Food Allergies: The Search for a Cure Reaches Prime Time

Plus: Expansion Update and Report on Giving
Dear Friends,

We are on the cusp of very exciting developments at Lucile Packard Children’s Hospital Stanford and Stanford University School of Medicine. As you’ll read in this issue of Lucile Packard Children’s News, we are literally and figuratively building the framework for future advancements in research and care.

Earlier this year, with the “topping off” of our hospital’s expansion project, we saw our dreams of healthier happy futures become tangible. As the final steel beam was raised and secured into place, we took an important step toward 2017 when the hospital expansion will open its doors to patients and their families.

We were also recently honored by a transformational gift by entrepreneur Sean Parker to establish the Sean N. Parker Center for Allergy Research at Stanford University. This gift, along with many others provided by supporters like you, will help us reach our ultimate goal of curing all allergies.

Within these pages you’ll meet some of the children who have overcome life-threatening food allergies to lead fuller, safer lives. Clinical trial participants like Keegan, Carter, Annie, Stefan, Matthew, Maya, Kieran, and Tessa have each helped us advance the world’s understanding of the mechanisms of allergies. Their brave families and the donors who support our research are truly making a difference for patients today and tomorrow.

What an exhilarating time we live in. We look forward to what the future holds, and are so grateful for your support to help propel us onward.

Sincerely yours,

David Alexander, MD
President and Chief Executive Officer
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Thirty years ago, Lucile Salter Packard envisioned a warm and welcoming hospital that would transform the way children and expectant mothers receive care.

To gather ideas, Mrs. Packard, along with a team of Stanford doctors and executives, toured several of the nation’s top children’s hospitals. Curiously, she would sometimes excuse herself from the group.

“My mother would later be found speaking directly with patients, families, and their care providers so she could hear what truly made a difference to them,” remembers Susan Orr, Mrs. Packard’s daughter.
What Mrs. Packard learned from those candid conversations was the importance of nature, play, and compassion when treating children, as well as keeping families at the heart of health care decisions. She recognized that these elements, in combination with state-of-the-art medicine, would improve the way children heal and make a lasting impact in the community.

With its child-friendly amenities and access to outdoor spaces, Lucile Packard Children’s Hospital Stanford was considered ahead of its time when it opened in 1991. It remains one of the few hospitals in the country exclusively dedicated to both pediatric and obstetric care and is nationally recognized for its exceptional programs in cardiology, neonatology, cancer, and transplantation. Each year more than 4,000 babies are born at the hospital, and its expanded network through Stanford Children’s Health receives more than 500,000 patient visits.

As demand continues to grow, the hospital is responding with a $1.1 billion expansion, supported by $262 million in philanthropic gifts, that builds on the powerful foundation first established by Mrs. Packard.

“We are building what will be the most technically advanced, family-friendly, and environmentally sustainable hospital for children and expectant mothers.”

Christopher Dawes

“While it needs to accommodate 21st-century medicine,” Guenther adds, “the building also needs to reflect that it is in a place that is like nowhere else in the world.”
The Bay Area’s deep sense of environmental responsibility is a driving force behind the design, which has put sustainability and “green” systems as a top priority. Almost four acres of gardens and green space will offer areas where patients, families, visitors, and staff can savor the sights, smells, and sounds of nature. The landscaping will feature native and adapted plants, including flowering shrubs and trees, that can thrive in the California climate while providing spots for quiet visits or active play. Heritage oaks and redwood trees from the original site were carefully relocated in oversized containers to be replanted when construction is complete. This environment also will provide inviting habitats for local birds.

The building site was formerly a large expanse of asphalt parking lots, which tend to raise surrounding temperatures by reflecting sunlight and subsequently increase the need for air conditioning. The expanses of green space and permeable paving can absorb storm drainage better than paved areas, since they allow rain to enter into the region’s groundwater system rather than running off into the bay, Guenther notes.

**Bringing the Outdoors In**

The sense of outdoors will pervade the interior of the new hospital as well. Courtyards and roof gardens will be easily accessible to patients and visitors and enable natural light to filter into the corridors. Patient room windows will feature planter boxes so that a child confined to bed will have a view of flowers, much like the current hospital building.

“From the very beginning, we knew that the new building would be highly sustainable and that thematically it would be all about nature,” Guenther says. “As a way-
finding guide for families who come from all over the state, the building is themed around the ecoregions of California, from the Rocky Shore to the Sierra Nevada Mountains."

Each floor theme highlights a specific ecosystem that includes native animals and plants, both to help visitors find their way around the building and to serve as an educational experience for young patients. The hospital’s child life staff and the design team polled patients and their families to determine favorite plants and animals, and engaged Stanford University ecology faculty to ensure accuracy. The fourth floor, for example, is themed to the California foothills with their indigenous cottontail rabbits, burrowing owls, and California poppies; the desert theme on the third floor will showcase bighorn sheep, valley quail, and saguaro cacti.

Water Wise

No potable water will be used for landscaping, Guenther says, which will save more than 684,000 gallons of water per year.

Rainwater will be harvested for landscape irrigation, and condensate water — water collected from dehumidifying indoor air — will be used to irrigate the gardens. All collected water is gathered in two 55,000-gallon underground cisterns. Harvested water will be used by a highly efficient drip irrigation system.

Water-cooled pumps and air compressors will be eliminated to reduce water usage. Dishwashers and sterilizers are projected to use about 80 percent less water than their standard counterparts, and low-flow bathroom fixtures along with a system of sensors and controls will reduce potable water usage in the new building by as much as 40 percent.
Energy Efficiency

Hospitals by their very nature are energy-intensive facilities, operating around the clock, and using complex medical systems and equipment critical to patient care. They also include heating and cooling systems that require a lot of energy, as do specialty support services such as laundry, sterilization services, food service, and complex computer centers. Lane and his team have been working closely with the architects and contractors to identify ways to make these systems energy efficient and to reduce waste.

An extensive external solar shading system will minimize direct sunlight, and window configurations in each direction can be altered to accommodate the sun’s orientation over the year, Guenther says.

Instead of overhead air conditioning, the new hospital will incorporate a highly efficient displacement ventilation system that introduces air at the floor level. “Air naturally rises as it gets warmer from equipment and people, so it takes less fan energy to deliver it to the space,” she says, adding that the system uses 55 to 60 percent less thermal energy than a standard hospital cooling system.

The goal is to qualify for LEED gold status, says Michele Charles, a project engineer for the expansion project. LEED (Leadership in Energy & Environmental Design) is a national certification program that recognizes sustainable building strategies and practices. An energy dashboard in the main lobby will display how much energy is being used — and saved — at any time.

Full Circle

Lane says that the building’s construction also adheres to the highest standards of environmentally sensitive practices. On site, a quarter of the vehicles and equipment are powered by electric or alternative fuel. Thanks to diligent recycling practices, more than 1,200 tons of scrap metal, paper, and construction material have been sorted and diverted from local landfills. More than 70 percent of the steel used in the building comes from recycled sources.

And, in an ultimate measure of using recycled or reclaimed materials, the main elevator tower will be paneled in redwood slats harvested from the recently demolished roof infrastructure of the zeppelin hangar at Moffett Field in Mountain View. “The elevator tower will look and feel like being inside a redwood tree,” Guenther explains.

Next Steps

The expansion project remains on schedule for a summer 2017 opening, says Lane. By mid-May of this year, the metal decks and concrete floors will be in place, and the steel framework will be coated with fireproofing. The prefabricated components that make up the exterior skin are being installed throughout this spring and summer.

By mid-fall the hospital will look more like a building than a construction site, he adds, and interior walls will start going up floor by floor. By the end of 2015 the overhead utilities, water pipes, electrical conduits, and basic infrastructure will be in place.

Finally, by late 2016 construction will be completed as equipment and staff are brought on board to prepare for patients.

In the meantime, the planning team attends ongoing safety meetings with the construction crew. “Some of our crew members’ own children were born at our hospital,” says Charles. “It’s an ongoing reminder of the positive impact this hospital makes on people’s lives.”

As one parent of a current patient says, “2017 can’t come soon enough. It’s so critically important to help advance the healing for children.”
Food allergies are a peculiar disease.

Unlike other life-threatening conditions, the people they affect are completely healthy unless they are exposed to the allergen. They and their families live a life of unremitting worry, with the constant mental refrain that any mistake can be a fatal mistake. And there are always mistakes.

For Michelle Sandberg, MD, and Marc Bodnick, it was the time their 9-year-old daughter, Maya, went on a skiing trip with her cousin. Her aunt let Maya pick out some malt balls from a candy bin after checking with the staff that none of the candies contained nuts, which Maya was allergic to. But the candies had been contaminated, and Maya’s face began to swell, her throat hurt, and she vomited. Her aunt, an ER doctor, dosed her with Benadryl and she conked out for 14 hours.

Kim Yates Grosso and Andy Grosso recall the time their 8-year-old daughter, Tessa, almost died when she ate a spring roll with “rice” noodles that turned out to be made of wheat, which she was allergic to, and she began to lose consciousness.

When my son, Kieran, was a toddler he got hold of a cookie that contained egg and nuts, both of which he was allergic to.
Writer Melanie Thernstrom recounts her family's experience overcoming her son Kieran's deadly food allergies.
I grabbed it out of his hand just as he began to put the cookie in his mouth and rinsed his mouth out with water. I mistakenly believed then that an allergic reaction would be in proportion to the exposure to the allergen and, since he hadn’t bitten down on the cookie, I thought if he had any reaction, it would be slight. But as a precaution I decided to drive him to the hospital and sit in the parking lot.

He was screaming energetically as we pulled out, but on the way he quieted and began to seem glazed. His face was white, spotted with crimson hives, and his lips were oddly blue. I didn’t know then that blue lips are a sign of oxygen deprivation, but I saw the terrible hives spreading down his trunk and I stabbed him in the thigh with an EpiPen — an adrenaline-loaded syringe. (Adrenaline — also called epinephrine — interrupts the allergic reaction by relaxing airways and tightening blood vessels.)

I promised myself that day that nothing — nothing, nothing, nothing — would ever cross his lips again unless I had prepared it myself and, when he was released from the hospital the next day, I threw out all the processed foods in the house. But it was not his last reaction — by the time he was 3, he had needed an EpiPen three times.

In a severe allergic reaction known as anaphylaxis, the body misidentifies the protein of a harmless food as the protein of a pathogen. The immune system mounts an attack that spirals out of control, turning into a terrible, self-sustaining feedback loop that — unless interrupted by a shot of epinephrine — causes tissues throughout the body to swell until the airways close and the heart and lungs fail.

**A Mysterious Epidemic**

Currently, about 8 percent of children in the United States and about 2 percent of adults have diagnosed food allergies. It’s a mysterious epidemic. The rate of food allergies has more than doubled over the past decade and appears to be rising, with the rate highest among preschoolers. (Many more people self-identify as food allergic, but they are actually suffering from food intolerances or sensitivities.) An estimated one-quarter of people with food allergies will have an episode of anaphylaxis in their lifetime. These rarely result in death — the fatality rate is hard to quantify because such deaths are often coded as cardiac arrest — but they are the cause of 90,000 emergency room visits a year. Until recently, no effective therapy for the problem existed.

Maya, Tessa, and Kieran were rescued from this life by being among the first children to be treated in a medical trial at Stanford of a treatment called oral immunotherapy, or OIT, led by Kari Nadeau, MD, PhD, associate professor of pediatrics and an immunologist at Stanford University School of Medicine, Stanford Hospital, and Lucile Packard Children’s Hospital Stanford. The treat-
ment involves retraining the immune system through eating the allergen, beginning with microdoses and slowly increasing until the patient can safely eat a full serving of the food. Nadeau and her colleagues have recently discovered that the treatment changes the way patients’ genes function.

For decades, immunotherapy has successfully treated environmental allergies (giving injections of cat dander, tree grass and so forth), but had been considered too risky to try with food allergies. However, in the 1980s researchers in Europe experimented with food allergies and, in the past decade, trials conducted at Duke, Johns Hopkins, the Mount Sinai School of Medicine, and other places showed that children could be safely desensitized to peanut, milk, and egg. Each of these trials had involved desensitizing children to a single food at a time, yet a third of people with allergies suffer from more than one allergy.

In April 2009, Kim Yates Grosso attended a lecture on food allergies by Nadeau. Afterward, she asked Nadeau what she could do for her daughter Tessa — severely allergic to milk, wheat, egg, nuts, shellfish, and some other foods. To desensitize Tessa to her major allergens one by one would take more than a decade.

Nadeau promised to help her — and she did.

The two women worked together to raise the money to conduct a trial of OIT in which patients would be desensitized to up to five foods simultaneously. Yates Grosso led a volunteer coalition, then called the Stanford Alliance for Food Allergy Research (SAFAR) Community Council, which raised 95 percent of the money for the trials from private donors, with the balance made up by grants from the National Institutes of Health. Entrepreneur Sean Parker later made a visionary $24 million gift to establish the Sean N. Parker Center for Allergy Research at Stanford University (see “A Catalytic Investment in Allergy Research,” page 18). In total the Center has raised $38 million, thanks to the philanthropic community, since October 2013.

So far, more than 440 patients have undergone a food allergy clinical trial at Stanford; unlike other trials, Nadeau accepts both adult and pediatric patients. (Another 1,300 patients are on the waiting list.)

We began oral immunotherapy when Kieran was 2. The first doses — made from the protein of the allergens — are so small they look like sprinkles of cinnamon. Every two weeks or so, he would return to the hospital for an “updose” in which he would try to eat a slightly larger amount. Every day at the same time, he would eat a dose at home and then we would anxiously monitor him for...
reactions for two hours. Like almost all the patients, he had reactions: he got hives on his face, his eyes became itchy, his tongue became swollen, or he vomited. If he reacted, we would stay on that dose an extra few weeks until his body adjusted to it. (Reactions severe enough to use an EpiPen are rare; out of 440 patients, only 15 had a reaction in which an EpiPen was used.)

Tessa was in a smaller, multiallergy OIT trial in which patients received injections of an asthma drug, Xolair, that suppresses a critical antibody in anaphylaxis known as IgE. Because of this, Tessa was able to complete a treatment in just four months. After about two years of OIT, Maya switched to a Xolair trial and finished her treatment in eight months.
We pinched ourselves at Kieran’s fourth birthday, when we were able to serve chocolate cake made with eggs. On his first birthday, before we knew he had an egg allergy, a few bites of cake had put him in the hospital. Like most allergy parents, I had come to think of eggs and nuts — formerly favorite foods of mine — as positively evil and shunned them myself, even when I was traveling.

Then suddenly the curse was lifted: we took down the sign on our front door forbidding them and we served peanut butter on toast for breakfast, almond and cashew butter sandwiches for lunch, hazelnuts for snack, and eggs for dinner every night.

Indeed, we had to serve them (this is the catch of the treatment) because the patient needs to continue eating the food to prevent a return of the allergy. Suddenly the food that has always been strictly avoided has to be eaten every day — a surreal state of affairs. Patients must initially eat full servings of the food every day (the program is now experimenting with having patients eat them every other day instead). Eventually however, when their blood work and skin testing shows no traces of the allergy (which happens sometime between six months and three years), they can consume a much smaller amount — say a few peanuts, or the amount of egg in a muffin.

Innovative Science, Compassionate Care

For some kids the food that once was poisonous to them still tastes like poison. Tessa, now 12, finds milk and eggs revolting — she will eat them only in the form of ice cream and egg chips. For a long time, Maya, 11, could consume her nuts only in a vanilla frozen yogurt and pineapple smoothie, but she eventually graduated to eating them straight.

Because of kids’ aversion to their former allergens (not to mention the general difficulty of getting kids to eat anything their parents want them to), trials at other centers in the United States and Europe have lost up to a third of their patients. Nadeau and her team have gone to extraordinary lengths to avoid this. They bond with the patients and their families and are accessible to them day and night. When one boy decided he would take his dose only if Tina Dominguez, the program’s beloved physician assistant, would stay on the phone with him, she did it. Families can join a support group and work with a therapist to treat anxieties about eating the foods and a nutritionist to find creative ways to eat the foods, such as placing nuts under the cheese on a pizza. Out of 440 patients, only 12 dropped out. (Three moved away, two suffered from unrelated health problems, two found taking the dose caused the child or their parent too much anxiety, and five were terminated because they failed to take their doses more than six days in a row.)

“For everyone who has stayed in the study, the treatment has been 100 percent successful,” says Nadeau. “It turns out that everyone’s immune system is capable of adapting — and surprisingly, it is as true of adults as children.” She and her team now have a nine-year study of OIT — the longest record in the United States — in which they found that everyone who was compliant with the treatment and continued to eat the foods has kept their allergies from returning.

What happens if the patients stop eating the foods altogether? Nadeau recently published the results of a withdrawal study, where 20 formerly peanut-allergic patients who had completed two years of OIT and were able to eat a full serving (1 tablespoon of peanut butter or 20 peanuts) without any reaction stopped eating peanuts altogether. After three months, more than half (13 out of 20) had regained the allergy to peanut, although their reactions were no longer as
severe. By six months, almost everyone (17 of 20) had regained the allergy.

Cracking the Code

Why? How does OIT work — and why doesn’t it last without continuous exposure? Is it possible to understand at a molecular level what causes food allergies, and how OIT changes those processes?

These are among the questions Nadeau and others at Stanford have been exploring. The Sean N. Parker Center for Allergy Research at Stanford University is bringing together researchers and clinicians, geneticists, engineers, chemists, psychologists, and nutritionists to understand and treat all types of allergies, including allergies to drugs, the environment, and other triggers.

Parker’s gift focuses on clinical trials in adults with food allergies and on extensive immune monitoring for all clinical trials. His gift also provides the infrastructure for multi-disciplinary collaborations across Stanford and across the globe. The Center’s discoveries in treating and understanding food allergies pave the way for finding the underlying cause and a more effective treatment strategy for all allergies. “We are dedicated to transforming the lives of patients and families through innovative science and compassionate care,” says Nadeau.

“I am excited about the Center because there is enormous clinical need,” says Lloyd Minor, MD, dean of Stanford University School of Medicine. “This profound increase in the incidence of serious food allergies that has occurred in a relatively short space of time is fascinating and deeply concerning at the same time.”

“Stanford nurtures innovation like no other place does,” Minor adds. “One reason I’m so excited about the Center is that, with Dr. Nadeau’s leadership, we are establishing and leveraging interactions with departments around the entire university in truly innovative ways.”

The Center will also research and treat food sensitivities and intolerances. “Our researchers are trying to understand why some people are skewed toward autoimmunity, like gluten intolerance or celiac, while others

“It turns out that everyone’s immune system is capable of adapting — and surprisingly, it is as true of adults as children.”

— Kari Nadeau, MD, PhD

Research staff in the allergy center prepare carefully measured cups of food allergens for use in clinical trials.
are skewed toward allergy,” Nadeau says. “Both involve misdirected immunity — one is dysfunctional and leads to autoimmunity, and one is dysfunctional in a very different way and leads to food allergies.”

Nadeau and her colleagues are also working on a type of immunotherapy that circumvents the need to eat the allergens. Patients receive injections in which the food protein — cloaked in a nanoparticle that will fool the body and thus avoid anaphylaxis — travels directly to the lymph nodes and re-educates the immune system. This approach has been tried successfully in Switzerland and Canada to treat allergies to grass pollen and cat dander, respectively, in just a few injections rather than the usual regimen which can take a year.

Another focus of Nadeau’s work has been the development of a predictive food allergy test. Pilot studies have found that the test — which is being developed in collaboration with the laboratories of professor of microbiology and immunology Stephen Galli, MD, and professor of genetics Leonore Herzenberg, PhD — can identify food allergies with 95 percent accuracy using just three drops of blood from a newborn. The hope is that this test will eventually not only identify an allergy, but also predict how severe that allergy will be.

Allergies in the Genes

Food allergies are thought to be largely genetic (one study with twins found them to be about 70 percent genetic and 30 percent environmental). The environmental theories include exposure to toxins, pollution, the Western diet, and excessive cleanliness — “the hygiene hypothesis” — that has deregulated the immune system. But if food allergies are largely genetic, then how has there been such a rapid increase?

Genetic changes used to be believed to take place only through natural selection, over vast periods of time. But the new field of epigenetics has discovered that, although the genetic code itself is fixed at birth, the environment can radically modify how genes behave through chemicals that attach themselves to the genes. Moreover, these acquired epigenetic changes can actually be passed on to later generations.

“What we discovered is that allergy treatment causes changes at the epigenetic level,” Nadeau says.

Nadeau and her colleagues focused on a type of white blood cell known as regulatory T cells, or Tregs. Tregs

How Your Support Helps

The Sean N. Parker Center for Allergy Research at Stanford University was established through the generous support of many donors, including Sean Parker’s founding gift to fund adult-based clinical studies, immune monitoring, and expansion of infrastructure; Jeff and MacKenzie Bezos’ matching funds for a multi-site phase 2 study throughout the U.S. for children and adults with multiple food allergies; and four endowments from Beth and Larry Gies, Nancy and Steve Carell, Kathryn and Orlando Bravo, and Sean Parker for faculty scholars and fellows at the Center.

“Our vision is to find the cause and the cure for all allergies,” says Kari Nadeau, MD, PhD. “I use the word ‘cure’ very carefully. We have successfully desensitized many food-allergic individuals, but we don’t know yet if they are cured for life. We are deeply grateful to our donors for helping advance research toward a lasting cure for all allergies, including food, drug, and environmental allergies that affect millions of people worldwide.”

Continued philanthropic support for the Center is essential and will accelerate pioneering work in the following areas:

- **Laboratory research** to advance the scientific understanding of allergies
- **Clinical trials** to translate research discoveries into treatments for patients
- **Ambulatory clinic** to provide multidisciplinary care to patients and families from around the world
- **Training and education** for the next generation of allergy leaders
- **Community outreach** to connect, educate, and support patients and families
- **Computational biology research** to create and leverage a database of research findings from leading institutions around the world

Every gift allows the Center to deliver on the hope and promise of finding the cause and the cure for allergies.

For more information about the Center or to participate in this important work, please contact Brian Panique at (650) 497-9951 or brian.panique@lpfch.org.

Gifts can also be made online at supportLPCH.org/allergy.
are called “peacekeeper” cells because they modulate the immune system and allergic response (preventing autoimmune disease, for example). Treg cells suppress other cells that are overactive or inflamed — a system that dramatically fails in the case of anaphylaxis. Her lab examined a gene within these cells called FOXP3. In the case of allergic subjects, she discovered FOXP3 had been disabled because it had become coated with methyl groups. Methyl groups (groups of three hydrogen atoms bonded to a carbon atom) affect different genes differently, but in the case of FOXP3, the methyl groups suppressed the gene, rendering it useless.

In a recent study, Nadeau compared blood samples from peanut-allergic patients who had been desensitized through OIT with blood from peanut-allergic patients who had not undergone the therapy. The untreated group had a high level of DNA methylation in the FOXP3 gene, but the patients who had undergone OIT had a low level. The therapy had caused the gene to demethylate and become active again. Indeed, the level of methylation in patients who had undergone OIT was so low as to be indistinguishable from that of people who had never been allergic.

Other work by Nadeau and her colleagues has found that environmental stressors such as tobacco smoke and pollution can cause FOXP3 to methylate.

People who have food allergies have a 65 percent chance of passing those allergies to their children. Will OIT change that? In animal models, the epigenetic changes last three generations — for good (in the demethylated FOXP3 gene) or for bad (exposure to toxins such as cigarette smoke and pollution). Perhaps Tessa and Maya and Kieran will pass the demethylated FOXP3 to their children, and spare them the burdens of their experiences.

Fear-free Eating

Nadeau recently published a study that attempted to document the vast improvements in quality of life of patients and their families after they were desensitized. Of the 75 families who filled out a questionnaire, more than 92 percent reported a significant improvement in their quality of life.

Kieran’s allergies were the deepest worry my husband, Michael, and I had ever faced that truly evaporated. “You’ll have to figure out something else to worry about now,” a friend joked. But we didn’t; it turns out our other worries aren’t as worrisome as the fear that our child may die because we were insufficiently worried, as it were, and failed to protect him. The long vigil was over.

For Kieran, completing the therapy meant no longer being excluded from the food at every preschool party and gathering. For Maya it meant being able to go to sleep-away camp with her bag of nuts and eat the same food as the other campers. For Tessa it meant she was able to go on an overnight trip and feel safe being away from her family.

“She’s a completely different kid and we are a completely different family,” Tessa’s mother, Kim Yates Grosso, says. “She has less anxiety, she’s more confident, more social.” For the first time, Tessa’s parents are able to go out by themselves — something they never used to do because they couldn’t trust a babysitter with Tessa.

“Every single time she walked out the door I never knew if I’d see her again,” Andy Grosso says. Tessa didn’t feel safe either — she was afraid whenever she had to leave her family. “Now she hops out of the car with her backpack and tennis racket and runs into school without looking back.”
“She’s a completely different kid and we are a completely different family.”

- Kim Yates Grosso, Tessa’s mother
A Catalytic Investment

Q&A with Sean Parker

In December, entrepreneur and philanthropist Sean Parker donated $24 million to establish the Sean N. Parker Center for Allergy Research at Stanford University. His gift, one of the largest private donations to allergy research in the United States to date, provides both expendable and endowed support for innovative clinical research and care, state-of-the-art equipment, and top-ranked research scientists. Of the $24 million total, $4 million will be used as a dollar-for-dollar challenge match for all other new gifts to the Center.

Why is the subject of allergy research so important to you?

I understand the dramatic effect allergies can have on someone’s life and how difficult it can be to manage them. Unfortunately, there are many misconceptions that allergies are simply a nuisance, but in fact, they can be debilitating. I’ve personally dealt with anaphylactic allergies to a number of foods, and despite carrying EpiPens and a variety of other medications designed to stop the reaction, I know I’m not safe until I get to an emergency room and am able to get treatment. As a new parent, I also understand the anxiety that parents feel about every meal in a restaurant or when they send their child off to school or to a friend’s house.

Finding a safe and durable treatment for allergies would transform the lives of patients and their families, but we need to make catalytic changes to allergy research. I believe that allergies are an immunological problem that should be tackled by immunologists. Given how far the field of immunology has come in the last decade, I began to think that allergy research was not benefiting from the recent breakthroughs in basic immunology. Allergy research, it seemed, was lagging behind.

In addition, there was a critical need for funding the basic science around immune mechanisms driving the sensitization and desensitization in allergy. I wanted to help close this gap by funding the basic science as well as the translational clinical research intended to accelerate the development of new treatments for patients so more people can be enrolled and better treatments can be applied more quickly.

Your experience with food allergies led you to learn about how allergies are currently treated and understood. What did you find?

Since non-food allergies such as ragweed, pollen, and cat dander have been treated with desensitization therapies for decades, it was frustrating to find that clinicians were unwilling to consider this approach in the case of food allergy. I was told over and over by renowned allergists that this approach would not work. But nobody ever offered
ventures, I wanted to very cautiously and carefully look at the field because it didn’t make sense to deploy a lot of capital if the timing wasn’t exactly right. The goal is really important to keep in mind. It’s not just enough to come up with slightly better incremental improvements on the kind of treatments that are out there. The goal is actually to achieve a cure for all allergies.

Like any good venture investment, you need the right group of people, the right team that really understands the problem and approaches it in the right way at the right time. You need certain resources available to you that weren’t available to you before, and you need certain technologies that weren’t available before.

I have a lot of respect for Stanford’s immunology program and have always thought we need to figure out a way to combine all of the genomics and immune marker monitoring in this context.

It was abundantly clear that the team at Stanford led by Dr. Nadeau is taking a very different approach from other programs and really wants to get beyond the conventional therapeutic interventions. It doesn’t mean the medical community stops pursuing oral immunotherapy, but researchers have to approach allergies in a much more scientifically rigorous way.

What is your vision of the future for children and adults with allergies?

My vision is that someone with allergies will be able to go to their neighborhood allergist—in a non-hospital setting—and receive a safe treatment that is permanently effective.

I believe we are relatively close to a point where all allergies can be cured, and that’s why I’m committed to supporting Dr. Nadeau and her research through a catalytic grant to conduct trials at levels capable of moving the entire field forward.
It Takes a Village
Rallying Support to Cure Food Allergies

By Jennifer Yuan

Nine years ago, David and Kori Shaw moved to Palo Alto with their 3-year-old daughter, Keegan, and 1-year-old son, Carter. Along with the usual adjustments of relocating — new job for dad, new preschool for their daughter, making new friends — there was one additional challenge to tackle.

Both Keegan and Carter had been diagnosed with severe allergies to peanut, and Carter was also allergic to milk, egg, and tree nuts. The family consulted multiple allergists in hopes of understanding their children’s allergies and keeping their kids safe.

Strict avoidance, they were told — but the danger was ever present.

With David serving as the new offensive coordinator for the Stanford football team, Kori would arrive at the stadium with Keegan and Carter in tow and find peanuts at their feet. During one game, some spectators were throwing peanuts and the airborne dust alone was enough to trigger an allergic reaction for Carter.

This was less than a decade ago, notes Kori, yet food allergies had not yet entered the general public’s awareness and were often misunderstood as merely an annoyance — or worse, as a figment of overprotective parents’ imaginations. Families facing these deadly allergies often felt isolated.

One day at Keegan’s preschool, Kori noticed another little girl’s nametag: “Tessa,” it read, and below that, “Allergies: milk, wheat, egg, nuts, shellfish.” Kori sought out and met Tessa’s mom, Kim Yates Grosso, and the two women instantly bonded over the experiences, fears, and hopes that both their families had faced in living with dangerous food allergies.

“We were literally just trying to figure out how to live,” Kori explains, “and getting to know another family with food allergies made a world of difference. I remember walking through the grocery store, trying to find foods that were safe for my kids, and Kim on the phone talking me through it — go to aisle six and get this bread and so on — while I cried with relief.”
A few years later, Kim met Stanford immunologist Kari Nadeau, MD, PhD (see “I Can Eat It,” page 8), the first doctor she had ever encountered who was willing to try to treat Tessa’s multiple allergies. A lack of funding for food allergy research, however, was a major limiting factor in moving the work forward.

“It was evident that we needed to fundraise so Dr. Nadeau could do the trial and prove that it was possible to desensitize these deadly allergies — especially for kids with multiple allergies,” Kori notes.

Kim, Kori, and several other moms banded together and began rallying families — to build a community, host events, raise awareness of food allergies, and generate funding for clinical trials. Their grassroots efforts started small but grew as more and more families facing the emerging epidemic of food allergies began joining together and providing private philanthropic support for research.

Five years after the Shaws moved to Palo Alto, 8-year-old Keegan and 6-year-old Carter joined the first cohort of children to undergo Nadeau’s oral immunotherapy trial with the drug Xolair to desensitize patients to multiple allergens at the same time. Over the course of two years under the supervision of Nadeau’s team, Keegan and Carter consumed and tolerated a carefully measured, increasing dose of their allergens and were eventually desensitized to a point where accidental exposure or cross-contamination was no longer a fear.

The results were life-changing for their entire family.

“She changed our family — our whole dynamic,” Kori says. “We’re not stressed. On Sunday we took a bike ride and went downtown and had dinner in a restaurant. She gave us normal family life.”

**Spreading the Word**

In the meantime, word of Nadeau’s successful research had also reached another concerned set of parents — actors Nancy and Steve Carell, whose daughter, Annie, had a severe dairy allergy.

As Annie described it, having food allergies was “like living in a box.” No playdates outside their own home, no sleepovers, anxious meals at restaurants. When the family traveled, they dragged along a cooler full of food.

“Every time we arrived at a hotel, it looked like we were tailgating!” Nancy recalls.

“The second I read about Kari’s success in desensitizing another child to dairy, I thought, ‘Sign us up!’” Nancy says. “Annie was 8 years old, and she hated feeling different from her classmates. I couldn’t believe that there was a possibility that she wouldn’t have to live with this the rest of her life.”

As Annie started in a clinical trial at Stanford, the Carells’ hopes were modest. “Our dream was that she could come out of an accidental exposure to dairy without serious consequences,” notes Nancy. “We weren’t thinking, ‘I hope she can eat pizza.’ We were thinking, ‘Maybe now she can hold hands with somebody who just ate pizza.’”

The experience of oral immunotherapy was not without anxiety. “We were traveling back and forth from Los Angeles, and we were basically saying to Annie, ‘Remember the food we’ve been telling you not to eat because it’s poisonous to your body? We want you to start eating it now,’” says Nancy. “I would be lying if I said it was smooth sailing...
from the get-go. Annie went through a lot. She has our admiration for life.”

What immediately stood out to the Carells — and what got them through — was Nadeau’s compassion and the entire research team’s support.

“We call Kari a gentle genius,” says Nancy. “During the trial [which can result in allergic reactions at home], we besieged her with phone calls. She answered every time and stayed on the phone with us until everything was under control. I trust her completely.”

When Annie successfully completed the trial, the Carells wanted other families facing food allergies to have the same opportunity. They have played an active role in supporting Nadeau’s research and in raising the public’s awareness of food allergies. In 2011, Steve volunteered to host a fundraising gala and recruited his friend and fellow actor Dana Carvey to help him raise support for food allergy research at Stanford. Steve has also narrated an hour-long documentary and participated in public service announcements to help raise awareness.

“Living with food allergies can be extremely difficult but should be approached in a positive, proactive way,” says Steve. “It’s important to support allergy research because every day they are coming closer to a permanent cure for food allergies. So there is hope.”

**Advocating Early**

Stefan Lainovic, 22, was the first New Yorker to join one of Nadeau’s clinical trials at Stanford. When Stefan was an infant, his doctors described him as “wildly allergic” to dairy and egg. Restaurant meals and processed foods were out of the question. Any food prepared on equipment shared with egg or dairy ingredients could cause a deadly anaphylactic reaction. Like other parents of food-allergic children, his mother, Rebecca, monitored everything he put in his mouth.

Stefan’s parents also took another important step: they encouraged him from a young age to advocate for himself.

“We wanted to empower him even as a little boy,” Rebecca explains, “to speak up for himself in an assertive way and be taken seriously. We knew we couldn’t always be there speaking for him. As parents, you blink and suddenly they’re off to grade school and then it’s high school, college.”

As early as age 2 or 3, any time Stefan could speak on his own behalf, he did. When the family went out to a restaurant, it was Stefan’s job to explain that he didn’t need a menu, thank you, because he had brought his own food.

Starting in preschool, Stefan carried his own EpiPen in a waist-pack along with pre-measured Benadryl. Though his family and the school staff always had backups at the ready, Stefan’s parents instilled in him that he was solely responsible, that he was in charge of his own destiny. This sense of responsibility served him well in his teenage years — a risky period when many food-allergic kids fail to carry their own medications — and saved his life on at least one occasion.
It wasn’t until Stefan was 19 years old that he finally qualified for a food allergy clinical trial. By then he was enrolled at Williams College in Massachusetts and the trial was across the country at Stanford — seemingly a deal-breaker. Thanks to what Rebecca describes as Nadeau’s resourceful and get-it-done attitude, they soon found a unique solution: it turned out Stefan could enroll in classes at Stanford while undergoing the clinical trial and earn academic credits that would transfer to Williams.

For much of the next 13 months, Stefan lived at Stanford, attending classes and working part-time in Palo Alto. Though Rebecca flew out for monthly visits, the ongoing reality of the trial was that Stefan was individually responsible for attending his “updosing” appointments (when the research team would introduce a higher dose of his allergen), ingesting his prescribed dose of milk at home each day, and keeping himself safe from possible reactions.

But in many ways, Stefan didn’t go through the experience alone.

“They say it takes a village to raise a child,” Rebecca notes, “and this is never more true than in the food allergy community.” Everyone from Kari Nadeau to fellow parent Kim Yates Grosso to physician assistant Tina Dominguez offered support, friendship, and watchful eyes to ensure that Stefan would succeed in completing the trial.

Since then, the Lainovics have become more committed to the food allergy community than ever before. Rebecca serves on the board of directors of Food Allergy Research & Education (FARE), and she and her husband, Sacha, made strategic philanthropic gifts to sustain and further advance Nadeau’s groundbreaking work.

While Stefan has also taken part in raising awareness, he says food allergies do not define him. He now works in investment banking in New York at Centerview Partners, a demanding career that involves seven-day work weeks and eating out daily — without fear.

The Future is Bright

Today, patients from all over the country are participating in Nadeau’s clinical trials. Matthew Friend, a high school junior from Chicago, is proud to be one of them.

Matthew’s life-threatening allergies to wheat, barley, rye, and oat were discovered when he was 8 months old and broke out in full-body hives after his first taste of Gerber multigrain baby cereal. The hardest thing to avoid was wheat, which his parents soon learned was literally everywhere: in root beer, Pringles, brownies — even hand cream, shampoo, and sunblock. By the time Matthew entered high school, he had been to the emergency room at least 10 times despite his family’s vigilant efforts to keep him safe.

“We saw Dr. Nadeau’s work as the first glimmer of hope in 14 years for our child,” says Matthew’s mother, Linda Levinson Friend. “While other physicians were directing us to carry epi and avoid wheat, Dr. Nadeau was willing and able to set the stage for Matthew to lead a full and normal life.”

When Matthew began the trial in August 2012, just a miniscule speck of his allergens could cause anaphylaxis. Eight weeks
into the trial, Nadeau instructed him to “go and get cross-contaminated” and Matthew successfully tolerated the exposure. By the end of the trial, he was eating a daily regimen of one cupcake, six Oreos, and one graham cracker containing wheat; one granola bar containing oat; and four cookies made with rye and barley flour, all of which he still continues every day in order to maintain his desensitization to the previously deadly allergens.

“We are forever indebted to Dr. Nadeau and her incredible staff,” Linda says. “They are desensitizing kids like Matthew with multiple food allergies, and exciting results are happening. It is surreal and amazing to be part of this process.”

When Matthew’s family began looking for a way to give back, they reached out to their local network in Chicago and convinced their friends and colleagues that supporting research at Stanford would actually have a national impact. Today, thanks to Linda and her husband, Bill, and the other donors they have mobilized, the clinical trials have opened sites in Chicago, New York, and Los Angeles so that more families can participate in life-changing research in their own hometowns.

For Matthew, the trial made such an important difference that he began blogging for *The Huffington Post* about his experiences “as a human lab rat” in food allergy research, recounting his experiences and wanting other teens with potentially deadly food allergies to know there is hope for a normal life. Matthew is also quick to point out that he still carries two EpiPens — because although he is desensitized and protected from cross-contamination, the treatment is experimental and he can still have reactions.

“Whenever we are presented with an opportunity, we are happy to speak to or guide other families,” Matthew writes. “Because of the innovative and incredible work that Dr. Kari Nadeau and her team are doing at Stanford and now in other sites across the country, people with food allergies can look forward to full lives. I am living proof that the future is extremely bright for people with food allergies.”
In Memory of Pete Harman

On November 19, 2014, the Lucile Packard Children’s Hospital community lost a dear friend and supporter, Leon W. “Pete” Harman. Born near Salt Lake City in 1919, Harman and his wife, Arline, founded the Kentucky Fried Chicken chain in Utah. The couple saw the franchise grow, with the Harman Management Corp. overseeing more than 230 KFC locations with 4,000 employees. The Harmans shared their success with a number of philanthropic causes. When the couple retired and moved to the Bay Area, they formed a connection with our hospital that would change the lives of countless patients and their families.

Over the years, the Harmans gave selflessly to wherever the need was greatest, including several key areas that have made a tremendous difference in how the hospital attracts, trains, and retains top physicians and promising scientists. The Arline and Pete Harman Professor and Chair of Pediatrics is currently held by Hugh O’Brodovich, MD, an internationally renowned pediatric pulmonologist and chair of the department of pediatrics at Stanford University School of Medicine. The Harmans also established the Harman Clinical Endowment for Neurosciences, which promotes research into new tools and technologies that involve less-invasive procedures and better outcomes for children with brain cancer, epilepsy, cerebral palsy, and other neurological disorders.

The family created endowed funds for fellows and faculty scholars in pediatric subspecialties to encourage young physician-scientists and trainees to merge pediatric research with innovative, family-centered care. And for many years, the Harmans made annual commitments to the Lucile Packard Children’s Fund to help support care for families who lack sufficient insurance, as well as important services like the chaplaincy, Hospital School, recreation therapy, and more.

Arline Harman passed away in 2013 at the age of 96.

“I am honored to have known the Harmans and worked in partnership by their side,” said Harvey Cohen, MD, PhD, former chief of staff at Lucile Packard Children’s Hospital Stanford and the first holder of the Harman professorship. “They truly made a transformative difference that continues to benefit children and families in our community and around the world, and will do so for generations to come.”

Roberts Honored with 2015 Tribute to Women Award

This May, YWCA Silicon Valley honored Kim Roberts, our Interim Chief Strategy Officer, Chief Administrative Officer of Physician Practices, and Chief Executive Officer of Packard Children’s Health Alliance, as one of 36 recipients of the 2015 Tribute to Women Award. Roberts has been instrumental in building Stanford Children’s Health, Northern California’s largest healthcare enterprise for children and expectant mothers.

Childx Offers a Look at the Future

In April, Stanford Medicine held its inaugural Childx Conference, a TED-style event focused on innovation in maternal and child health. Internationally recognized thought leaders shared insights on solving health problems in pregnancy, infancy, and childhood. The conference, hosted by the Stanford Child Health Research Institute, covered an array of topics, from gene therapy and precision medicine to the life course from fetal to adult.
IN THE
news

Sager Named a ‘2015 Woman of Influence’

Our Chief Government and Community Relations Officer, Sherri Sager, has been honored by the Silicon Valley Business Journal as one of 2015’s Women of Influence. For more than two decades, Sager has represented the hospital to government agencies and community groups, and also advocated for children and expectant mothers through work on policy issues.

Spunt Receives Endowed Professorship

Sherri Spunt, MD, professor of pediatric oncology, has been appointed an Endowed Professor of Pediatric Cancer. Spunt works at the Bass Center for Childhood Cancers and Blood Diseases to improve the treatment of children and young adults with soft tissue sarcomas, a type of cancer that can be found in any part of the body. Her research focuses on the development of drugs to treat solid tumors in children and to understand the long-term effects of childhood cancer therapy.

The position was established by a gift from 14 donors with an interest in supporting pediatric cancer programs, in appreciation of the work of Harvey Cohen, MD, PhD, the Deborah E. Addicott – John A. Kriewall and Betsy A. Haehl Family Professor in Pediatrics and former chair of pediatrics.

Sunshine Honored as Legend of Neonatology

Philip Sunshine, MD, was honored as a 2015 “Legend of Neonatology” at The Legends Gala and Awards Ceremony in Orlando this February. Part of the annual NEO: Conference for Neonatology, the event honors remarkable individuals whose efforts have contributed to the care of critically-ill newborns.

Sunshine’s career of caring for preemies spans more than 50 years, and the honoring organization aptly described Sunshine as, “One of the ‘originals’ in neonatology, a neonatologist’s neonatologist, one of history’s best, and an endearing and enduring figure.”

Since arriving at Stanford in 1957, Sunshine has cared for 40,000 babies. He was one of the first doctors to put babies on ventilators and to let parents spend time with their premature babies. Over the years, he has seen the premature infant survival rate increase from 50 percent to over 90 percent.

Happy Birthday, Boo!

Internet sensation — and our furriest donor — Boo the dog generously donated his 9th birthday to our hospital. More than 400 of Boo’s fans donated more than $10,000 in his honor to the Lucile Packard Children’s Fund, which was then doubled to $20,000 with a matching gift from Boo’s owner. To celebrate his big day, Boo stopped by our hospital to deliver 200 birthday gift bags for our patients.
WWE Superstars Bring Hope

In March four WWE Superstars and two WWE Divas took time out of preparations for WrestleMania 31 at Levi’s Stadium to visit our hospital and meet some of our patients and their families. Not only did the larger-than-life heroes bring toys and goodies, but through the Superstars for Hope online fundraiser, WWE raised more than $140,000 for our cancer programs.

Stanford Researcher Follows Students Through Mindfulness Curriculum

Thanks to the Sonima Foundation, 3,400 students from seven schools in the Ravenswood City School District in East Palo Alto will participate in yoga-based exercises, mindfulness practices, and nutritional education. Leading a study on the program’s effectiveness is Victor Carrion, MD, director of the Stanford Early Life Stress and Pediatric Anxiety Research Program at Lucile Packard Children’s Hospital Stanford and associate chair and professor of psychiatry and behavioral sciences at Stanford University School of Medicine.

Carrion and his team will follow a group of students over the next four years to evaluate how yoga and mindfulness can help in their emotional and social lives. Carrion hypothesizes that students enrolled in the Health and Wellness programs will display emotional regulation, higher academic performance, and a generally healthier lifestyle.

Transplant Center Remains Top in Nation

Newly released information from the Organ Procurement and Transplantation Network named our hospital’s Transplant Center as the national leader in pediatric organ transplantation. Among our accomplishments in the past year: 91 organs transplanted (highest volume in the country), a three-year patient survival rate of 100 percent for liver and kidney transplants, and the ongoing support of 15 outreach locations that help us serve transplant patients closer to their homes.

Associate Deans Appointed for Maternal and Child Health

Stanford University School of Medicine has named three new associate deans in the area of Maternal and Child Health: Mary Leonard, MD, MSCE; pediatric surgeon Dennis Lund, MD; and global health expert Gary Darmstadt, MD. The positions will serve under the direction of David K. Stevenson, MD, Senior Associate Dean for Maternal and Child Health, and in concert with Harry Greenberg, Senior Associate Dean for Research.
Governor appoints Carmichael to DART Committee

In January California Governor Jerry Brown announced that Suzan Carmichael, PhD, associate professor in the Division of Neonatal and Developmental Medicine at the School of Medicine, had been appointed to the Developmental and Reproductive Toxicant (DART) Identification Committee. The group comprises expert scientists appointed by the Governor to identify chemicals that have been shown through scientifically valid testing to cause reproductive toxicity.

Esquivel Receives Honor for Mentorship

Transplant pioneer Carlos Esquivel, MD, PhD, the Arnold and Barbara Silverman Professor in Pediatric Transplantation, received the 2015 Francis Moore Excellence in Mentorship in the Field of Transplantation Award.

Granted in January by the American Society of Transplant Surgeons and the Vanguard Committee, this award honors extraordinary surgeons for their stewardship of fellowship trainees and junior faculty. Last year Esquivel celebrated 30 years as a transplant surgeon.

Comprehensive Neuromuscular Clinic a Certified Duchenne Care Center

The Comprehensive Neuromuscular Clinic at Lucile Packard Children’s Hospital Stanford was named a Certified Duchenne Care Center by Parent Project Muscular Dystrophy (PPMD), a nonprofit organization leading the fight to end Duchenne muscular dystrophy and demanding optimal care for all people with Duchenne. The clinic, led by John Day, MD, PhD, is the eighth center to be certified by PPMD, recognizing the Clinic’s dedication to improving care for people living with Duchenne.

Carrion Elected to Lead State Commission

California’s Mental Health Services Oversight and Accountability Commission (MHSOAC) announced that Victor Carrion, MD, has been elected the new Chair of the Commission. Carrion, who has been a MHSOAC commissioner since 2011, is a child and adolescent psychiatrist at Lucile Packard Children’s Hospital Stanford. Additionally, he directs the Early Life Stress Research Program at Stanford, and is associate chair of the department of psychiatry and behavioral sciences.

Hintz Appointed Robert L. Hess Family Professor

Susan Hintz, MD, MS Epi, professor of pediatrics (neonatology), was appointed the Robert L. Hess Family Professor. Hintz is a neonatologist and perinatal epidemiologist who works to improve the survival and health of extremely premature and high-risk infants. She helped to create, and currently directs, the Fetal and Pregnancy Health Program at Lucile Packard Children’s Hospital Stanford.
Champions for Children

Champions for Children events come in all sizes. Every toy and book collected, and every dollar raised directly benefits the children and expectant mothers we serve. Meet some of the fantastic Champions for Children who are fundraising for our hospital:

**Luke of San Jose: Kickball Dinner**

When Luke and his friend Miranda decided to throw a kickball dinner, they kicked it up a notch and turned the party into a fundraiser for our Bass Center for Childhood Cancer and Blood Diseases. In honor of Luke’s nephew Ellio and the outstanding care he received at the Bass Center, Luke and Miranda raised more than $1,000 through their kickball dinner, held March 13 in Sunnyvale. More than 40 of their friends and family joined in to support our hospital.

**Aeshaan and Garima of Santa Clara: Talent Show**

Six-year-old Aeshaan donated his birthday to patients at our hospital, raising $250. His mother, Garima, was so inspired by her little boy that she helped him organize a talent show for children ages 4-12. More than 70 people attended the event, which included musical performances, karate demonstrations, and more. With Garima serving as emcee, the show was a smashing success, raising more than $1,900 for cancer research.

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**Check Out Our New Champions Pages!**

We’re thrilled to introduce the new and improved Champions for Children website! Now it is even easier to plan a fundraiser, gather helpful tips and resources, and build your own fundraising page. Follow the lead of Champions like Jennifer, who raised over $8,000. Visit ChampionsPages.org to learn more.
5th Annual Summer Scamper

Benefiting Lucile Packard Children's Hospital Stanford

6k, 10k & kids’ fun run
June 21 • Stanford
SummerScamper.org

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