Blood test can predict premature birth

By Erin Digitale

A new blood test for pregnant women detects with 75-80 percent accuracy whether their pregnancies will end in premature birth. The technique can also be used to estimate the gestational age of a fetus — or the mother’s due date — as reliably as and less expensively than ultrasound.

Developed by a team of scientists led by researchers at Stanford University, the tests could help reduce problems related to premature birth, which affects 15 million infants worldwide each year. Until now, doctors have lacked a reliable way to predict whether pregnancies will end prematurely, and have struggled to accurately predict delivery dates for all types of pregnancies, especially in low-resource settings.

The blood tests are described in a paper that was published online June 7 in Science. Stephen Quake, PhD, professor of bioengineering and of applied physics at Stanford, shares senior authorship with Mads Melbye, MD, visiting professor of medicine. The lead authors are former Stanford postdoctoral scholar Thuy Ngo, PhD, and Stanford graduate student Mira Moufarrige.

“This work is the result of a fantastic collaboration between researchers around the world,” said Quake, who is also Lee Ottersen Professor in the School of Medicine. “We have worked closely with the team at the Stanford March of Dimes Prematurity Research Center, and the research involved collaborations with scientists in Denmark, Pennsylvania and Alabama. It’s really team science at its finest.”

The tests measure the activity of maternal, placental and fetal genes by assessing maternal blood levels of cell-free RNA, tiny bits of the messenger molecule that carry the body’s genetic instructions to its protein-making factories. The team used blood samples collected during pregnancy to identify which genes gave reliable signals about gestational age and prematurity risk.

“We found that a handful of genes are very highly predictive of which women are at risk for preterm delivery,” said Melbye, who is also president and CEO of the Statens Serum Institut in Copenhagen. “I’ve spent a lot of time over the years working to understand preterm delivery. This is the first real, significant scientific progress on this problem in a long time.

Toll of preterm births

Pregnancy birth, in which a baby arrives at least three weeks early, affects 9 percent of U.S. births. It is the largest cause of infant mortality in the United States and the largest contributor to death before age 5 among children worldwide. In two-thirds of preterm births, the mother goes into labor spontaneously; doctors usually do not know why. Previously, the best available tests for predicting premature birth worked only in high-risk women, such as those who had already given birth prematurely, and were correct only about 20 percent of the time.

Quake first took an interest in this problem when he became a parent: His daughter was born nearly a month early. “She’s now a very healthy and active 16-year-old, but it certainly stuck in my mind that this is an important problem to work on,” Quake said.

Doctors also need better methods for measuring gestational age, he added. Obstetricians now use ultrasound scans from the first trimester of pregnancy to estimate a woman’s due date. 

Compound found in citrus oil could reduce dry mouth in head, neck cancer patients

By Becky Bach

A compound found in citrus oils could help alleviate dry mouth caused by radiation therapy in head and neck cancer patients, according to a new study by researchers at the School of Medicine.

The compound, called d-limonene, protected cells that produce saliva in mice exposed to radiation therapy — without diminishing the tumor-fighting effects of the radiation. The researchers, led by graduate student Julie Saiki, also showed that taken orally, d-limonene is transported to the salivary gland in humans.

The study was published online May 21 in the Proceedings of the National Academy of Sciences. The finding was possible because of a close collaboration between clinicians and basic scientists, said co-senior author Daria Mochly-Rosen, PhD, professor of chemical and systems biology. “This is a perfect example of two pieces that could not work alone.”

“Stanford is a fertile ground for collaboration,” added Quynh-Thu Le, co-senior author and professor and chair of radiation oncology.

About 40 percent of head and neck cancer patients who receive radiation therapy develop dry mouth, known clinically as xerostomia. It’s more than uncomfortable. Patients struggle to speak and swallow and are more likely to develop oral pain or dental cavities, and the condition can lead to tooth removal, in some cases, Le said. And, although some recovery can occur in the first years after the therapy, once saliva production is impaired, it is usually gone for life.

Radiation can kill salivary cells

One drug, called amifostine, is approved for use during radiation therapy to try to protect the salivary gland. But it is not always effective, Le said. And although some recovery can occur in the first years after the therapy, once saliva production is impaired, it is usually gone for life.

“Blood is one of the easiest biological samples to obtain,” said Marius Wernig, MD, associate professor of pathology and a member of Stanford’s Institute for Stem Cell Biology and Regenerative Medicine. “Nearly every patient who walks into a doctors’ office has a blood test done.”
Stanford has been selected as one of five universities to receive a Physician Scientist Institutional Award from the Burroughs Wellcome Fund. The grant, announced June 1, provides the School of Medicine with $2.5 million over five years to support novel programs that enhance career development for medical students who wish to strengthen their research skills. Physician-scientists are essential bridges between clinics and labs, and are defined as physicians who spend a majority of their time conducting research. Most physician-scientists hold both an MD and PhD. The grant is designed to encourage research among the group of nearly 20,000 MD-only physicians who graduate annually from medical schools in the United States. Medical students at Stanford are required to complete a scholarly concentration to graduate, and many want to pursue longer-term research projects by spending an extra year on campus.

With funding from the award, Stanford will take this five-year curriculum a step further, allowing students to add a sixth year of full-time research as a Burroughs Wellcome Fund Scholar, said PJ Utz, MD, professor of medicine and associate dean of medical student research, who is also one of the three principal investigators for the grant. The grant, together with financial commitments from the school’s Medical Scholars Program and the Dean’s Office, will help fund students’ research in years 2 and 3, and will fully fund research and clinical clerkships during the last three years of training. As many as five students per year will be recruited, with a goal of matching the students to research-intensive residences at top-tier programs. Utz said an effort is underway to develop an associated master’s degree in the biosciences at Stanford for MD students.

“In addition to our outstanding, almost 50-year-old MD-PhD program, our new Burroughs Wellcome Fund Scholars Program will generate MD-only physician-scientists who are curious, outstanding researchers and caring clinicians,” Utz said. “They will take questions from their patients back to their research groups to figure out solutions to unsolved problems.”

Utz said he is stepping down as director of Stanford’s Biomedical Sciences Graduate Program to direct the new Burroughs Wellcome Fund Scholars Program. His fellow principal investigator for the grant is Noel Bel laureates Paul Berg, PhD, professor emeritus of biochemistry, and Brian Kolbka, MD, professor of molecular and cellular physiology.
Four recipients of Spirit, Inspiring Change awards announced

By Kira Newby

The School of Medicine has announced the winners of the annual Anne G. Crowe Spirit Award and Inspiring Change Leadership Award.

Spirit Award winners are selected for their outstanding dedication, initiative, motivation, positive attitude and customer service. This year’s recipients are Misty Mazzara, an educational program manager in the Department of Health Research Policy, and Michela Pilo, an administrative associate in the Department of Dermatology.

The Inspiring Change Leadership Award, which goes to staff members who have implemented processes that improve the school, was given to both Kim Osborn, administrative director of clinical education in School of Medicine Student Affairs, and Shannon Monahan, a research analyst in the Office of Postdoctoral Affairs. Each winner receives $3,000.

Misty Mazzara

With gusto and pizzazz, Misty Mazzara manages the four graduate-level educational programs in the Department of Health Research and Policy. In this role, she juggles the tasks associated with admissions, orientation and graduation for the master of science and PhD degree programs in epidemiology and clinical research and in policy and several other units at the university. For example: We are now building human connections between caregivers, medical students, physician-as-teachers and patients, which has allowed her to spend more time with Stanford students with early patient experience, and this innovative new course that provides first-year medical students with a more realistic sense of patient care.

“Misty is incredibly helpful in guiding students through the graduate program application process and tracking the myriad details necessary for completing the degrees,” said Martha Kessler, executive director of finance and administration in health research and policy. “She makes sure supplies never run out. She solves technical problems with the computer-based systems. She keeps the office neat. She also likes her co-workers. “There are very smart, humble people here, and it’s hard not to love working with them,” she said.

Before Pilo moved to Stanford four years ago, she worked for 12 years as a jack-of-all-trades at a nonprofit arts foundation. The thing she appreciates about her current position is its healthy work-life balance, which has allowed her to spend more time with her husband and two teenagers, as well as indulge in her passion for Italian cooking.

“She is tenacious and does not give up until she has explored every option and found a solution. She doesn’t see the boundaries of her job description, but rather looks for opportunities that allow those around her to work more efficiently. The department is fortunate to have someone whose spirit and work ethic inspires others.”

One of the things Pilo likes about her job is that every day is different. On a daily basis she manages seemingly does the work of a multitude. And she seems the most capable of making things seem easy — and they are.”

Shannon Monahan

Shannon Monahan won an Inspiring Change Leadership Award for her dedication to continuous improvement in the systems and processes that support postdoctoral training at Stanford University.

When she joined the office in March 2006, postdoctoral scholars were appointed through a laborious paper-based process. Monahan served as the technical lead in designing an online platform that streamlined the appointment processes and enabled the collection of data that could be used to understand the postdoctoral experience at Stanford. Since that time, she has continued to work for improvements to the myriad systems that impact postdoctoral administration. For example, she pushed for a policy change that allowed postdoctoral registration fees to be automatically charged to applicable projects. This saved hundreds of hours of administrative work each year over all the schools and eliminated the surprise collection notices delivered to postdocs who were unaware of the erroneous bills. She also helped guide the redesign of the online platform that streamlines the process for postdocs to request a travel award, and recently announced by the provost.

“Monahan’s analytical talents, attention to detail, understanding of arcane systems and ability to work with a wide range of people have made her an immeasurably effective change agent,” said Sofie Kleppner, PhD, associate dean for postdoctoral affairs.

“My goal has always been to put myself out of a job by automating things,” said Monahan. “If I can get systems to a point where my colleagues can access the data that they need anytime and anywhere, that’d be terrific.”

She was also instrumental in the establishment and administration of a hardship fund for postdoctoral scholars, which covers expenses such as housing and child care for postdocs. Her analyses were invaluable in modeling the impact of the recent increase in the minimum postdoctoral salary to $60,000, as was recently announced by the provost.

“Through her outstanding ability and remarkable dedication, Shannon has generated and analyzed the data supporting the efforts of university leadership and the faculty to provide the best possible environment for postdoctoral training,” said Will Talbott, PhD, senior associate dean for graduate education and postdoctoral affairs. “Her deep knowledge and thoughtful approach to solving challenging problems, continuous improvement and collaboration, Monahan sets a unique and powerful standard,” Kleppner said.

Monahan attributes her success, at least in part, to the work ethic that her parents instilled in her while growing up on the Upper East Side. She won the award money for a trip to Ireland to visit her ancestral homeland and meet a few long-lost relatives.
Experts discuss ways to improve electronic health records

By Amy Jeter Hansen

A Stanford Medicine survey conducted by The Harris Poll found that more than 6 in 10 primary care doctors say electronic health records have led to improved patient care. However, a majority also report frustration with how the demands of the digital systems affect their relationships with patients.

Presenting the results June 4 at Stanford Medicine's EHR National Symposium, Lloyd Minor, MD, dean of the School of Medicine, said the survey illustrates the gap between the potential and current reality of the documentation technology. He charged the attendees — leaders in patient care, technology, design thinking and public Good Friday. A future that fulfills the clinical promise of EHRs while reducing the administrative burdens.

“We absolutely don’t want today to be about pointing fingers or trying to assign blame,” Minor said. “The goal of today’s conference is to define where we are today, identify the opportunities for the future, and begin to form a road map about how we succeed in achieving those opportunities.”

With panel discussions and breakout sessions focused on problem-solving, the daylong symposium touched on fixed inefficiencies in EHRs, harnessing data for population health management, building on successes and overcoming obstacles. The online survey — of more than 500 primary care physicians throughout the United States — provided a baseline of opinions and experiences.

What doctors report

Two-thirds of doctors reporting at least somewhat satisfied with their electronic health records system, though 4 in 10 say the records bring more challenges than benefits, according to the survey. About 7 in 10 physicians say EHRs take valuable time away from patients, and an equal percentage say the systems contribute greatly to burnout.

Of 31 centers devoted to a patient, doctors estimate they spend 12 interacting with the records systems during the visit, and another 11 minutes on the computer after the visit, according to the poll.

Though data entry required by digital systems can be burdensome, local culture and workflow can influence how physicians regard their EHR experience, panels at the symposium said.

Christine Sinsky, MD, vice president of professional satisfaction at the American Medical Association, said that over 16 years, she’s seen expectations for digital documentation grow. “The expectations that every act must go through the EHR, that we translate the clinical experience into digital data for the convenience of others and not for advancement of the care — those pressures have increased.”

Taylor Davis of KLAS, a company with the records, said: “That has been a huge boon to the way we think about care in the United States.”

Most trial participants favor sharing personal data for research

By Beth Duff-Brown

Most participants in clinical trials believe the benefits of broadly sharing person-level data outweigh the risks, according to a new survey by Stanford University researchers. And despite low levels of trust in pharmaceutical companies, most of those who take part in clinical trials are willing to share their data with drug firms.

The study was published in the June 7 issue of The New England Journal of Medicine.

The lead author is Michelle Mello, JD, PhD, professor of law and of health research and policy, by Stanford University School of Law.

The researchers surveyed 771 current and recent participants from a diverse sample of clinical trials at three academic medical centers in the United States. They asked about the participants’ interest in data collected in medical research widely available after the removal of information that could identify individual participants. Nearly 80 percent of those surveyed expressed willingness to allow their data to be shared with scientists for-for-profit companies. The researchers found that the willingness to share was high regardless of the purpose for which their data would be used, unless that purpose was litigation.

Although some researchers and trial funders have worried that participants might object to data-sharing as an invasion of privacy, the respondents’ greatest concern was expressed about discrimination (22 percent) and exploitation of data for profit (20 percent).” The authors wrote.

The API will allow developers to create apps that can use electronic health records to help people manage their health. The API will also allow developers to create apps that can use electronic health records to help people manage their health.

“We are rapidly moving toward a world in which broad sharing of participant-level clinical trial data is the norm,” Rucker said. "The way it does in other industries, the way it does in other industries, the way it does in other industries."
Conference focuses on how to make tech work for patient care

By Hanee Armitage

As vast troves of health data accumulate through wearable technologies, genome sequencing and an increased interest from patients in monitoring their own health, scientists and doctors face a challenge: how to get this data into the hands of those who need it the most — health care professionals, doctors and a growing list of researchers applying new technologies to patient care.

Spearheading that discussion was the challenge the School of Medicine’s Big Data in Precision Health Conference, which was held on May 23 at the Li Ka Shing Center for Learning and Knowledge. Speakers from academia, government and industry shared lessons on wrangling immense data sets to develop usable, actionable solutions in health care and new lines of research.

“We’ve translated fundamental discoveries into advances in therapeutics, and we’ll continue to do that,” said medical school Dean Lloyd Minor, MD. “But now we also have the unique opportunity to make discoveries not necessarily based on mechanistic analyses, but on deriving information from vast treasure troves of data that already exist.... That’s really the power of big data.”

Keynote speaker Eric Dishman, director of the National Institutes of Health’s All of Us research program, explained the program’s mission: to gather health data from more than 1 million people in the United States to improve and accelerate health research and care.

While describing the aims of the program, Dishman related the story of his diagnosis, at age 19, with a rare form of kidney cancer. Doctors who saw the diagnosis extrapolated information from the 90 people who had his disease, most of whom were ages 65 to 70. He was told he had nine months to live. “It was a wake-up call to me,” said Dishman. “It’s like everyone is doing the best they can with the data they have, but it doesn’t mean that’s the truth for any given individual.”

**Precision health for the masses**

The morning session of May 23 focused on questions about the body’s transition from health to disease. Susie Spielman, director of strategic initiatives for Stanford’s Department of Radiology, is a program leader for Project Baseline, a collaboration between Stanford, Duke and VA that aims to map human health in unprecedented detail. She led off the session, detailing the project’s goal of analyzing 10,000 individuals’ health data to answer a question that’s key to nearly all precision health research efforts: How do you define “normal” for any given individual?

“As we move to population cohorts, the scale increases to millions of individuals, and genome sequencing continues to roll out, tens of millions of generic variants. Data at that scale becomes quite challenging,” said Manuel Rivas, PhD, an assistant professor of biomedical data science, who spoke on population health. That challenge, he said, is what motivates him to think about statistical methods and computational tools capable of carrying out analyses on massive amounts of data, creating summaries that are useful in answering questions fundamental to biology.

In the afternoon, the focus shifted to a high-profile embodiment of precision health today: cancer immunotherapy. Crystal Mackall, MD, professor of medicine and pediatrics at Stanford, who is leading a researcher in engineering immune cells to fight cancer. In back-to-back talks, she and Adnan Jaitar, MD, a medical officer at the Food and Drug Administration, explained the yin and yang of innovation and regulation: how cutting-edge treatments that reprogram a patient’s own immune cells to fight tumors make it out of the lab and into the hands of doctors.

Topping off the discussion on cancer immunotherapies, Jennifer Wargo, MD, associate professor of surgical oncology and of genomic medicine at MD Anderson Cancer Center, highlighted what she believes is an emerging frontier in precision health: the microbiome, or the makeup of the gut microbiome and immunotherapy success. Indeed, the type and number of bacteria living in a person’s gut actually does alter the outcome of immunotherapies — a result that theoretically could enhance success of these kinds of cancer treatments, Wargo said.

**Man plus machine**

Day Two of the conference opened with a focus on machine learning and artificial intelligence, highlighting its purpose and potential in health care. Dekel Gelbman, the CEO of FDNA, a digital health platform that harnesses artificial intelligence to identify rare diseases based on physical facial features, said that the role of the company’s facial recognition capabilities is to augment diagnoses. Clinicians using the technology report accurate diagnoses, and that’s, he said. But the best feedback is when they say the platform helped show them diagnostic information they wouldn’t have otherwise seen.

Andrew Ng, PhD, an adjunct professor of computer science at Stanford and a globally recognized leader in artificial intelligence, brought the power of AI to diagnostics to the stage in a demonstration of a smartphone app that processes pictures of X-ray images and spits out the likely medical conditions associated with the X-ray’s composition.

“Because AI technology is still evolving … only AI experts have a very good sense of the potential of AI, while only health care experts have a very good sense of how health care could benefit,” Ng said. “The approach that I believe will be successful in this era in getting AI people to learn more about health care, and get health care people to learn more about AI.”

The final conference session focused on digital health. Four speakers discussed the intersection of health, digital technologies, venture capitalism, quality of life and behavior as it relates to health.

“We often hear about the fear that robots are going to take over and kill us all,” said Rich Mahoney, PhD, CEO of Seismic, which creates wearable robots. Mahoney’s technology is called Powered Clothing and looks like a pliable combination of undergarments and a bodysuit. But integrated into the fabric are electromechanical muscles that work to boost the wearer’s core muscles. With sensors that can feel the motion of the person, Powered Clothing is designed to tell when a person is, for example, standing up, and physically helps to bring them upright. The technology could help improve the quality of life for older individuals who may be experiencing a loss of mobility.

“We don’t specify other industries as ‘digital.’ It’s not ‘digital transportation’ or ‘digital manufacturing,’” said Lisa Suennen, senior managing director at GE Ventures, who said she views technology as a means to better patient care.

“We need to get to a point where we’re comfortable enough with technology in health care that it’s simply part of health care.”

**Data**

Most of those participants, along with clinical researchers, believe the benefits of sharing data include accelerating scientific discovery and improving accurate reporting of trial results.

**Companies leery of data sharing**

Yet some investigators and industry sponsors of clinical trials are leery of the swift move toward broad data sharing because of “potential harm to research partici- pants,” said the authors. “Investigators express worry that patients’ privacy cannot be adequately protected, particularly in light of the fact that experts have demonstrated that it is possible to reidentify participant-level data.”

Furthermore, the authors wrote, some pharmaceutical companies have warned that data sharing could chill people’s willingness to participate in trials, thereby delaying the availability of new therapies. In fact, 31 percent of those surveyed were somewhat or very concerned about having their personal information stolen. Nevertheless, most felt the benefits of data sharing were more important.

“Reaching a world in which the sharing of clinical trial data is routine requires surmounting several challenges — financial, technical and operational,” the authors wrote. “But in this survey, participants’ objections to data sharing did not appear to be a viable barrier.”

Former Stanford researcher Van Lieou also co-authored the study.

The study was funded by the Greenwall Foundation and the National Institutes of Health.

Stanford’s departments of HealthResearch and Policy and of Medicine and the Stanford Law School also supported the work.

**Clockwise from top:** Dean Lloyd Minor gave introductory remarks at the Big Data in Precision Health conference, which was held at the Li Ka Shing Center for Learning and Knowledge. Computer scientist Andrew Ng discussed artificial intelligence at the conference. Carla Pugh, far left, moderated a panel on digital health and technology featuring Jennifer Schneider, Leanne Williams, Lisa Suennen and Rich Mahoney.

**INSIDE STANFORD MEDICINE**

JUNE 11, 2018

PHOTOS BY BRI HAMMES

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Mello said she was somewhat surprised by the survey results, “given the amount of consternation one hears at conferences about data sharing.”

“Interestingly, nearly half our sample had experi- enced a breach of their personal data privacy in another context, yet were still willing to share their clinical trial data,” she said.

Then again, she said, people who take part in clinical trials are leery because “I suspect that clinical trial participants may be different from the public at large,” Mello said. “They are already incurring risks to benefit science by dint of their trial participation.”

**New guidelines**

Participants were asked if they would be more willing to share their data if there were clearer guidelines for the types of data that could be shared. Approximately 39 percent of those surveyed said they would be more willing to share data under these circumstances.

“I think that making the data available in some form would be beneficial to the scientific community,” one of them wrote. “But at the same time, we need to think about maintaining confidentiality and the privacy of the individuals involved.”

Several others who said they would not share data under any circumstances also noted the importance of ensuring the confidentially of participants.

“I think that a balance needs to be found between useful research and protecting participant confidentiality,” said one.

While participants were less willing to share data if there were no guidelines, Mello reported in her analysis that participants who were more concerned about the privacy of the data they would share were also more concerned about the confidentiality of the data collected on them.

“Protected health information [PHI] is a complex issue, and we need to be careful about how we handle it,” wrote one participant.

**Human subjects research**

When asked if they were concerned about the safety of those involved in clinical trials, 15 percent of those surveyed said they were worried that participants’ privacy could be inadequately protected, particularly in light of the fact that experts have demonstrated that it is possible to reidentify participant-level data.

**Compliance with human subjects research guidelines**

The majority of those surveyed — 53 percent — said they were concerned about being compliant with the human subjects research guidelines that govern such trials.

But a number of participants still felt the guidelines did not do enough to protect the confidentiality of data collected on them.

“I believe current human subjects research guidelines are not adequate to protect privacy,” wrote one. “There are too many exceptions that allow access to data.”

**New guidelines**

While many participants expressed concerns about privacy, 30 percent of those surveyed were somewhat or very concerned about having their personal information stolen.

“While we’re concerned about the confidentiality of the data we generate in research, we’re also concerned about the potential misuse or theft of that data,” wrote one.

“Data protection is a concern,” wrote another. “There is concern about sharing data with those who would misuse it.”

While many participants expressed concerns about privacy, 30 percent of those surveyed were somewhat or very concerned about having their personal information stolen.

“While we’re concerned about the confidentiality of the data we generate in research, we’re also concerned about the potential misuse or theft of that data,” wrote one.

“Data protection is a concern,” wrote another. “There is concern about sharing data with those who would misuse it.”

**CONTINUED ON PAGE 5**
More than 11 million Americans may have incorrect prescriptions for aspirin, statins and blood pressure medications, according to a study led by researchers at the University of Washington.

Their findings are based on an updated set of calculations—known as pooled cohort equations, or PCEs—that are used to determine the risk of a heart attack or stroke.

The PCEs are the foundation for cardiovascular-disease-prevention guidelines in the United States. They are based on often outdated data and therefore putting some patients at risk for over- or under-medication.

“We found that there are probably at least two major ways to improve the 2013 equations,” said Sanjay Basu, MD, PhD, assistant professor of primary care outcomes medicine at Stanford. “They are based on outdated data and therefore putting some patients at risk for a heart attack or stroke. Most physicians calculate a patient’s risk using a PCE software calculator or a smartphone app; the equations are also built into many electronic health records so the patient’s risk is automatically calculated during an office visit.

But there has been debate over whether the PCEs are based on outdated data and therefore putting some patients at risk for over- or under-medication.

“The first was well-known: that the data used to derive the equations could be updated. Old equations

For example, he said, one of the main data sets used to develop the equations has information on people who were 50-62 years old in 1948, and who would therefore be 100 to 132 years old in 2018—that is, they are no longer alive. Another concern is that the equations were often estimating people’s risk as too high, possibly by an average of 20 percent across risk groups.

“A lot has changed in terms of diets, environments and medical treatments,” Basu said. “So, it is relying on our grandparents’ data to make our treatment choices is probably not the best idea.”

But there has also been discussion surrounding a second improvement to the equations, the authors found that the old data may not have had a sufficient sample of African-Americans. For many African-American physicians may have been estimating the risks of heart attacks or strokes as too low.

So while many Americans were being recommended aggressive treatments that may not have been according to current guidelines, some Americans—particularly African-Americans—may have been given false reassurance and probably need to start treatment sooner.

“Somewhat mindboggling”

In the new study, Wernig and his colleagues focused on highly specialized immune cells called T cells that circulate in the blood. T cells protect us from disease by recognizing and killing infected or cancerous cells. Infections can cause our T cells to become long and skinny cells capable of conducting electrical impulses along their length and passing them from cell to cell. But because the cells’ vastly different shapes, locations and biological missions, the researchers found it unexpectedly easy to complete their quest.

“It’s kind of shocking how simple it is to convert T cells into functional neurons in just a single iteration of the complex reprogramming process.”

Although it’s possible to directly convert skin cells to neurons, the biopsied skin cells first have to be grown in the laboratory for a period of time until their nuclei fuse together and introduce genetic mutations not found in the person from whom the cells were obtained. The researchers wondered if there was an easier, more efficient way to generate patient-specific neurons.

To figure out how to predict preterm birth, the researchers used blood samples from 58 American women who were at risk for premature delivery because they had already had early contractions or had given birth to a preterm baby before. These women each gave one blood sample during the second or third trimester of their pregnancies. Of this group, 13 delivered prematurely and the remaining 25 delivered at term. The scientists looked to identify unique cell-free DNA from seven genes from the mother and the placenta that could predict which pregnancies would end early.

“Mostly maternal genes,” Mouradjee said, noting that the genes that predict preterm delivery are different and unique to each pregnancy. “We think it’s mom sending a signal that she’s ready to pull the ripcord.”

“I think it’s less likely to be something that the children’s nervous system or skin cells are involved in. But it is a signal that the mother and the baby are ready to end the pregnancy.”

The results of the study have important implications for the diagnosis and treatment of preterm birth, a leading cause of death among newborns. Preterm birth can cause a range of serious health problems in newborns, and is associated with an increased risk of death, developmental delays and lifelong disabilities.

In the meantime, they’ve started to collect blood samples from women with autism.

“We now have a way to directly study the neuronal function of, in principle, hundreds of women with schizophrenia and autism,” Basu said. “So, we have very few clues about the origins of these disorders or how to treat them. Now we can start to answer so many questions.”

Other Stanford co-authors are postdoctoral scholars Shoham Chanda, PhD, and Daniel Haag, PhD; undergraduate student Victor Olmos; professor of psychiatry and behavioral sciences Douglas Levinson, MD; and a few days ago, the director of molecular and cellular physiology Thomas Südhof, MD.

The research was supported by the National Institutes of Health, the California Institute for Regenerative Medicine and the New York Stem Cell Foundation, the Howard Hughes Medical Institute, the Siebel Foundation and the Stanford Schizophrenia Genetics Research Fund.

Stanford’s Department of Pathology also supported the work.

Scientists from the Statens Serum Institute in Copenhagen, the University of Pennsylvania School of Medicine and the University of Alabama-Birmingham also contributed to the study.

Contributors: Tibshirani, Shaw and Stevenson are members of Stanford Bio-X; Tibshirani, Shaw and Stevenson are members of the Stanford Child Health Research Institute; and Quake is a member of the Stanford Children’s Health Research Institute.

The research was funded by the Bill and Melinda Gates Foundation, the March of Dimes Prematurity Research Center at Stanford University, the March of Dimes Prematurity Initiative Grant at the University of Pennsylvania and the Chan Zuckerberg Biohub, of which Quake is co-president.

The Chan Zuckerberg Biohub has submitted a patent application for the technology.

Stanford’s department of Bioengineering, Applied Physics and Pediatrics also supported the work. The Department of Bioengineering is jointly operated by the schools of Electrical Engineering, and Medicine.
### 1. How might Nipah adapt to more efficient human-to-human transmission and thereby become a global pandemic threat?

**Luby:** It is conceivable that there is currently a strain of Nipah virus circulating among bats that, if it infected people, would efficiently transmit from person to person. That would be very troubling.

### 2. What role, if any, does land conversion have in altering the epidemiology of infectious diseases, including the emergence of novel infections such as Nipah?

**Luby:** The natural habitat for Nipah-carrying Pteropus bats is tropical forests. As these forests have been converted into agricultural lands, the bats have sought out other locations to rest and feed, and they have likely moved from bats to people because the bats are licking fresh date palm sap and so passing their saliva — which occurs in the crevices of the bat's chin. Because of habitat loss, Pteropus bats in Australia are more likely to stay in suburbs where fruit trees are available, and people and horses are nearby. The bats have halted much of their annual migration because of habitat loss.

### 3. Why are emerging diseases such as Nipah important to study?

**Luby:** Emergent infections have resulted in some of the most devastating infectious diseases that humanity has ever faced. These include HIV, tuberculosis, measles and smallpox.

### 4. How can the global community thoughtfully respond to the threat?

**Luby:** Both Ebola outbreaks and hospital-based transmission of Nipah illustrate that hospitals in low-income countries are important sites for transmission of potential pandemic organisms. We cannot predict which organism is likely to be the next pandemic, nor can we predict against which targets it will attack unknown threats. There has been much less enthusiasm for efforts to reduce the risk of transmission in hospital settings, perhaps because hospital-acquired infections can cause difficult problems with adequate supplies, behavior and accountability. In addition to developing vaccines and drugs, improving conditions in health care facilities is a key step for reducing global risk. As an example, a doctoral student at Stanford has published nice work on the difficulty of implementing basic hand-hygiene practices in resource-poor settings.

### 5. Was Nipah discovered 20 years ago, and there is still no vaccine? Why?

**Luby:** Vaccine development requires large amounts of money. The number of people infected with Nipah is relatively small, and so it is a difficult disease to invest in developing a vaccine. The Coalition for Epidemic Preparedness Innovations recently announced plans to fund the development of a human vaccine against Nipah.
Grant awarded to study whether stem cells can treat urinary incontinence

School of Medicine researcher Bertha Chen, MD, has been awarded $5.98 million by the California Institute for Regenerative Medicine to investigate ways of using a person’s own stem cells to treat urinary incontinence.

The award was one of four given out May 24 by the state stem cell agency as part of its Translation Research Program, which aims to help move promising stem cell research out of the laboratory and into the clinic.

Urinary incontinence affects about 30 percent of adult women ages 30 to 60 and is one of the most common indications for surgery in elderly women. However, as many as one-third of the women either cannot undergo surgery or will not benefit from surgery. The condition can have a significant impact on quality of life and be emotionally devastating.

Chen, professor of obstetrics and gynecology, and her team are exploring ways to use stem cells to generate the smooth muscle cells in the urinary tract that are lost in a person with urinary incontinence. If the approach works, it could also lead to new ways to treat other urinary or digestive problems caused by a loss of smooth muscle.

Other translational grants announced at the meeting included $1.7 million to Max BioPharma Inc. to pursue a stem-cell-based treatment for osteoporosis; $4.77 million to researchers at the University of California Irvine to investigate how to regenerate damaged retinas; and $1.17 million to researchers at Children’s Hospital Oakland Research Institute to develop a prenatal test for some types of blood cell disorders that could be amenable to early stem-cell-based treatments.

The institute also awarded nearly $1.2 million to researchers at UCLA to test a therapy for advanced nonsmall cell lung cancer that combines a well-known immunotherapy called pembrolizumab with an approach that genetically modifies immune cells called dendritic cells to enhance their ability to activate cancer-fighting T cells.

Howard Chang named Howard Hughes Medical Institute investigator

Howard Chang, MD, PhD, professor of dermatology and genetics at the School of Medicine, is among 19 scientists from 15 institutions announced as new Howard Hughes Medical Institute investigators.

HHMI provides each investigator with a full salary, benefits and a research budget over the initial seven-year appointment, which may be renewed for additional terms. The institute also covers other expenses, including research space and the purchase of critical equipment.

Stanford’s other new HHMI investigator is Elizabeth Sattely, PhD, assistant professor of chemical engineering. With today’s appointments, the university now has 24 HHMI investigators.

“Every scientist is unique, but they all need one thing—time,” said HHMI President Erin O’Shea in announcing the new recipients. “HHMI is dedicated to providing outstanding biomedical scientists with the time and resources to do their best work. We think of this as investing in people, not just projects.”

Chang’s research focuses on understanding how small molecules attached to the DNA affect gene expression and coordinate cell fate and function, as well as on the role played by metabolic disorders to cell structure and tissue of the human brain. His work focuses on human brain organoids to gain insights into psychiatric disorders. The program celebrates physicians who have made significant contributions to cure and treat cancer. MICHAL TAL, PhD, a postdoctoral scholar in immunology and in stem cell biology and regenerative medicine, received a 2018 Emerging Leader Award from the Bay Area Lyme Foundation. The $100,000 award is designed to encourage promising scientists who are the future of Lyme disease-research leadership. She will study how the bacterium that causes Lyme disease uses the protein CDN7 to evade the immune system.

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