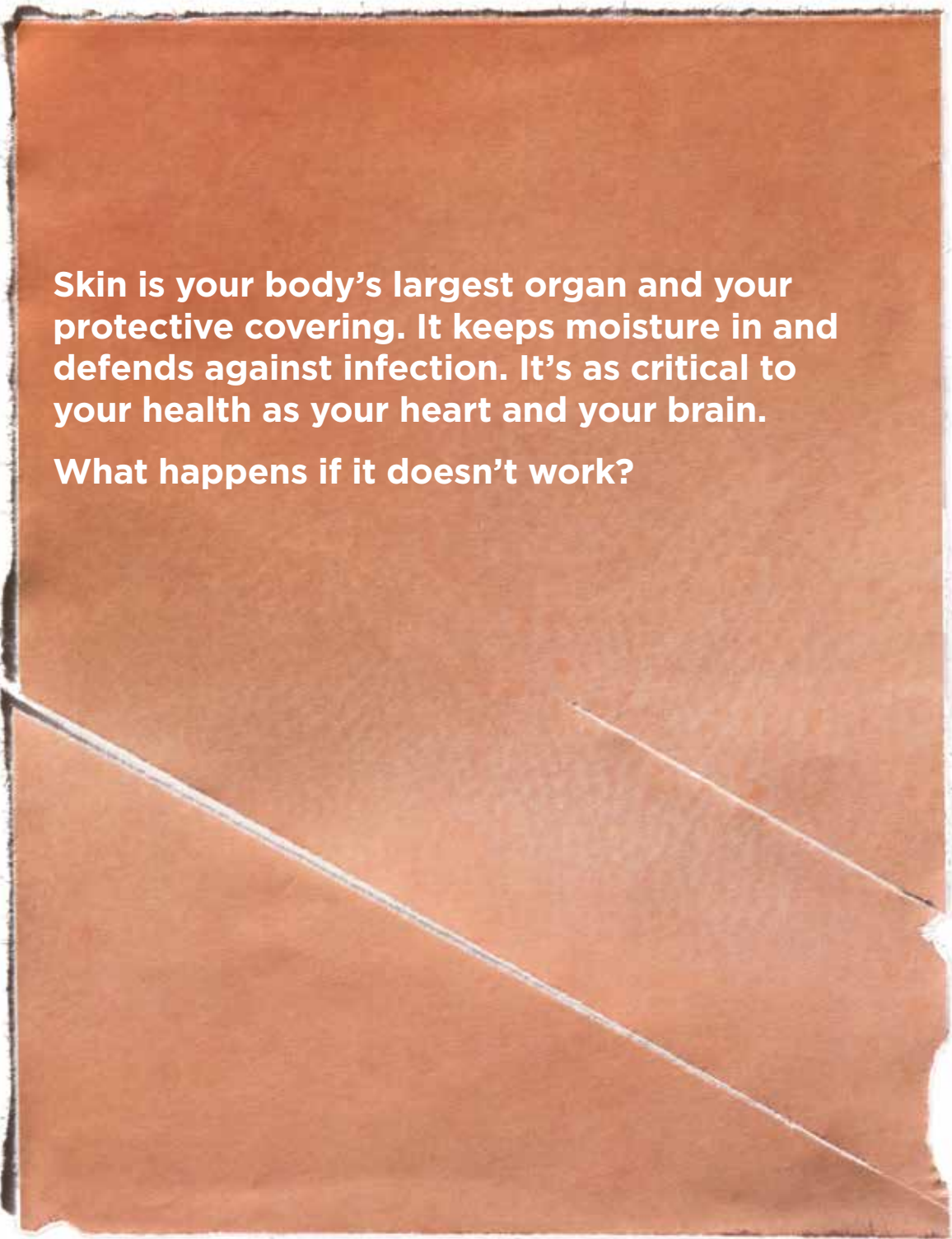




one  
day  
every  
day

Pursuing a Cure for  
**Epidermolysis Bullosa (EB)**

A piece of brown, textured paper, possibly leather or heavy cardstock, with a diagonal crease running from the bottom left towards the top right. The edges are slightly worn and frayed. The text is printed in white on the upper left portion of the paper.

**Skin is your body's largest organ and your protective covering. It keeps moisture in and defends against infection. It's as critical to your health as your heart and your brain.**

**What happens if it doesn't work?**

**At the EB Research Partnership,  
we think about skin every day  
because we are pursuing a cure  
for the genetic skin disease  
Epidermolysis Bullosa, or EB.**

Affecting children from birth, EB encompasses a group of life-threatening skin fragility disorders that occur when genetic mutations rob a body of critical proteins that bind skin together. Our organization supports research for all forms of EB. One of the worst forms, Recessive Dystrophic EB, or RDEB, is an area that many of today's therapies are focused on. Those living with RDEB and other forms of EB experience severe pain, disfigurement and wounds that never heal – even inside the eyes, mouth and internal organs.



**WE PARTNER**

EBRP creates and supports research-enabling infrastructure to help bring treatments to those in need as swiftly as possible.

**WE FUND**

EBRP is the largest nonprofit dedicated to funding research aimed at treating and ultimately curing EB. We funded more than \$1.8 million for research grants in 2015 alone and have been instrumental in securing an additional \$35 million for critical EB research.

**WE HELP HEAL**

EBRP has supported a broad array of potential treatments under investigation by academic institutions and their commercial partners, from stem cell therapies to protein replacement therapy and gene therapy.

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# **one organization: eb research partnership (ebrp)**

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**EB Research Partnership grew from the collaboration of the Jackson Gabriel Silver Foundation, founded on the East Coast by Jamie and Alex Silver; and Heal EB, established on the West Coast by Heather and Ryan Fullmer, and Jill and Eddie Vedder, the lead singer of Pearl Jam. Both organizations shared an urgency based on first-hand experience: To find a cure for Jackson Silver and Michael Fullmer, and all other children and adults who suffer from EB.**

With the support of individual donors, the EB community and experts in the field, we partner with nonprofit organizations, for profit companies and research institutions to develop treatments as quickly as possible. Game-changing work is in progress and innovative therapies are emerging. Our nimble, sustainable model allows us to both fund a broad range of research and target the most likely to succeed.

When we make a research grant, we retain or influence intellectual property rights, which generates a recurring revenue stream if the therapy or product is commercially successful. That money is then used to fund additional research.



**It's about the most insane skin disorder you can imagine. And when you realize it also affects the internal organs, then you see it as diabolical.”**

**eddie vedder, ebrp co-founder**

**BY THE NUMBERS:**

**30,000**

Estimated number of people with EB in the United States

**5,400+**

EB shares a common genetic platform with more than 5,400 other ailments

**THREE MAJOR SUBTYPES OF EB:**

1. **Simplex:** Related to the protein keratin
  2. **Dystrophic:** Collagen Type VII, or C7, is missing
  3. **Junctional:** The protein laminin-332 is missing
- 

# every day enemy: epidermolysis bullosa (EB)

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**Epidermolysis Bullosa is a group of life-threatening skin disorders that occur in the absence of a protein that binds skin together. EB can be evident from the moment a baby is born. Blisters form and skin comes away at the softest touch. Soon, all the joyful milestones of early life – learning to crawl, walk, talk and play – also bring anxiety.**

Children with severe forms of EB must be continually aware that even gentle contact can harm their skin. Hugging, picking things up, standing, sitting, even sleeping – anything that creates friction. Regardless of how careful they are, those with EB can also experience alopecia, nail dystrophy, corneal abrasions and wounds to internal organs. Because food can damage esophageal tissue they struggle to eat and drink. Their skin is extremely sensitive to hot and cold. Their bodies lose fluids easily, they have chronic blood loss and dental problems. The frequent skin injury and impaired ability to heal result in scarring. The process of break and repair between their fingers and toes causes mitten deformities and loss of dexterity. With persistent wounds, they are highly vulnerable to infections and aggressive, metastatic and lethal skin cancers.



**Even though EB is so obvious on the skin – so visible and painful – it is not a local disease. These children are sick throughout their bodies.”**

**dr jakub tolar, md, phD**



one mutation

In normal skin, collagen type VII forms the “velcro” that holds certain layers of the skin together. When a mutation occurs with the gene encoding these molecules, the collagen is either diminished or absent. This disrupts what one leading researcher describes as the “body’s biological Velcro” and results in RDEB.



one  
day  
at a  
time

for patients and families,  
an excruciating routine

# every day: a fragile situation

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## reid

Brian and Audra Underwood of Atlanta had no reason to expect anything would be wrong with their third child when he was born. They were shocked when they saw Reid was missing a large portion of skin on his right leg, his left foot and the backs of both hands. Just as surreal was the reaction of the doctors.

“It was the craziest thing to see staff at a big Atlanta hospital looking through textbooks, trying to figure out what was wrong with our son,” Brian said.

Reid’s case was dire. His parents couldn’t put him into a car seat without damaging his skin. He couldn’t even wear clothes. A doctor in their family encouraged them to contact Dr. Jakub Tolar at the University of Minnesota, who was in the midst of a Phase II trial involving a high-risk bone marrow stem-cell transplant for young EB sufferers.

Reid had the transplant in December, 2014. The process took several months of preparation, starting with the extraction of healthy marrow from the hipbone of a sibling. Reid’s sister Avery, who was four at the time, was his donor. Her marrow, mixed with her blood, was eventually delivered through a catheter into Reid’s heart.

Some of Reid’s chronic wounds showed dramatic improvement within a month. His skin still damages, and he suffers from itching, but he now eats soft foods and is able to venture out a little bit with his family. He loves to play with his brother and sister. “We have to reel them in sometimes, but they’re very good with him. They know how fragile he is,” Brian said. “Their lives are very affected. We couldn’t just pick up and go to a baseball game.”

Now that they are able to go out sometimes, the whole family is learning how to deal with the stares Reid inevitably attracts. “It’s a learning process for us,” Brian said. “You wish EB was more widely known.”



reid's parents,  
audra and  
brian underwood

“

Yes, a transplant may be risky. But living a life with EB is pretty risky, too.”



“Audra has to be with him all day. She is essentially the only person who can take care of him.”



# one focus



Parents of Dr. Tolar's young patients appreciate not only his research, but his special rapport with their children.

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## university of minnesota

**By advancing the stem cell treatment for children with severe forms of EB, Dr. Jakub Tolar hopes to provide the first systemic treatment for the disorder.**

The procedure, a bone marrow transplant, aims to correct the deficient protein – collagen laminin, integrin or plakin – and reduce skin fragility. Dr. Tolar hopes that the healthy cells will continue to circulate, regenerate and stay with his patients their entire lives.

But the work does not stop there. Dr. Tolar is applying what he's learned from transplants to develop an innovative gene therapy treatment for EB. He is optimistic that improvements to this approach will enable a new level of systemic treatment that utilizes a patient's own corrected cells. This is the groundbreaking research that EBRP is supporting.

"Ten years ago I would not have thought it was possible to shift our focus to more targeted treatments using the patient's own cells," he said.

To date, none of the therapeutic approaches developed by EB researchers across the U.S. have been completely successful. The potential for a cure most likely lies in a combined approach of both local and systemic therapies, individualized to specific patients.

"The key is a broader platform of combination therapy, brought about by the collective intelligence and collaborative work of investigators in EB research," Dr. Tolar wrote in a recent article published in the *New England Journal of Medicine*. "In this scenario of the future, additions or corrections to COL7A1, which is the replacement of C7 protein, and cellular therapy would be applied locally or systemically, once or serially, alone or in combination with other interventions that cooperatively establish a portfolio of options enabling truly personalized and clinically meaningful changes in the practice of medicine for children and adults with RDEB."



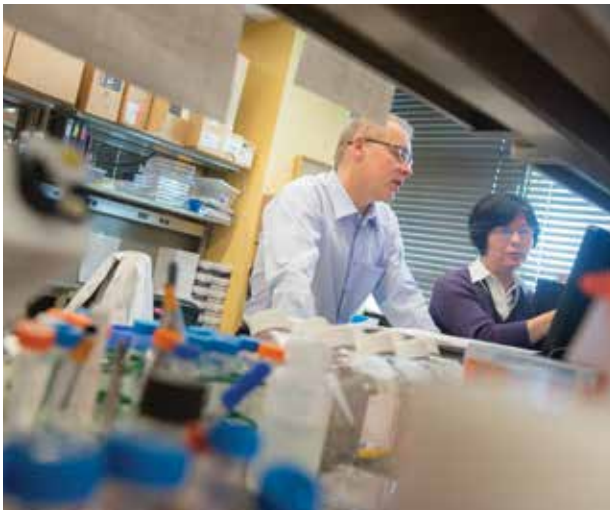
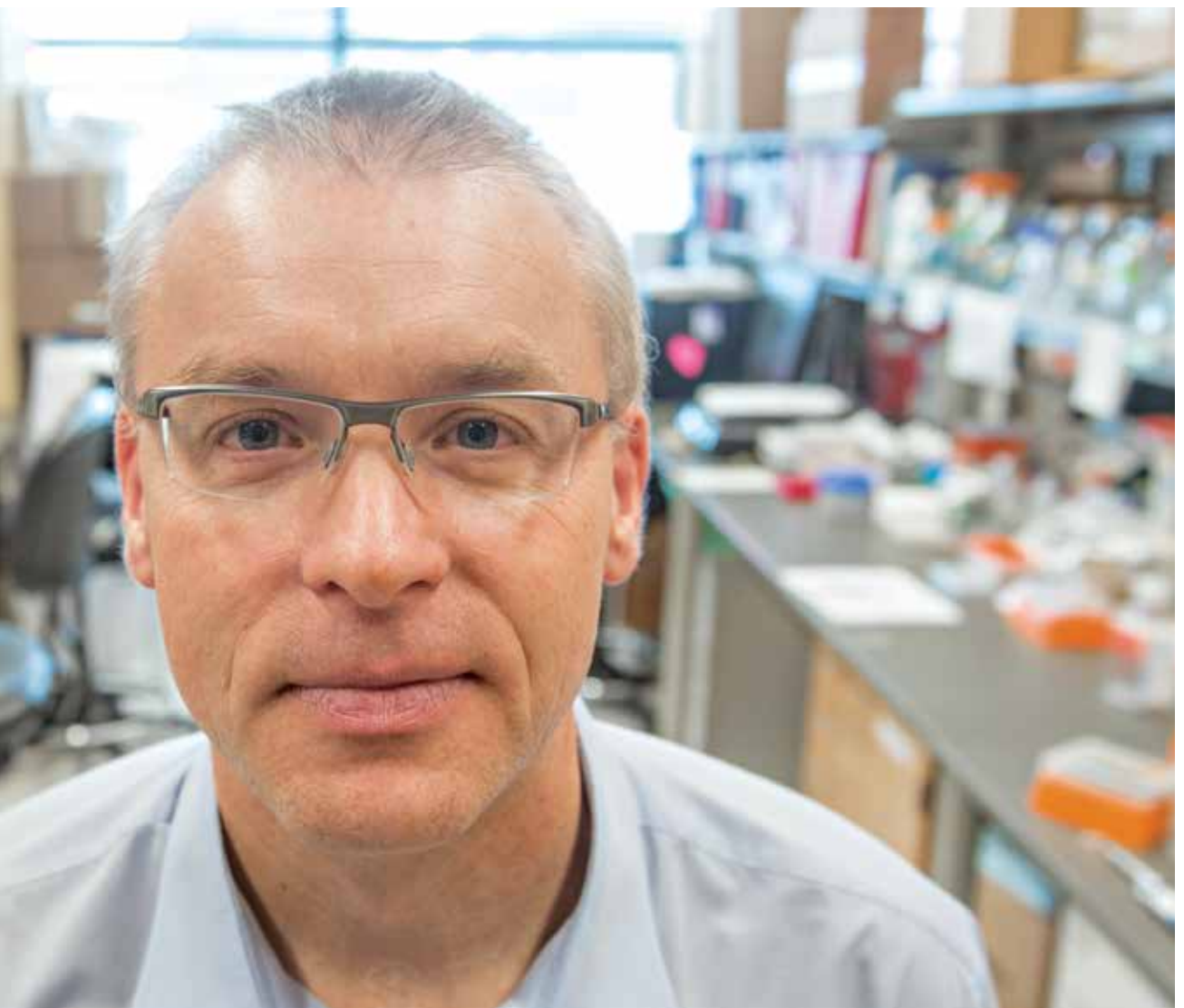
**Jakub Tolar, MD, PhD**  
distinguished McKnight professor,  
department of pediatrics  
Tulloch chair in stem cell biology,  
genetics & genomics  
director, Stem Cell Institute  
University of Minnesota



**Some of these individuals cannot wait a decade or two for the next breakthrough. We are in a position to develop treatments collaboratively and bring them to the next level.**









# every day: a positive attitude

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## paul

Paul Martinez knew better than to hope for too much when he qualified for a Phase 1 clinical trial to test the safety of a new gene transfer technique at Stanford University in late 2014. He was already an old man in the EB world, a guy who had far exceeded his life expectancy.

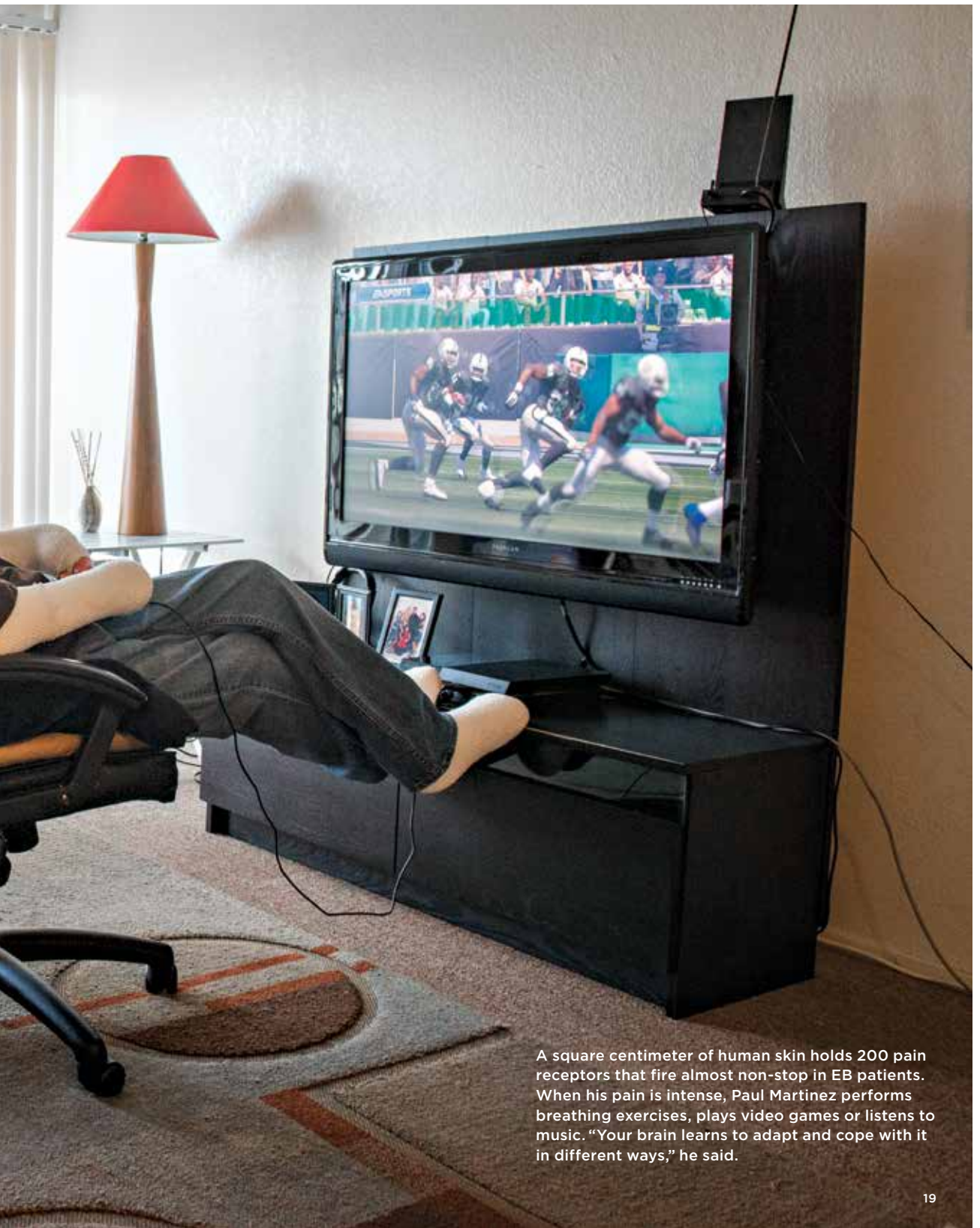
Paul, who is now in his 30s, has always lived about an hour and a half away from Stanford. When he was born with severe EB, doctors in his hometown of Stockton, California did not expect him to survive more than a few years. He was six when researchers at the university established one of the nation's leading EB clinics, aiming to develop genetic treatments, but there were research protocols and regulations to meet, labs to build, mice to test – a process that can take decades. Stanford's doctors tried to slow the mitting of Paul's hands when he was 10, but the deformity seemed inevitable, so he didn't go back for a repeat procedure in his teens. His last working finger disappeared when he was 25. It's still there, but trapped, as if inside a cocoon.

The gene transfer process took several months, as the researchers took biopsies of his skin, attached a vector virus to C7 cells that "corrected" them, grew out playing-card sized patches in the lab, then grafted the patches onto five of Paul's many dozens of existing wounds and one onto a test wound they created. He believes his skin heals faster where the grafts adhered. But that's not why he participated. He just wanted to help the next generation of EB patients, he said. "No one should have to live with this."

Paul feels every wound on his body, every minute of every day. And he doesn't take pain medications. "It dulls you," he said. "I might not have been blessed physically, but I feel I've been blessed mentally, and I don't want to lose my mind. In a psychotic way, I'd rather feel pain because it makes me feel alive."

**"I don't know the sense of normal. Every second of my life has been pain. Taking a shower is one of the most grueling things. It feels like needles hitting your skin."**





A square centimeter of human skin holds 200 pain receptors that fire almost non-stop in EB patients. When his pain is intense, Paul Martinez performs breathing exercises, plays video games or listens to music. "Your brain learns to adapt and cope with it in different ways," he said.

# one hope, multiple therapies

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## stanford university

**A team of researchers in the department of dermatology at Stanford University has dedicated more than 20 years to improving life for those with EB.**

“We’re stepping up to the plate and taking as many swings as we can, to develop as many therapies as we can,” said Dr. Anthony Oro.

Dr. Al Lane, who led the program for many years, said the most recent strides involve the use of inducible pluripotent stem cells, or iPSCs, that can be genetically reprogrammed to produce healthy organ tissue, including skin.

“The important thing is that we have a pipeline, and we are trying to develop multiple therapies,” said Dr. Jean Tang, who leads the clinical trials and manages the regulatory side of EB research. Her next Phase 1 trial involves protein therapy in which normal C7 will be injected near wounds. She is also testing a pill and a topical cream that could relieve itching.

Those therapies were tested first with animal models in the laboratory led by Dr. Peter Marinkovich. His current projects include making C7 protein and working with corporate partners to develop a shelf-stable delivery method for protein therapy that will release C7 locally through dissolvable “micro-needles.” Collaborating with the EB Research Partnership and Dr. Vicki M. Chen at Tufts University, Dr. Marinkovich’s lab is also manufacturing C7 protein for eye drops that could help young EB patients with corneal abrasions.

Dr. Oro’s lab performs genome editing and tissue engineering for EB trials. His goal is to use patients’ own tissue, correct it or make it better, and put it back on. “With genome editing, you can correct the DNA so that an EB patient’s genes no longer have mutations. And if you can make enough, you have a lifetime supply of tissue,” he said.



**al lane, md**  
professor of dermatology and pediatrics, emeritus  
lucile packard children's hospital at  
stanford department of dermatology



**jean tang, md**  
associate professor of dermatology



**peter marinkovich, md**  
associate professor, director, blistering disease clinic  
department of dermatology



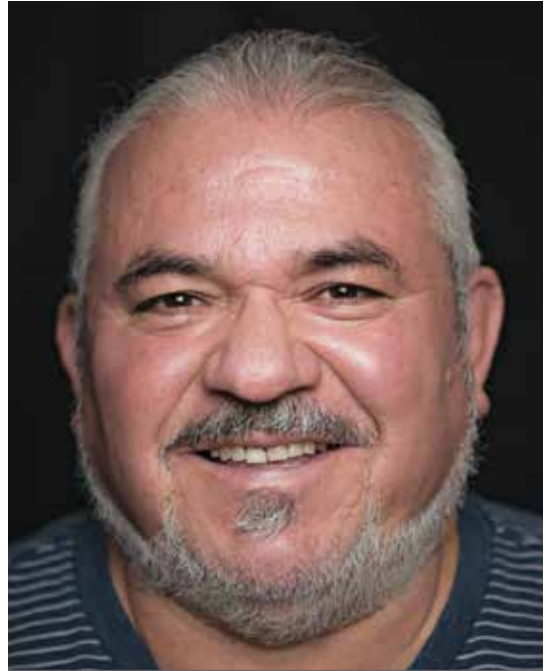
**anthony oro, md, phd**  
professor, program in epithelial biology

jose



## every day: a family copes

fernando



the chavez family

For Fernando and Lourdes Chavez and their three grown sons, every day is an exercise in patience, love and surviving together. Brothers Jose, Abraham and Marlon all have RDEB. Jose and Abraham, the first two participants in Stanford University's skin grafting trial, both attend City College. Jose studies bioengineering and Abraham's courses include nutritional education and graphic design. Marlon is in high school and enjoys helping his dad rebuild cars. The Chavez family tries hard to live normally. "Everything is not negative," Fernando says. "There are many positive things about these guys."



**abraham**

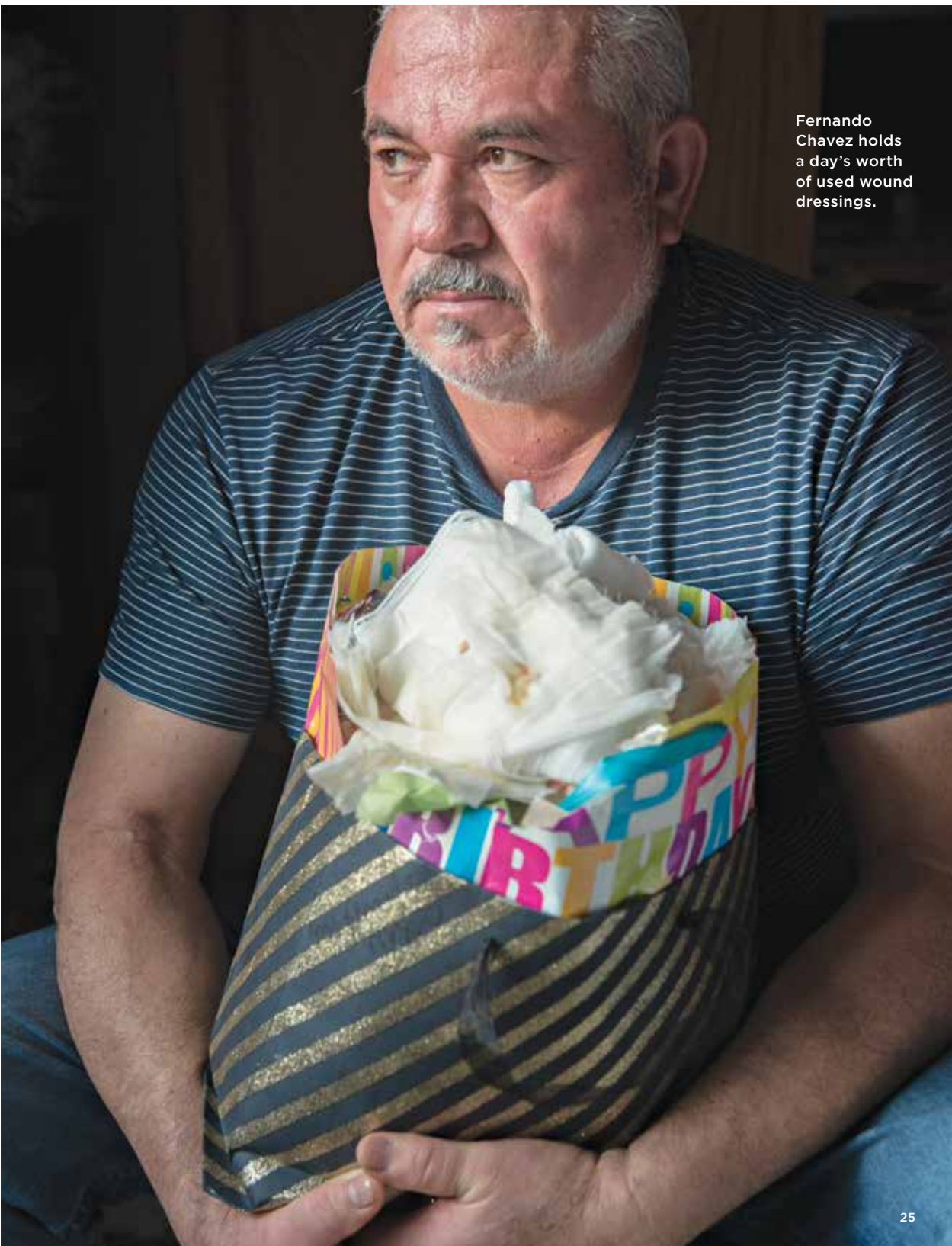


**marlon**



Most of us relish the comfort of sinking into bed each night. But an EB patient's skin can bleed and blister even from contact with the softest sheets. Jose Chavez often wakes up in the mornings with a soiled pillow.





Fernando Chavez holds a day's worth of used wound dressings.

One day's dressings: To help protect skin from trauma and promote wound healing, EB patients need an arsenal of specialized medical supplies that can cost as much as \$14,000 per month.

Fernando Chavez estimates how many of these supplies he uses daily for his three boys:

**8**

1/16"-thick foam Mepilex Transfer pads to cover shoulder wounds

**12**

1/8"-thick Mepilex pads for back and chest wounds

**12**

6"x36" sterile petrolatum Vaseline gauze pads for large wounds (1 box)

**24**

3"x36" sterile petrolatum Vaseline gauze pads for small wounds (2 boxes)

**3**


25-gauge needles to puncture new blisters so they won't grow

**6**

4"x4" gauze sponges for cleaning wounds

**12**

Rolls of 2", 3" and 4" gauze to hold bandages in place



Caregivers of EB patients build their wound protection and healing regimens from an array of commercially available bandages, topical ointments and dressings, based on personal preference and pain tolerance. After they cleanse wounds, they usually apply a topical moisture or antibiotic ointment. A “contact” dressing allows fluids to drain. A secondary dressing adds padding. A third, elastic layer of gauze helps to keep the other dressings in place. Adhesive tape or ordinary bandages would tear the skin.

Fernando spreads healing ointment on a layer of gauze for one of Marlon’s elbows. He saves time by preparing bandages in multiples rather than treating one wound at a time.

Mepilex foam pads help cushion damaged skin from further trauma.

Hydrogen peroxide and antibiotic ointments (generally Aquaphor, but something stronger, like Bacitracin, for open wounds), are often mixed with a custom herbal compound of medicinal plant powders.



**Zurab Siprashvili and Ngon Nguyen lead the team that is growing skin for grafts in Stanford's gene transfer trials. It is the hope that Phase II trials will allow participants as young as 13 to receive the transfers as the researchers focus on the treatment's efficacy.**

---

**ngon nguyen, bs** (left)  
life science research professional III

**zurab siprashvili, PhD** (right)  
senior research scientist

Stanford's clinical researchers grow patches of skin for experimental treatments from cellular tissue in a sterilized "clean room" purpose-built for the job. Starting with small skin biopsies from a participant that yield several million keratinocytes, or skin cells, scientists infect the isolated cells with a genetically-engineered virus that carries the corrected gene. They continue to manipulate the microscopic cells, coaxing them to grow into opaque sheets of healthy skin. About three weeks later, after the new skin tissue is tested for safety, a delicate dance ensues: The sheets must be delivered to the operating room and grafted onto the patient's skin within 24 hours.



Jose Chavez was the first participant in Phase I of Stanford's gene transfer trial, which aimed to show that the procedure was safe. His arm (inset) shows improvement in the area where it received a graft. The healthier patch also appears to stop the spread of adjacent wounds. While not a cure, gene transfers can modify the effects of EB.

# every day: a determined spirit

---

## darren

He's all boy. He wants to play baseball. He jumps on a trampoline and also has a swing set in the back yard. He wants to wrestle his older brother. Recently he also started to love skating, even though a fall gave him a wound that didn't heal for two and a half weeks. That meant especially painful bandage changes. He said it was worth it.

Darren Martinez doesn't let RDEB slow him down, said his mother, Krystal Martinez. That makes her nervous, but she's torn because she also wants him to be happy. "If he gets hurt, we patch him up," she said. "He goes through cycles of pain, but it's what he wants to do."

Blood flowed from Darren's mouth when he was born, and skin on his hands and feet sheared away as doctors rushed him to a neonatal intensive care unit. The first time his mother saw him, about six hours later, her second son was bandaged from head to toe. His fingernails and toenails fell off within his first week. But Krystal and Michael Martinez feel lucky that they live near Children's Hospital Colorado, where a team of doctors trained in EB treatment now oversee every aspect of Darren's ongoing care. It takes a village: A gastrointestinal specialist, an anesthesiologist, two primary care doctors, a dermatologist, an ophthalmologist and a dentist.

Darren needs to have his esophagus cleared every three to six months. His eyes often get abrasions in the middle of the night, so he can't open them for a day or two afterward. He uses a wheelchair at school because he tires easily.

In spite of it all, Darren doesn't focus on EB, and he has a very big heart. Writing a school essay recently about his hopes and dreams, he didn't mention his disability: He expressed concern for kids who don't have families. He wants to be an art teacher when he grows up. He's really good at drawing.

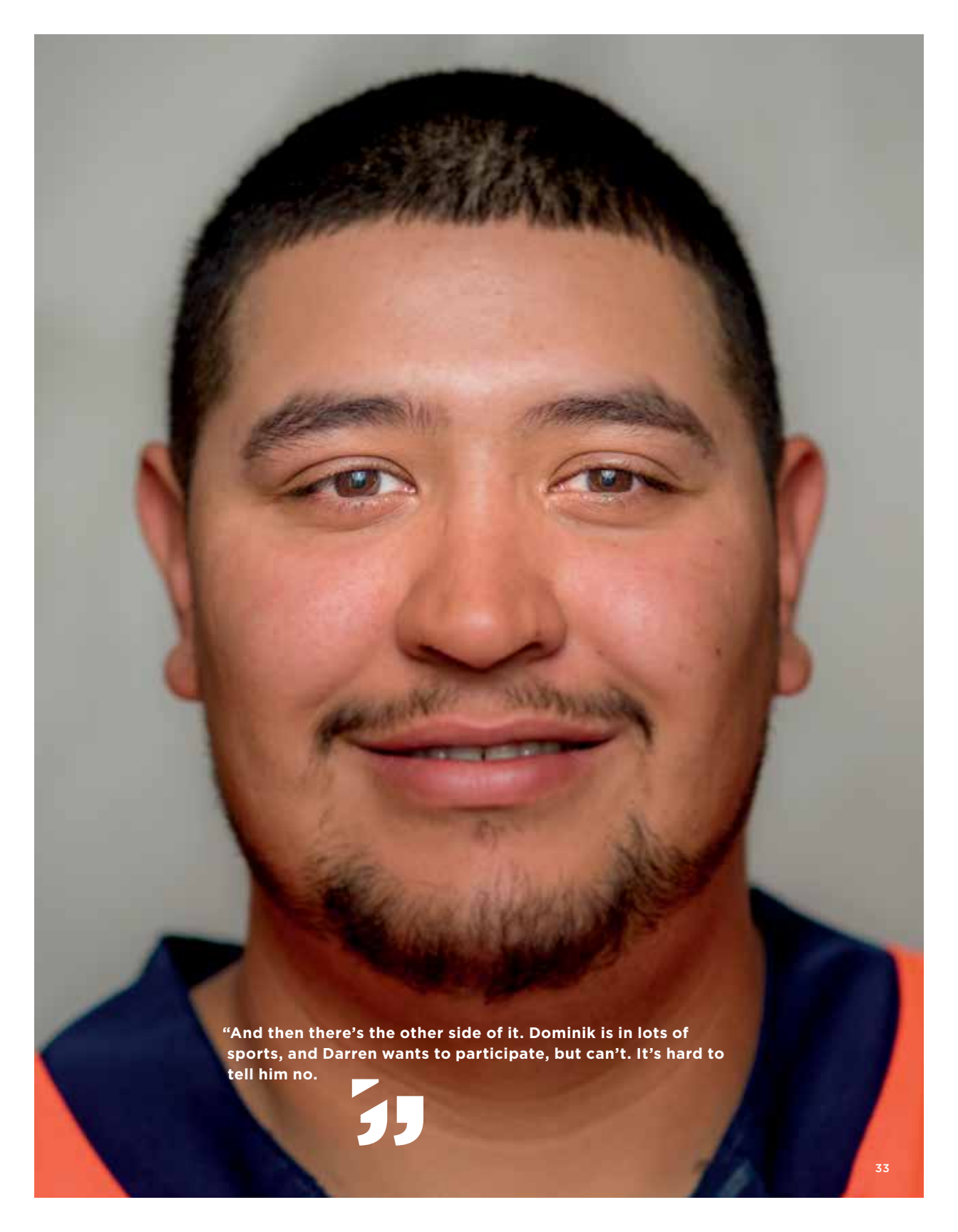




darren's parents,  
krystal and  
michael martinez

“

**It's hard to find a balance when you have one healthy child and one with EB. Our older son, Dominik, feels left out, not because we don't care about him but because Darren requires so much medical attention.”**

A close-up portrait of a man with short, dark hair and a goatee. He is looking directly at the camera with a slight smile. He is wearing a dark blue shirt with orange accents on the shoulders. The background is a plain, light-colored wall.

“And then there’s the other side of it. Dominik is in lots of sports, and Darren wants to participate, but can’t. It’s hard to tell him no.

”



**“I have to step out because I get emotional,” Krystal said. Her son’s screams are too hard to bear.**

this is **one** reality of EB.





On a good day, Darren's bandaging routine takes about 90 minutes. He endures more - up to 3.5 hours - on bathing days and during the summer, when he gets hotter and sweats, and bandages slide off easily.

"As he's grown, we've got the routine down. But he's also more active, so there are more wounds to cover," said Krystal Martinez.

Darren needs to be bandaged from head to toe while he is participating in a study for a promising new wound healing and itch-reducing ointment, SD-101, by Amicus Therapeutics. His parents apply the cream to his body before the usual layer of Aquaphor and bandages.

Darren enjoys a playful moment with his dad, Michael Martinez. His itching and wounds have decreased significantly since he has been treated with the new SD-101 ointment.

hope is real too –  
and it is part of  
**every**  
single **day.**





Every day, people with EB face obstacles that could be diminished – or overcome entirely – when a cure for the disorder is achieved. We asked them how they would measure progress from a successful treatment. Here's what they said:





"I wish my son could do something spontaneously,  
so he wouldn't have to decline invitations  
from friends because he was in the middle of a bath  
or getting fed through his G-tube.  
He never tells friends why he can't make it.  
He just says he can't."



"I would measure progress by the act of sitting.  
I dream about my son sitting in a chair without pain and injury  
to his back and thighs."



"I would rejoice if he were able to use his hands for writing in school or to feed himself."



"My daughter loves to sing and also loves to be in the water. To be able to swim is her dream. Progress would mean healing her esophagus and removing her tracheotomy tube. Then she could sing like an angel and swim like a mermaid."



"I would watch him carry his backpack without getting blisters."



"I would echo his excitement for activities he loves instead of having to temper his expectations."



"Recently my little girls had their dance recital. I kept wishing their costumes could have covered the bandages that showed through their fights. I know it's not an everyday thing, but they should enjoy those great moments EB free. And they love shoes. I wish they could wear the sparkly dress shoes that light up their eyes."



"Everything in my life would be better. I can't think of one thing. It would mean every single aspect of my life would be better."



"I would be able to brush my son's teeth without tearing his gums."



"Progress would be wearing jeans. I can't wear them because the seams tear the skin off my body."



"Progress would mean time. I would like to have more time to be a mother. The constant preparation of medications, bandages, nutrition and ointments is relentless. EB robs our family of quality time together. I miss being 'just a mom.'"



"I want to be able to participate in more things. EB is so much of me."

# one strategy: support multiple, collaborative solutions

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**On the forefront of supporting the new paradigm of collaborative “team science,” the EB Research Partnership partners with non-profit and for-profit entities and individual donors, as well as with the EB and research communities, to co-fund the development of treatments that address the gamut of issues facing those who suffer from EB.**

Our projects are helping EB investigators find a cure for the disorder faster than they could with a traditional, siloed research approach that can consume decades before treatments are brought to the market. In a world where NIH funding is rare, this kind of progressive collaboration is increasingly important.

EBRP helped create and continues to support research enabling infrastructure to ensure that treatments will get to those in need as swiftly as possible.

Among EBRP’s projects:

- **The iPS Cell Consortium.** Researchers at Stanford University, Columbia University Medical Center and the University of Colorado Anschutz Medical Campus are collaborating on the development of one of most promising therapies for EB - the manufacture and delivery of induced pluripotent stem (iPS) cells - reprogrammed cells that can be generated from a patient’s own body.
- **Protein replacement therapies.** A world-wide, multi-center study led by the Hospital for Sick Children, Toronto to examine the treatment of esophageal strictures, one of the most common gastrointestinal complications for those with EB.

With Tufts University, Boston, we are testing the feasibility of an eye drop that could deliver C7 to the eyes to reduce or prevent the corneal abrasions that cause vision loss in up to 40% of those with EB.

- **Novel use of antibiotics.** With the University of Southern California, Los Angeles, we are supporting a pilot clinical trial to test the use of gentamicin in EB patients. This aminoglycoside antibiotic is known to suppress genetic mutations and restore protein synthesis in the treatment of other genetic disorders.
- **The Epidermolysis Bullosa Clinical Research Consortium.** This group of 16 institutions conducts multi-site, clinical and translational research in EB. It is developing the infrastructure necessary to enhance collaborative multi-site clinical research and to secure funding for additional translational EB research.



**The EB Research Partnership co-funds all of these projects with the Epidermolysis Bullosa Medical Research Foundation.**

# one goal

eb research partnership (ebrp)

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#### **VENTURE PHILANTHROPY**

When we make a traditional donation to a research project, we retain the added upside of generating a recurring donation stream. If the therapy or product that is developed becomes commercially successful, we employ that revenue to fund additional EB research.

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# **Leading researchers say treatments and a cure are within reach.**

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**Every day, Reid, Jose, Abraham, Marlon, Paul, Darren and all the others suffering from EB have reason to feel hope.**

The potential for successful treatment is astounding. More EB trials are anticipated in the next three years than have taken place in the last 10 combined.

An army of professionals is working across America to help, including physicians and researchers at Children's Hospital of San Antonio, Cincinnati's Children's Hospital Medical Center, Columbia University, Dell Children's Medical Center, Austin, Henry Ford Hospital in Detroit, Northwestern University, Phoenix Children's Hospital, Sainte-Justine Hospital University Center (Quebec), Stanford University, Toronto's Children's Hospital (SickKids), University of California San Diego, University of Colorado, University of Massachusetts, University of Miami, University of Minnesota and Washington University.

# one ask

help us find a cure



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# Right now the biggest obstacle to finding a cure for EB isn't science. It is money.

---

**While life-altering treatments are on the horizon, EBRP's venture philanthropy model is critical to realizing those advancements.**

We facilitate partnerships between academic institutions and for-profit companies in ways that speed the time to market for treatments. And if a therapy or product is commercially successful, our interest generates recurring revenue for additional EB research.

Your generous donation has the potential to fund multiples of its original value, for years to come - not just to cure EB, but to cure hundreds of other genetic diseases with the knowledge gained in EB-related studies.

**Find a Cure.  
Heal EB.**

**(212) 554-1467**

**www.ebresearch.org**

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email:

**info@ebresearch.org**

**Every day  
we work  
so that  
EB will be  
no more.**

**One day,  
with your  
help, we  
will cure  
EB.**

sappi | ideas  
that  
matter

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