A novel immunotherapy appears safe for use in patients with a type of blood cancer called non-Hodgkin’s lymphoma, according to a phase-1 multicenter clinical trial led by a researcher at the School of Medicine.

Although some patients showed signs of transient anemia or reactions at the injection site, there were few other significant side effects to the treatment, the researchers said.

The therapy combines an experimental antibody developed by researchers at Stanford and a commercially available anti-cancer antibody called rituximab. The experimental antibody, known as Hu5F9-G4, blocks the protein CD47, a “don’t eat me” signal that inhibits immune attacks on cancer cells. The antibody combination was used to treat people with two types of non-Hodgkin’s lymphoma: diffuse large B-cell lymphoma and follicular lymphoma.

Half of the 22 people enrolled in phase 1 of the trial had a positive response to the therapy, and about one-third went into complete remission from their cancer.

“It was very gratifying to see how the treatment was well-tolerated and showed a clinically meaningful response,” said Ranjana Advani, MD, professor of medicine at Stanford.

A paper describing the results of the phase-1 trial was published Nov. 1 in The New England Journal of Medicine. Advani is the lead author. The senior author is Sonali Smith, MD, a professor of medicine at the University of Chicago.

The trial was funded by Forty Seven Inc., the company that licensed the patent from Stanford to produce Hu5F9-G4, and by the Leukemia and Lymphoma Society.

Silencing “don’t eat me” signal

In 2010, researchers led by Irving Weissman, MD, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, showed that nearly all cancer cells cover themselves with a protein known as CD47, which acts as a “don’t eat me” signal to immune cells called macrophages.

Weissman and his colleagues later developed an antibody called Hu5F9-G4 that blocks the CD47 protein, prompting macrophages to engulf and devour cancer cells. Rituximab is an antibody that has been shown to amplify positive “eat me” signals.

See CD47, page 6

Heart study enrolls more than 400,000 people

By Tracie White

A clinical trial to determine whether a smartwatch app that analyzes pulse-rate data can screen for a heart-rhythm disorder has enrolled more than 400,000 participants.

Researchers at Stanford Medicine, in collaboration with Apple, launched the Apple Heart Study last November to determine whether a mobile app that uses the optical sensor on the Apple Watch to analyze pulse-rate data can identify atrial fibrillation. The condition, which is characterized by an irregular heartbeat, often remains hidden because many people don’t experience symptoms. Atrial fibrillation can increase the risk of stroke and heart failure.

A paper describing the design of this unique clinical trial, the largest screening study on atrial fibrillation ever done, was published online Nov. 1 in the American Heart Journal. Enrollment, which was conducted through an iPhone app, is now closed.

The study has entered the final phase of data collection and will be completed early next year, the researchers said. The Stanford team is led by principal investigators Mintra Tzika, MD, associate professor of cardiovascular medicine, and Marco Perez, MD, assistant professor of cardiovascular medicine, and by study chair Kenneth Mahaffey, MD, professor of cardiovascular medicine.

“We hope this study will help us better understand how wearable technologies can inform precision health,” said Lloyd Minor, MD, dean of the School of Medicine.

“These new tools, which have the potential to predict, prevent and manage disease, are finally within our reach,” Minor said.

The Food and Drug Administration announced Sept. 11 that it had cleared two mobile medical apps designed by Apple to work on the Apple Watch. One app uses data from new hardware on the Apple Watch Series 4 to take an electrocardiogram by touching the button on the side of the device. The other app uses data from an optical sensor available on the Apple Watch Series 1 and later to analyze pulse data to identify irregular heart rhythms suggestive of atrial fibrillation and notify the user. The Apple Heart Study involves only participants in the Apple Heart Study who get a notification if the optical sensor on the Apple Watch detects an irregular pulse.

See APPLE, page 7

Secret behind Bambi’s fast-growing antlers revealed in research

By Hanae Armitage

Each spring, male deer sprout a new pair of antlers, which are essentially temporary external bones, at a speed unparalleled by the bone growth of other mammals. Now, research led by scientists at the School of Medicine has identified a key element that makes antlers sprout so quickly.

Researchers have long known that antler growth is driven by a type of hormone called IGF-1, or insulin-like growth factor 1. Using a technique to specifically deactivate the IGF-1 receptor in antlers, scientists found that this receptor controls the speed of growth significantly and that it is usually only active during the spring.

“Although IGF-1 plays a critical role in antler growth, it has been difficult to understand how this hormone has such tremendous effects,” said study leader Weissman. “Our findings indicate that the receptor, which acts to initiate antler growth, is responsible for the spring upsurge in antler growth.”

See ANTLER, page 6
Three are awarded the School of Medicine's highest honor

By Julie Greicius

Three are awarded the School of Medicine's highest honor. Carla Shatz, PhD, the Sapp Family Provostial Professor, the David Starr Jordan Director of Stanford Bio-X and a professor of biology and of neurobiology; Don Listwin, founder and chairman of the Canary Foundation, which supports programs for early cancer detection; and Ron Johnson, founder and CEO of Enjoy, a company that hand-delivers technology and helps customers set up.

The collaborative effort to advance the biomedicinal revolution in precision health takes many forms, said Lloyd Minor, MD, dean of the School of Medicine. "This year's medal recipients have used their passions for innovation, philanthropy and service to help bring about exceptional progress in research and clinical care. I'm proud to honor their work."

Improving brain plasticity

Shatz's interest in the brain's visual system began as an undergraduate at Radcliffe College. She went on to study how the eye and brain connect during development, and her lab discovered that, in the earliest stages before the eye can even see, it sends coordinated test patterns of neural activity to the brain. Those test patterns, said Shatz, "give the brain a chance to develop.

Shatz has gone on to discover that this early neural signaling, which is needed for synapse plasticity and later memory, involves interactions common to both the brain and immune systems. Her discoveries have implications for improving brain plasticity and memory.

"It's an immense honor to be recognized with the Dean's Medal," Shatz said. "I want to recognize and thank the incredible students and postdocs in my lab. Without them, none of our discoveries would have happened. What's more, it is a great privilege to be included in Stanford Bio-X, where transforming, high-risk ideas emanating at the crossroads of disciplines are encouraged."

Earliest cancer detection

Living through her mother's death from ovarian cancer left an indelible mark on Listwin and inspired him to work toward progress in early cancer detection. Listwin's role in helping to create today's global internet infrastructure through multibillion-dollar technology investing and management, including a decade at Cisco Systems, enabled him to step back from his operating roles to build the Canary Foundation.

Today, 15 years later, the Canary Foundation has grown from a startup nonprofit to a leader in the development of early cancer detection programs, including the Canary Center at Stanford and many others in the United States and abroad. The Canary Foundation is the only nonprofit exclusively dedicated to research in the field of early detection of cancer. The Deal's Medal honors Listwin for his service in the scientific and philanthropic communities that have advanced precision health.

"My thanks to Dean Minor and the entire School of Medicine organization," Listwin said. "Over the past decade, a theme of partnership has emerged in my pursuits in the medical field, and none has been stronger than at Stanford. Whether working with Dr. Sam Gambhir to build the first comprehensive early cancer detection center or launching a modest vision clinic in Belize with Dr. Caroline Fisher, there has always been support from the School of Medicine. My current pursuit is the field of precision medicine. At Stanford, it is a privilege to be able to engage in a spectrum of work in the field of medicine with the best in the world to help solve these critical problems."

Designing the ideal hospital

Known as the executive team member at Apple who founded its stores and helped create a unique user experience for its customers, Johnson had also transformed merchandising at Target through a focus on design.

"Volunteering for Stanford Medicine over the past decade has been a gift," Johnson said. "To be able to work with such incredibly talented people to deliver on our vision of precision health has been among the most gratifying experiences of my life. The new Stanford Hospital will be a symbol of excellence for Stanford for decades to come," he added.
Skeletal stem cells revert to primitive state to fix major damage

By Krista Conger

Adult mouse skeletal stem cells in the jaw revert to a more developmentally flexible state when called upon to regenerate a birth defect, according to a study by researchers at the School of Medicine.

"It's pretty remarkable that this would happen in an adult animal," said Michael Longaker, MD, professor of plastic and reconstructive surgery. "It changes the way we look at skeletal development and regeneration."

A paper describing the research was published online Oct. 24 in Nature. Longaker, the Deane P. and Louise Mitchell Professor in the School of Medicine and co-director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, shares senior authorship with Changting Chai, PhD, PhD, professor of dermatology and as genetics and director of Stanford's Center for Personal Dynamic Regulomes. Graduate students Ava Carter and Ryan Ransom are the lead authors.

Aiding stunted bones

The researchers were studying a common surgical technique called distraction osteogenesis, in which the bone ends are repeatedly moved further apart, is much more extensive. "How do they know to reform a mandible with the correct shape and function?" said Longaker. "Are they somehow reprogramming normal development?"

Tracking cellular reversion

Carter and Ransom used a technique developed in the Chang laboratory called ATAC-seq to identify gene switches that are turned on in mouse skeletal stem cells in response to the mechanical force of distraction. They found that the cells began to express normally found in cranial neural crest cells that arise in humans about five to six weeks after the bone has been fractured and the bone, cartilage and connective tissue of the head and face. At the same time, the cells tapped down the expression of genes involved in normal fracture repair.

"This was really a surprise," Longaker said. "These cells appear to revert back to a cell type responsible for forming the jaw during early development. That's why the regenerated mandible looks like one formed in early embryogenesis."

In the absence of mechanical force to separate the bone, the skeletal stem cells repaired the fracture without expressing cranial neural crest genes. Further research identified the focal adhesion kinase molecular pathway as a key player in the ability of the skeletal stem cells to detect and respond to mechanical force. Inhibiting this pathway abolished the ability of the cells to make new bone during distraction osteogenesis.

The finding has provocative clinical implications, the researchers believe. "Now that we've identified one of the molecular pathways responsible for this developmental shift, it may be possible to target the proteins in that pathway to achieve a similar outcome without the requirement for physical force," Carter said.

"We're beginning to understand in detail how skeletal stem cells are likely to respond to environmental cues in humans," Longaker said. "This is an opportunity to change how we think about the development of not just the skeleton, but also other tissues and organs. Can we go back in time after an organ is formed to trigger more extensive regeneration? This at least opens the door to that possibility." Longaker is a member of the Stanford Child Health Research Institute, the Stanford Cardiovascular Institute, the Stanford Cancer Institute and Stanford Bio-X. Chang is a member of the Stanford Child Health Research Institute, the Stanford Cancer Institute and the Stanford Bio-X. Other Stanford authors are research associate Ankit Salthoria; former research associate Tripp Leavitt, MD; medical student Owen Marecic; CIRM scholar Michael Lopez; postdoctoral scholars Matthew P. Murphy, MD, Yuning Wei, PhD, and Ruth Ellen Jones, MIT; surgical resident Clement Marshall, MD; undergraduate student Ethan Shen; asstistant professor of surgery Charles K.F. Chan, PhD; and associate professor of surgery Derek Wan, MD.

The research was supported by the National Institutes of Health, the HHMI, the Stanford Child Health Research Institute, the Hagey Laboratory for Pediatric Regenerative Medicine, a Steinhardt/Reed Award, the Gunn-Oliver Fund and the Scleroderma Research Foundation. Stanford's departments of Surgery and of Dermatology also supported the work.

Chromatin

creating a new and accessible site where a transcription factor can bind. Once the protein attaches to the site, a new gene is expressed, causing significant biological changes. An example of this occurred with bladder cancer tissue that Chang examined. When the team performed ATAC-seq on the tissue, they noticed that a chromatin mutation created a new protein-binding site that was associated with increased in the activity of a marker gene that regulates cell size, motility and shape — all of which are critical factors in cancer growth. Even more interesting, the researchers found that the transcription factor was not pres- ent in the other cancer tissues analyzed in the study, suggesting that different cancer types may arise from different chromatin mutations.

"We believe that gene activity were our missing component," Chang said. "We can now find how these switches are changing cancer, including mutations that are stably inherited in the organism.

The tip of the iceberg

The vast amount of genetic research is focused on the 2 percent of our DNA that is used to create proteins. In the current study, Chang wanted to explore the other 98 percent, known as the "junk DNA." This part of the genome is used to make crucial regulatory components that control gene behavior and activation. It also includes information that is pertinent to cancer.

During distraction osteogenesis, the bone is surgically fractured, and an adjustable device is inserted to gradually increase the distance between the ends of the bone over the course of weeks. This encourages new bone growth, but it also stimulates the gap and create what resembles a normally developed mandible.

"This is a very large system of regulation that echoes what normally happens in development," said Chang, who is the Virginia and D.K. Ludwig Professor of Cancer Sciences and a Howard Hughes Medical Institute investigator. "If you cut the bone, and stretch it, you get more bone. But this regeneration requires mechanical force. We wanted to know how skeletal stem cells respond to this kind of environmental signal.

Recently, Stanford researchers identified the skeletal stem cell in both mice and humans. Like other stem cells that occur in adult animals, skeletal stem cells are restricted in their ability to generate different cell types. In particular, they can generate bone, cartilage and stroma (the bone's spongy interior) to repair normal damage like fractures. But the regeneration required for distraction osteogenesis, in which the bone ends are repeatedly moved further apart, is much more extensive.

"How do they know to reform a mandible with the correct shape and function?" said Longaker. "Are they somehow reprogramming normal development? And, if so, how?"

Researchers awarded nearly $5 million to map cells of colon

Scientists at the School of Medicine will launch a center to map the mosaics of cells that comprise the human colon.

Michael Snyder, PhD, professor and chair of genetics, and Gary Nolan, PhD, professor of microbiology and immunology, will lead the Stanford Tissue Mapping Center, which is being funded by $4.9 million from the National Institutes of Health. In addition to mapping the types of cells that make up colon tissue, the center aims to reveal the spatial organization of the cells, with the intention of providing insights into how cell types and their locations contribute to the function of the colon. Through the center, the scientists also aim to understand and treat many intestinal and colorectal diseases, such as inflammatory bowel disease, ulcerative colitis and colon cancer.

The research will contribute to the Human Biomolecular Atlas Program, a larger effort supported by the NIH to map the entire human body at the level of individual cells.
Heart recipient: ‘Stanford has saved my life not once, but twice’

By Grace Hammerstrom

Today, Yolanda Ishaq’s “miracle baby” is 25 years old, and Ishaq herself is a grandmother. She continues to thrive after undergoing two heart transplants and a kidney transplant at Stanford Hospital in 2015.

“Stanford has saved my life not once, but twice,” said Ishaq, who lives in Oakland, California. “They’ve also given my daughter life. It was unheard of to have a baby like her.”

Ishaq’s story began about two decades after Norman Shumway, MD, PhD, a cardiothoracic surgeon at Stanford, performed the first successful adult human heart transplant in the United States in 1968. Since Shumway’s time, Stanford’s heart transplant operation, heart transplantation continues to be one of the few treatment options available for end-stage heart disease.

“Heart transplantation opened up a potential life-saving treatment for people who were dying of heart disease,” said Sharon Hunt, MD, PhD, a professor emerita of medicine who was a Stanford medical student when Shumway performed his first transplant. She later became Ishaq’s transplant cardiologist.

Life was ‘literally hell’

For Ishaq, a nagging cold was the first sign that something was wrong. After multiple trips to the doctor she was diagnosed with an enlarged heart. It could no longer pump blood effectively to her body. She went from working full-time and enjoying life to barely being able to walk from one room to another without getting out of breath.

“Life before my first heart transplant was literally hell,” she said. “I couldn’t function or do anything on a day-to-day basis with the heart that I had.”

When medical therapy failed to improve her condition, Ishaq’s doctor referred her to Stanford. At her first appointment, she knew she was in the right place.

Her Stanford cardiology team continued to monitor her enlarged heart, and placed her on the transplant list when it was clear that her right side had completely failed, and her left side was on its way to failing. “I believed they would make me better,” she said. “I love my entire transplant team. Without them, I would not be here.”

She underwent a heart transplant in 1991 and, when she became pregnant a year later, she asked Hunt, “Can I keep it?” At the time, the Stanford transplant team discouraged heart recipients from conceiving a child because of the risk of complications to the organ, such as rejection, infection and graft dysfunction, a life-threatening complication that affects the hearts ability to circulate blood effectively. But Ishaq was willing to do whatever it would take to have a baby, and Hunt was ready to help.

“Because I left her mother, Mo-nique, Ishaq said. “She is the first baby born to a heart transplant recipient at Stanford. The delivery room was packed with 28 people, all of whom wanted to witness the historic birth.”

Ishaq was fine for 24 years with her new heart, and Hunt continued to care for her. But she had a setback in mid-2015 when her heart and kidneys began to fail. Her blood pressure periodically plummeted, causing fainting spells. The first time it occurred, it was the middle of the night. Ishaq woke up on the floor, her dog persistently nudging and licking her.

Ishaq received a second heart transplant on Nov. 9, 2015. Because her body was also showing signs of kidney failure, her Stanford transplant team decided to simultaneously conduct a kidney transplant.

Stanford at ‘heart’ of innovation

Today, approximately 50 patients undergo heart transplantation at Stanford each year, and the program has performed more than 1,200 heart transplants over five decades. Stanford remains the oldest, continuously operating heart transplant center in the world, and its physicians are responsible for many of the innovations that continue to improve long-term survival.

Research conducted by Shumway and his team led to the use of the antirejection immunosuppressive drugs, which help weaken hearts continue to circulate blood. Additional Stanford contributions to the field include the creation of the classification system used to determine rejection, and the development of a noninvasive way to detect rejection earlier than previously possible.

“Stanford really is the birthplace of heart transplantation,” said Kiran Khush, MD, associate professor of medicine at the Stanford School of Medicine and a transplant cardiologist who works as part of a team of physicians, nurses, physical therapists, social workers, dieticians and pharmacists to care for patients before, during and after heart transplantation at Stanford Hospital.

For Ishaq’s daughter Monique Crawford, Stanford is simply home. “It’s where my mom Jonaih was born. It’s where I was born, and it’s where my mom got both of her new lives. Stanford is definitely a special place for us.”

‘DNA origami’ triggers tissue generation in early development

By Krista Conger

A developing embryo faces the difficult task of concentrating morphogens — proteins that are responsible for the body patterning of wings and the head, for example. Varying concentrations and types of morphogens affect a developing embryo is so dramatic. Subsequent days of developmental biology, in part because their expression by directing the looping of DNA in a cell.

The researchers were particularly interested in learning more about how to stimulate the production of a type of skin cell called keratinocytes to treat epidermolysis bullosa, a blisters disease with few treatments, they believe their findings may have implications for the derivation of other therapeutically useful tissue types.

“For the first time, we were able to see how morphogens and master transcriptional regulators work together to control the development of keratinocytes,” said Anthony Oro, MD, PhD, professor of dermatology. “We’ve always wondered how a transcription factor required for the development of vastly different cell types knows which genes to make into proteins in which situation. Now we’ve answered that question: morphogens help the master transcription factors hook up to the right targets, and the transcription factor is responsible for the body, causes dramatically different outcomes.”

A paper describing the research was published online Nov. 5 in Nature Genetics.

Oro, who is also the Eugene and Gloria Bauer Professor, is the senior author. Postdoctoral scholar Jillian Patterson, PhD, former postdoctoral scholar Sandra Melo, PhD; and graduate student Samantha Pieckos share lead authorship.

Putting body parts in the right place

Morphogens are responsible for the body patterning that occurs, for example, that the fly’s wing ends up on its thorax rather than the top of its head. They were the first important class of proteins identified in the early days of developmental biology, in part because their effect on a developing embryo is so dramatic. Subsequent studies showed that they work through the process of diffusion and can have different effects based on their concentration throughout the embryo. Cells that are near other cells making and releasing the morphogen are exposed to a much higher concentration than those farther away, as waves of varying morphogens overlap and interact, they direct the proper placement of legs, wings and the head, for example.

Researchers also identified other types of proteins called master transcriptional regulators that bind to DNA to control the expression of specific genes throughout the cell. These cell proteins that control the expression of specific genes throughout the cell.

Anthony Oro and his colleagues have identified a key regulatory hierarchy in which proteins called morphogens control gene expression by directing the looping of DNA in a cell.
Older fathers associated with increased risks for their newborns

By Hanea Armitage

A decade of data documenting live births in the United States links babies of older fathers with a variety of increased risks at birth, including low birth weight and seizures, according to a new study by researchers at the School of Medicine.

The data even suggest that the age of the father can sway the health of the mother during pregnancy, specifically her risk for developing diabetes.

“We tend to look at maternal factors in evaluating associated birth risks, but this study shows that having a healthy baby is a team sport, and the father’s age contributes to the baby’s health, too,” said Michael Eisenberg, MD, associate professor of urology.

Data from more than 40 million births showed that babies born to fathers of an “advanced paternal age,” which roughly equates to older than 35, were at a higher risk for adverse birth outcomes, such as low birth weight, birth defects, and seizures, according to a new study by researchers at Stanford, Florida.

Michael Eisenberg and his colleagues examined data from more than 40 million births and found links between older fathers and increased health risks for their infant children.

By Erin Digitale

Gun deaths among children and teenagers are twice as common in U.S. states with the most lax gun laws compared with states with the strictest gun control legislation, a study from the School of Medicine has found.

In addition, states with laws that restrict children’s access to guns have lower rates of firearm-related suicides among youth, even after controlling for other factors, the study said.

The research will be presented in a scientific talk today at the American Academy of Pediatrics 2018 National Conference & Exhibition in Orlando, Florida.

The title of the presentation is “Strict Firearm Legislation Is Associated With Lower Firearm-Related Fatalities Among Children and Teens in the United States.”

“Children are 82 times more likely to die in our country of a firearm injury than in any other developed nation,” said senior author Stephanie Chao, MD, assistant professor of surgery at Stanford. “We focus a lot on the federal government and the laws that they make, and the things they can do to protect our children from firearms. But our study shows that what states do at the state level really does have an impact.”

The lead authors of the study are professor of pediatrics Gary Shapira, MD, PhD; professor of pediatric surgery and graduate student in surgery and graduate student in biomedical sciences David Stevenson, MD; and professor of biomedical data Ying Lu, PhD.

Eisenberg is a member of Stanford Bio-X, the Stanford Child Health Research Institute and the Stanford Cancer Institute.

Stanford’s Department of Urology also supported the work.
The combination of rituximab and Hu5F9-G4 has previously been shown to work well in fighting human cancers in animal models, but this is the first published study of a clinical trial of this therapy in humans. The trial builds upon previous studies of CD47 and its role in cancer that published result of a clinical trial of this therapy in humans,“Yang said.

“Knowing the genetics behind antler regeneration, fast to this field and mineralization is fundamental to our ultimate therapeutic goal and is critical to understanding rapid bone generation in other species, like humans,” Yang said.

The genes Yang and his collaborators identified are uhrf1, which supports rapid bone cell proliferation, and s100a10, which supports rapid mineralization, or the hardening of bone tissue. Together, the genes work in a one-two punch fashion, with uhrf1 spurring bone cell generation and s100a10 working to cement the bone’s structural matrix. What lends even more transformative potential to Yang’s research is that both uhrf1 and s100a10 are linked to bone development in humans.

"Right now, we have two focuses: To understand the genetic regulation of deer antler growth, and to see if we can use this information to build therapeutic agents to potentially prevent or treat bone diseases such as osteoporosis, or more quickly repair bone fractures,” said Peter Yang, PhD, associate professor of orthopedic surgery.

Antlers are essentially regenerating bone, which is rare in the animal kingdom. During the spring, antlers begin to sprout; by winter, they start to shed. Antler regeneration is a unique phenomenon that, “for me, is worth studying just out of pure curiosity, but also to help, it may have some really interesting applications for human health,” Yang said.

Applying antler genetics to humans

The researchers hope that their insights into antler genes might inform new approaches for treating disease. Yang plans to pursue deer antler genetics. But while on vacation in Alaska in 2009, Yang’s tour guide rattled off some fun facts about wild deer, and it piqued his curiosity.

“Deer antlers can grow a whopping 2 centimeters per day when it’s summertime and their antlers are growing at full speed,” Yang said. “From that guide’s spiel, it made me wonder: Are there special genes that are behind this unusually fast bone growth?”

To investigate, Yang and his lab traveled to a deer farm in California where they collected samples of early antler tissue, which is primarily made up of skeletal stem cells. Antlers grow from the top down, so as they grow upward, a reservoir of stem cells remains at the top of the antlers, continuing to produce large quantities of tissue. In early development, antler tissue is soft, much like the cartilage of your nose, making cell sampling an easy task for Yang and harmless for the buck. Only in the second stage of development does the antler mineralize and become rigid.

Back in the lab, the scientists used a variety of techniques to decipher the genetics behind antler growth, including analyses of RNA, a molecule that helps carry out specific gene instructions, and gene “knock-down” and “over-expression” studies, which hinder gene function or rev it up, respectively. Comparative RNA analyses between stem cells in deer antlers and human stem cells from bone marrow led Yang to a collection of genes that play an important role in driving the process of rapid bone growth.

Yuiling Cheng, a PhD student in Yang’s lab, helped stretch the antler and mineralize tissue in culture from deer to confirm that uhrf1 and s100a10 work in a yin and yang style to continuously form and destroy bone. Osteoblasts break down old bone. The two cell types work in a yin and yang form and degrade bone to maintain balanced bone structure. In osteoporosis, osteoclast function overacts osteoblasts, and the bone starts to break down. "We're just at the beginning of this research, but our ultimate goal is to figure out how we can apply the same underlying biology that allows for rapid bone regeneration in deer antlers to help treat human bone conditions, such as osteoporosis,” Yang said.

Yang plans to conduct research on multiple kinds of deer to confirm that uhrf1 and s100a10 back speedy antler growth across species. In addition, he plans to test how the genes function in human cell lines, while continuing to parse how uhrf1 and s100a10 work on a molecular level, looking into possible functional pathways.

“There's a lot of work to be done, but this could be a unique model of bone regeneration, and our initial work has started to lay a foundation for future studies,” Yang said.

Other Stanford co-authors of the paper are postdoctoral scholars Dan Wang, PhD, and Bin Zhang, PhD; Norma Neff, PhD, former DNA sequencing core director; former undergraduate researcher Rashmi Sharma; William Maloney, MD, the Boswell Chair of Orthopedics and professor of orthopedic surgery; and Steven Quake, PhD, professor of bioengineering and of applied physics and co-chair of the Chan Zuckerberg Biohub.

Peter Yang is a member of Stanford Bio-X, the interdisciplinary program that is fast-tracking the study of diseases in cross-disciplinary teams.

"Antler regeneration is a unique phenomenon that, for me, is worth studying just out of pure curiosity, but also to help, it may have some really interesting applications for human health,” Yang said.
What parents should know about poliomyelitis

Recently, cases of a polio-like illness have occurred among children in the United States. The illness has been identified as acute flaccid myelitis (AFM), a rare complication of enterovirus infection, which can cause paralysis in one or more limbs and strikes mostly children. Keith Van Haren, MD, assistant professor of neurology and Dubravka Volavsek, MD, assistant professor of pediatric infectious disease at the Stanford University School of Medicine, discuss the condition.

What is AFM?
AFM is a condition in which the nerves that control voluntary movement become infected and inflamed. It’s not known why some people develop AFM while others do not. The Centers for Disease Control and Prevention (CDC) reports that between 2014 and 2018, more than 130,000 people were diagnosed with AFM. Although the condition is rare, it is a serious illness that can lead to permanent paralysis in some cases. The CDC advises parents to be on the lookout for the symptoms of AFM and to seek medical attention if they occur.

What are the symptoms of AFM?
Symptoms of AFM may include weakness or loss of movement in one or more limbs, including the arms and legs. Other symptoms may include difficulty with balance, coordination, or speech. Symptoms can develop over a few days or weeks, and may get better or worse over time.

Who gets AFM?
AFM affects people of all ages, but most cases occur in children younger than 5 years old. Boys are affected more often than girls. There is no known way to prevent AFM, but the best way to protect children is to keep them healthy and clean.

What are the causes of AFM?
AFM is caused by a virus called enterovirus 68. The virus is spread by direct contact with infected people or through the air when people who are infected cough or sneeze. The virus can be found in the throat and the nose of infected people.

How is AFM treated?
There is no cure for AFM, but treatment can help manage symptoms. In some cases, physical therapy, occupational therapy, and speech therapy may be needed. In other cases, medication may be prescribed to reduce pain or improve movement.

How to protect children from AFM?
- Keep children healthy and clean by washing their hands frequently and keeping their surroundings clean.
- Avoid close contact with people who have AFM.
- Get vaccinated for other viral illnesses to reduce the risk of AFM.
- Practice good hygiene, such as washing hands with soap and water, to reduce the spread of the virus.

What should parents do if they think their child has AFM?
If you think your child has AFM, take them to the hospital immediately. A doctor will perform tests to determine if the child has AFM. If the child is diagnosed with AFM, the doctor will work with the child and their family to create a treatment plan.

How can AFM be prevented?
There is no vaccine for AFM, but there are steps you can take to reduce the risk of infection. These include:

- Washing hands frequently with soap and water.
- Avoiding contact with people who have respiratory illnesses.
- Covering the mouth and nose with a tissue when coughing or sneezing.
- Disinfecting frequently touched surfaces.
- Avoiding close contact with people who are sick.
- Getting vaccinated for other viral illnesses.

It’s important to remember that AFM is a serious illness that can lead to permanent paralysis in some cases. The best way to protect children is to keep them healthy and clean. If you have questions about AFM, contact your child’s doctor or a health care provider.

Keith Van Haren, MD
Assistant Professor of Neurology
Paul King has been selected as the new president and CEO of Lucile Packard Children’s Hospital Stanford and Stanford Children’s Health. The organization’s board of directors announced King’s appointment Nov. 2.

“With more than 35 years in health care, including 22 years in executive roles leading pediatric healthcare enterprises, Paul brings a wealth of experiences and achievements and contributions to the understanding and treatment of benign and malignant breast tumors. His specific interests are identifying and understanding pathologic and genomic features of breast cancer subtypes, precursor lesions and tumor progression.”

Paul King

“As we plan for the continued growth of Stanford Children’s Health and expansion of innovation across the entire continuum of care, Paul’s distinguished record of accomplishment and dedication to the critically important role of pediatric and academic care will undoubtedly help us achieve our vision of precision health at Stanford Medicine,” said Lloyd Minor, MD, dean of the School of Medicine.

“I am thrilled to be joining Stanford Children’s Health at a time of flourishing innovation in pediatric health care and leadership expertise to Stanford Children’s Health,” said Jeff Chambers, chair of the board of Stanford Children’s Health.

King has led Mort Children’s since 2013, where his management efforts helped the organization achieve the highest patient satisfaction and employee engagement levels across the entire University of Michigan Health System. Prior to that, he served as president and CEO of the Pediatric Management Group, a 550-physician academic pediatric subspecialty group practice affiliated with Children’s Hospital Los Angeles.

Lund stepped into the interim CEO role at Stanford Children’s Health in March, when Christopher Dawes announced his retirement and medical leave of absence. Dawes had served as president and CEO since 2000.

In a joint statement, Minor and Chambers said that Lund “has demonstrated exceptional leadership during this challenging time while also successfully spearheading the opening of the new state of the art Bonnie Uytengsu and Family Surgery and Interventional Center. We also thank Chris for his extraordinary contributions to Packard, Stanford and children’s health nationwide over his remarkable career.”

King is expected to begin his new role at Stanford Children’s Health in early 2019. More detailed plans for his transition will be announced in the coming weeks.