Vol. 8 No. 2, Winter 2007

Packard Children's NEWS

Lucile Packard Foundation for Children's Health

Inside:

The Promise of Regenerative Medicine

New Dialysis Center Opens

Lucile Packard
FOUNDATION *for Children's Health*

Dear Friends,

You may have read recently that Packard Children's once again has been named to the Top 10 list of U.S. children's hospitals by *U.S.News & World Report*, and ranked No. 1 in California. This national recognition results from the Hospital's innovative work, which is supported by your philanthropy.

In this issue of *Packard Children's News* we focus on one of those areas in which our Hospital is leading the way: regenerative medicine. This evolving field pursues therapies that will enable the body to repair, replace, and restore diseased cells, organs, and systems. One center of this work is our new Stanford/Packard Program in Cardiovascular Regenerative Medicine, where scientists are exploring how tissue engineering can be used to treat congenital heart defects and other cardiovascular diseases.

Regenerative medicine also may help address epidermolysis bullosa, an agonizing disease in which a child's skin is unable to withstand normal stress, and blisters easily. Researchers are using a promising experimental technique known as gene therapy—inserting normal copies of the defective gene into skin cells in the lab, and then grafting those cells back onto the wounds—to restore normal adhesion between the skin layers.

In another example, regenerative medicine illustrates the contributions made by the postdoctoral fellows who work in our clinical research laboratories. Former postdoc Karen Liu, PhD, identified the exact window of time when cleft palates and sternum clefts occur in mice. The molecular mechanisms that she identified one day may allow scientists to correct these conditions in a human fetus before birth.

Also in this issue, we highlight Packard's new 3,000-square-foot dialysis unit, which opened this spring. Expanded in size and featuring the latest equipment, this outpatient facility is designed to make our patients' treatment not only effective, but also as pleasant and comfortable as possible.

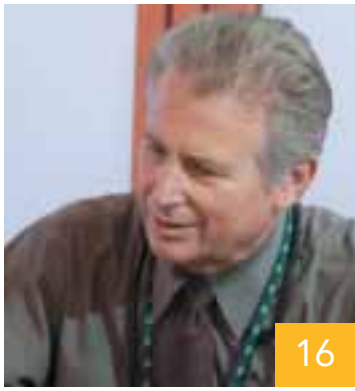
All of these innovations, which are made possible by your generosity, improve the health of children and help keep Packard in the top tier of children's hospitals. We are grateful for your ongoing support.

Sincerely,

David Alexander, MD
President and Chief Executive Officer

Packard Children's NEWS
Vol. 8 No. 2, Winter 2007

Contents



PACKARD Children's News is published by the Lucile Packard Foundation for Children's Health, an independent public charity incorporated in 1996. For more information about the Foundation, call **(650) 497-8365** or visit **www.lpfch.org**.

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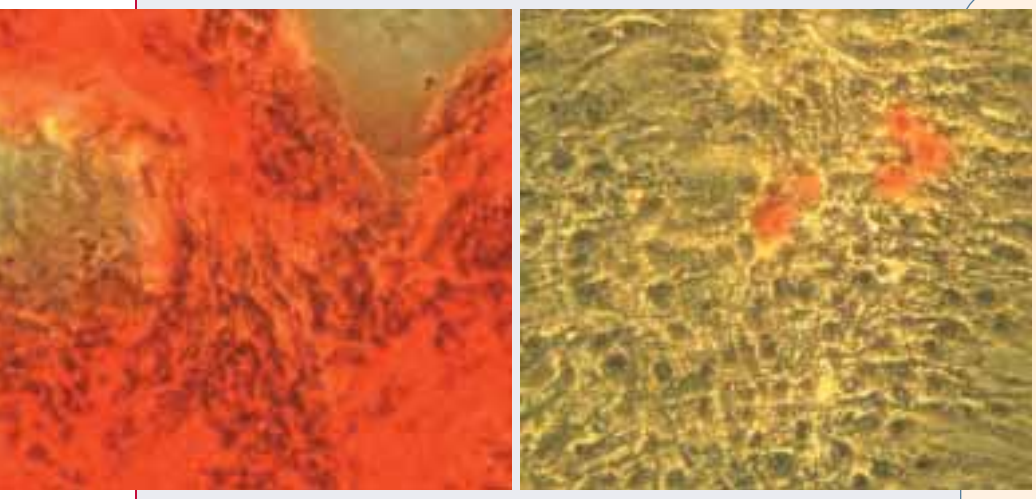
Cover: Three-year-old Noelle Takagi and mom, Matsumi.

The Promise of Regenerative Medicine

by Mark Shwartz



These images show stem cells grown in culture to produce mature bone marrow, as indicated by red staining (left). Loss of function of the retinoblastoma (RB) tumor-suppressor gene in the cells blocks their maturation (right), possibly explaining why RB deficit is an initiating event in pediatric bone cancers.

> "Many genetic diseases of tissue and organ failure begin in children. Therefore, children are the most likely recipients of stem cell or regenerative medicine therapies."
>
> ■ Irving L. Weissman, MD, the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research

Imagine a time when laboratories can grow healthy hearts for children in need of cardiac transplants. Or picture a future in which pediatricians treat severe skin diseases by grafting genetically engineered skin cells onto the patient's body. And what if doctors had the ability to prevent the formation of cleft palates and other birth defects while the baby is still in the womb.

These distant scenarios are coming closer to reality, thanks to pioneering research in stem cells and regenerative medicine now under way at Stanford University and Packard Children's Hospital.

"Stem cell biology and regenerative medicine are fundamental to our understanding of human development," says Philip A. Pizzo, MD, the Carl and Elizabeth Naumann Professor and dean of the Stanford School of Medicine. "How cells, organs, and systems are formed and regulated, how they are sustained and overcome injury with repair, and how they might go awry in the case of cancer are among the fundamental questions we are now addressing."

This promising new field also offers many potential benefits for pediatric medicine. "Congenital malformations of the heart, lungs, and nervous system are major causes of disease and death during the first years of life," Pizzo says. "The knowledge gained from stem cell biology and regenerative medicine may help us better understand how some of these abnormalities arise, and could lead to new ways to repair damaged organs and systems—even during fetal development."

To illustrate the university's commitment to this emerging field, Pizzo points to the creation of the Stanford Institute for Stem Cell Biology and Regenerative Medicine in 2005. The Institute is led by Stanford's Irving L. Weissman, MD, the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research and professor of pathology and of developmental biology.

"Many genetic diseases of tissue and organ failure begin in children," Weissman says. "Therefore, children are the most likely recipients of stem cell or regenerative medicine therapies."

An internationally recognized leader in developmental medicine, Weissman was the first scientist to isolate animal stem cells, in the 1980s. Today, he and his Institute colleagues are expanding that groundbreaking work to include human embryonic stem cells, which have the potential to regenerate tissues and organs, and to cure cancers and genetic diseases such as Alzheimer's and Parkinson's.

In November 2004, Stanford and other medical research institutions in California received a tremendous boost when voters passed Proposition 71, providing $3 billion over 10 years for statewide stem cell research. So far, the Stanford Institute for Stem Cell Biology and Regenerative Medicine has received more funding than any other institution—nearly $29 million, of which more than $1.8 million has been awarded to three faculty members in the Department of Pediatrics:

- Mark A. Kay, MD, PhD, the Dennis Farrey Family Professor in Pediatrics and professor of genetics
- Kenneth Weinberg, MD, the Anne T. and Robert M. Bass Professor in Pediatric Cancer and Blood Diseases
- Julien Sage, PhD, assistant professor of pediatrics and of genetics


Mark A. Kay, MD, PhD


Kenneth Weinberg, MD


Julien Sage, PhD

"One way to enhance adult and embryonic stem cells so that they are resistant to viral infections is through genetic modification," Weissman says. "Mark Kay is one of the leading investigators in the world in this area. Ken Weinberg is a world leader in finding out how certain types of blood stem cells can regenerate the immune system rapidly and effectively. Julien Sage is a promising young investigator studying cancer gene pathways in cancer stem cells."

A great deal of fundamental research will be needed to make the promise of stem cell and regenerative medicine therapies a reality for patients, Pizzo adds. "This will require time, careful study, and, of course, resources," he says. "But the extraordinary research at Stanford and the plethora of biotechnology in our surrounding communities will one day provide unique opportunities to translate laboratory discoveries into therapies for children who truly need them." ●

A Change

# of Heart

by Ruth Schechter

"So many lives could be dramatically improved by being treated with living, growing tissue rather than through surgery."

■ Frank Hanley, MD, director of the Children's Heart Center at Packard and the Lawrence Crowley, MD, Endowed Professor in Child Health

Frank Hanley, MD, (right) delivered a new valve to Noelle's heart on a catheter, avoiding the need for a transplant or open heart surgery.

Three-year-old Noelle Takagi goes to summer camp, loves to play in the water, shows a knack for drawing, and sings a mean karaoke. To her parents, these activities are genuine miracles.

Noelle was born with a defective aortic valve that required open-heart surgery when she was 10 days old. At nine months, her replacement valve started leaking, and she faced the prospect of an innovative but difficult valve replacement surgery or a transplant that had a 50 percent survival rate after five years. "I believe we made the right choice, but we appreciate that the doctors gave us an option," says her father, Naoyuki Takagi.

Noelle's valve replacement surgery made headlines because she was the youngest person to undergo a unique procedure that used a catheter to position the valve without opening her chest. While the results have been positive, she still will face additional surgeries as she grows older to replace the outgrown valve.

Each year about 40,000 infants are born with a heart defect in the United States. While new technology and surgical innovations have made a tremendous difference in the outcome and quality of life of these young patients, the harsh reality remains that an infant born with congenital heart disease often faces a future of repeated surgeries to replace an outgrown valve or one that has deteriorated from use.

But breakthrough insights in stem cell biology and tissue engineering are pointing to a day when that situation finally may change. Research indicates that stem cells could play an important role in repairing damaged hearts, and that tissue engineering someday could be used to regenerate malformed or missing heart tissue.

Noelle Takagi with her parents, Naoyuki (left) and Matsumi.

Building a Better Valve

Approximately eight out of every 1,000 children are born with a congenital heart condition. While these problems still can't be prevented, great strides have been made in diagnosing and treating heart defects.

Defective heart valves usually are replaced with a mechanical heart valve made of plastic or Dacron, or of biologic material taken from a pig, cow, or deceased human donor. Like a normal valve, the replacement valve opens and closes with each heartbeat, permitting proper blood flow through the heart. After surgery, patients must take anticoagulant medications to prevent blood clots, and a child may face a half dozen or more operations over his or her lifetime.

An alternative involving tissue engineering would allow doctors to use a simple procedure to induce stem cells to specialize into a new heart valve, ready to place in the infant at birth. Because the valve would be living tissue derived from the baby's own cells, it would grow and repair itself, and the child's immune system would accept the material as its own.

Both Hanley and Longaker emphasize that there are many questions to answer before it will be possible to construct and introduce a replacement organ like a heart valve. Laboratory conditions cannot duplicate the complexity of a human being, and many factors involved in how cells differentiate and specialize still need to be clarified.

Packard physicians and Stanford scientists are developing a new **Program in Cardiovascular Regenerative Medicine** to apply the great potential of tissue engineering toward the creation of new ways to treat congenital heart defects and other cardiovascular diseases.

"Regenerative medicine is a relatively new field, and we are still defining the niche areas that may have the highest impact," says Frank Hanley, MD, director of the Children's Heart Center at Packard and the Lawrence Crowley, MD, Endowed Professor in Child Health. "But the promise is immense, and so many lives could be dramatically improved by being treated with living, growing tissue rather than through surgery."

Hanley and program co-director Michael Longaker, MD, director of the Children's Surgical Research Program and the Deane P. and Louise Mitchell Professor in the School of Medicine, are helping to coordinate the work of Packard's heart specialists with Stanford's basic and clinical science investigators. While researchers continue to make great headway into the basic biology of stem

cells and the process by which they differentiate and specialize, Packard physicians are identifying the most pressing needs and potential strategies to improve care for children with heart conditions.

"At this point there is almost no heart defect we can't repair with surgery. But there are limitations: prosthetic valves must be replaced as the child grows older, and transplanted tissue tends to deteriorate over time," says Hanley. "But that's what we have to work with in terms of reconstruction—we can't make something out of nothing."

An additional problem is that heart tissue is subjected to ongoing stress and strain: a valve, for example, moves 60 to 80 times each minute.

These challenges make a coordinated, collaborative effort all that more important, says Longaker. "While growing a replacement organ is still at least a decade away, the program may help get us to that point. It is designed to incorporate some of the most promising biomedical research under way into a comprehensive program that will accelerate the process of designing —and applying—new therapies."

What makes the program unique and particularly promising, he adds, is its breadth of expertise. As part of Stanford's Institute for Stem Cell Biology and Regenerative Medicine, the program integrates specialists from throughout the university, from chemists and biologists in the School of Humanities and Sciences to experts in business, law, engineering, physics, and biomechanics.

"The program extends far beyond the boundaries of the medical center," says Longaker. "The problems we need to solve come from the clinic, but the answers may come from some unexpected source. That's why it's so important we involve the entire university and organize teams: the answer is far beyond the scope of just one person."

This new endeavor is very appealing to Naoyuki Takagi. "When your child has a disease, one of the parents' responsibilities is to provide the best health care available. For me, as a person from a different country, the care at Packard is something to be proud of. I thought that a miracle really happened to Noelle, and I'm happy that more improvements may happen." ●

Breaking New Ground at Lucile Packard Children's Hospital

Strengthened by Philanthropy

Generous philanthropic support has helped to establish the Hospital's preeminence in pediatric medicine, especially in surgery for congenital heart disease, where treatment requires unusual expertise and specialized skill. Led by internationally renowned surgeon Frank Hanley, MD, Packard's pediatric cardiac surgical team has become one of the largest and most experienced in the world.

The following lead donors to the **Breaking New Ground** campaign have made gifts totaling $3.4 million in support of the Children's Heart Center:

Roma M. Auerback

Alex Vibber Foundation

Dora and James L. Fergason

Kathleen Justice-Moore and Steve Moore

Andrew David Sit Foundation

Kunio Takagi

For more information about gift opportunities, please call ***(650) 498-7641*** *or visit* ***www.supportLPCH.org****.*

Nailing Down the Window

by Ruth Schechter

Research Fellow Pinpoints Exact Time When Cleft Palate Occurs in Womb

For thousands of babies born with a cleft palate, early life can involve multiple surgeries, followed by specialized care and therapy. But what if it were possible to repair the cleft before birth? Or better yet, prevent the damage altogether?

That challenge got postdoctoral fellow Karen Liu, PhD, thinking. Straight out of graduate school, and putting in the laboratory hours required to qualify for a career in research, Liu wanted to combine her interests in molecular biology, embryonic development, and basic science. Using specially designed mouse models, she and her team used a technique called chemical genetics to explore the exact window of time when cleft palates and sternum clefts occur, allowing the scientists to potentially modify the condition in the unborn fetus.

A Big First Step

The results of Liu's investigation—though still too early to apply to humans—show great promise in terms of understanding how and when clefts form in the womb and for the possibility of preventing conditions in unborn patients rather than trying to treat them after birth.

"It's an important first step in the development of fetal therapies," says Michael Longaker, MD, director of the Children's Surgical Research Program and the Deane

"It's possible that someone in the next building has a new way of doing things that will completely change the way you approach your project. A program like Regenerative Medicine is great because it forces cross-disciplinary interactions and allows you to work with a wide range of people."

■ Karen Liu, PhD

P. and Louise Mitchell Professor in the School of Medicine. "Our hope is that this basic advance eventually will make a significant difference for children with clefts and other birth defects."

The research creates new insights into how palates are formed and fuse, which in turn may lead to better understanding of what goes wrong in congenital disorders. Cleft palates are one of the most common birth defects in the world, affecting about one in every 2,000 births.

A Two-Day Timeframe

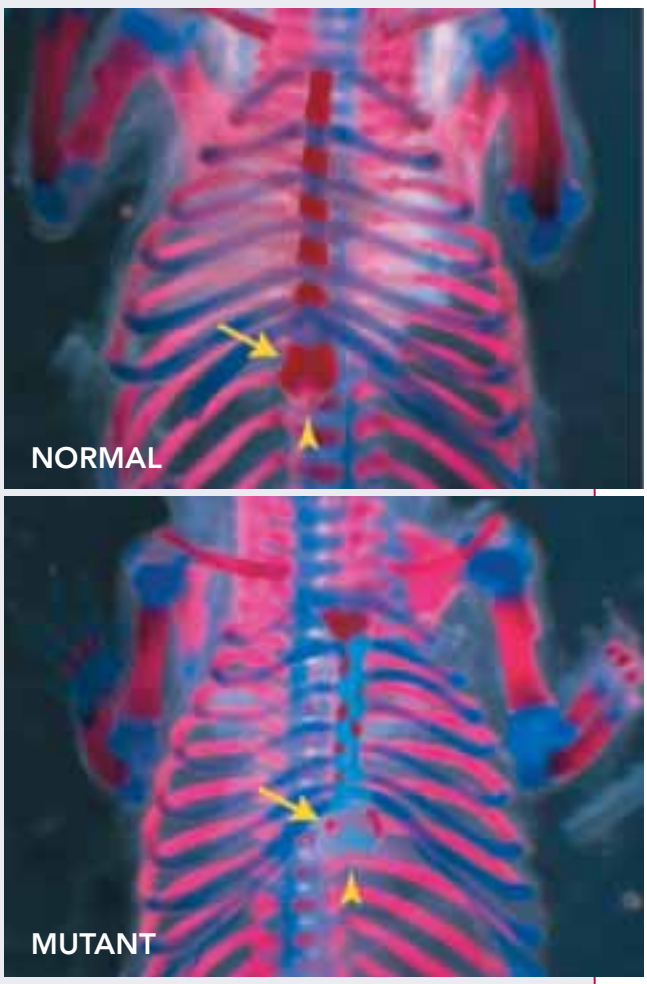
Liu took advantage of a strategy to disrupt the function of GSK-3beta, a protein that plays an important role in biological development. Mice that had been genetically engineered to make GSK-3beta unstable developed cleft palates. Liu found she could reverse the defect by injecting the pregnant mother with a drug called rapamycin, which returned the protein's function to normal. She also determined that she needed to normalize the protein during a very specific timeframe: In these mice, cleft palate is the result of growth imperfections that occur in a two-day window during embryo development, while sternum development takes place—with normal protein function—two days later.

"The beauty of the technique is that it nails down the developmental window for a specific embryonic event," Longaker says. "We don't need to treat the mother long term, but just during the time that the organ or structure is forming."

Fellows Play Key Role

Liu, who now has her own laboratory at Kings College London, was one of the more than 1,000 postdoctoral fellows working in basic science and clinical research laboratories throughout Stanford. Fellows play a critical role in moving science forward, and they are encouraged to think in terms of translational medicine—the integration of scientific studies to the diagnosis and treatment of disease—that has the most potential for improving children's health.

Liu was prompted to "think outside the box" and to take a collaborative approach to solving her research questions, which led to close interactions with mathematicians, chemists, and neurobiologists. She then was able to blend her interests in developmental biology with Longaker's expertise in craniofacial surgery and stem cell biology, benefiting from the insights of experts who normally might not work together.



Mice lacking the GSK-3beta gene are born with congenital defects of the sternum, which is important for protecting the heart and lungs from trauma. These images show ribcages of fetal mice where bone is stained red and cartilage is stained blue. "Normal" reveals a properly formed lower sternum, while the sternal structure in "Mutant" has very little mineralized bone.

Breaking New Ground at Lucile Packard Children's Hospital

Investing in the Next Generation

In addition to raising funds for an expansion of Lucile Packard Children's Hospital, a key objective of the **Breaking New Ground** campaign is to enhance training and support for pediatric faculty. Thanks to the influx of world-class pediatric clinicians and researchers, Packard and Stanford now have the opportunity to transfer this valuable expertise to the next generation by creating support programs to retain exceptional young faculty and allow them to build careers in clinical care and research.

Gift Opportunities:

The Campaign seeks to establish 15 endowed fellowships and 15 endowed faculty scholar awards for post-doctoral specialists and young faculty in pediatric programs at the Stanford University School of Medicine. Fellowships and Faculty Scholar Funds can be named in recognition of the donor or someone of the donor's preference.

Endowed Fellowship	$2 million each
Endowed Faculty Scholar Fund	$2 million each

The following lead donors to the **Breaking New Ground** campaign have made gifts totaling $16.5 million in support of training and faculty support:

Roma M. Auerback
The Eucalyptus Foundation
Marion and Jack Euphrat
Shirley and Harry Hagey

For more information about fellowships and faculty support, please call ***(650) 498-7641*** *or visit* ***www.supportLPCH.org****.*

"I wanted to pick up some new 'tools' for my developmental studies, so I guess I was already thinking in a multidisciplinary direction," says Liu. "This project required coordination of a diverse group of people—and their skills. I think it is important to talk to a variety of people about your project. It's possible that someone in the next building has a new way of doing things that will completely change the way you approach your project. A program like Regenerative Medicine is great because it forces cross-disciplinary interactions and allows you to work with a wide range of people."

How Research Helps

Several key advances are required before Liu's research can have clinical relevance, but the results demonstrate that chemical genetics strategies can prevent a birth defect in mice—an important breakthrough concept. Her work sheds light on a vital part of the intricate process of fetal development, and moves science one step closer to the possibility of new therapies.

"It is quite amazing that a single fertilized egg can develop to become this incredibly complex creature," she says. "The process is so complicated and there is so much that is unknown. It's important for us to 'translate' basic science and explain the medical impact of this work. I think it's reasonable for the public to ask, 'What good is this research? How does it help people?' And we should be able to explain." ●

"This research is an important first step in the development of fetal therapies. Our hope is that this basic advance will eventually make a significant difference for children with clefts and other birth defects."

- Michael Longaker, MD, director of the Children's Surgical Research Program and the Deane P. and Louise Mitchell Professor in the School of Medicine

Anna L. Bruckner, MD, examines EB patient Abraham Chavez.

Battling "EB"

Gene Therapy Holds Hope for Rare, Devastating Skin Disease

by Mark Shwartz

For most kids, running, skating, and other physical activities are just a normal part of growing up. But for the Chavez brothers—José, age 17, Abraham, 12, and Marlon, 9—even the simplest act, such as riding a bicycle or hugging their dog, can have painful consequences. All three brothers were born with a severe form of epidermolysis bullosa, or EB, an inherited skin disease in which even the slightest physical contact can cause blisters that turn into agonizing sores, which are slow to heal.

"Sometimes I don't want to go out, because everybody stares at me," says Abraham, an eighth grader, whose young body is riddled with scars and lesions from the disease.

"Some forms of EB are fairly mild, but Abraham and his brothers have a rare, severe type called recessive dystrophic EB, or RDEB," says Anna L. Bruckner, MD, assistant professor of dermatology and of pediatrics at Stanford University. "Their skin is incredibly fragile, so they need frequent bandaging—a painful ordeal that can take several hours a day."

As director of pediatric dermatology at Packard Children's Hospital, Bruckner heads the only clinic in the western United States that specializes in treating children with EB. "We regularly see about 35 patients with severe RDEB a year," she says. "They come from all over—California, Nevada, Washington, even overseas. We provide them a full suite of clinical services, including a pediatric pain specialist, physical and occupational therapists, a nurse specialist, a social worker, and a nutritionist."

> "Their skin is incredibly fragile, so they need frequent bandaging—a painful ordeal that can take several hours a day."
>
> ■ Anna L. Bruckner, MD, assistant professor of dermatology and of pediatrics at Stanford University

The Chavez family has been coming to Packard for 11 years—a 200-mile round-trip drive from their home in Stockton, Calif. "My wife and I are constantly changing their bandages," says Fernando Chavez, the boys' father. "It's a full-time job taking care of these guys."

During one recent clinic visit, Bruckner examined the bandaged wounds on the boys' legs, hands, and torsos for signs of infection.

"Basically, these kids are wrapped like mummies, because any trauma will tear their skin off," says Alfred T. Lane, MD, professor of dermatology and of

> "These patients and their families are truly heroic, because they are living with a disease that causes suffering virtually every moment of every day."
>
> ■ Paul A. Khavari, MD, PhD, the Carl J. Herzog Professor in Dermatology at Stanford

Paul A. Khavari, MD, PhD, and Isaias Zarate (inset).

pediatrics at Stanford. "Bandages may cost as much as $40,000 a year, and insurance won't cover it. So if you're not poor when you have the disease, you're poor when you treat the child."

Diet and nutrition is another major challenge for EB patients and their families. "Blistering can occur in the mouth and esophagus, which makes it hard for them to eat," Bruckner explains. "As a result, they become very undernourished. Their food has to be liquefied and supplemented with vitamins and other nutrients."

Some children, like 9-year-old Isaias Zarate, require surgery to keep their esophagus open. Isaias also has severe scarring that has caused his fingers and joints to contract, making it difficult for him to hold a fork or dress himself. This year, he and his mother, Eliut Dominguez, made two trips from their home in Los Angeles to Packard Children's, where Stanford surgeon James Chang, MD, performed hand surgery to separate the boy's fingers.

"These patients and their families are truly heroic, because they are living with a disease that causes suffering virtually every moment of every day," says Paul A. Khavari, MD, PhD, the Carl J. Herzog Professor in Dermatology at Stanford. "There is almost nothing I've experienced in medicine that is so heartbreaking as seeing a young child who can't play or run normally and is covered with bandages, wounds, and bleeding sores."

Because no standard medications are available to treat this traumatic blistering, Khavari has turned to a promising experimental technique known as gene therapy.

RDEB is caused by a defect in a gene that produces collagen VII, a protein that helps glue the epidermis, or top layer of skin, to the dermis, the deeper layer below. Without collagen VII, the skin is unable to withstand normal stress, and blisters easily.

The idea behind gene therapy is to insert normal copies of the defective gene into the patient's skin cells in a laboratory Petri dish, then graft those cells back onto the patient's wounds. "If it works, the new skin cells will produce the missing collagen VII glue, which will restore normal adhesion between the epidermis and the dermis," Khavari says.

He and his co-workers successfully demonstrated the technique in a recent experiment using human skin cells grafted onto immune-deficient mice. Now, Khavari, Lane, and Stanford colleagues M. Peter Marinkovich, MD, and Zurab Siprashvili, PhD, are seeking approval from the Food and Drug Administration to conduct similar trials on RDEB patients who are 18 or older.

"We hope that gene therapy will stop the blistering for more than a year," says Marinkovich, associate professor of dermatology at Stanford. "If it proves successful on adults, then perhaps we can begin testing it on children."

In the past, kids with severe RDEB often died before adulthood. Today, with advances in nutrition and basic care, many survive into their 20s and 30s, only to succumb to a lethal form of skin cancer. "The lessons we learn from gene therapy and EB may enhance our understanding of that kind of cancer, as well as the more than 175 genetic diseases that affect the skin," Khavari says. "Stanford and Packard have become world leaders in this kind of research."

For Fernando Chavez and his three sons, help cannot come too soon. "The boys have good times and bad times, but I tell them not to give up," he says. "Right now, the number one priority for all of us is to find a cure." ●

Breaking New Ground at Lucile Packard Children's Hospital

Striving for a Cure

Illnesses such as EB pose serious threats to the well being of children and require ever more effective treatments. Packard's location at the center of a leading research university is an ideal environment for pediatric discovery, virtually unmatched at other academic medical centers or stand-alone children's hospitals. The integration of Packard Children's with the School of Medicine gives the best minds in pediatrics the opportunity to pursue promising scientific investigations and translate their discoveries quickly into life-saving care for sick children.

Gift Opportunities:

The Campaign seeks to establish 15 endowed fellowships and 15 endowed faculty scholar awards for post-doctoral specialists and young faculty in pediatric programs at the Stanford University School of Medicine. Fellowships and Faculty Scholar Funds can be named in recognition of the donor or someone of the donor's preference.

Endowed Fellowship	$2 million each
Endowed Faculty Scholar Fund	$2 million each

The following lead donors to the **Breaking New Ground** campaign have made gifts totaling $7 million to fund research and program support for pediatric diseases:

- John A. and Cynthia Fry Gunn
- Hilibrand Foundation
- Don Listwin and Hilary Valentine
- Price Charities

*For more information about gift opportunities, please call **(650) 498-7641** or visit **www.supportLPCH.org**.*

16-year-old Valerie Retiz (left) shares a laugh with sister, Vanessa.

by Theresa Johnston

A Room of Its Own

New Dialysis Center Opens

Steven Alexander, MD, explains a procedure to dialysis patient Ricky Jolivette.

It's a typically busy Wednesday afternoon in the new Pediatric Dialysis Treatment Unit at Lucile Packard Children's Hospital. At one station, 16-year-old Valerie Retiz of Watsonville, Calif., works intently on a jigsaw puzzle, seemingly oblivious to the lifesaving machine at her side that's filtering impurities from her blood. At the next station, 13-year-old Jacqueline Castillo of San Jose, Calif., quietly passes time watching the Disney Channel. Not far from her, a yellow Labrador is visiting patients as part of the hospital's pet therapy program.

As he makes his rounds, Steven Alexander, MD, couldn't be more pleased. For years, he notes, Packard Children's outpatient dialysis unit was isolated from the rest of the hospital in a stuffy, narrow room that was depressing for kids and nurses alike. The biggest drawback was its small size—only two young patients could be accommodated at any one time. "We had to send most kids over 15 out to other facilities," recalls Alexander, who serves as medical director of dialysis and kidney transplantation at Packard, and director of pediatric nephrology. "We had teenage dialysis patients in adult dialysis units with 60-year-olds up and down the Peninsula."

> "The new unit is another sign of the commitment this hospital has made to providing first-rate, absolutely top-of-the-line care in everything."
>
> ■ Steven Alexander, MD, medical director of dialysis and kidney transplantation at Packard, and director of pediatric nephrology.

Packard's new 3,000-square-foot dialysis unit, which opened in April off a sunny courtyard near the Day Hospital, can handle six young patients at a time, up to 24 a week. Its equipment—including new dialysis machines donated by the Hospital's San Francisco Auxiliary—is state-of-the-art. And depressing it is not.

On one end of the long, citrus-colored room, children can gaze out onto a patio planted with bright pink-and-white impatiens. On the other end, drawers

A Room of Its Own

Jacqueline Castillo enjoys coloring with siblings Jose Luis and Sofia while she undergoes treatment.

are loaded with coloring books, puzzles, and other toys. Overhead, new flat television/computer screens hang above each reclining chair, allowing patients to play video games, watch TV, or keep up with their homework. If a child wants privacy or a nurse needs to perform a dialysis procedure, a touch of a button lowers shades from the ceiling.

"I just like the way you feel when you walk into it," Alexander says of the unit, which he lovingly designed with the help of Packard Children's chief biomedical engineer, Dean Peterson, and a team of physicians, nurses, social workers, and child life therapists, headed by the architectural firm of Hawley Peterson & Snyder. "Yes, you're entering a dialysis unit. But it's light, it's cheerful, and the colors are bright. If you stand on your tiptoes you can see the mountains."

Dialysis, of course, would not be high on any kid's list of fun things to do. The procedure involves connecting a patient, via two long, flexible catheters, to a hemodialysis machine about the size of a home water heater. Then the child must stay put for three to four hours while the dialyzer circulates his or her blood through a filter that gently extracts waste substances and excess fluid. Usually the treatment is prescribed three times a week to support children while they wait for kidney transplants.

Alexander is particularly eager to show off his new unit's water filtration system, which ensures that the dialysate solution used to cleanse his young patients' blood is completely sterile and free of undesirable trace elements. When visitors come in to see the water treatment room, he proudly passes out samples of the "ultra-pure" water in plastic wine goblets. "You can't make it any purer," he shouts over the hum of the pumps.

Water quality is extremely important in these systems, Alexander explains, because when the dialysis water contains contaminants like bacteria or chlorine, infections can occur and patients tend to suffer more from

chronic inflammation—and that can lead to long-term health problems like hardening of the arteries. "Life expectancy is now up to 50-plus years for a child with end-stage renal disease," he notes, "so we have to be thinking now about their health as adults."

The new equipment should be particularly helpful for long-term dialysis patients like 17-year-old Ricky Jolivette, of Pacifica, Calif. Ricky has had problems with his kidneys since infancy; he's already had two transplants, and is now waiting for his third. Three times a week, for the past year, his grandparents have been shuttling him to Packard for his three-and-a-half-hour treatments.

Alexander with the new unit's water filtration system.

In the old dialysis unit, Ricky says, there was only one television set, and he had to wait for a nurse to change the channel. Now, with the big, new flat screens, it's easy for him to surf the auto websites he enjoys, or catch up on his favorite television show, *Law & Order*.

Another person who appreciates the new unit is Chris Holzberger, of Watsonville, Calif. Working around her job at Safeway, she brings in her 16-year-old niece, Valerie, three times a week. Valerie has suffered from lupus since she was 7 years old, and now her kidneys are failing. The family is hoping for a transplant within a year.

Holzberger has nothing but kind words to say about Packard's staff. But the old unit was so cramped that there was barely any place for her to sit. "This place is much roomier, and they've got TV, games, and puzzles to keep her occupied so she doesn't get squeamish," she says, nodding at Valerie. Another plus is that the girl can interact with more kids in the new unit. "It makes her feel not so alone."

Packard's new 3,000-square-foot dialysis unit opened in April.

Alexander's next goal for the unit is to set up a training room, furnished like a child's bedroom, where parents can learn how to administer home peritoneal dialysis. In those treatments, the dialysate solution is instilled through a tube into the child's lower abdomen, where it absorbs waste products and toxins before being drained, measured, and discarded.

Usually it takes a couple of weeks for parents to feel comfortable doing peritoneal dialysis. But at least in the new unit they'll have a pleasant place where they can learn—and nurses to teach them. One of the best things about the new unit, Alexander says, is that it has allowed him to recruit a full team of "rare and wonderful" nurses who are specialists in pediatric dialysis.

In fact, he says, it's pretty rare and wonderful to have an on-site outpatient dialysis unit at all. "What this allows us to do is have sicker kids in an outpatient dialysis setting whom we can see as part of our daily rounds. It really increases the opportunities for physician-patient-family interaction," he says. "It's another sign of the commitment this hospital has made to providing first-rate, absolutely top-of-the-line care in everything."

In the NEWS

Packard Children's: Top 10 in Nation, No. 1 in State

Packard Children's Hospital has once again made the *U.S.News & World Report* Top 10 list of the finest pediatric institutions in the country. In its 2007 "America's Best Children's Hospitals" issue, the magazine places Packard #10 among pediatric hospitals nationwide and #1 in California based on reputation, as well as on data and statistics about hospital performance and quality of care.

Founded in 1991, Packard Children's is the youngest hospital on the Top 10 list. Christopher Dawes, president and CEO, noted, "Our placement on the *U.S.News* Top 10 list is recognition of what our faculty and staff have built and continue to build—a nationally and internationally preeminent children's hospital."

Cohen and Golden Honored with Endowed Professorships

The Lucile Packard Foundation for Children's Health and the School of Medicine recently established two new endowed professorships. Harvey Cohen, MD, PhD, was named the Deborah E. Addicott-John A. Kriewall and Elizabeth A. Haehl Family Professor in Pediatrics, and Neville Golden, MD, was appointed the Marron and Mary Elizabeth Kendrick Professor in Pediatrics.

Cohen is the former Adalyn Jay Chief of Staff at Packard Children's and the Arline and Pete Harman Professor and Chairman of the Department of Pediatrics. He stepped down from those posts last November to return to medicine and research. The endowment will allow him to continue his research in devising new ways to diagnose and treat pediatric diseases. The donors of the professorship, created in 2006, requested that the first holder be a senior member of the department of pediatrics whose clinical and academic focus lies in the field of pediatric oncology and hematology.

Golden arrived at Packard recently to serve as chief of adolescent medicine and director of the Center for Adolescent Health. As former director of the eating disorders center at Schneider Children's Hospital in New York, he is renowned for his expertise in the medical complications of eating disorders. Golden is studying the use of hormone replacement therapies to improve bone mineral density in patients with anorexia nervosa. The Marron and Mary Elizabeth Kendrick Professorship, established in 1976, was the second endowed chair in the pediatrics department. •

DORIS DUKE
CHARITABLE FOUNDATION

Sweet-Cordero Wins Award from Doris Duke Foundation

Alejandro Sweet-Cordero, MD, assistant professor of pediatrics (cancer biology) has received a Doris Duke Clinical Scientist Development Award of $135,000 per year for three years to support his research on pediatric sarcomas—cancers that appear in the bone, muscle, and connective tissue.

The Doris Duke Charitable Foundation provides grants to strengthen and support clinical research that advances the translation of basic biomedical discoveries into new treatments, preventions, and cures for human diseases. The Development Award helps promising junior faculty successfully move into independent clinical research careers by providing start-up funding to establish their own investigative teams. •

Hart Family Foundation Supports Palliative Care

The Hart Family Foundation has pledged $160,000 for the Pediatric Palliative Care Program at Packard Children's. The funds will support efforts to enhance the quality of life for young patients who are facing a life-limiting illness. The program, led by Barbara Sourkes, PhD, the John A. Kriewall and

Elizabeth A. Haehl Director of Pediatric Palliative Care, provides a range of care for patients and their families.

The foundation's pledge ensures the continued work of pain management physician Julie Good, MD, DABMA, and clinical nurse specialist Sandy Sentivany-Collins, RN, MS, CNS, and will enable the Hospital to hire a social worker to assist patients transitioning to hospice care. ●

Benjamin Arias

5,000 Kids Safely Seated

Certified technicians who install and check car seats at Packard's Maggie Adalyn Otto Safely Home Car Seat Fitting Station recently reached a milestone of 5,000 car seats installed since the program's inception in 2004. Community outreach liaison Benjamin Arias, with the help of two part-time assistants, provides free and friendly instruction to about 40 families a week, showing parents and guardians the safest way to position and fasten their newborns' seats. ●

Feinstein, Albanese Appointed to Endowed Directorships

Packard Children's recently announced the appointees to two new endowed directorships. Carl Feinstein, MD, was named the first Endowed Director of Child and Adolescent Psychiatry, and Craig Albanese, MD, was installed as the John A. and Cynthia Fry Gunn Director of Pediatric Surgical Services.

Feinstein is currently the division chief of child and adolescent psychiatry, and a professor of psychiatry and behavioral sciences and, by courtesy, of pediatrics, at the School of Medicine. He is known for his expertise in biological and developmental psychiatry, particularly in developmentally disabled children and adolescents. The directorship is endowed by The Eucalyptus Foundation, which supports a variety of environmental, educational, and cultural causes.

Albanese, professor of surgery, pediatrics, and obstetrics and gynecology, serves as the chief of pediatric general surgery and director of pediatric surgical services. He is also the surgical director of the Hospital's Center for Healthy Weight. Albanese has achieved prominence as a pioneer and leader in minimally invasive pediatric endoscopic surgery, fetal surgery, and bariatric surgery. The directorship was established in 2006 through a gift from John A. and Cynthia Fry Gunn, long-time friends of Packard Children's, the School of Medicine, and Stanford. ●

Sobrato Family Foundation Boosts Campaign

SOBRATO FAMILY FOUNDATION

Building Community • Investing In People & Places

The **Breaking New Ground** Campaign is off to a tremendous start thanks to an early $20 million commitment from John A. Sobrato and his family for the construction of a proposed addition to Packard Children's Hospital. The planned expansion will double the number of beds available to care for children and allow Packard to meet growing demand for its services.

Sobrato is founder and principal of Sobrato Development Companies, one of the largest real estate development firms in California. He currently serves as a trustee of Santa Clara University and vice chairman of the National Hispanic University. He and his family are well known for their philanthropy throughout Silicon Valley, particularly in providing general operating and capital grant support, in-kind office and meeting space, and loans to create affordable housing locally.

In the NEWS

Antonio Hardan, MD

Escher Family Gift Funds Autism Research

The Escher family has given $50,000 to support autism research by Antonio Hardan, MD, director of the Autism and Developmental Disabilities clinic at Packard Children's and assistant professor of child and adolescent psychiatry in the School of Medicine. The gift allows Hardan to conduct a 12-week pilot study of N-Acetylcysteine (NAC), a drug that may help better treat children with autism.

Chris and Jill Escher have three children, one of whom has autism, and have dedicated themselves to helping find a cure for the disorder. Chris serves on the Autism Education Network's board of directors. Jill serves on the Autism Advisory Committee for the San Jose Unified School District and is a board member of Walk San Jose. ●

Protein May Hold Key to Multiple Sclerosis

Stanford researchers, led by Lawrence Steinman, MD, professor of pediatrics and of neurology, have detected a protein that they believe will help doctors understand what causes multiple sclerosis.

Doctors traditionally have believed that the disease is caused by a mixture of defective genes and environmental factors. But the work by Steinman and his team, recently published in the journal *Nature*, implicates a protein, alphaB-crystallin, that they believe normally regulates the human immune system, but doesn't do so in people with the lifelong illness. The researchers hope the discovery will lead to new treatments and a way to stop the disease's progression. ●

Foundation Names New Board Members

Three new members were recently elected to the board of directors of the Lucile Packard Foundation for Children's Health.

Edward L. Schor, MD, is vice president at the New York-based Commonwealth Fund, where he leads the Child Development and Preventive Care program. Schor previously was medical director for the Iowa Department of Public Health, Division of Family and Community Health. He has chaired both the Committee on Early Childhood, Adoption, and Dependent Care and the national Task Force on the Family for the American Academy of Pediatrics.

George J. Still Jr. is managing partner of Norwest Venture Partners in Palo Alto. He served on the Stanford Business School Venture Capital Trust from 1997 to 2001 and is currently on the board of the Center for Private Equity and Entrepreneurship at the Tuck School of Business at Dartmouth.

Christopher Dawes, president and CEO of Packard Children's, was appointed an ex officio member of the board. ●

William C. Mobley, MD, PhD

Kirwan and Rizzi Families Hold Benefit for Down Syndrome Research

A benefit held by the Kirwan and Rizzi families in Greenwich, Conn., raised $100,000 to fund research at Stanford for the treatment of Down syndrome. Both families have daughters with the genetic disorder and hosted the event to support the research of William C. Mobley, MD, PhD, the Cahill Family Professor and director of the Center for Research and Treatment of Down Syndrome at the School of Medicine. At the event, Mobley discussed his research on the extra chromosome that causes cognitive problems in people with Down syndrome. ●

Circle of Care Spotlight

Dianne and Tad Taube

Dianne and Tad Taube are well known in the Bay Area and beyond as leaders in business and philanthropy. With a strong commitment to improving the well being of the community, they feel it is only natural to support Lucile Packard Children's Hospital.

As members of the **Children's Circle of Care**, the Taubes are helping to ensure that children and families benefit from the expertise of Packard Children's. Their unrestricted gifts to the *Lucile Packard Children's Fund* provide the greatest flexibility for the Hospital to meet critical needs.

The Taubes' sons, Travis, 9, and Zakary, 4, both were born at Packard. "With two young children, our eyes have been opened to the need for good pediatric care," says Dianne. On a recent tour, she was impressed by the Hospital's outstanding medical services and by the dedication of its physicians, nurses, and staff.

Recognizing that few communities have a top-tier children's hospital, the Taubes want to make sure Packard is always there for families who need it. In addition to their own giving, they have encouraged friends and colleagues to become involved as well.

"Packard Children's is a vital treasure," Dianne says. "We believe it takes the whole community to support a hospital of such high caliber."

The Taubes' philanthropic efforts have included lead gifts to Stanford University for the Taube Family Tennis Stadium, the Taube Tennis Center, the Center for Jewish Studies, and the Taube Hillel House. They also have supported the Taube-Koret Campus for Jewish Life in Palo Alto, and the Conservatory of Flowers and the Palace of Fine Arts in San Francisco.

Dianne is a board member of the San Francisco Opera Association, the San Francisco Zoological Society, and the ARCS Foundation, and is an active volunteer for Youth Tennis Advantage. Tad has served as chairman and CEO of Koracorp Industries, Inc. (formerly Koret of California) and founder and chairman of the Woodmont Companies, and is currently president of the Koret Foundation. He is also a member of the Board of Overseers and a member of the Executive Committee of the Hoover Institution at Stanford.

Tad and Dianne Taube

"We try to support institutions that make a fundamental impact on people's lives," says Tad. "Packard Children's Hospital is a perfect fit."

Children's Circle of Care
Leaders in Annual Giving...

The Children's Circle of Care recognizes individuals and family foundations whose annual gifts of $10,000 or more help advance pediatric patient care, research, and teaching.

For more information about the Children's Circle of Care please contact Michelle Heeseman at **(650) 724-2783** or **michelle.heeseman@lpfch.org**. You may also visit our website at **www.supportLPCH.org**.

Planning Your Gift to Packard

New Law Allows Lifetime Gifts from Retirement Accounts

John Working Jr. has turned his lifelong connection to Stanford into lasting support of Lucile Packard Children's Hospital. After many years of annual giving, Working recently made a special planned gift to Packard Children's directly from his Individual Retirement Account (IRA), as allowed under new legislation for a limited time (see sidebar).

The son of a Stanford University economics professor, Working grew up on campus and stayed on as a student. He volunteered at the Stanford Home for Convalescent Children, the earliest predecessor of Packard Hospital, and served on the board of the former Children's Hospital at Stanford with Mrs. Lucile Packard. He still lives nearby today.

Working's IRA gift supports the research of Harvey Cohen, MD, PhD, the Deborah E. Addicott-John A. Kriewall and Elizabeth A. Haehl Family Professor in Pediatrics and former chief of staff of Packard Children's. Cohen's lab is using comparative proteomics—the statistical analysis of proteins and peptides—to better diagnose, understand, and treat childhood diseases.

"Imagine being able to predict whether a child will develop diseases such as asthma, diabetes, or cancer, to anticipate how they will respond to treatment, and to intervene in the most effective way," says Cohen. "Proteomics offers us the potential to do this, and we are grateful for John's help in moving our work forward."

"I think of the enduring contributions Harvey is making to improve the lives of children," says Working. "With my father's research in statistics and my love of Packard Children's, I feel I've come full circle by supporting Harvey's work."

In addition to this gift, Working has included Packard Children's in his estate plans and is a member of the *Lucile Salter Packard Society*.

John Working Jr. and his wife, Lysbeth (left), join Victoria Applegate, director of auxiliaries relations, at the 2006 *Lucile Salter Packard Society* Holiday Tea.

Make a Tax-Free Contribution

A new federal tax law makes it possible to give up to $100,000 tax-free from your Individual Retirement Account to Packard Children's Hospital. This is a great solution if you need to take a minimum distribution this year and want to avoid tax consequences.

To qualify:

- You must be 70 ½ or older at the time of your distribution.
- Your IRA administrator must transfer your contribution directly to Packard Children's.

Act now—this new federal legislation applies only to gifts made in 2007 and will expire at the end of the year.

For more information, please contact Donna Bandelloni, director of gift planning, at **(650) 736-1211** or visit our website at **www.lpfch.org/plannedgiving**.

Please be sure to consult your tax advisor when considering a gift through your IRA. Gifts made under this federal tax law cannot count as a charitable deduction on your income tax return.

Circles of Leadership

Become a Leader in Annual Giving

Making a *Circles of Leadership* gift to Lucile Packard Children's Hospital is a generous way to demonstrate your commitment to children's health. Your leadership gift will help ensure that our young patients receive the most advanced care possible, and help fund groundbreaking research to develop new treatments for childhood diseases.

Circles of Leadership	
Circle of Care	$10,000 or more
Circle of Vision	$5,000 to $9,999
Circle of Hope	$2,500 to $4,999
Circle of Courage	$1,000 to $2,499

By joining the *Circles of Leadership*, you help build a foundation of support for the Hospital. The more you give, the greater your impact on Packard's patient care, and the more you will inspire others in the community to follow your generous example.

We invite you to make your leadership gift today! For more information about the *Circles of Leadership* please call **(650) 736-8282**.

Lucile Packard
FOUNDATION *for Children's Health*

2007 Board of Directors

Packard Children's EVENTS Calendar

Community Health Classes at Lucile Packard Children's Hospital

To register, please call (650) 724-3783

Heart to Heart: A Seminar on Growing Up for Parents and Kids

This informative, humorous, and lively discussion sets parents and their preteens on a straight course for talking about puberty, the opposite sex, and growing up.

Tuesdays, October 30 and November 6
6:30 p.m., *for boys and their fathers*

Mondays, December 3 and 10
6:30 p.m., *for girls and their mothers*

Please visit **www.LPCH.org** to see a full listing of community classes and programs.

Packard Kids Connection

Packard Children's recently launched a new website just for patients. Located at **http://kids.lpch.org**, the playfully animated, bilingual site shows children what to expect when they arrive for a visit. Interactive games help kids prepare for tests and treatments, and photos and on-location videos allow them to check out the Hospital's activities and resources.

Upcoming Auxiliary Events

For more information, please call (650) 497-8591

Jewel Ball
Saturday, October 27
Palace Hotel, San Francisco
San Francisco Auxiliary

Holiday Gala
Saturday, November 3
Peninsula Country Club, San Mateo
San Mateo-Burlingame Auxiliary

American Girl Doll Event
Friday and Saturday, November 9 and 10
Christ Episcopal Church, Los Altos
Palo Alto Auxiliary

Holiday Boutique Sale
Friday and Saturday, November 16 and 17
472 Oak Road, Stanford
Charter Auxiliary

Special Sale
Friday, December 7
472 Oak Road, Stanford
Charter Auxiliary

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