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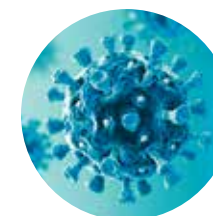
Stanford MEDICINE | Sean N. Parker Center
for Allergy & Asthma Research

2021

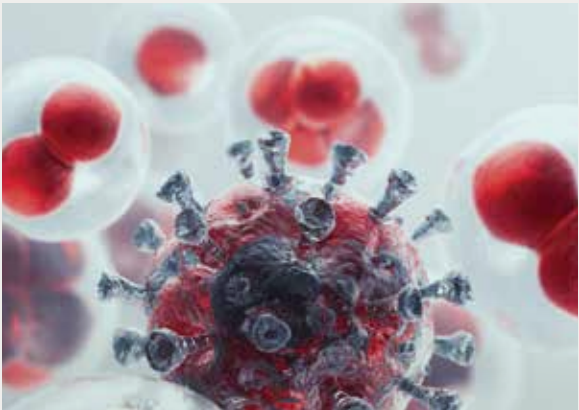
ALLERGY AND ASTHMA UPDATE

Transforming Lives with Innovative
Science and Compassionate Care

Responding to the Call



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My Heartfelt Thanks Go to You— Our Donors, Patients, and Friends

Because of your generosity, the Sean N. Parker Center for Allergy & Asthma Research has continued to expand and improve innovative science and compassionate care. You have our deepest gratitude for enabling us to further our mission during a challenging time. **We became first responders in 2020, answering the call sparked by three pandemics—allergies, COVID-19, and wildfires.** Positioned on the front lines, we took actions to address the long-running surge in food allergies globally and the public health and environmental changes in the world around us. Our Center pushed the leading edge in allergy science, using the most advanced tools and technologies to investigate the molecules, proteins, and genes underlying allergies and asthma.

During a tough year when COVID-19 transformed ordinary activities and human interactions, our Center marched ahead in clinical trials, patient care, and lab research. As you will read in this report:

- **We investigated how the SARS-CoV-2 virus affects the immune system**, revealing insights useful in studying immune antibodies, developing COVID-19 vaccines, and strengthening treatments for allergies and asthma. We launched a long-term study of immune changes in people who contracted COVID-19.
- **We advanced our goal to treat, prevent, and cure allergies and asthma.** These efforts included oral immunotherapy for multiple allergens with use of multiple biologic drugs as well as testing a DNA vaccine for peanut allergy and improving the skin in eczema patients to reduce the likelihood of food allergies later in life.
- As the threat of wildfires grew amid drought and climate change, **we revealed damaging molecular changes to the immune system linked to the inhalation of wildfire smoke.**

On all these fronts, we met the most current challenges to health and safety brought on by these pandemics.

You made all of our work possible. The vast majority of our funding comes from our donors, including many families affected by allergies and asthma. Because of your commitment, we elevated the best of science and the best of care for allergies and asthma and we reached new heights in investigating COVID-19 and wildfires. Thank you so much for providing inspiration and encouragement in 2020!

All the best,

Kari C Nadeau



Kari C. Nadeau, MD, PhD, FAAAAI
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Our Dream Team Takes on COVID-19

Early in the coronavirus pandemic, Kari Nadeau, MD, PhD, FAAAAI, started receiving fervent calls and emails from her patients asking: How would contracting COVID-19 affect their allergies or asthma? Would allergies or asthma make them more likely to become seriously ill if infected with the SARS-CoV-2 virus?

These inquiries sparked larger questions for the allergist and immunologist about the overall immune response to the virus and whether doctors could find ways to reduce the severity of the disease and hospitalization for those at greatest risk.

With critical seed funding from donors, Dr. Nadeau sprang into action, starting the Long-Term COVID-19 Immunity Study.

“I am grateful to our donors for initiating discussion central to this study as well as making it possible to launch,” says Dr. Nadeau. “We are looking at how COVID-19 symptoms match up with what is going on in the immune system.”

To do this, Dr. Nadeau has enlisted a dream team of scientists to conduct research into the immune response. Two of her top collaborators are Scott Boyd, MD, PhD, a Stanford associate professor of pathology and endowed faculty scholar in allergy and immunology at our Center, and Bali Pulendran, PhD, professor of microbiology and immunology at Stanford.



Dr. Boyd is looking at the acquired immune response, which involves how our bodies produce antibodies that can eliminate foreign invaders. Dr. Pulendran is delving into the innate immune system, which employs a complex of cellular reactions to form the inflammatory response as the first line of defense to pathogens.

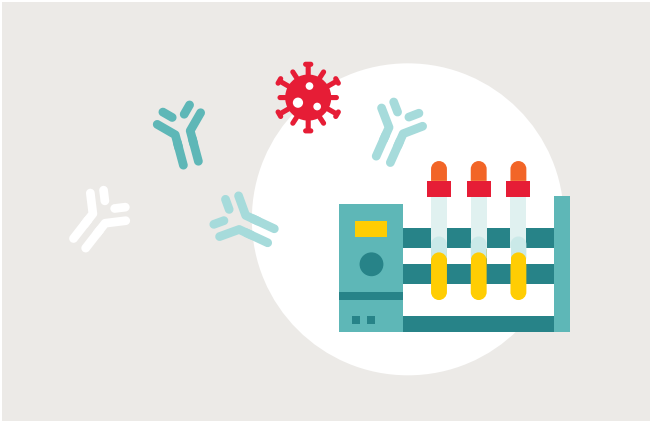
Their work has already uncovered a treasure trove of new information about the immunological capabilities of our bodies. Findings from them and from other researchers working on the coronavirus could help in treating allergies and asthma. As Dr. Nadeau points out,

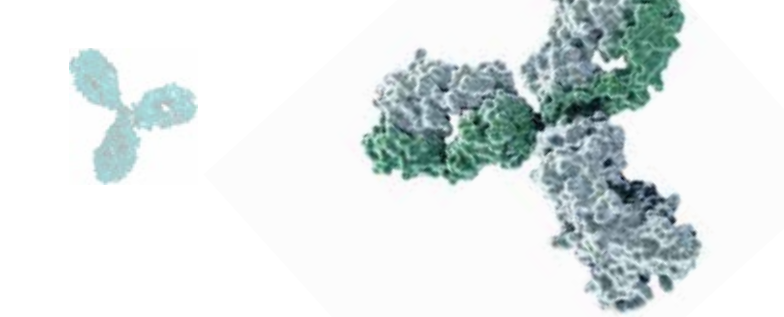
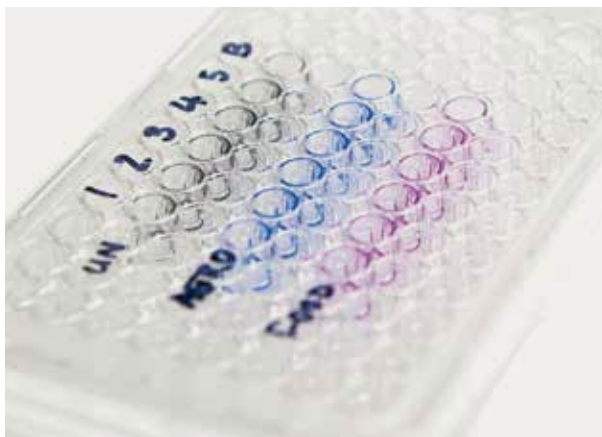
“What we learn about the human immune system will bring new insights for developing therapies for our allergy and asthma patients.”

As designer and principal investigator in the Long-Term COVID-19 Immunity Study, Dr. Nadeau began enrolling patients receiving treatment for COVID-19 at Stanford Hospital and Lucile Packard Children’s Hospital Stanford in April 2020. The study will track patients for up to four years. Thus far, nearly 800 participants have provided monthly blood and saliva samples and report any symptoms they are experiencing.

Early data show that women are more likely than men to report headaches, fatigue, loss of smell, and diarrhea. People with hypertension, diabetes, and immunocompromised conditions are at the greatest risk for hospitalization, and Hispanic participants made up 58 percent of all cases in the severe and critical COVID-19 categories.

Manisha Desai, PhD, director of the Quantitative Sciences Unit at Stanford and another frequent collaborator of Dr. Nadeau’s, will develop computational analysis of these symptoms to predict which interventions will work best for different patient populations.



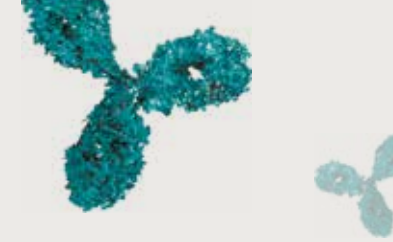


Investigating Weapons of Immunity

But scientists are probing well beyond patient symptoms to determine the mechanisms of immunity. Dr. Boyd has been looking at the type and quantity of protective antibodies produced in response to COVID-19 to see if he can identify differences in antibodies in those who developed severe versus mild disease. He observed that patients with more severe illness had higher levels of COVID-19 antibodies in their blood than those with mild symptoms, but that the antibodies in patients with mild illness were better able to target the vulnerable parts of the virus. **This observation suggests that replication of the virus was more effectively controlled in those with mild disease, so their antibody levels did not rise as much as in those with serious COVID-19.**

Collaborating with Benjamin Pinsky, MD, PhD, medical director of the clinical virology lab at Stanford, Dr. Boyd is measuring how much viral RNA can be detected in the blood of patients and has noted a correlation between higher antibody levels and greater viral load. Their investigation should yield valuable information that can better predict the severity of COVID-19 and make earlier interventions possible. Dr. Boyd's lab is also analyzing the degree to which antibodies generated against one variant of the virus during infection or vaccination can protect against new viral variants that have arisen across the world. This knowledge will be critical for planning strategies to prevent new waves of infection from variant viruses, such as the more contagious Delta variant that emerged in 2021.

Antibodies aren't the only weapon in our immune system repertoire. Dr. Pulendran specializes in how the innate immune system can be harnessed to develop vaccines. **Using the most advanced tools available to capture information about these immune cells from all angles, Dr. Pulendran has made novel observations that have already translated into life-saving therapies for the sickest COVID-19 patients.** (See sidebar on page 6.) His research provided some of the earliest insights into why some people develop serious clinical symptoms when infected with SARS-CoV-2 and was published in the leading journal *Science* in September 2020.



Assessing Allergy and Asthma Risks

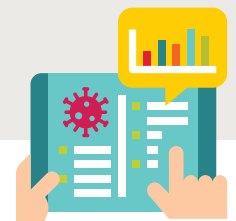
But what about people with allergies and asthma? Are they at greater risk?

Early evidence suggests some good news. Working with collaborators at the Philips University of Marburg in Germany, Dr. Nadeau examined the interplay of the virus and common allergens. The researchers learned that some patients with allergies to airborne peanut particles could already have protection, because protein sequences on the surfaces of the virus and airborne allergens are similar enough that patients might already have memory T cells geared up to battle the SARS-CoV-2 virus.

Sharon Chinthrajah, MD, director of our Center's clinical translational research unit, is looking at the intersection of COVID-19 and asthma. Studies have shown that not all asthma patients become severely ill from SARS-CoV-2. The reasons might depend on whether a patient's asthma is caused by allergy or another factor. The medication that asthma patients take could also play a role in protecting patients from severe COVID-19 disease. Dr. Chinthrajah has been analyzing data from almost 170,000 COVID-19 tests taken at Stanford and focusing on asthma patients to determine what may or may not put them at greater risk

for being hospitalized or having severe COVID-19. The team is also exploring how "long COVID," where symptoms linger months after contracting the virus, may affect asthma patients.

With generous investment from the Parker Foundation, Dr. Nadeau's lab has investigated risks of allergic reaction to the vaccine. Based on one week of data in December from everyone who received the Pfizer vaccine in the U.S., very few people have an allergic reaction or go into anaphylactic shock. These reactions usually occur quickly, before patients leave the vaccination site.



STANFORD GETS ON BOARD WITH COVID-19 DRUG TRIALS

While the world watched the pandemic spread, Stanford joined the global effort to release life-saving COVID-19 drugs. In March 2020, the National Institute of Allergy and Infectious Diseases (NIAID) selected Stanford as one of approximately 100 sites to participate in the Adaptive COVID-19 Treatment Trial (ACTT). The purpose was to test drugs that could stem the destruction caused by SARS-CoV-2.

When NIAID tapped Dr. Nadeau to lead the trials at Stanford, she immediately connected with hospital medicine staff to begin testing remdesivir, an antiviral drug, for hospitalized COVID-19 patients. As co-principal investigators, Dr. Nadeau and Neera Ahuja, MD, division chief of hospital medicine at Stanford University School of Medicine, led a team of 20 physicians and specialists to run trials treating patients.

"We were part of the seminal paper published in the *New England Journal of Medicine* that led to the emergency authorization of remdesivir for use in COVID-19 patients by the Food and Drug Administration," says Dr. Nadeau.

Trials showed that infusions of remdesivir reduced length of hospital stays, especially when administered early. ACTT sites then moved on to test remdesivir in combination with baricitinib, an anti-inflammatory medication. Results were even more promising, helping COVID-19 patients recover even faster. The ACTT sites continue to test other drugs selected by NIAID.



HOW CURIOSITY DRIVES CARE FOR COVID-19

In a happy accident of scientific research, Bali Pulendran, PhD, made a novel discovery in his Stanford lab that inspired a life-saving treatment for COVID-19 patients.

Science, a leading peer-reviewed journal, published Dr. Pulendran's research in September 2020, documenting something new arising in the immune system of COVID-19 patients.

Looking at blood from COVID-19 patients, Dr. Pulendran's lab detected higher levels of three inflammatory mediators, including a molecule known as LIGHT, in patients with severe clinical symptoms. LIGHT was so strongly associated with disease severity that Dr. Pulendran and his team concluded in the paper that LIGHT and the other mediators could "represent attractive therapeutic targets against COVID-19."

What happened next was a speedy translation of benchside science to bedside care. Shortly after publishing his findings, Dr. Pulendran received a call from the chief scientific officer at the pharmaceutical firm Cerecor, who had read the *Science* article.

Fortuitously, Cerecor had already developed an antibody to block LIGHT, for use in Crohn's disease. Cerecor quickly launched a clinical trial of the drug, treating 82 patients with acute respiratory distress syndrome (ARDS) from COVID-19, and showed a single dose resulted in a jump in the proportion of patients alive and free of ARDS.

"It was tremendously gratifying to learn that patients at death's door survived, thanks in part to our discovery and Cerecor's drug," remarks Dr. Pulendran.



Putting COVID-19 Vaccines to the Test

The greatest question at the heart of all this work is about when we can return to our regular pre-pandemic lives. **Scientists will first need to determine how long the protection brought on by vaccines will last.** Indeed, Drs. Nadeau, Pulendran, and Boyd are working closely on this effort.

Using samples from people who received the Pfizer vaccine, Dr. Boyd began examining how it helps people form immune system memory cells that will protect them if they get exposed again. A vaccine should boost antibody levels higher than our own natural immune response. Even after antibody levels drop off, the cells that produced them are still in the body, and they can be reignited to meet the enemy again.

Dr. Pulendran used a biological systems approach, which involves using multiple cell-probing tools and computational analysis, to get a full picture of the response—from genes to proteins—that is being induced by vaccines. He worked with a Stanford computational lab run by Purvesh Khatri, PhD, to crunch the data into a prediction model for long-term immunity.

In collaboration with Washington University, Dr. Pulendran has applied his expertise in adjuvants, or potency enhancers, toward development of a new vaccine for SARS-CoV-2 infection. Initial tests in primates have been very promising and clinical

trials of the vaccine, which bears some similarity to the vaccines we use for tetanus and shingles, are already underway in South Korea. If approved, a pharmaceutical company has committed to manufacturing one billion doses specifically for the many developing nations in dire need of COVID-19 vaccines. At the same time, Dr. Pulendran is working with another pharmaceutical company on modifications to the mRNA vaccines from Pfizer and Moderna that will protect against new variants of the virus.

With many more questions still to be answered, these leading scientists won't give up until the global pandemic is beaten and long-term solutions are created. But the most inspiring player is not in the lab or clinic. "I am eternally grateful to the donors," adds Dr. Pulendran. "If we had to write grants for this work, we would not be where we are right now. Donors can move mountains—and make an unbelievable impact on human health." 🙏

Thank You

We investigated the impact of the SARS-CoV-2 virus on the human immune system through generous gifts from **Sean N. Parker**, an **anonymous donor**, the **Bunning family**, and **Jacquelyn Soffer**.



Thank you!

Your commitment helps children
enjoy healthy and active lives.



ALLERGY TREATMENTS

Oral immunotherapy (OIT) has become an important tool to protect people from allergens, but the long, sometimes uncomfortable process of building up tolerance through OIT can cause some patients to quit treatment. **Today, our Center is poised to dramatically improve OIT, boosting its chance of success by speeding up treatment and lessening its side effects.**

The COMBINE trial is the first OIT to use two biologic drugs in a patient. It is testing omalizumab to reduce the antibodies that cause allergic reactions and dupilumab to inhibit certain cell signaling that occurs



JACOB DREAMS OF
NON-ALLERGIC TREATS

A peanut butter sandwich and a slice of cake.

That’s what 14-year-old Jacob Sam would like to be able to eat as a result of participating in the COMBINE trial. He is allergic to peanuts, eggs, and chickpeas, making him an ideal candidate for this multi-allergen immunotherapy trial.

For Jacob’s mom, success would be developing a tolerance that would keep Jacob safer in the years ahead. Jacob’s two older brothers have allergies, and one had a harrowing experience in the emergency room when he was away at school. **“This trial provides relief for me when Jacob goes to college. It definitely has been life-changing,”** explains Sharon Sam.

Because of his siblings’ allergies, Jacob’s parents tested him early—at age 4—for allergies. He carries an epinephrine auto-injector in case of inadvertent exposure to contaminants.

Jacob was a little nervous at the start of COMBINE, especially about having an allergic reaction to peanuts. But he became more comfortable with eating the allergen powder every day and has become more confident as his tolerance increases. **“As it went on, I became more okay with it. I don’t know how to explain it, but the trial has been fun,”** says Jacob.

At the outset, Jacob could tolerate just 3 milligrams of peanut. Now he is up to 1,000 milligrams (about three to four peanuts). For eggs, he started at 30 milligrams and now can consume 1,000 milligrams (about a quarter teaspoon). Not yet enough for that sandwich and cake, but Jacob is well on his way.

Increasing the Winds Behind Immunotherapy



in allergic responses. It builds on the success of previous OIT, in which patients eat tiny but growing doses of an allergen to build tolerance. COMBINE aims to desensitize participants to peanuts, along with one or two other allergens. This is vitally important as approximately 40 percent of the 6 million U.S. children with food allergies have reactions to more than one food.

COMBINE shows how far allergy immunotherapy has come, even though it is a newer area of research compared to other fields, like cancer therapy. “How amazing it is to be where cancer is, where you’re giving combination treatments to cure disease. That’s pretty cool,” notes Kari Nadeau, MD, PhD.

Our Center was a global leader in establishing the effectiveness of oral immunotherapy for a single allergen. Then we added the drug omalizumab to speed up desensitization from the years it can take with OIT alone. We were the first to successfully

use OIT for multiple allergens. Now, COMBINE seeks to desensitize patients to two or three allergens at once, helped by two drugs already approved for use with asthma (omalizumab) and eczema (dupilumab).

The trial is enrolling 110 participants, ages 5 to 55, at Stanford, the University of California, Los Angeles, and the University of California, San Diego. For the first eight weeks, participants receive shots of omalizumab, which suppresses the immunoglobulin E (IgE) antibody that is the most responsible for allergic responses. Then, they undergo oral immunotherapy over six months, eating an allergen powder every day. Half of the participants are also receiving dupilumab to reduce gastrointestinal distress, a common challenge of OIT that can make kids quit the therapy. Dupilumab inhibits signaling of interleukin-4 and interleukin-13, molecules that create inflammation in allergic responses. At the end of six months, participants undergo an oral food challenge to test tolerance, then stop therapy for two months before undertaking another food challenge to see if desensitization has been sustained.

With protection from multiple allergens, kids with allergies can feel freer to eat at a bakery or restaurant. **“Building the confidence of the kids in this trial is the best part for me. They have been so afraid,”** shares MacKenzie Cox, clinical research coordinator. ●

Thank You

We treated allergy patients with leading-edge therapies, including the COMBINE multi-allergen, multi-drug trial. COMBINE is funded by the **Amouyal, Bing, Bunning, Cowan, and Franey-Coopman families**, as well as **The Safe + Fair Food Company** and **Food Allergy Research & Education (FARE)**, which matched donor gifts to COMBINE. The **Chang family**, the **Levin Family Foundation**, and **Kori Shaw** supported our collaboration with the Mayo Clinic on milk oral immunotherapy.



KELLY REACHES MUCH SAFER GROUND

As an infant, Kelly was tested and found to be allergic to peanuts. She sailed through much of childhood, avoiding peanuts, going to a nut-free nursery school, and having her parents bring their own food to social gatherings. Yet her parents wanted Kelly to do more than avoid eating peanuts; they wanted her to be protected from any minute accidental exposure.

At age 8, Kelly entered an oral immunotherapy trial at our Center. For more than a year, she ate tiny doses of peanut powder, with the quantity increased every two weeks. Eventually, Kelly built up a tolerance. She continued her immunotherapy by eating one real peanut every day to maintain her protection.



At times, immunotherapy was a challenge for Kelly.

She did not enjoy the chocolate pudding to which the peanut was added. Periodic food challenges, which tested how much of the allergen she could safely eat, were especially tough because they involved a blood draw and skin prick. Kelly has needle-phobia, says her mom, Kristina.

Kelly, now 10, recalls that the immunotherapy was difficult. “I had to get a shot every time, or almost every time. I don’t really like pudding.” But, she adds, “I feel a little safer [after immunotherapy].”

Her mom recommends immunotherapy as the best way to ensure safety from allergy hazards.

Shown left: Tina Sindher, MD, Kelly, and Melanie Shojinaga, clinical research coordinator associate.

“Kelly still has the allergy, but we know we can do something about it. We can increase her tolerance toward peanuts, and she can have a normal life,” says her mother, Kristina.



FAMILY GETS PEACE OF MIND FOR ALEXA AND NIKHIL

Two of the three Moorti children, Alexa, 11, and Nikhil, 9, are each allergic to multiple types of nuts and have received different treatments at different times.

When Alexa was 1½ years old, her mom gave her a peanut bar. Within two hours, Alexa was vomiting violently. The family soon discovered that she was allergic not only to peanuts but also to hazelnuts, cashews, walnuts, and pecans. They avoided these allergens and carried an epinephrine pen.

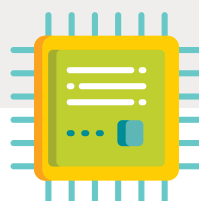
At age 4, Alexa entered an oral immunotherapy trial at our Center for her multiple allergies. Aided by injections of omalizumab—an immunoglobulin E (IgE) blocker that is anti-inflammatory—she progressed quickly through the trial. After several months, she could safely tolerate up to 2 grams of each allergen.

Nikhil was also allergic to peanuts, walnuts, cashews, and pecans, but he was too young for an oral immunotherapy trial. Instead, he joined a skin patch trial for peanut allergy at age 5, wearing an adhesive patch on his back over the course of three years to be desensitized. He is now eating small but increasing amounts of the other allergens to build up his tolerance.

Both kids are continuing their maintenance doses every day. Alexa consumes eight peanuts, 10 hazelnuts, six walnut halves, and seven cashews daily. Nikhil eats eight peanuts.

The family now has peace of mind about any accidental consumption. In fact, their dad, Tushar, recently boiled a pot of peanuts. Nikhil had 20 of them. Alexa, the girl who once violently reacted to a peanut bar, ate 50 peanuts that day!

New Tools Help Replace Food Challenges



Ten-year-old Kelly is grateful for the peace of mind she gets from oral immunotherapy (OIT) for a peanut allergy. But she spent more than a year building up tolerance, which was not easy. Periodic food challenges, which test how much peanut she can safely eat, involved extensive blood draws and scary needles.

OIT has helped hundreds of children like Kelly, but negative experiences with the therapy are also common. Children and teens do not relish eating long-term maintenance doses of a food they spent years avoiding. Food challenges—the gold standard for identifying an allergy—are extremely stressful, not only because of the blood draws but also because they could trigger an anaphylactic reaction.

Many of the things that make OIT uncomfortable or stressful are avoidable. For example, Kari Nadeau, MD, PhD, notes:

“Science shows already that half of food challenges aren’t necessary. In two or three years, we can have a composite biomarker to predict food challenge outcomes and no longer will need food challenges.”

Our Center’s researchers are working to improve both diagnosing allergies and predicting responsiveness to treatment. Using sophisticated genetic sequencing and computational tools, they are looking for molecular changes in the immune system linked to food allergies and OIT. **These changes, or biomarkers, found in a single drop of blood, can indicate when someone has or does not have a serious food allergy—without undergoing a food challenge.**

After analyzing many blood samples, researchers can create a composite biomarker of chemical reactions that lead to anaphylaxis. This biomarker should also be able to predict who will do well on OIT, who might be able to go off a maintenance dose, and who would have the greatest success with OIT in combination with other drugs.

Stanford’s Stephen Galli, MD, has already developed a highly accurate test for food allergies that measures certain molecules on the surface of basophils, white blood cells involved in inflammation. Bioengineer Sindy Tang, PhD, and her Stanford team have miniaturized this process, fitting it onto a microchip that tests chemical reactions in a drop of blood stimulated with a suspected allergen. They are building a device that could eventually test for many different food allergies simultaneously. Once complete, perhaps within a year or two, the test might be used in a doctor’s office, a pharmacy, or even a patient’s home.

Sharon Chinthrajah, MD, our Center’s clinical translational research director, has already shown that measuring basophil activation and certain antibodies can predict how well and for how long OIT will work for people with peanut allergies. Center researchers are now gathering many more samples from patients with multiple food allergies and analyzing changes over time in a variety of immune cells. Eventually, they will use data collected from thousands of patients worldwide to create an algorithm for a prognostic device that can run many molecular tests at once and produce an accurate assessment of OIT response, including risk of serious side effects for each patient.

Researchers believe these emerging tools will eventually provide safer, more personalized options for people with allergies. **“We want to help people to manage their allergies with a variety of tailored treatments,” says Dr. Chinthrajah, “rather than just telling someone to avoid a certain food.”** ●

Thank You

We are delving into molecular biology that will improve diagnosis and prognosis of allergy and asthma, funded by an **anonymous donor** as well as the **Kepner** and **Orsak families**.



THOMAS GAINS FREEDOM IN EATING

At age 2, Thomas put his mouth on the lid of a jar that contained mixed nuts. He broke out in hives. He was tested and found to be allergic to peanuts, tree nuts, eggs, shellfish, and milk. It flipped the family’s life upside down. “I felt very hopeless and not empowered,” recalls his mother, Felicia.

Through much of childhood, Thomas carefully avoided all his allergens. When he went to a friend’s house, he had to bring his own food, or his mom had to learn what might be eaten there. Birthday gatherings and school parties required her to prepare allergy-free treats.

Finally, at age 10, **Thomas was admitted into a clinical trial of an adhesive patch that exposes immune cells in the skin to small doses of peanut protein.** In the trial at our Center, he wore a patch on his back for three years, swapping it out daily for a fresh patch. Eventually, he was desensitized enough so that he could eat five peanuts safely until he had an allergic reaction. Since finishing the patch trial, Thomas has maintained his tolerance by eating a peanut every day.

Before the trial, Thomas sometimes would develop hives and his throat would swell upon just being around peanut dust. But now, “I have more freedom to try more foods,” says the 15-year-old. He is also eating small but increasing amounts of egg to build up his tolerance to that food.

“Food is a huge part of our lives. I didn’t want him to be limited by what he could not eat,” explains Felicia.



Ushering in a New Era

“It’s really the beginning of the end of allergies,” says Dr. Kari Nadeau. “We are at an inflection point. We now have information on how to prevent and to try to cure food allergies.”



For decades, children with food allergies have painstakingly avoided the slightest crumb of foods that might trigger a deadly reaction. Nonetheless, allergy prevalence rose to astronomical heights, with one in 13 children in the U.S. now suffering reactions to wheat, nuts, milk, eggs, and other foods.

Our Center is ushering in a new era, with revolutionary treatments and approaches that could prevent allergies altogether. **One focus is on proactively moisturizing the skin of babies to break the connection between eczema and food allergies later in life.** Another target is creating vaccines to block allergies from even developing.

To many allergists, breaking the link between eczema and food allergies represents a major step forward. Our Center is testing a novel approach that begins very early in life. It is based on the finding that babies with the red, itchy skin condition known as eczema are more prone to developing food allergies, as well as hay fever and asthma, later in childhood. This progression is known as the allergic or atopic march.

Eczema leaves the skin vulnerable to allergens, allowing particles of food proteins carried by dust through the air to enter the body through skin. That triggers an abnormal immune response that makes the child more sensitive, or allergic, to the food later.

Researchers aim to intervene by using a cream that moisturizes the skin and forms a natural barrier. It contains ceramide, cholesterol, and fatty acids—three lipids that mirror the normal fat content in skin. In a trial funded by the National Institutes of Health (NIH), they will track 875 infants who have developed eczema by 10 weeks of age. One group will receive twice-daily trilipid cream plus steroidal cream when needed. Another set will get twice-daily petroleum-based moisturizer plus steroidal cream when needed. And a third group will receive standard care with steroidal cream for flare-ups.



“Once a food allergy has developed, you’re stuck with it for life. With this study, if we find out we can break the cycle from skin to food allergies, hopefully it will turn back this upward trend,” says Tina Sindher, MD, a clinical associate professor of allergy and immunology and the principal investigator at Stanford.

Besides skin moisturizing, **we are moving ahead on food allergy vaccines to create long-term tolerance.** Our Center is testing a vaccine with peptides (short chains of amino acids) that injects patients with DNA producing three peanut proteins. Administered in four doses, the vaccine is designed to desensitize an individual to peanuts without having to eat them. In an industry-sponsored trial, we have begun using this peptide vaccine among peanut-allergic adolescents for the first time.

We also are doing lab work on wheat epitopes, parts of the allergen that are involved in chemical reactions leading to allergic response. Epitopes will be critical in developing a wheat vaccine. ●

Thank You

Our research into allergy preventions, such as vaccines and skin treatments, benefited from partnerships with an **anonymous donor** and the **Barakett, Friend, Hartman, Hill, and Lubetzky families.**



VARIED DIET OFFERS AN OUNCE OF PREVENTION

A simple strategy is giving parents an important tool to help their kids avoid food allergies.

“If you can diversify the diet early and often in children, you can decrease the risk,” says Kari Nadeau, MD, PhD.

The approach, based on new research, represents a radical departure from 20 years ago, when the American Academy of Pediatrics encouraged parents to delay introduction of milk, peanuts, shrimp, and other foods to their babies. Instead, studies by Dr. Nadeau and other scientists have found that children who eat very small amounts of potential allergens at an early age are less likely to develop an allergic response later in life.

“Parents should know that the knowledge is in their hands to do something now, rather than just passively wait for their child to develop allergies,” adds Dr. Nadeau.

She advises parents to offer their babies very small amounts of potential allergens, such as nuts, soy, milk, wheat, and eggs, every day starting at around four to six months of age. Some companies even sell mix-in powders that can be combined with solid foods for easier introduction.





COMMUNITY

Connecting with Our Community

Thanks to generous donors, our Center communicated broadly about allergies and asthma and helped underserved communities in 2020—despite the obstacles presented by the COVID-19 pandemic.

Patient Referrals

Our Center is now linked with Lucile Packard Children's Hospital Stanford and Stanford Hospital in new ways. With donor funding, we are setting up a method to automatically refer any patients to our Center who were seen for anaphylaxis, or severe allergic reaction, at the emergency departments of the hospitals. We will then reach out to the patient's family with information on our services and trials. After developing an algorithm that uses billing codes for anaphylaxis, our Center is set to receive notification through a Stanford database that tracks clinical data for research purposes. We hired a Stanford emergency physician, Youyou Duanmu, MD, MPH, part time to serve as a first point of contact and to secure the family's contact information. We have started receiving referrals and expect this to be a fruitful way to expand our patient base.

Toxic Stress and Asthma

We continued working with the Center for Youth Wellness, a San Francisco nonprofit, to raise awareness about the link between toxic stress and asthma, especially for people from underserved communities who are exposed to higher levels of stress, such as physical or emotional abuse. Our Center's Tina Sindher, MD, helped establish the National Committee on Asthma and Toxic Stress (NCATS), which in 2020 held an educational webinar that attracted 268 primary care physicians, mental health workers, educators, and families.

The committee aims to approve guidelines in 2021 that clinicians consider toxic stress when treating and preventing asthma. Once approved, NCATS hopes to launch a pilot program to test and evaluate the guidelines in clinical settings.

A Passport for Allergy Families

Lower-income families are more likely to need urgent care and extra support for their children with allergies. Working with patients on public insurance in Chicago, a group of physicians and researchers running the FAMILY Study created a colorful toolkit called a "passport" to help caregivers navigate the needs of children with allergies—from managing symptoms to advocating in school.

Because of COVID-19, the FAMILY Study group was not able to test the toolkit in person but conducted telehealth check-ins to fill out the passport with allergy families and followed up with them to find out how much the toolkit helped. The group is developing an app of the toolkit for caregivers to load onto their phones. Our Center sponsored the FAMILY Study and provided expert advice on allergy care.

Reaching Homeless Families from a Distance

In partnership with Dare2B in New York, our Center has led workshops the last few years to help homeless families manage their children's allergies and asthma. With in-person sessions no longer safe due to the coronavirus, Dare2B connected with Katharine Fast, MD, a faculty member at our Center, to launch a virtual program in 2021. ☀

Thank You

Gifts from the **Barakett, Canfield, Friedheim, and Giorgi families** enabled us to reach underserved communities with help on allergies and asthma. Through its funding of Dr. Nadeau, the **Lainovic family** is generously supporting patient

referrals to our Center from the emergency departments of Packard Children's and Stanford Hospital.

The **Hill family** funded our data science team that supports clinical trials. The team is led by Manisha Desai, PhD, the **Kim and Ping Li Director of Computational Biology at Stanford University**.

Donors endowed key researchers and clinicians. The **Carell family** funded Sharon Chinthrajah, MD. **Jacquelyn Soffer** supported Bali Pulendran, PhD. An **anonymous donor** funded Scott Boyd, MD, PhD. The **Gies Foundation** supported Tina Sindher, MD. **Sean Parker** funded Maya Kasowski, MD, PhD.



Smoke Exposure's Hidden Harm to Children's Health

It has become an all too familiar scene—wildfires burning across much of North America, darkening the skies with plumes of toxic smoke that fills people's lungs. Although the smoke eventually dissipates, there is increasing evidence that its damage to human health remains.

The problem is expected to get worse as hotter summers, drought, and climate change contribute to a wildfire season in the West that in recent years has extended to become almost year-round.

The threat is particularly great for those who breathe the smoke for weeks or months or who have chronic exposure to smoky or

polluted air. These populations include children living in dusty, polluted communities whose parents cannot afford air purifiers or travel to get away from the smoke.

Yearly, about 7.4 million children and teens are exposed to wildfire smoke across the United States.

There are more than 400 toxins associated with wildfire smoke.

Our Center gathers evidence to show how wildfires affect children's health at the molecular level as well as to help guide policy decisions, such as whether controlled burns aimed at fire prevention are less toxic than actual wildfires or whether air purifiers can reduce or prevent damage from smoke inhalation.

"Ultimately our goal is to change policy," explains Mary Prunicki, MD, PhD, director of air pollution and health research at our Center. (For information about Dr. Prunicki's research on wildfires and climate change, visit our website at climatehealth.stanford.edu.)

Dr. Prunicki and her team are finding that wildfire smoke not only exacerbates allergies and asthma but also changes the immune system—perhaps permanently—at the molecular level. Dr. Prunicki and other researchers are discovering increasing connections between smoke exposure and other kinds of disease.

About 80 percent of wildfire smoke consists of particulate matter called PM 2.5, particles about one-thirtieth the width of a human hair. When inhaled, these particles are small enough to get into the bloodstream and cause damage. Using sophisticated imaging and cell sorting tools, Dr. Prunicki and her team are examining changes in saliva, blood, and other samples collected from those exposed to fires, searching for markers that indicate immune dysfunction.



In previous work involving teenagers and children exposed to high levels of air pollution in Fresno, California, Dr. Prunicki documented changes in immune activity and inflammation as well as increases in blood pressure and cellular changes associated with heart failure.

Her more recent investigations of wildfire smoke exposure among Fresno teens are finding similar changes in a gene involved in the development and function of T cells—white blood cells that are an important part of the immune system. This alteration can make the gene less capable of producing T regulatory cells, which modulate immune responses. Smoke-exposed children also have significantly fewer Th1 cells, which are helper cells that promote immune response, compared with unexposed kids. **All these immune changes put children at greater risk of developing allergies, infections, and possibly other illness as well.**

Computational studies of large data sets also show a strong connection between wildfire exposure and a variety of illnesses. Data scientist Bibek Paudel, PhD, has analyzed 240 different diseases for which patients nationwide were hospitalized, comparing their health data with air quality readings in the areas where they lived.

Among the top 20 diseases linked to communities with high smoke exposure, he and other researchers found increased risks for asthma and respiratory distress, which they expected. But they also found increased risk for liver disease, dementia, mood disorders, and pregnancy complications. In the same way that counties and hospitals have used predictive tools to forecast whether they have enough beds for COVID-19 patients, Dr. Paudel is using these data to build an algorithm that can predict an increase in hospitalizations due to wildfire smoke. This tool could help hospitals determine whether they have enough beds during a fire season. ●

Thank You

Our research into wildfires and the environment benefited from donors who supported Mary Prunicki, MD, PhD, the **Barakett Endowed Faculty Scholar of Expanded Access**, and Bibek Paudel, PhD, the **Bravo Family Endowed Faculty Scholar for Food Allergy and Immunology Research**.





Dr. Mary Prunicki holds a mail-in kit that collects information on firefighters throughout California.



New Research Focuses on Firefighters

Whether battling a raging blaze on a mountainside or entering a burning apartment building, firefighters are hailed as heroes who risk their lives to save people, homes, and wilderness. But scant attention has been paid to how constant exposure to smoke and to equipment containing chemicals and heavy metals affects their long-term health.

Despite having higher rates of allergies, asthma, and respiratory disease than the general population and higher death rates from heart disease and cancer, firefighters have been notably understudied by researchers, says Mary Prunicki, MD, PhD.

She and her team, led by life science researcher Eric Smith, are seeking to change this. **Using surveys and mail-in kits, they are collecting information and samples such as blood and hair from retired and active firefighters throughout California.** They plan to analyze the samples and identify biomarkers of disease in retired firefighters, who have had chronic smoke exposure, and younger firefighters, who have acute exposure every time they go to a fire. Using these immunological

profiles, they hope to answer questions such as: Is smoke from prescribed burns less hazardous than smoke from wildfires? Are firefighters, because of immune system alterations caused by smoke, more at risk for severe COVID-19? Does exposure to heavy metals and toxins in firefighting equipment cause changes to their immune systems?

Eventually, the team hopes its findings will lead to better ways to protect the people whose jobs often put their well-being and lives at risk.

“Firefighters really appreciate the focus on their health because it’s been lacking for so long,” notes Dr. Prunicki.

At least one study estimates that up to 16 percent of firefighter deaths are cancer related. Firefighters have higher rates of testicular cancer, non-Hodgkin’s lymphoma, most myelomas, and brain cancer, adds Dr. Prunicki. Heart attacks are the leading cause of death for on-duty firefighters, according to the U.S. Fire Administration.

Dr. Prunicki is one of very few researchers looking at biochemical health effects on firefighters, says Arlene Nuñez, a San Francisco firefighter involved in Dr. Prunicki’s studies. A former infectious disease researcher, Nuñez understands the value of bringing attention to the long-term health of firefighters. “Almost every week, we get a notice about a retired firefighter who has died of leukemia or throat cancer or something similar,” she says.

The information Dr. Prunicki uncovers, adds Nuñez, will contribute to safer practices and even new technologies to offer better protection. “We want to educate people, so they are proud of what they do, but are safe in how they do it.”



Arlene Nuñez, a San Francisco firefighter involved in the studies.

What Your Gifts Made Possible in 2020 at Our Center:



See our Center’s research articles published in peer-reviewed academic journals:
med.stanford.edu/allergyandasthma/research/ResearchPublications.html

FUNDING NEEDS

Looking Toward the Future with Hope



Thanks to you—our philanthropic community—clinicians and researchers at our Center are successfully treating people with food allergies and asthma in clinical trials and advancing the science in our laboratories.

We are making remarkable discoveries about molecular changes involved in allergies and asthma, changes we can possibly redirect with drugs under development and approved for other uses. By collaborating with researchers around the globe and with community health professionals, we are reaching people who may not be aware of the latest treatments. We are broadening access and education nationwide to disadvantaged communities where the COVID-19 pandemic further revealed disparities in health equity. By using our expertise in immunology and clinical trials, we are stepping in to serve Stanford University and the world in COVID-19 research. We are locking arms to combat climate change, investing in data-driven studies to document how pollution and wildfires damage the immune system at the molecular level, and developing strategies to limit this damage.

With your support, we can do much more.

Investing in Innovation. Situated in Silicon Valley on Stanford’s campus, our Center is uniquely positioned to bring the most cutting-edge treatment and care to our patients. Through the accessibility and computing power of mobile phones, our Center is making use of a digital, patient engagement app to assess the psychosocial aspect of food allergies and asthma. Addressing the anxiety surrounding oral food challenges, several pilot studies using virtual reality are being created, including a game for children with celiac disease to select “safe” food items and an instructional game featuring an interactive epinephrine pen for children with allergies. **This fund provides the creative and scientific freedom for our staff to explore out-of-the-box innovation for more children to live happier and healthier lives.**

Investing in Science. Our Center is one of the foremost in the nation for food allergy and asthma research. Under the leadership of Drs. Kari Nadeau and Sharon Chinthrajah, and fielding a talented staff of more than 50, we tackle the hardest scientific challenges. This includes improving diagnostics, finding new biomarkers for disease, studying changes in the microbiome, using bioinformatics to create large cohorts to study, exploring prevention therapies, and much more. **Dedicated to our robust pipeline of key projects, this fund ensures that our brilliant scientists and physicians do not need to stop their research to write grant applications.**

Investing in Community. As COVID-19 raged, every person in the world was affected, but this epidemic brought the harshest realities for vulnerable populations. Families already at risk for food insecurity were forced to not only find safe and allergen-free foods in grocery stores, but also faced economic instability in paying for these foods. **This fund will allow our Center to continue our civic duty of helping all people, regardless of a family’s financial ability.** Providing education and resources to these underserved communities nationwide continues to be one of our guiding principles.

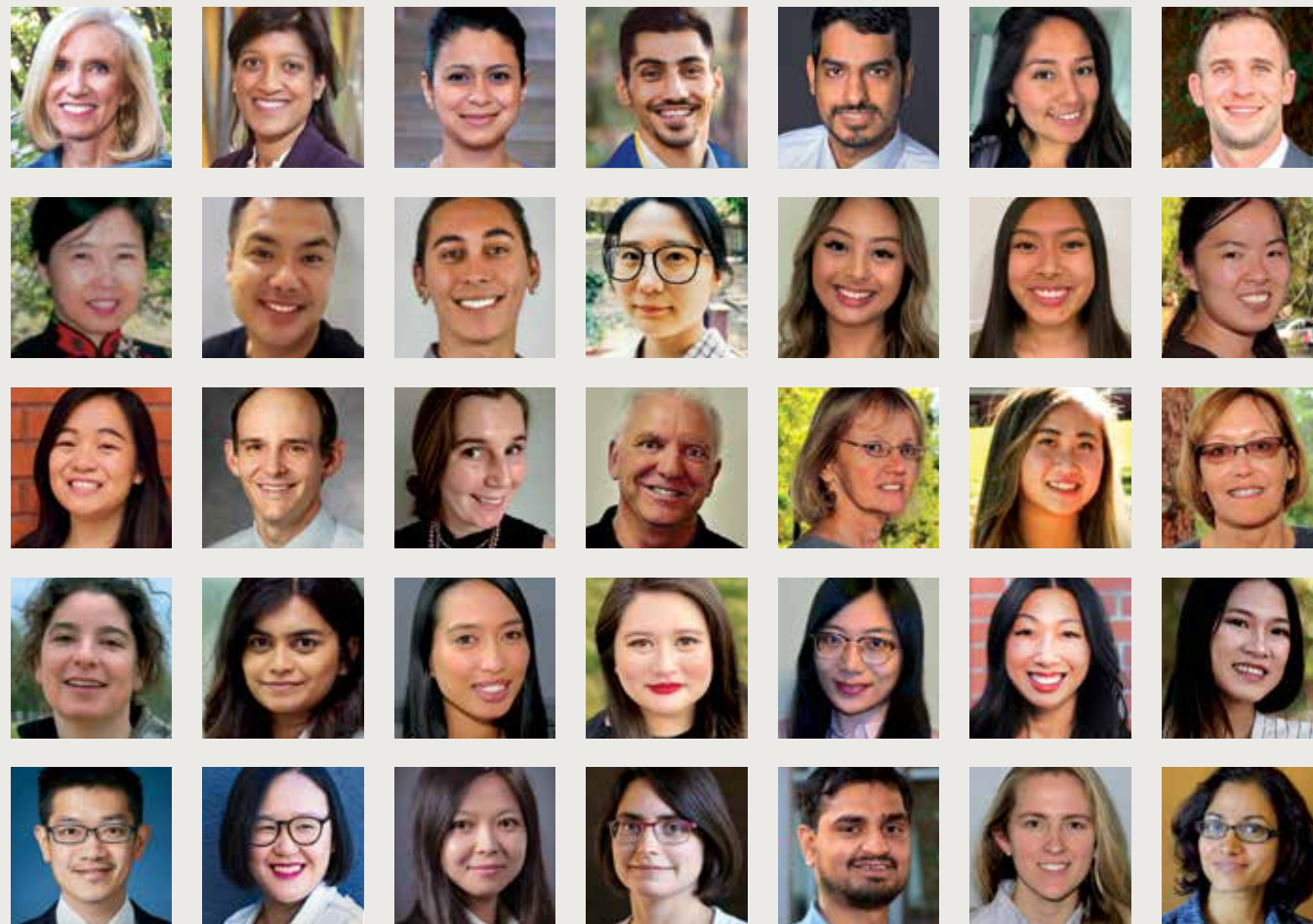
To donate online, please visit supportlpch.org/SNP.

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

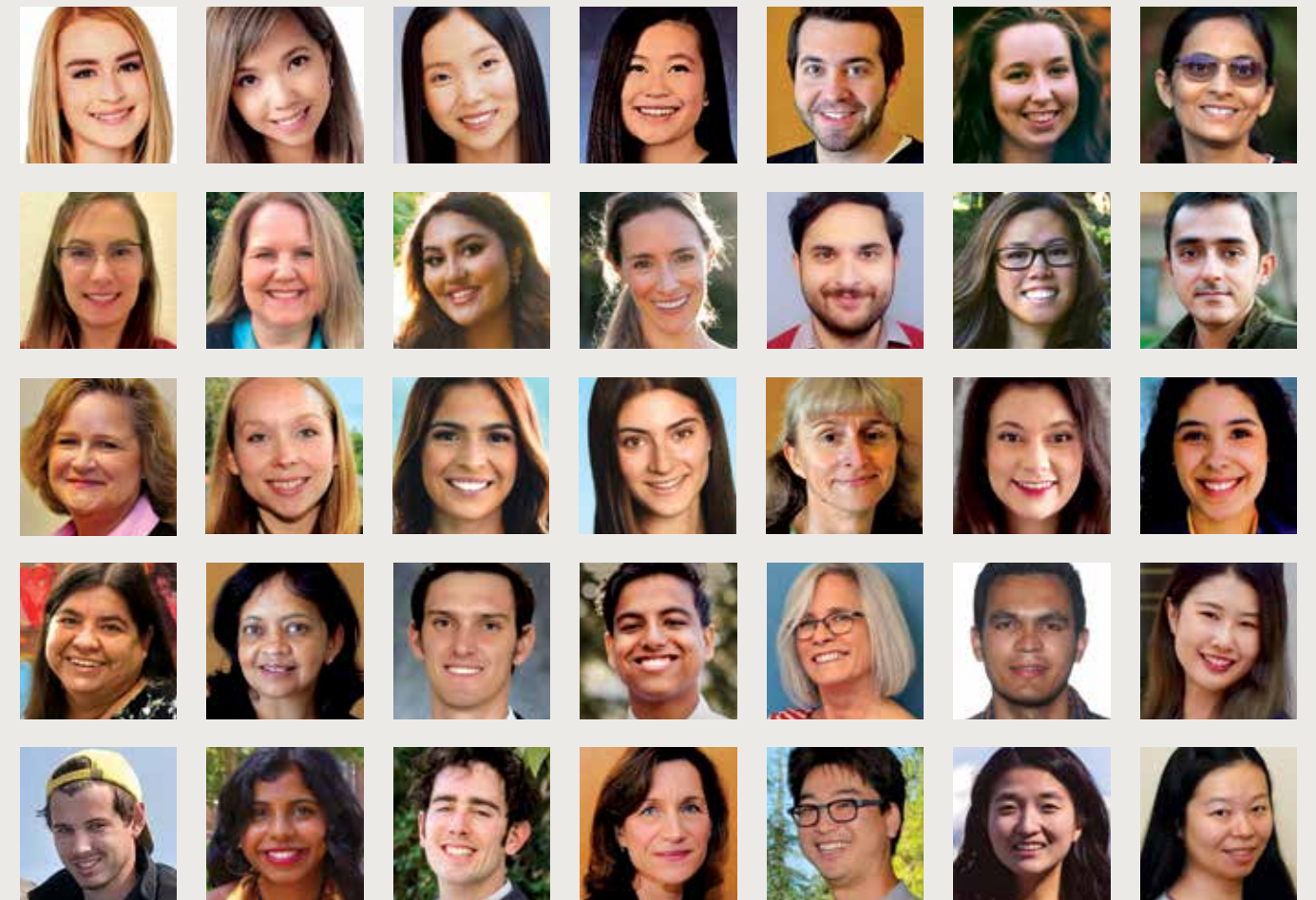
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With Deepest Gratitude

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



Pictured on this page, Row 1 – Kari C. Nadeau, MD, PhD; Sharon Chinthrajah, MD; Sayantani (Tina) Sindher, MD; Bahman Adlou; Juan Aguilera, MD, PhD; Marleni Albarran; Brent Anderson, PharmD; Row 2 – Maolin Bai; Angelo Buendia; Stuart Cansdale; Shu Cao; Lauren Casareno; Jhanelle Celiz Cervantes; Iris Chang; Row 3 – Elizabeth Chen; William Collins, MD; MacKenzie Cox; Christopher Dant; Rosemarie DeKruyff, PhD; Evan Do; Diane Dunham, MSc; Row 4 – Katie (Katharine) Fast, MD; Andrea Fernandes; Roxanne Garcia; Quinlan Hampton; Xiaorui Han, PhD; Lindsey Hincks; Vivian Hoang; Row 5 – Yuan-Pang Hsieh, PhD; Angela Hy; Sophie Yufei Jie; Maya Kasowski, MD, PhD; Abhinav Kaushik, PhD; Laurie Kost, and Divya Kumar, PhD.

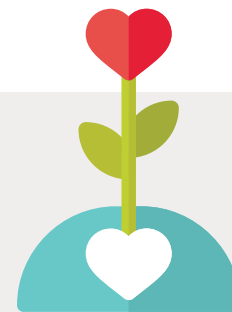


Pictured on this page, Row 1 – Gabriella Landes; My-Linh (Mimi) Le; Allie Lee; Zoe Lew; Andrew Long, PharmD; Rose Madison; Monali Manohar, PhD; Row 2 – Kristine Martinez; Marté Matthews, MA, MFT; Humayra Mohiuddin; Andrea Bunt Nadosy; Ceena Nafarzadegan; Tina Nguyen; Bibek Paudel, PhD; Row 3 – Mary Prunicki, MD, PhD; Natasha Purington; Karina Quezada; Grace Rabinowitz; Olivia Raeber, PhD; Alyssa Rodriguez; Jessica Rogers; Row 4 – Maribel Gonzalez Ruiz; Vanitha Sampath, PhD; Chris Schumacher; Mihir Shah; Barrie Ann Shapiro, PhD; Abhay Singh; Cillione Tan; Row 5 – Meije (Mark) Benjamins Tiersma; Monica Vel; Christopher Michael Warren, PhD; Margie Woch, RDN; Yu Wong, MD, PhD; Julia Ye, and Xiaoying Zhou, MD, PhD. Not shown: Catherine Ghodrat; Debjani Goshal; Heather Ha, PhD; Isabelle Patricia Hickey; Taryn Audrey Liu; Ella Parsons, and Kiara Anesu Revels.



Our Scientific Advisory Board offers high-level expertise to improve diagnostics, prognostics, and therapies:

med.stanford.edu/allergyandasthma/about-us/our-team.html



Thank You

Your generosity strengthens our ability to bring care, comfort, and science to people with allergies and asthma.

Congratulations to Our Doctors

Sharon Chinthrajah, MD, was named associate professor of medicine in November 2020. An endowed faculty member, she has established herself as a physician-scientist and leader in investigating immune mechanisms in food allergy and asthma. She is director of the Clinical Translational Research Unit at our Center, leading our team in conducting innovative studies in food allergy, asthma, hay fever, and eczema. She is funded by the National Institutes of Health and is licensed in both pulmonary/critical care and allergy/immunology.



Tina Sindher, MD, was promoted to clinical associate professor in April 2021. Endowed by the Gies Foundation, she has used cutting-edge research to not only better understand the mechanisms behind food allergy but also develop treatments and preventions. Joining Stanford as a clinical assistant professor of allergy/immunology in 2017, she is active in our outpatient clinics and serves as the principal investigator of several clinical research trials at our Center.



For more information about our Center, including how to join clinical trials, see:
med.stanford.edu/allergyandasthma/about-us.html