Researchers invent inexpensive nanotech microchips for diagnosing type-1 diabetes

By Erin Digitale

A n inexpensive, portable, microchip-based test for diagnosing type-1 diabetes could improve patient care worldwide and help researchers better understand the disease, according to the device’s inventors at the School of Medicine.

Described in a paper published online July 13 in *Nature Medicine*, the test employs nanotechnology to detect type-1 diabetes outside hospital settings. The handheld microchips distinguish between the two main forms of diabetes mellitus, which are both characterized by high blood-sugar levels but have different causes and treatments. Until now, making the distinction has required a slow, expensive test available only in sophisticated health-care settings. The researchers are seeking Food and Drug Administration approval of the device.

“We think the new test, not only do we anticipate being able to diagnose diabetes more efficiently and more broadly, we will also understand diabetes better — both the natural history and how new therapies impact the body,” said Brian Feldman, MD, PhD, assistant professor of pediatrics and lead author of the study. “Although we cannot draw conclusions about cause and effect from our study, our findings support the notion that exercise and physical activity are important determinants of the trends in obesity.”

The study will appear in the August issue of *The American Journal of Medicine*. It’s also available online now in a draft form.

The researchers analyzed data from the National Health and Nutrition Examination Survey, a long-term project of the Centers for Disease Control and Prevention that collects information from both surveys and physical examinations to assess Americans’ health. The researchers considered survey results from 17,438 participants from 1988 through 1994 and from approximately 5,000 participants each year from 1995 through 2010.

Survey participants recorded the frequency, duration and intensity of their exercise within the previous month. The team defined “ideal” exercise as more than 150 minutes per week of moderate exercise or more than 75 minutes a week of vigorous exercise.

The research highlights the correlation between obesity and sedentary lifestyles, but because it is an observational study, it does not establish a cause-and-effect relationship.

Lack of exercise, not diet, may explain rise in obesity, according to a new study

By Becky Bach

Inactivity rather than overeating could be driving the rise in Americans’ obesity, according to a study by a team of School of Medicine researchers.

Examining national health survey results from 1988 through 2010, the researchers found huge increases in both obesity and inactivity, but not in the overall number of calories consumed.

“The what struck us the most was just how dramatic the change in leisure time physical activity was,” said Uri Ladabaum, MD, associate professor of gastroenterology and lead author of the study. “Although we cannot draw conclusions about cause and effect from our study, our findings support the notion that exercise and physical activity are important determinants of the trends in obesity.”

The study will appear in the August issue of *The American Journal of Medicine*. It’s also available online now in a draft form.

The researchers analyzed data from the National Health and Nutrition Examination Survey, a long-term project of the Centers for Disease Control and Prevention that collects information from both surveys and physical examinations to assess Americans’ health. The researchers considered survey results from 17,438 participants from 1988 through 1994 and from approximately 5,000 participants each year from 1995 through 2010.

Survey participants recorded the frequency, duration and intensity of their exercise within the previous month. The team defined “ideal” exercise as more than 150 minutes per week of moderate exercise or more than 75 minutes a week of vigorous exercise.

The research highlights the correlation between obesity and sedentary lifestyles, but because it is an observational study, it does not establish a cause-and-effect relationship.

Flight irregularity leaves Navy pilot with unusual constellation of symptoms

By Sara Wykes

Edward Damrose, MD, chief of the Division of Laryngology, has nearly 20 years of practice under his belt, but what he observed in U.S. Navy Cmdr. Robert Buchanan stumped him. “I had never encountered anything quite like it before,” Damrose said.

When he had done what he could, he sent Buchanan to Jayakar Nayak, MD, PhD, one of Stanford’s top specialists in the workings of the nasal cavity and sinuses. After Buchanan shared his symptoms with Nayak, he, too, was puzzled.

Nayak, assistant professor of otolaryngology, thought some of Buchanan’s issues might be related to a problem with his left ear duct, so he called Andrea Kessler, MD, assistant professor of ophthalmology and co-director of the Ophthalmic Plastic, Reconstructive Surgery and Orbital Oncology Service at the Byers Eye Institute at Stanford. She looked at Buchanan and agreed with Damrose and Nayak. Whatever it was that was plaguing Buchanan “was something we had never seen,” Kessler said.

What these three expert doctors were chasing was an explanation for air — harmless when it goes where it is needed. Buchanan, however, came to Stanford exhibiting a strange phe-
By Christopher Vaughan

Researchers at the Stanford Institute for Stem Cell Biology and Regenerative Medicine have shown how the kidneys constantly grow and have surprising ability to regenerate themselves, overturning decades of accepted wisdom that such regeneration didn’t happen. It also opens a path toward new ways of repairing and even growing kidneys.

“These are basic findings that have direct implications for kidney disease and kidney regeneration,” said Yuval Rinkevich, PhD, the lead author of the paper and a postdoctoral scholar at the institute. The findings were published online May 15 in Cell Reports.

It has long been thought that kidney cells didn’t reproduce much once the organ was fully formed. The new research shows how the kidneys are continuously regenerating and repairing themselves throughout life.

“This research tells us that the kidney is in no way a static organ,” said Benjamin Dekel, MD, PhD, a senior author of the paper and associate professor of pediatrics at Sackler, as well as head of the Pediatric Stem Cell Research Institute at the Sheba Medical Center in Israel.

“The kidney, incredibly, rejuvenates itself and continues to generate specialized kidney cells all the time,” said Irving Weissman, MD, professor of pathology and of developmental biology and director of the Stanford institute, is the other senior author.

“The research, which was done in mice, also shows how the kidney regenerates the tissue. Instead of a single type of kidney stem cell that can replace any lost or damaged kidney tissue, slightly more specific kidney stem cells that reside in different segments of the kidney give rise to new cells within each type of kidney tissue. It’s like a tree with branches in which each branch takes care of its own growth instead of being dependent on the trunk,” Dekel said.

The scientists also showed that the decision these cells make to grow is through the activation of a cellular pathway involving a protein called Wnt.

Even though populations of kidney (mesenchymal) cells look identical, the robust kidney-forming capacity can be traced back to precursor cells in which Wnt is activated and that can only grow into one of two types of specialized kidney tissue, Rinkevich said. “The realization that Wnt signaling is responsible for the generation of new kidney tissue offers a therapeutic target to promote or restore the regenerative capacity of the kidneys,” he said. “We may be able to turn on the Wnt pathway to generate new kidney-forming cells.”

“This finding will be important for scientists who attempt to create kidney parts in the lab, the researchers said. However, they cautioned that such advances are not imminent. To grow a whole kidney in the laboratory would be complicated because we would need to orchestrate the activities of many different kinds of precursor cells using just the right stimuli,” Dekel said. It might be possible to grow a kidney in a complex system that includes the blood and immune system, which can be reconstituted from one type of stem cell.

Other Stanford co-authors of the study are Michael Longaker, MD, MBA, professor of surgery; and Deidre Lyell, PhD, associate professor of developmental biology.

Send letters, comments and story ideas to John Sanford at 723-8309 or at johnsanford@stanford.edu. Please also direct him to receive an e-mail version of InsIde Stanford Medicine.
Researchers develop technique to help unravel cancer’s secrets

By Shara Tonn

An interdiscipli- nary team of chem- ists, oncologists and one statistician at Stanford has taken the first step toward developing a technique that can identify the origin of certain types of cancer — a potential boon to doctors prescribing therapies for their patients.

The researchers' findings were published July 3 in the Proceedings of the Na- tional Academy of Sciences.

"The same cancer can occur because of different genes, but in certain cases the aggressiveness and the type of treatment actually depend on a lot on what oncogene caused that cancer," said Livia Eberlin, PhD, a postdoctoral scholar in chemistry and lead author of the paper.

An oncogene is a normal gene that has mutated, causing cells to become cancerous. In this study, the team members looked at one that is related to lymphoma and responsible for approximately half of all human cancers. They wanted to find a biological signature that would trace the mutating cancer cells back to the original oncogene.

"When cancer takes place, the cell loves to gobble up glucose — that's a sugar — and glutamine," said Richard Zare, PhD, professor of chemistry and senior author of the paper. "It takes these and makes different lipids — different fatty molecules than what it normally makes.

Using a statistical method from co-au- thor Robert Tibshirani, PhD, professor of health research and policy and of sta- tistics, the team was able to identify not just one but 86 lipids that can be traced back to an oncogene.

"It’s not just diagnostic," Eberlin said. "It gives extra information that could be prognostic."

Depending on the bio-signature of the cancer cells, physicians will have a better idea of the aggressiveness of a pa- tient’s cancer. In the future, this research may lead to a better knowledge of cancer in general.

"The next step is to use this as a way to figure out the causal mechanism," said Dean Felscher, MD, PhD, professor of medicine and of pathology and co-au- thor of the paper. "Though the connec- tion between the cancer cells and their origin is clear, the actual cause of cancer — the biological trigger that pushes can- cer to progress — is still mysterious.

As Zare mused, "How does cancer re- ally work? This is a tool to understand the nature of how cancer progresses."

Other co-authors of the paper are Al- ice Fan, assistant professor of medicine, and postdoctoral scholars Mettal Gabay, PhD, and Arvin Gouw, PhD.

The research was supported by grants from the National Science Foundation, the National Institutes of Health and the Air Force Office of Scientific Research, as well as by a Stanford Hospital & Clin- ics Cancer Innovation Fund award.

Livia Eberlin was the lead researcher of a study examining biological signatures in cancer cells.

Stanford to become a clinical site for Undiagnosed Diseases Network

By Erin Digitale

Stanford has received a $7.2 million, four-year grant from the National Institutes of Health to fund a clinical site for the NIH’s new Undiagnosed Diseases Network.

The network expands the NIH Undiagnosed Diseases Program, which was launched in 2008 to help patients who have conditions that skilled physicians have been unable to diagnose despite extensive clini- cal investigation.

To date, approximately 600 patients from across the United States and seven foreign countries have been evaluated at the program’s pilot site at the NIH Clini- cal Center in Bethesda, Md. The NIH team has di- agnosed about 100 of these patients, discovered two unknown diseases and identified 15 genes not previ- ously associated with any other human disease. These successes prompted the NIH to expand to a network of six more clinical sites across the country, including one at Stanford.

The grant to Stanford will be shared by a multidis- ciplinary team from the School of Medicine, Stanford Hospital & Clinics and Lucile Packard Children’s Hos- pital Stanford, and will be used for helping both pedi- atric and adult patients.

"It’s exciting to be able to offer the latest diagnostic testing, including genome sequencing, to these patients who have often traveled around the country looking for answers," said Euan Ashley, MD, PhD, principal investigator for the Stanford grant. Ashley, as- sociate professor of medicine and of genetics, is also director of the Clinical Genome Service and the Center for Inherited Cardiovascu- lar Disease at Stanford Hospital & Clinics.

"I’m particularly excited now to bring Stanford’s cutting edge to the bedside of these patients," he said.

Matthew Wheeler, MD, instructor of medicine and the medical director for the grant at Stanford Hospital & Clinics, said, "Stanford was chosen for our infor- matics expertise, our experience with clinical interpre- tation of whole-exome and whole-genome data, and our scientific potential to follow up any lead."

The team will use cutting-edge genomics and medi- cal phenotyping techniques to diagnose patients, and will also aim to understand the underlying biology of patients’ conditions so they can generate targets for new therapies, Wheeler said. "We aim to make a deep dive into each patient’s biology."

Matthew Wheeler, MD, instructor of medicine and the medical director for the grant at Stanford Hospital & Clinics, said, "Stanford was chosen for our infor-

The team receives funding from SPARK, Stanford’s bioscience incubator, and is seeking funds to commercialize the technology.

School of Medicine team wins start-up competition with plan for commercializing allergy test

A School of Medicine team has won the 2014 Stanford BASES E-Challenge for its plan to commercialize a better diagnostic test for food allergies.

The team, Allertope, was awarded $15,000 from the Business Asso- ciation of Stanford En- trepreneurial Students. The association’s annual start-up competition, the BASES Challenge, gives prizes in three cat- egories: E-Challenge (entrepreneurship), So- cial E-Challenge (social entrepreneurship) and Product Showcase (prod- uct prototype).

Led by Manish Butte, MD, PhD, assistant professor of pediatric immunology and allergy, and Yasmin Chandrasekher, PhD, business ad- viser to Allertope and former Stanford postdoc- toral scholar, the team invented a method to test the severity of a person’s food allergies.

Current food allergy tests provide no infor- mation about whether an allergy is mild, mod- erate or life-threatening. The team’s test uses microspheres made from rapidly dissolvable polymer to painlessly prick the skin with dozens of tiny doses of epitopes, small portions of protein molecules, from an allergenic food. Re- actions to a greater variety of different epitopes from a food indicate a more dangerous allergy.

The team receives funding from SPARK, Stanford’s bioscience incubator, and is seeking funds to commercialize the technology.
Seeing inner workings of brain with CLARITY made easier

By Amy Adams

Last year, Karl Deisseroth, MD, PhD, professor of bioengineering and of psychiatry and behavioral sciences, announced a new way of peering into a disembodied brain that provided spectacular fly-through views of its inner connections. Since then, laboratories around the world have begun using the technique, called CLARITY, with some success to better understand the brain’s wiring.

But two technological hurdles have kept the technique from being more broadly adopted. The first was the problem of removing fat from the brain without damaging the organ’s complex wiring. Second, the most commonly available microscopy methods were not designed to image the whole transparent brain.

“There have been a number of remarkable results described using CLARITY,” Deisseroth said, “but we needed to address these two distinct challenges to make the technology easier to use.”

“A three-dimensional rendering of clarified brain imaged as seen from below (ventral half).”

In a Nature Protocols paper published June 19, Deisseroth and his team described solutions to both of those challenges. “These transform CLARITY, making the overall process much easier and the data collection much faster,” he said.

Deisseroth, who is senior author of the paper, anticipates that even more scientists will now be able to take advantage of the technique to better understand the brain at a fundamental level, and also to probe the origins of brain diseases. The paper’s lead author is Rebecca McKenzie, MD, a postdoctoral fellow in Deisseroth’s lab, who was also a Stanford Bio-X affiliated faculty member.

“This work shares the spirit of the BRAIN Initiative goal of building new technologies to understand the brain — including the human brain,” said Deisseroth, who is also a Stanford Bio-X affiliated faculty member.

Eliminating fat

When you look at the brain, what you see is the fatty outer covering of the nerve cells within, which blocks microscopes from taking images of the intricate connections between deep brain cells. The idea behind CLARITY was to eliminate that fatty covering while keeping the brain intact, complete with all its intricate inner wiring.

The way Deisseroth and his team eliminated the fat was to build a gel within the intact brain that helps hold all the structures and proteins in place. They then used an electric field to pull out the fat layer that had been dissolved in an electrically charged detergent, leav- ing behind all the brain’s structures embedded in the firm water-based gel, or hydrogel. This is called electrophoretic CLARITY.

The electric field aspect was a challenge for some labs. “About half the people who tried it got it working right away,” Deisseroth said, “but others had problems with the voltage damaging tissue.”

Deisseroth and his team had solved that problem when introducing new technologies. When he first introduced optogenetics, which allows scientists to control light-activated neurons with light, a similar proportion of labs were not initially set up to easily implement the new technology, and ran into challenges.

To help expand the use of CLARITY, the team devised an alternate way of pulling out the fat from the hydrogel-embedded brain. A similar proportion of labs were not initially set up to easily implement the new technology, and ran into challenges.

“Probably a good majority of these children, if they’re treated early, don’t need a liver transplant.”

By Erin Digitale

A new mode of treating a sudden, severe form of childhood liver disease could potentially avert dozens of pediatric liver transplants in the United States each year, according to research from the School of Medicine and Lucile Packard Children’s Hospital Stanford.

The new study, a series of nine case reports published, found that an immune-system attack on the liver may explain many cases of pediatric acute liver failure, a condition in which a child’s liver fails without apparent cause over a few days or weeks. Until now, the cause of this disease has been mysterious, and liver transplant has been the only treatment. The findings show that early, aggressive use of existing immune-suppressing therapies could save many children’s lives.

“We believe the large majority of these cases could be explained by dysfunction of the immune system,” said Rebecca McKenzie, MD, a postdoctoral scholar in gastroenterology and the lead author of the study, which is posted online in Pediatric Transplantation. “And probably a good majority of these children, if they’re treated early, don’t need a liver transplant.”

Acute liver failure is responsible for 10-15 percent of pediatric liver transplants, or about 50-80 U.S. transplants each year. Unlike heart- and kidney-failure patients, who can be temporarily supported with a pump or dialysis to assist their failing organs, children with acute liver failure often need an immediate organ transplant to survive. But receiving a transplant has drawbacks, such as a risk of organ rejection and also side effects from a lifetime of immune-suppressing medications. In addition, because donor organs are in short supply, receiving an immune treatment derived from donor blood that can counteract antibodies from the patient’s blood or modulate the immune system in other ways. All patients showed improved liver function, as assessed by blood tests, within 24-72 hours, and one patient who had already been placed on the waiting list for transplant recovered enough to be removed from the list. Four other patients stayed healthy enough to remain off the list for, and not need, liver transplants.

However, the remaining four patients did need a liver transplant. All of the patients who received transplants had liver biopsies showing extensive necrosis — a lack of blood cells caused by bone marrow failure — a lack of blood cells caused by bone marrow failure — suggests that in some patients, liver and bone marrow fail-
Preventing chronic illness in developing nations

There’s a new health policy challenge in developing countries. Though many see chronic conditions like type-2 diabetes and heart disease as problems plaguing the wealthiest nations, “nearly 80 percent of the deaths worldwide from these two diseases are coming from the developing world,” said Sanjay Basu, MD, PhD, assistant professor of medicine with the Stanford Prevention Research Center.

But Basu is working to change this statistic, and his efforts just earned him the $100,000 George Rosenkranz Prize for Health Care Research in Developing Countries.

Administered by the Center for Health Policy/Center for Primary Care and Outcomes Research at Stanford’s Freeman Spogli Institute for International Studies, the award will help fund Basu’s large-scale data collection project in India. With health data on more than 65,000 people in the country, Basu hopes to improve diabetes screening there at a step toward better prevention and treatment of the disease.

A researcher focused primarily on global development and human health, Basu is also an internal medicine physician with a master’s degree in medical anthropology and a doctorate in epidemiology. Writer Kylie Gordon recently interviewed Basu about his research interests and plans for the future.

1 How did you first become interested in global health policy and the developing world?

**Basu**: As a child, our family went back and forth between the United States and India, and the contrast in daily life were striking and overwhelming. There is a sense in many parts of India that life is a privilege and a constant struggle to maintain.

2 Your research in India will involve data collection and mathematical modeling. Sounds rather abstract. How does this work translate into real-world improvements in people’s health?

**Basu**: Our research serves as a bridge between the clinical science of how to prevent and treat disease, and the detailed operations of how to actually deliver better prevention and treatment in the real world. What we specifically do is combine biological and clinical science of how to prevent and treat disease, and the detailed operations of how to actually deliver better prevention and treatment programs. And we’ve looked into reducing intake as a strategy to lower hypertension and cardiovascular disease. But we also have to make sure that we don’t generate iodine deficiency, since salt is the major delivery strategy for iodine and, unlike in the United States, iodine deficiency is a serious concern in India.

3 What’s different about approaching chronic disease prevention in India versus in the United States?

**Basu**: The sheer size and diversity of the population is one big difference. India is four times the size of the United States and far more diverse. There is simultaneously malnutrition and obesity, starvation and type-2 diabetes, vitamin deficiency and heart attacks — often in the same city. That means designing programs for a country — or a province, or even a city — requires a lot of attention to complicated, perverse outcomes that may happen. For example, we’ve recently looked into reducing sodium intake as a strategy to lower hypertension and cardiovascular disease. But salt may be a single syndrome, perhaps caused by an immune-system attack on both organs. A widely used treatment for bone-marrow failure involves using medications to suppress the immune system that are similar to those administered after liver transplant,” McKenzie said. “When someone receives a liver transplant, the new organ gives them a bit of protection from the system. And so the key question right now is how to find these folks within the limits of current infrastructure, or how to build better infrastructure without taking away funding from other important programs.

5 What’s next for you? What other research projects might your laboratory pursue down the road?

**Basu**: We are expanding our analysis of actual health-care outcomes among populations. We’re studying “natural experiments” in which similar populations experience very different health policies — such as new insurance, prevention and treatment programs. And then we follow those folks as they move through similar processes of economic development, urbanization and cultural change to find out what works and what fails in improving population-health outcomes.

The research was supported by Defense Advanced Research Projects Agency, the National Institute of Mental Health, the National Science Foundation, the National Institute on Drug Abuse, the Stanford Prevention Research and the Wiegars Family Fund.

Amy Adams is the director of interdisciplinary life sciences communications for Stanford.
Stanford University will name a new home for bioengineering and chemical engineering in recognition of gifts from university trustee Kantvir "Ram" Shriram and his wife, Vidjaleatchoumy "Vijay" Shriram. The couple have provided $57 million in support for the new Shriram Center for Bioengineering & Chemical Engineering, the fourth and final building in the university's new Science and Engineering Quad. The couple also will endow the chair in the Department of Bioengineering.

"The Shriram Center will unite innovators in science, engineering and medicine, enabling them to work together more closely and more quickly," said Vidjaleatchoumy "Vijay" Shriram, left, and Kantvir "Ram" Shriram helped to fund the Shriram Center for Bioengineering & Chemical Engineering, the fourth and final building in the university's new Science and Engineering Quad. The couple also will endow the chair in the Department of Bioengineering.

$57 million for bioengineering, chemical engineering center

Diabetes

requireing a lab-based blood draw, it can be done with just a finger prick.

The microchip relies on a fluorescence-based method for detecting the antibodies. The team's innovation is that the glass plates forming the base of each microchip are coated with an array of nanoparticle-sized golds, which intensify the fluorescent signal, enabling reliable antibody detection. The test was validated with blood samples from people newly diagnosed with diabetes and tested from people without diabetes. Both groups had the old test and the microchip-based test performed on their blood.

In addition to new diabetics, people who are at risk of developing type-1 diabetes, such patients' close relatives, also may benefit from the test because it will allow doctors to quickly and cheaply track their auto-antibody levels before they show symptoms. Because it is so inexpensive, the test may also allow the first broad screening for diabetes auto-antibodies in the population at large.

"Auto-antibodies as a 'crystal ball'"

"The auto-antibodies truly are a crystal ball," Feldman said. "Even if you don’t have diabetes yet, if you have one auto-antibody linked to diabetes in your blood, you are at significant risk; with multiple auto-antibodies, it’s more than 90 percent risk."

Type-1 diabetes patient Scott Gualdoni, of Palo Alto, and his 9-year-old daughter, Mia, are excited about the new test. Gualdoni was diagnosed with diabetes in 2011, at age 41. Because of his age, his primary care physician began treating him for type-2 diabetes without checking for type-1 auto-antibodies.

After a few months, Gualdoni returned to his doctor and asked for an antibody test. "I was just feeling like something wasn't right," he said. His suspicions were confirmed: He had type-1.

"Doctors may not be thinking adults can get late-onset type-1," he said. "I slipped through the cracks."

He’s eager to see the microchip test implemented because a cheap handheld test in the doctor’s office would have saved him months of incorrect treatment. "If you’re not treated the right disease, you’re really doing damage to your body," he said.

The test also holds promise for Mia, who was found to have five kinds of diabetes auto-antibodies in her blood when she volunteered for TrialNet, a nationwide study that tracks relatives of people with type-1 diabetes to monitor their risk.

"I’m really excited for other people who are at high risk for diabetes that this new technology is available for them now," Mia said.

"There is great potential to capture people before they develop the disease, and prevent diabetes or prevent its complications by starting therapy early," Feldman said.

But it was prohibited for that type of thinking because it was so costly and time-consuming.

Stanford University and the researchers have filed for a patent on the microchip, and the researchers also are working to launch a startup company to help get the method approved by the FDA and bring it to market, both in the United States and in parts of the world where the old test is too expensive and difficult to use.

"We would like this to be a technology that satisfies global need," Feldman said.

Bo Zhang, a graduate student in chemistry, and Rajiv Kumar, MD, clinical assistant professor of pediatric endocrinology and diabetes, are lead authors of the paper. Another Stanford co-author is Hongjie Dai, PhD, professor of chemistry. Feldman and Dai are members of Stanford’s Child Health Research Institute.

The work was supported by grants from Stanford’s SPARK program; the National Institutes of Health; the National Cancer Institute; JDRF, a type-1 diabetes research foundation; Stanford Bio-X; Gerentech; and the Child Health Research Institute at Stanford.

Stanford’s Department of Pediatrics also supported the work.

Obesity

address the possible causal link between inactivity and weight gain.

"We have not found a consistent pattern day per day did not change substantially during those periods, it didn’t mean that the number of calories consumed were optimal. "We simply didn’t have the statistical increase over time," he said, noting that caloric intake and physical activity are both important determinants of weight.

Both obesity and abdomi-

nul girth, which the team analyzed independently, con- tributed to a variety of well-documented conditions, such as diabetes and cardiovascular disease, as well as increased mortality.

Department 2010, 61 percent of women and 42 percent of men had too much belly fat, up from 46 percent and 29 percent in 1999-2000. In addition, one out of three waist of even normal-weight women swelled between 1988 and 2010, the study shows.

Ladabaum noted that the study did not follow one group of participants over that 22-year span; instead, the data came from different samples in each survey cycle. But the samples are constructed to be representative of the population.

In an accompanying editorial, the journal’s managing editor, Pamela Powers Hann- ley, MPH, called the study “a clarion call.”

"Obesity is a complex, multifaceted problem linked to a variety of societal factors," Hanley said in an interview.

"There are societal and eco-

nomic forces at work that we must address," she said.

"Take, for example, the struggle of single mothers who are trying to balance work and child care. They may lack the time or resources to exercise. We shouldn’t as- sume that people are just lazy. Their lives may be overwhelming to them." Recommendations to exercise 30

minutes a day aren’t enough, Hanley added.

"It’s going to take widespread change," she said. "We shouldn’t just tell patients they need to work out. We need to work with communities, employers, and local governments to enable healthy lifestyles by ensuring that there are safe spaces to exercise that are cheap or free.”

Other Stanford co-authors of the study are Ajitha Mannalithara, PhD, a social science research associate; Parvati Myer, MD, a former postdoctoral scholar who is now at Kaiser Permanente, and Gurmikul Singh, MD, adjunct professor of gastroenterology.

The study was funded by the National Institutes of Health.

Stanford’s Department of Medicine also supported the research.

Becky Bach is a science-writing intern for the medical school’s Office of Communicati-
on July 14, 2014

INSIDE STANFORD MEDICINE
**Pilot continued from page 1**

nommenon: If he pushed his hand along his neck, he could produce a sound like a knocking. Air had entered the tissues of his neck and was trapped, causing a painful constellation of symptoms. Before coming to Stanford, Buchanan had gone from doctor to doctor — to dozens, in fact — hoping for treatment, but finding none. Sometimes, he was told, “Learn to live with it.” Sometimes, he was doubted. “I knew myself well enough to know I wasn’t crazy,” Buchanan said. “There was something physiological happening to me.”

**Decompression injury**

What no one could explain was how to find that misplaced air and the tumorous system it caused: a pulsating heartbeat and a cluster of issues on his left side — a drooping eyelid, constricted pupil, hyper-sensitive sinuses, jaw pain and neck swelling.

Buchanan had lived most of his adult life as a U.S. Navy aviator, flying combat jets at hundreds of miles per hour at thousands of feet in the air. By the time he arrived at Stanford in 2012, he had been grounded from flight since March 20, 2006, a day that changed everything for him.

Flying back to the aircraft carrier after a mission in the Middle East, he began to notice some powerful pressure fluctuations in the cockpit of the jet. He was wearing an oxygen mask and, as all aviators do, knew how to react to the symptoms of oxygen deprivation. But what he was feeling was different from lack of oxygen. “I remember the feeling of incapacitation,” Buchanan said, “and then there was some sort of lapse.”

When his awareness faded out, he was flying at about 27,000 feet above the sea and 450 miles from the nearest U.S. Air Force base. After a few minutes, Buchanan regained consciousness to the voice of a fellow pilot, flying nearby, repeatedly yelling his call sign over the radio. With help, Buchanan managed to fly back to the aircraft carrier. He remembers getting out of the plane and having a hard time keeping his balance. (Buchanan said he could not share further details about the incident.)

The aviator’s career was only one of a common phenomenon,” Damrose said. He believed that air was traveling toward Buchanan’s eye and brain, into his ves-tibular system — a nest of canals and capsules in the inner ear — and back down into his chest. “Air escaping throughout the body can kill a person,” Damrose said. “We could not find a source”

He surgically removed the sac, but Buchanan’s symp-toms continued, and the mystery remained. Damrose looked again, this time at Buchanan’s esophagus, lungs and voice box. “Once we knew where the air was not coming from, we were concerned about where it was really going,” Damrose said. “We looked every-where that would be expected, and we could not find a source.”

An extensive search of medical literature and con-sultations with colleagues at other medical institutions didn’t get them closer to a diagnosis, either. Damrose turned to Nayak. “I needed somebody who could take a fresh look at this evidence and say, ‘This might be something new that we’ve not encountered before,’” Damrose said. Nayak looked at Buchanan’s CT scans and found only changes in his sinuses typical of those caused by years of high-altitude flying.

Bit by bit, Nayak explored the interior cavities of Bu-chanan’s face and skull endoscopically and with medical imaging. “There were areas that looked entirely normal,” he stated, “but if you touched them, they were exquisitely tender,” Nayak said. “That’s when you realize it was a combination of factors that most likely caused by high-altitude flying, Dr. Nayak told me it looked as if a bomb had gone off in my sinuses,” Buchanan said. “I needed somebody who could take a fresh look at this evidence and say, ‘This might be something new that we’ve not encountered before,’” Damrose said. Nayak looked at Buchanan’s CT scans and found only changes in his sinuses typical of those caused by years of high-altitude flying. “I knew myself well enough to know I wasn’t crazy,” Buchanan said. “There was something physiological happening to me.”

Nayak said. First, he repaired the damage typically caused by high-altitude flying. “That’s the pinnacle of an aviator’s career,” he said. “Through this process, we learned of two other Navy pilots with similar decompression injuries that hadn’t been previously reported,” Kossler said.

The Stanford doctors did have to come up with a name for this now-identified decompression injury. It doesn’t exactly roll off the tongue, but it’s finally part of medicine’s lexicon: a sino-cervical fistula.

Nayak is waiting for one small token of thanks he still receives from Buchanan. “I want him to call me from somewhere higher than 20,000 feet, from the cockpit of his F-18, doing what he does best and what he loves to do.”

Sara Wykes is a writer for the Stanford Hospital & Clinics communications office.

The opinions contained in this presentation are solely those of Cone. Buchanan and are not intended to represent the opinions of the Department of Defense, Department of the Navy or any part of the United States Government. Furthermore, the opinions and information contained in this presentation should not be construed as implying an endorsement of any organization by the Department of Defense, Department of the Navy, or any part of the United States Government.
Sergiu Pasca, age 36, during vertebrate embryonic development. The Pew Scholars program supports assistant professors in Biomedical Sciences by The Pew Charitable Trusts. His work focuses on neural development and the disorders that arise with funding over four years to help them start their careers as clinical and translational researchers.

University-wide, these two programs are administered by Spectrum, the Stanford Center for Clinical and Translational Research and Education. Both programs provide promising young scholars with financial support, training and mentoring to help them initiate research that accelerates the translation of medical discoveries into better health.

K2L program

Five scholars will join the K2L Mentored Career Development Program, which provides financial support and advanced training in clinical and translational research in health-related fields. The new K2L program participants are:

- Rira Hamad, MD, MPH, family medicine
- Rebecca McKenzie, MD, pediatric gastroenterology and hepatology
- Joshua Mooney, MD, pulmonary and critical care
- Mary-Beth Percival, MD, hematology-oncology
- Sidhartha Sinha, MD, gastroenterology and hepatology

TL1 program

Another five have been accepted into the TL1 Predoctoral and Postdoctoral Research Training Program, which provides partial tuition and stipend support for a year of full-time instruction in research methods or pointed toward research. The new TL1 program participants are:

- Colleen Craig, MD, endocrinology
- Christine Chen, medical student
- Andrew South, MD, pediatric nephrology
- Erick Sullivan, medical student
- John Openshaw, MD, infectious disease

Both programs are funded by an institutional Clinical and Translational Science Award from the NIH.

Information on these programs is available on the Spectrum website for more information, contact Anandi Krishnan, PhD, academic and research program officer at Spectrum, at anandi.krishnan@stanford.edu, or Steven Goodman, MD, MHS, PhD, director of research education and training at Spectrum, at steve.goodman@stanford.edu.

Menon, Roncarolo appointed to endowed professorships

Two Stanford Medicine faculty have recently been named to endowed professorships:

- Vinod Menon, PhD, professor of psychiatry and behavioral sciences and of neuroscience, was appointed the Rachael L. and Walters F. Nichols, MD, professor, effective June 12. The professorship was established by Rachael L. and Walters F. Nichols, ‘37, MD ‘43, of Pasadena, Calif.

Menon’s lab uses advanced imaging and computational techniques to investigate the functional and structural architecture of cognitive networks in the human brain. His lab also investigates how disruptions in specific brain circuits impact behavior, cognition, emotion and learning in individuals with neurodevelopmental, psychiatric and neurological disorders. Menon is director of the Stanford Cognitive and Systems Neuroscience Laboratory.

The Nichols family has long supported the Department of Psychiatry and Behavioral Sciences at Stanford. In 1989, the couple created the Walter F. and Rachael L. Nichols Fund at the School of Medicine to encourage efforts to increase understanding, improve treatment, care, or prevent schizophrenia and other related disorders.

- Maria Grazia Roncarolo, MD, professor of pediatrics and medicine and chief of the Division of Pediatric Translational and Regenerative Medicine, was appointed the George D. Smith Professorship in Stem Cell and Regenerative Medicine, effective June 12. Roncarolo joined the Stanford faculty in June and will lead efforts to translate scientific discoveries in regenerative medicine into novel patient therapies, including treatments based on stem cells and gene therapy. She also serves as co-director of Stanford’s Institute for Stem Cell Biology and Regenerative Medicine.

The professorship was established with a gift from the George D. Smith Fund and is intended for a faculty member in the field of stem cell biology and regenerative medicine. It is the third professorship established at Stanford by the fund.