Rocket scientists apply engineering know-how to detecting disease through breath analysis

By Kris Newby

I n a dimly lit room, next to a super-	onic jet engine test rig, three Stan-
ford engineering graduate students sat
around a whiskey bottle.

All was quiet on this Friday evening in
2013 except for their lab’s visceral hum, a
rumbling of fans, flames and gases rush-

invasive way to detect everything from
diabetes to cancers. They take giant leaps for mankind.

By Jennie Dusheck

Researchers identify potential for compromising
security in network used to share genomic data

By Lindzi Wessel

How do we reduce health risk in the face of harm that

can’t be eradicated completely? That’s the question Lloyd
Minor, MD, dean of the School of Medicine, presented
to the audience at the recent Health Policy Forum on e-
cigarettes — a topic about which he said “intelligent and
reasonable people can disagree.”

E-cigarettes are a controversial subject in the public-
health community. Panelists at the event debated whether the
recently developed devices hold promise to help long-
time smokers move away from combustible cigarettes, or
whether they could abet a renormalization of smoking.
All panelists agreed that those under the age of 21
shouldn’t be using any nicotine delivery devices, and they
shared a goal of minimizing general use of harmful health

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In recent months, the World Health Organization (WHO) has declared red meat and processed meat to be carcinogenic. This classification is based on a review of more than 800 studies on cancer in humans to reach its conclusions. The reaction was noisy. Proponents in Parma, Italy, protested; vegetarians and some environmentalists saw it as an affirmation, and the rest of us wondered what it all meant. Must we swear off all these kinds of meats completely, or is it safe to consume a little now and then? If so, what are the recommended servings? Do we buy less or better quality meat because it is cleaner? Is it a clear direction pointing to cancer patients at Stanford Health Care. In an interview with writer Sara Wykes, Paliko shared his thoughts on the WHO report and offered some suggestions on what we might want to change about our food choices.

1 What did you notice first about the WHO report?

PALIKO: Many of its numbers and guidance on red meat and processed meat is what we’ve been using at Stanford Health Care for years. Caution on processed meats has been around since 2007. What I like is seeing how much fanfare it’s cause. It’s important to be having these conversations about meat consumption. The report itself will become another tool that dietitians can use when we talk to people about what they eat. No longer will this idea of lowering how much red and processed meat you eat be an idea we just made up. It does build a framework for what a cancer-prevention diet looks like. There’s been a lot of conversation about it in the context of cancer risk through the years, but no clear definition. It’s hard to measure and do not have the risk of the form of iron found in red meat — a form called heme iron. Animal evidence suggests heme iron contributes to chronic disease risk, such as heart disease and digestive tract cancers. Heme iron, a strong pro-oxidant, is also found in other meats like fish and poultry, but in much smaller quantities that aren’t associated with cancer risk.

2 What should people know about the relationship between cancer and the consumption of red meat and processed meat?

PALIKO: I do have an issue with any conclusion that says if you eat red or processed meat, you will get cancer. No matter what numbers you choose to accept about the increased risk related to eating these kinds of meats, it’s important to remember that cancer is a multifactorial disease. It’s not just diet alone. It’s diet, weight related to that diet, inherited risk and environmental exposures. Your cancer risk can also be raised by other illnesses you may have had and treatments for those illnesses. Diet is just one piece of the cancer risk, albeit an important one.

3 If you decide not to eat red meat, how can you get enough protein and iron?

PALIKO: Chicken, fish, turkey, eggs, dairy, beans, nuts and seeds are very good sources of protein. Plant foods like dark-green vegetables contain the iron we need, and do not have the risk of the form of iron found in red meat — a form called heme iron. Animal evidence suggests heme iron contributes to chronic disease risk, such as heart disease and digestive tract cancers. Heme iron, a strong pro-oxidant, is also found in other meats like fish and poultry, but in much smaller quantities that aren’t associated with cancer risk.

4 How do you respond to the suggestion that we need help losing weight?

PALIKO: I don’t have a problem with losing weight. A healthy body weight is healthy for a variety of reasons. We need to help patients with obesity. It’s good to see that expanded to a broader stage.

5 Is there such a thing as a cancer-prevention diet that’s trustworthy?

PALIKO: A cancer-prevention diet looks very similar to a heart-disease or diabetes-prevention diet: lots of vegetables and fruits, plenty of whole-grain plant food, low in sugar, legumes, nuts and seeds; high-fiber, low-fat, limited-fried, processed or salted foods; and alcohol in moderation. If you work with patients, you might want to change about our food choices. People have been eating fast-food burgers or burritos, washing them down with unhealthy beverages and just overconsuming calories. If you want to eat some red meat, how much is safe?

PALIKO: Our guidance on red meat is a maximum of 18 ounces a week. We tell our patients that the cancer-prevention diet involves a week of eating a variety of foods, and the idea is to have a food or vegetable protein meal instead of eating red meat.
New bioengineering major is off to its first academic year

By Tom Abate

Ever since the schools of Engineering and of Medicine jointly created the Department of Bioengineering in 2002, the plan was to eventually offer a bachelor’s degree program alongside its master’s degree and PhD programs.

The Faculty Senate brought this plan to fruition during the last academic year by approving an undergraduate bioengineering major in perpetuity. Senate Chair Russell Berman, PhD, described the new major as a milestone in Stanford’s academic life.

“Not only does it address an exciting and growing field of knowledge at the interface of the life sciences and engineering,” said Berman, professor of comparative literature and of German. “It also is the first time that the School of Medicine, working together with the School of Engineering, has offered an undergraduate degree.”

Norbert Pelc, ScD, professor and chair of bioengineering, said approval of the major culminated years of effort by faculty, graduate students and pioneering undergraduates.

“We grew this department gradually around a core faculty and graduate program, and began testing our undergraduate curriculum in the 2009-10 academic year,” said Pelc, who is also a professor of radiology. “One of our challenges has been that bioengineering is such a broad field that we had to distill it down to the essential foundations.”

An excellent start

Brad Ogosh, PhD, a professor of electrical engineering, was senior associate dean for student affairs at the School of Engineering during the lead-up to senate approval of the bioengineering program. He likened bioengineering to computer science: an important but rapidly evolving field in which it took some time for a foundational curriculum to come into focus.

“How we present new fields to undergraduates boils over with energy, enthusiasm and intelligence is the question,” Ogosh said. “I don’t think anyone would say that we have the one answer, but we’ve made an excellent start.”

Ogosh, who in this effort has been Karl Deisseroth, MD, PhD, professor of bioengineering and of psychiatry and behavioral sciences, in his capacity as the department’s associate chair for undergraduate education, added that undergraduates enrich the department.

“The opportunities created at the interface of biology and engineering are immense and only beginning to come into focus,” Ogosh said.

An illustration of osteoporotic bone structure. Osteoporosis afflicts bone structure, muscle mass and muscle function in those who have withstood childhood chronic diseases.

Anjur-Dietrich was among the Stanford undergraduates.

Karl Deisseroth, who played a leading role in creating the bioengineering major, teaches undergraduates.

Russhmi Sharma, Class of 2014, said the department evolved during mechanisms of cell signaling in animals.

Anjur-Dietrich was among the Stanford undergraduates who helped pioneer the major by pursuing a bachelor’s degree in engineering with a concentration in bioengineering.

“These students were our guinea pigs,” Pelc quipped. “They helped us refine and prove the curriculum.”

Another of these undergraduate pioneers, Evan Masutani, said bioengineers delve into chemistry, physics, biology, math, and computer science, giving them a profound respect for the experts in each field.

“To be a bioengineer is to be a jack-of-all-trades,” said Masutani, Class of 2014, who is now doing postdoctoral research at the National Institute of Allergy and Infectious Diseases.

Many of society’s biggest problems require interdisciplinary solutions, he said, adding, “The realization that one is not an expert fosters a strong drive for collaboration.”

The breadth of the major, coupled with the need for depth, made for a strenuous program of study, but

It’s bad for the bone: The toll of childhood chronic disease

By Kathy Zonana

Mary Leonard, MD, is pointing at a spine MRI scan of a young adult who had a bone marrow transplant in childhood.

“That vertebrae is compressed,” said Leonard, a professor of pediatrics and of medicine who serves as an associate dean for maternal and child health research. “These patients who are in their teens or early 20s have little-old-lady kinds of fractures.”

Preventing early osteoporotic fractures in those who have withstood childhood chronic diseases is a central aim of Leonard’s research program. She and her colleagues have documented abnormal bone structure and muscle strength in children and teens with conditions ranging from cancer to Crohn’s disease to transplant patients. They have evaluated bone mobility, inflammation, malabsorption of nutrients and treatment regimens or side effects of cancer drugs that can all pose threats to developing bones.

“We believe that once you go through puberty, you’re not getting that bone back,” Leonard said. “I feel like we’ve created a program that could address the problem, and now we need to do clinical trials to see what we can do to improve bone health in these patients. We just want to get these kids into adulthood with the best, strongest skeleton possible — with bones to last a lifetime.”

Clinical trials could assess the efficacy of exercise programs, compare kidney-transplant patients on a steroid-free protocol with those who are given steroids and, eventually, test pharmaceutical interventions. In a new Stanford research center on Arastradero Road in Palo Alto, both kids with chronic diseases and healthy control subjects will undergo three assessments: a muscle-strength exam; a full-body DXA scan to quantify bone, muscle and fat; and ankle scans in the latest-generation XtremeCT machine. The total radiation dose from the three tests, Leonard said, is less than a week of background radiation exposure from living on Earth.

The XtremeCT is one of 10 in the United States, and one of only two with general degree of freedom to move aggressively before and during puberty, to improve their overall health and enable them to build more bone. “If you want to treat the Crohn’s until their bones are done developing, or if they don’t get their kidney transplant until their bones are done developing, that window of opportunity may be lost,” she said. Second, as life expectancy improves for children with rare and once-fatal conditions, pediatricians need to anticipate the lasting effects of their illness and treatment.

“Some childhood heart disease or cancer are surviving well into adulthood, the focus of research has shifted from simply improving survival to understanding some of the long-term complications,” Leonard said. “And osteoporosis and fractures are part of it.”

Tom Abate is the associate director of communications for the Stanford School of Engineering.
Robert Chase, MD, founder of the Division of Plastic and Reconstructive Surgery, kicked off a recent celebration of the program’s 50th anniversary by recounting the history of an innovation with far-reaching consequences.

The celebration began at the past and present residents, fellows and faculty of the division. Chase, the Emilie Homan Professor of Surgery, Emeritus, said that when he arrived at Stanford in 1963, he proposed unifying how plastic surgeons learned their craft. The traditional five-year training in general surgery, followed by two years focused on plastic surgery — just didn’t make sense to him.

“General surgery was mostly about repairing intra-abdominal organs, and plastic surgery involves many different types: bone, nerves and tendons,” said James Chang, MD, current division chief and professor of plastic surgery, who co-chaired the celebration, which included a conference. “You would train for seven years to sew tissues you would never see again in practice.”

Chase recalled that, in the 1960s, the tools and techniques for craniofacial sur- gery, microsurgery and hand surgery were advancing at breakneck speed. “Learning all that in two years was not good for the doctor and not good for the patient,” said Chang, the John & Jordan Distinguis hed Professor in Surgery

Chase’s plan was to train surgeons in plastic surgery techniques from the very start, for five years of direct training in the specialty. It also included another innovation: a sixth year for residents to conduct research or concentrate on a particular kind of surgery — even outside the Stanford medical school.

For example, Chase encouraged one resident, Vincent Hentz, MD, to spend a year working at a hospital in New York City with hand surgeon William Littler, MD. Littler was Chase’s teacher and one of plastic surgery’s legendary innovators. Hentz also spent six months learning about surgical techniques for head and neck cancer. “It was a very nonstandard residency,” Hentz said. In 1975, he joined the Stanford division as faculty member No. 6 and, later, became its chief. Hentz, who co-chaired the celebration, is now a professor emeritus of surgery.

An idea that caught on

Fifty years on, Chase’s approach to plastic surgery residencies dominates the field nationwide. Stanford Medicine’s plastic and reconstructive surgery residency program, recently lengthened to seven years, is now directed by Gordon Lee, MD, associate professor of surgery. The program attracts more than 300 ap-

pli cants each year for three spots.

Andrew Zhang, MD, a recent alumnus of the program, was first drawn to Stanford by giving someone a donation and then as a resident in a fellow in hand sur- gery. Now, he is an assistant professor of surgery at the University of Texas Med- ical Branch at Galveston. The celebration also provided an opportunity for the division to gauge the accomplishments of its alumni: Twenty-nine alumni, including former residents and fellows, direct programs in plastic and reconstructive surgery. Thirty-nine have been hospital chiefs. Seventy-eight hold academic titles. More than 5,000 journal articles have come from the research and clinical work of the division’s former residents, who have also authored or co-authored 396 books and book chapters. Nearly 170 serve on the boards of professional journals.

Two of these alumni have served as president of the American Society for Surgery of the Hand, and Chang, another alumni of the residency program, will be president in 2018. In addition, alumnus Robert Pearl, MD, is executive director and CEO of the Permanente Medical Group, which operates 21 medical centers in California. And alumnus Ronald Iverson, MD, is a past president of the American Society of Plastic Sur- geons, the profession’s national organi- zation. Alumna Debra Johnson, MD, is the society’s next president. “We have a proud history,” Hentz said.

Donald Laub, MD, one of the pro- gram’s first graduates and, eventually, one of the division’s first chiefs, founded Interplast, now Resurge International, the first organization to send American surgeons to help reconstruct body parts after combat in Stan- ford, to developing countries to repair cleft palates, disabling wounds, burns and other injuries. Laub has also been a growns in number, too. When Chang became chief in 2006, there were just six full-time fac-

ulty members. Today, Chang has plans to add four more by 2020. “We have some huge names here,” Chang said. “We could all be chiefs and chairs in our own right, but we keep them here for fostering an environment they can thrive in. We give them the independence and acknowledgement and room to do their own thing.”

The division’s current faculty have been awarded more than $38 million in research grants. Two of them, Michael Longaker, MD, and Geoff Greumur, MD, have been laboratory directors; additional clinical training or work in biodis- eases, public health or government.

The division’s alumni network of alumni maintains close ties to each other, said Ronald Iverson, MD, who founded the alumni group. The 50th anniversary cel- ebration was “a great way for all of us to see what we’ve been doing, to share our memories” — and to find out about the newest generation of Stanford-trained plastic and reconstructive surgeons, he said.

Sara Wykes is a writer for Stanford Health Care’s communications office.
Online courses that doctors take to learn and maintain their skills have a reputation for being tedious. They are often just videotaped lectures or PowerPoint presentations sprinkled with examples that are too much in the way of graphic design, animation or video.

The Stanford Center for Continuing Medical Education, in the School of Medicine, aims to help amend that legacy. It has debuted new interactive online continuing medical education courses that show how information freed from words-only presentation can be an effective medical education tool. It’s not, nor tells, but, animation and video, and a minimum of talking heads.

Based on the knowledge that more than half of us are visual learners whose attention may drift during a video of a podium-bound lecture, online-course designers in all fields increasingly incorporate animation, infographics and videos to illustrate the material. The medical school’s new CME courses reflect this trend.

The new courses also include teaching topics that have become more important in recent years, such as antibiotic and opioid overuse, and national health issues now near the top of the priority list of the Centers for Disease Control and Prevention. Other courses are meant to engage primary care physicians as partners in prevention health care for conditions with serious consequences.

“The new courses are designed to be more engaging for learners,” said Griff Harsh, MD, associate dean for postgraduate medical education. “We believe they are also unique in quality and content. Their development also reflects the need we have at Stanford for evidence-based practice when and faculty, medical educators and our IT experts collaborate.”

Using actors

The new courses don’t resemble video games, as do Spielberg and Sack — two CME offerings recently developed at Stanford. They do, however, share the use of a teaching environment that is more image-driven than word-dependent, including some dramatic recreations based on real and fictional cases observed in practice.

“We wanted to break free of the passive culture of lecture and find ways to visualize what’s being taught,” said Kimberly Walker, PhD, the instructional designer with the Stanford Medicine Information Resource and Technology, who worked with Stanford Health Care doctors to design the courses.

The new CME course on prescription drug misuse is a good example of what Walker means. The course uses animation and portrayals in a series of videos that dramatize what actually happens in doctors’ offices. Anna Lemble, MD, assistant professor of psychiatry and behavioral sciences, wrote the scripts based on her knowledge and experience.

“You can’t start to understand what’s going on until you see what actually happens in doctors’ offices,” said Lemble. “We want to spark a level of conversation doctors experienced when patients are prescribing for medications.”

The video, far more interesting than a deck of slides, really pulls you into the situation,” Walker said.

That’s the kind of reaction Lemble wants for a topic she has usually seen addressed only with depictions of cases with perfect endings. Lemble wanted those cases to reflect the imperfections of typical conversations between doctors and patients. She designed the course’s videos “to show exactly what a doctor shouldn’t do,” she said. “I’ve found that in medicine we learn the most from our mistakes.”

Another new course, one that will feature an introduction by Arjan Srinivasan, MD, the CCR’s associate director for health-care-associated prevention programs, was developed because of the worldwide value of its content: the antibiotic timeout.

“Studies show that up to half of all antibiotic use in the hospital is inappropriate, and we know that antibiotic overuse leads to medication-resistant superbugs and can harm patients,” said course co-creator Maria Holubar, MD, clinical assistant professor of infectious diseases. “We also know that clinicians don’t necessarily have the right training to make these decisions. That’s why we developed the course.”

“Antibiotic timeout

The antibiotic timeout, a term promoted by the CDC, asks doctors to take some time 48-72 hours after a patient has started a first course of antibiotics to re-evaluate the prescription, using clinical information and laboratory data. The timeout allows doctors to think about the value of that medication, its dosage, delivery method and duration, Holubar said. It’s a question of teaching the kind of approach that will become second nature to physicians in all fields.

There’s no lecture in this online course, either. Holubar and her collaborators created five case studies, supported with illustrations that include the molecular structure of certain medications, photographic images of organisms and, instead of a talking head, a narrator’s voice. Each case presents a clinical indication — sepsis is included — followed by clinical treatment options that could be applied in that case. “We wanted to make it case-based and real-world and appropriate for learners with some experience,” Holubar said.

The antibiotic timeout is a priority for the CDC, and this course will be featured on its website and that of the California Department of Public Health.

An online course designed by Laura Bachrach, MD, professor of pediatric endocrinology and diabetes, aims to teach pediatricians about the testing and treatment of congenital hypothyroidism. It’s a common disorder but can be easily detected, and treated, with a blood test in newborns, Bachrach said. Without screening and proper treatment within the two to three months of life, followed by continued appropriate care, infants with the condition will suffer intellectual disabilities. By the time clinical symptoms appear, Bachrach said, it can be too late to reverse the damage. That’s why the mandatory screening of all infants is so important.

How to counsel patients

“We have many more babies with congenital hypothyroidism than we have pediatric endocrinologists, so we need the help of pediatricians to care for them,” Bachrach said. “These doctors may also need help teaching parents about the condition, so the course includes a piece in which Bachrach plays a primary care doctor working with parents upset by the news of their newborn’s condition.”

“Teaching physicians and families physicians through this online resource allows us to reach many more providers on the frontline,” she said. “I am so grateful to Stanford,” Bachrach added.

“This is the first time I’ve ever done anything like this,” she said. “I am so grateful to Stanford,” Bachrach added. “This is the first time I’ve ever done anything like this.”

She’s also happy that Stanford will offer the course for free and that the American Academy of Pediatrics will link to it in websites.

Linda Baer, director of the Center for Continuing Medical Education, said a second round of new courses will be available next year.

“We are now seeing early evidence of how this online space is evolving,” said Mark Rosenberg, the online program manager for Stanford’s CME center. “Each course has its own set of best practices. There are differences between online academic learning and professional development training. CME falls somewhere in the middle. What we’re doing now is very different from what’s typically out there. We think of ourselves as innovators, and we’ll continue to explore and experiment.”

Sara Wykes is a writer for Stanford Health Care’s communications office.

E-cigarettes

Stanford Medicine debuts new, more visually compelling formats for online continuing medical education courses

By Sara Wykes

Hopkins University, described himself as a harm reductionist. At the event, held Oct. 2, Jackler agreed that, as an alternative mode of nicotine delivery, e-cigarettes pave the way for saving lives by helping addicted smokers avoid traditional cigarettes.

“I do think the evidence is very solid that they are dramatically less harmful than cigarettes,” Jackler said. “We are far, far away from having very low, almost undetectable levels or trace amounts of the top eight carcinogens that are found in cigarettes, and they have no carbon monoxide,” he said.

But a lack of extensive research makes Stanford’s Robert Jackler, MD, professor and chair of otolaryngology, and Bonnie Halpern-Felsher, PhD, professor of adolescent medicine, question whether e-cigarettes are safe. And a prevalence of candy-flavored e-liquids leaves them concerned about the potential for harm to young patients.

“We are seeing early evidence that those ... who never would have used or intended on using a tobacco product, when you ask them about e-cigarettes, they do have an intention. They are more susceptible to it,” said Halpern-Felsher.

She explained that when teens claim they are concerned about the cessation benefits associated with e-cigarette use, they assume that it’s safe to start using them.

“Kids are seeing tons of advertisements about the benefits, but not about the risks,” she said.

Arams acknowledged these concerns but countered with an analogy to safe sex: “What we say to kids is that we’d rather you don’t have sex at all, but if you do please use a condom. We don’t go on and on [about the fact] that 2 percent of condoms fail and therefore you shouldn’t use them.

In the end, the three all agreed that marketing plays a huge role in the complicated social acceptability of smoking. “Brilliant marketing of a lethal product that nobody needed made half the population buy it,” Abrams said, referring to traditional cigarettes.

“Now we’ve seen it again with e-cigarettes,” Halpern-Felsher added.

Linda Wessel is a science-writing intern for the medical school’s Office of Communications & Public Affairs.
Rocket
continued from page 1

Ethan's heart. Then Enns tried to figure out why Ethan's blood sugar was so low. He suspected that Ethan had a genetic defect of the metabolic system. This could result in a buildup in the bloodstream of ammonia, a chemical that is toxic to the liver. The blood test for this condition, called hyperammonemia, is slow and unreliable. Its analysis takes about an hour. By the time the test was back, the level of ammonia was almost 10 times higher than normal. Even if Ethan survived, he would always be at risk of another ammonia surge that could cause serious brain damage if not treated.

Ammonia is a byproduct released when the human body turns digested protein molecules into energy. The body eliminates this toxic substance by converting it in the liver to nontoxic urea, then sending it through the kidneys so it can be eliminated in urine. If anything goes wrong in the metabolic process, ammonia builds up. At this point there wasn’t time to do an in-depth genetic analysis to figure out what was wrong, so Enns expedited a biochemical test that revealed Ethan’s body was unable to digest long-chain fatty acids, a major component of breast milk and its precursor, cow’s milk. Because of this, Ethan’s body lacked enough energy to fuel its vital organs.

So Enns fed Ethan intravenously with a solution of high-calorie sugar and medium-chain fats. Then he administered a drug to remove the excreta-laring in his bloodstream. Against the odds, this strategy saved Ethan’s life.

“Ethan was the sickest child in the intensive care unit I’ve ever seen turn around,” Enns said.

Once Ethan was out of danger, Enns sat down with the parents to talk about the vigilance required to care for a child with a metabolic disorder. They passed on to protect Ethan’s metabolism from stress, especially viruses. And they have to be alert to signs of lethargy and confusion — indicators of high ammonia. They must never see an excess of ammonia, a life-or-death drill will be initiated. Rush to the hospital. Watch a photoelectron peak on the child with needles. Wait an hour for blood-test results. If the result is high, hospital staff will administer ammonia-grabbing drugs and intravenous fluids, re-test ammonia levels. If ammonia is not delayed to reach normal levels, could lead to permanent brain damage or even death.

Enns has a superhuman ability to connect with patients and families in these difficult situations. Most of the children he works with have extremely rare conditions for which research is limited and treatment plans are based on comfort care, guesswork or some combination. He is able to talk with a 10-year-old with severe developmental disabilities at exactly the right level, then turn to offer advice to parents on health insurance issues, or explain into a child’s doctor-speak. When asked how he protects himself from the emotional stress associated with these conversations, Enns pointed to his loving, laugh-filled companions. This was the dilemma for Enns: He could save these newborns, but what then?

Hope came out of the blue two years later, when he received a call from Darlene Solomon, MD, senior associate dean for maternal and child health at Stanford. Stevenson told him he knew of three Stanford rocket engineers with a novel idea for analyzing human breath, and they were looking for a medical condition to try it on. Would Enns collaborate with them? Enns immediately thought about patients like Ethan, and he jumped at the chance.

“Maybe these engineers could succeed where many others had failed,” said Enns. “I thought it, after all, they could be the key.”

Mission control

The idea for the disease breath analyzer was born in Stanford’s High Temperature Gas Dynamics Laboratory. This lab, tucked into an unobtrusive, sandstone-and-tile building behind Stanford’s Main Quad, has served as a launching pad for many cutting-edge experiments. Some of the lab’s students were both finishing dissertations on supersonic combustion ramjets, or scramjets. Strand was working on breathing in the strategic management of unfamiliar gases using lasers. Miller was developing gas-flow visualization techniques using lasers and high-speed cameras.

Scramjet technology, conceptualized in the 1950s, still presents researchers with extreme technical challenges. These engines use atmospheric oxygen to burn their fuel rather than having to carry liquid oxygen along for the ride. This silences with having parked seen yet the to fly at speeds of more than five times the speed of sound. Theoretically, scramjet space planes could carry a payload of more than 20 tons and reach altitudes of 500,000 feet. This is why the gas dynamics of the burning gases, and a sensor on the other side of the beam measures the quantity of light that is transmitted through the beam. The beam is made of light of a wavelength that is different, from 10 to 500 nanometers. These wavelengths are sensitive to the presence of trace compounds in the breath. For detecting gases in combustion flows, the technology works like this: A laser beam is directed at a specified wavelength that is different, from 10 to 500 nanometers. This is why the gas dynamics of the beams are so difficult to measure accurately. But on the other side of the beam measures the quantity of light that is transmitted through the beam. The beam is made of light of a wavelength that is different, from 10 to 500 nanometers. These wavelengths are sensitive to the presence of trace compounds in the breath. For detecting gases in combustion flows, the technology works like this: A laser beam is directed at a specified wavelength that is different, from 10 to 500 nanometers. This is why the gas dynamics of the beams are so difficult to measure accurately.
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The first prototype, built on an 8-foot by 4-foot table, used a clear quartz tube for the gas cylinder, which Miller classed as “very, very small.” The breathing tube was attached to one end of the cylinder. Flow meters, pumps and valves were attached to the other end, all scarred up from the hard knocks of the rock-star lab. These would direct the gas stream across the laser beam. Optical mirrors directed the laser beam onto the photodetector. During the initial tests, they found that for no one had every over-developed an ammonia breath analyzer.

“Ammonia is a nightmare to work with,” said Spearin.

Because the molecules are highly soluble in water and have an unstable electrical charge, they tend to stick to everything, including the inside of the human mouth and stomach, so they switched to a stronger, more stable sten Telfon tubing. Temperature fluctuations distorted ammonia measurements, so they added an on-board heater.

Finally, after six months of tweaking, the team brought its second-generation prototype into a quart er-size lab. The prototype was packed inside a custom box, which was placed on a wheeled cart. Beneath were a data acquisition system and various measuring instruments, an array of which would be miniaturized into a more compact format in a commercial product.

A volunteer from the meeting blew into the tube, and a graph of the levels of ammonia and carbon dioxide in that given breath appeared on the computer screen.

Enns’ first impression of the rapid, easy-to-use device was “jaw-dropping amazement.”

“Maybe these engineers could succeed where many others had failed.”

Ethan was recovering from a surgical procedure to insert a tube through his chest into an artery of his heart. His major organ he was working on the breath analyzer project.

Their plan was to have the teens blow into the device’s breathing tube after each of their blood draws over the two or three days it would take to normalize their ammonia levels. But they soon realized it was difficult to explain to the teens how hard to blow.

Finally, Straub figured out a strategy that worked. He gave one boy the tube and said, “Pretend that this is your elephant nose and make a sound like an elephant.”

This insight prompted the team to redesign the software to provide visual feedback that showed patients when they were blowing hard enough. They also started designing a passive, under-nose breathing tube that could be used with a mask, which was necessary for some patients but requires more sensitive detection.

Patient testing also refined their thinking on the technology. The device brings to the field.

The major weakness of the ammonia blood test is that by the time the results are received by a treating physician, it is usually too late to correct ammonia surges. The breath analyzer enables super-fast, repeatable testing so ammonia levels can be verified and treatment can begin immediately.

In just a year, the team had gone from a rough idea on paper to a working prototype, patient-tested. This was a step ahead in the medical device world. They are also preparing articles for publication describing the underlying spectroscopy, the device and, ultimately, their clinical studies.

Spearin can’t realize how hard this project was supposed to be until he called a respected expert on hyperammonemia for advice. Before Spearin could ask his kicker question, the expert chose a challenging project because ammonia is the most difficult molecule to measure, and newborns are the most difficult to test.

Spearin replied, “But we’ve already built a working prototype and we’ve tested it on two patients.”

“Given the planning a second, larger patient trial that will involve more than 20 children. There’s a good chance Ethan will be in that trial. Since they finished their first prototype, they’ve received grants from the NIH’s Small Business Technology Transfer program and the Wallace H. Coulter Foundation. The Stanford Office of Technology and Licensing has filed a provisional patent on the team. The company, funded by the NIH small business grant, has established a research consortium with Enns and others.

“We impressed me about this development team is that they really listened to all the advisers’ technical comments, methodically addressing each one. And they did so while getting a prototype into testing remarkably quickly,” said Solomon.

Waiting to exhale

Five years after his birth, Ethan, Pham, with chubby cheeks and bear-cub ears, looks and acts like a typical kindergarten student. His major play with him as he sits in his hospital bed, happily singing with cartoon farm animals on TV. On the bed is a sheet of paper where he has practiced writing his name with crayons.

Ethan is recovering from a surgical procedure to insert a tube through his chest into an artery of his heart. This permanent IV port will make it easier for the care teams to quickly administer ammonia-abating drugs when needed. He’s also under observation for high, unexplained fluctuations of ammonia.

It takes a dedicated team to keep Ethan alive. His family, schoolteachers and medical practitioners are continually on the lookout for signs of high ammonia levels. Episodes can happen at any time. Each prototype test means a 30-minute drive to the critical care unit, where staff members stand ready to draw blood. Ethan’s medical team — his pediatrician, Rebecca Fazliz, MD, at Sutter Health San Jose, Enns; and the hospital staff at Stanford Children’s Health — is on call 24/7.

Many times the ammonia blood tests, which can be done only at the hospital, are wrong or ambiguous. If the test is positive, it typically takes a day or two in the hospital to normalize the ammonia levels, with repeated blood tests every few hours. Sometimes the family is halfway home when a nurse calls them back to redo a test. Ethan has spent about half of his kindergarten year in the hospital.

Ethan’s teachers have been trained to accommodate his condition. His work areas must be extra clean and sick kids need to be kept away. His diet is carefully monitored — no birthday cake, since he can’t digest it. Ethan doesn’t have the muscle strength to climb on the playground equipment, so he often sits on the side, playing with his plastic farm animals or trying to kiss Catherine, a girl in his class he really likes.

Nguyen and Pham, like most parents who have children with metabolic diseases at the hospital and at home. This would allow Ethan to stay home and be watched more closely. Nguyen uses this time to teach Ethan. When Nguyen is at his side and Pham joins her after work. They often eat dinner at the hospital cafeteria. Nguyen’s parents and sister live nearby, and they help out when they can.

Nguyen is a full-time job keeping Ethan from slipping into an ammonia-induced coma.

What keeps the couple going is their faith (Nguyen is a Catholic and Pham is a Buddhist) and the hope that someone, maybe even the rocket men, will find a better way to test ammonia levels in children with metabolic diseases.

Blue sky thinking

It’s worth looking at the breath analyzer project the way it might perk up the attention of future scientists.

Of course, anyone familiar with medical device development would be quick to add that there’s a tremendous amount of work to be done before the ammonia breath analyzer is widely available. There needs to be more prototypes. Clinical trials. Independent validations. But one thing we all can probably agree on is this: Medicine needs more rocket scientists.

Kris Newby is the communications manager for SpectraWorks Inc., the Stanford Center for Clinical and Translational Research and Education.

Mariani Byerwalter to serve as interim president, CEO of Stanford Health Care

Mariani Byerwalter will serve as interim president and CEO of Stanford Health Care beginning Jan. 2. To ensure a smooth changeover, she will transition into her new role over the final two months of current president and CEO Michael D. Zeineh’s term.

Byerwalter, who earned a bachelor’s degree from Stanford and an MBA from Harvard, has served on the school’s board of directors for more than 15 years, including eight as chair. She has a long history of service and commitment to the Stanford community.

She served on the board of directors of Packard Children’s Hospital Stanford board of directors and chairs the Stanford Medicine Academic Council. From 1999 through 2012, she served three terms on the Stanford Univer sity board of trustees, chairing the Trustee Committee on the Medical Center. In recognition of her dedication, Byerwalter received the 2015 Gold Spike Award, which recognizes exceptional volunteer service and leadership for the university. In addition, she was awarded a 2015 School of Medicine Dean’s Medal in recognition of her contributions to advancing Stanford Medicine.

Byerwalter also served as chief financial officer and vice president for business affairs at Stanford.

Currently, she is chair of the board of directors of SRI International, a nonprofit independent research center that was originally founded as a Stanford research institute. She also sits on the boards of Pacific Life Insurance Company, Franklin Resources Inc., WageWorks Inc., Redwood Trust Inc. and the Burlington Capital Group.

Byerwalter has years of leadership experience, deep understanding of Stanford’s culture, and exemplary dedication and commitment to the mission of Stanford Health Care. Mariani is uniquely equipped to serve in this interim capacity. A Stanford graduate who served as president of Medicine, and John Levin, chair of the SCh board of directors, said in a statement.

A committee co-chaired by Levin and Minor is conducting a nationwide search for a new president and CEO. Rubin will step down from his post in January to take a position as executive director of Stanford Health Group and its OAnton Organization. He served as the hospital’s president and CEO for five years, overseeing a period of expansion and innovation in patient-centered care.
Story of family’s tumor donation inspires others, helps launch research

By Erin Digitale

On her son’s first day as a brain tumor patient at Lucile Packard Children’s Hospital Stanford, Danah Jewett asked one of her doctors if her family could donate 5-year-old Dylan’s organs to other children when he died. Most organs from cancer patients can’t be transplanted, the pediatric neuro-oncologist, Michelle Monje, MD, PhD, explained. But the Jewetts could make an even bigger difference by giving Dylan’s tumor to other children when he died.

Michelle Monje decided as a medical student to research diffuse intrinsic pontine glioma, a brain tumor that one father called “a death sentence for kids.”

When she began her work, she hit a roadblock: Because of its location, the tumor isn’t usually biopsied. There were no DIPG cells to examine in the lab.

In 2008, when Monje received approval for a protocol to collect tumor tissue from recently deceased DIPG patients for research, she worried about how parents of dying children would feel about being asked to donate the tissue. Shortly thereafter, Dylan came to Stanford, and his parents wanted to help doctors change the course of a disease his dad, John, called “a death sentence for kids.”

Their generous donation and openness about sharing their story made a difference: Twenty-one families, many of whom learned of the need for donations by reading Dylan’s story in *Stanford Medicine*, have now donated tumor tissue to Monje’s lab.

With the donated tissue, Monje’s team created the first cell line and mouse model of the tumor, which they have shared with scientists around the world. They’ve identified a candidate cell of origin for DIPG, learned that the tumor hijacks part of the brain’s normal mechanism for neuroplasticity to promote its own growth, and identified an FDA-approved drug that extends the lives of mice with the disease. The team is now planning a clinical trial of this drug, panobinostat, to see if it will also help children.

Danah later met one family that donated tumor tissue after reading the story about Dylan: “I thought, ‘Wow, this really encouraged another family to do this,’” she said. “It was a really good feeling.”

Many families of DIPG patients have also raised money for Monje’s research, contributing a total of more than $1 million to date.

“The story doesn’t end when Dylan died,” Danah said. “It feels good to know that my child’s life wasn’t just those five years. He’s continuing to make a difference.”

Michelle Monje decided as a medical student to research diffuse intrinsic pontine glioma, a brain tumor that one father called “a death sentence for kids.”

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*OF NOTE*

Elizabeth Egan, MD, PhD, was appointed assistant professor of pediatrics, effective Oct. 1. Her clinical specialty is pediatric infectious diseases. Her research examines host-pathogen interactions in the parasitic disease malaria, with a focus on how genetic variation in human blood influences parasite biology and virulence.

Paige Fox, MD, PhD, was appointed assistant professor of surgery, effective Sept. 1. She specializes in disorders of the arm, armpit and shoulder in adults and children. In her research, she aims to optimize care for hand infection patients and to use tissue engineering to improve outcomes after hand and upper-extremity trauma.

Anson Lee, MD, was appointed assistant professor of cardiothoracic surgery, effective Aug. 1. Lee leads the surgical arrhythmia program at Stanford, working closely with his colleagues who specialize in electrophysiology. Lee is also collaborating with the Stanford Cardiovascular Institute and the Department of Electrical Engineering to establish a basic and translational research laboratory that will explore the processes that underlie cardiac arrhythmias.

Lingyun Li, PhD, was appointed assistant professor of biochemistry, effective Sept. 1. Li’s research uses chemical biology to investigate cancer’s fighting mechanisms of innate immune pathways, an emerging field called chemical cancer immunology. Her lab aims to improve the understanding of these mechanisms so that more precise drugs can be developed to prevent or treat specific diseases.

Vj Periyakoil, MD, is pediatric associate professor of dermatology and director of palliative care education and training. She received a Practice Innovation Challenge award from the American Medical Association and the Medical Group Management Association for the Letter Project. The project provides templates that help patients identify and communicate their wishes for end-of-life care to their doctors and families. The five winners, announced at the MGMA annual conference on Oct. 12, will receive $10,000 and will have the opportunity to disseminate their work through the AMA.

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Blood type needed: AB-

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Elizabeth Egan
Paige Fox
Anson Lee
Lingyun Li
VJ Periyakoil