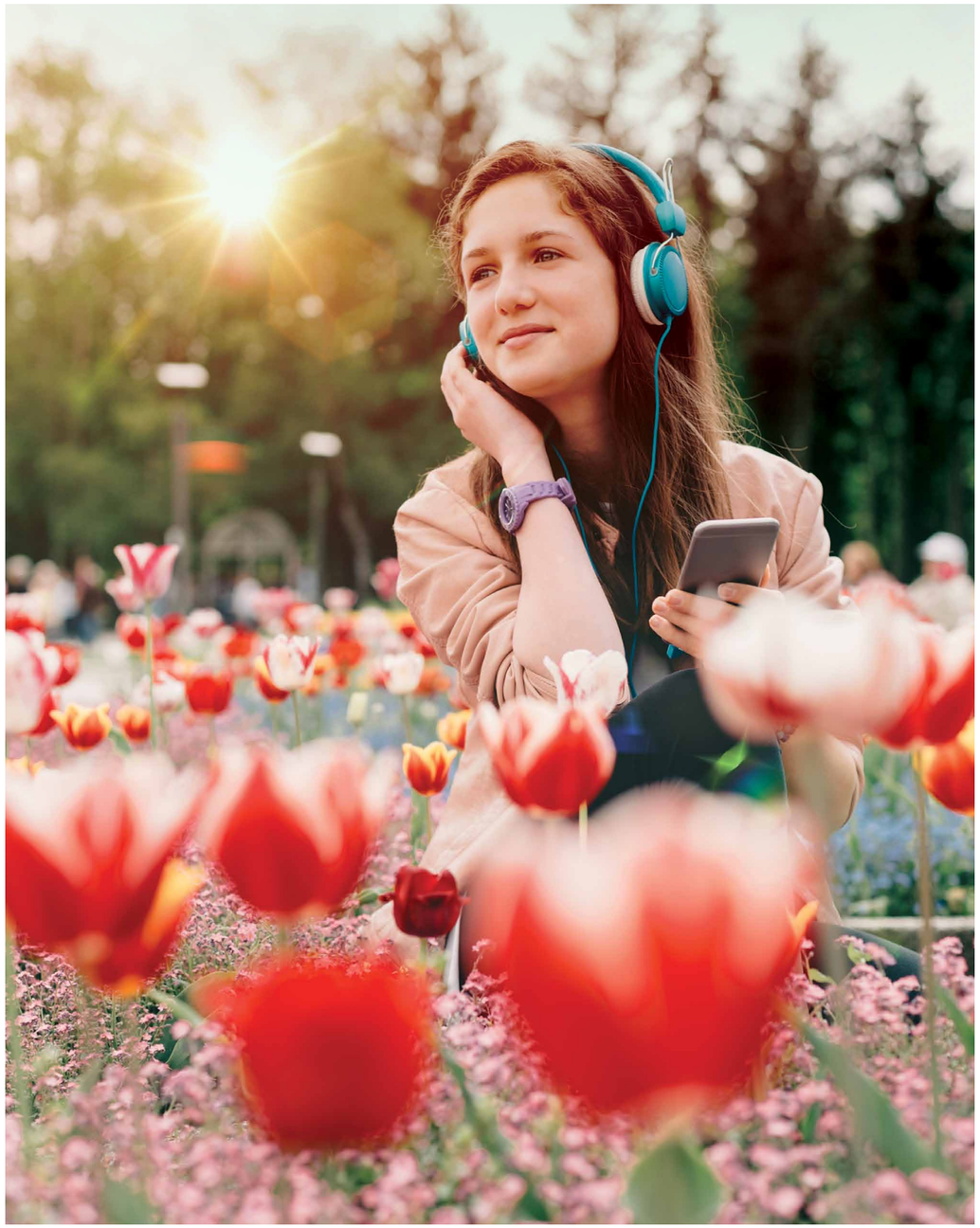
- Our Center, in collaboration with the Swiss Institute, is investigating exciting ways in which different allergic diseases carry overlapping immune signals. Your investment in this fund will allow Stanford and SIAF researchers to look for biomarkers in the circulatory systems of patients that might reveal these commonalities, pointing to new targets for treatment. It will also help recruit top new talent to join this project.

King's College London and National Jewish Health in Denver

- A worldwide clinical study involving Stanford, National Jewish Health in Denver, and King's College London focuses on how chronic allergic inflammation presents throughout the entire body, which could hold the key to how we treat and prevent allergic diseases—and possibly other autoimmune disorders. Your partnership would enable this international team to test their hypothesis that improvement in the skin barrier of infants can decrease their risk of food allergy.

Dupilumab Trial

- OIT has proven highly effective in reducing allergic sensitivities in patients. However, some patients develop gastrointestinal symptoms, which can cause them to stop treatment. Dupilumab, a medication already approved for treatment of eczema, has shown promise in treating asthma and gastrointestinal disease. With your support, this study—a unique collaboration between Stanford and Mayo Clinic Arizona—will evaluate dupilumab as a treatment for gastrointestinal symptoms in patients receiving OIT.



Because of You

We are able to bring the best science to help some of the world's most vulnerable people.

With Deepest Gratitude

We thank you on behalf of our Center team, our research partners, our patients and their families, and all who will benefit from our shared mission to cure allergies and asthma.

Your generosity gives people peace of mind to live full and healthy lives.

Thank you

We are dedicated to finding causes, treatments, and cures for allergic diseases, bringing greater peace of mind to children, adults, and families locally and globally.

For more information about our Center or how to participate in this important work, please contact:

Lindsey Hincks
Associate Director, Major Gifts
Lucile Packard Foundation for Children's Health
(650) 736-1021, Lindsey.Hincks@lpfch.org