WE ARE THE MEDICINE MAKERS, AND WE ARE THE DREAMERS OF DREAMS

DREAMERS, DRUGS,

INSPIRED MEDICINE

BY RACHEL WILKINSON AND HEATHER BOERNER, WITH ERICA LLOYD AND MICHELE BAUM | ILLUSTRATION BY FRANK HARRIS

For a second consecutive year, the University of Pittsburgh has broken its patent record. The end of the fiscal year on June 30 saw a total of 102 patents issued, topping last year's record of 80. That puts Pitt in the top third of universities granted utility patents worldwide; many of the University's patents are in biomedicine and biotech. Last year, Pitt also spawned 29 start-ups (14 of which are student run).

This didn't just happen overnight, of course. To understand what's going on, you have to go back to 1980. That year saw the passage of the Bayh-Dole Act, cosponsored by Senators Birch Bayh and Robert Dole. The legislation allowed nonprofit institutions to own, patent, and commercialize inventions developed with federal research monies.

Before Bayh-Dole, any products of federally funded research were strictly owned by the government and difficult to gain the rights to. Potential advances often languished in labs with no clear path to get to the marketplace—or to the clinic.

Since 1980, more than 5,000 new companies have been launched from federally funded university research, contributing about $30 billion to the U.S. economy annually. In a 2002 op-ed called "Innovation's Golden Goose," *The Economist* argued that Bayh-Dole resulted in a "sudden reversal of fortunes" for a then-sluggish U.S. economy, bringing about "a flowering of innovation unlike anything seen before."

In the past couple of decades, people have been dreaming big around here. Chancellor Patrick Gallagher recently wrote in *Science*: "The [Pittsburgh] region clawed back from its economic breakdown by refocusing on technology innovation fueled by federally funded research at its major universities. . . . It is no accident that the top of the city's tallest building now advertises the University of Pittsburgh Medical Center—not U.S. Steel." Gallagher, who previously served as director of the National Institute for Standards and Technology, has strengthened Pitt's commitment to commercialization.

When Pitt people apply their ingenuity to human health, things get really inspiring. We've devoted the next several pages to showing you what their dreams are made of.

THOSE BLASTED KIDS

Pitt students are teeming with idealism and great ideas. The Blast Furnace was founded in 2015 to support the entrepreneurs among them.

9 weeks of intensive classes and mentorship

32 mentors in the program's history

6 cohorts of student entrepreneurs

13 health care concepts to go through the program

36 projects total to make it to market

OPEN-CONCEPT WEB SPACE

Ray Funahashi hasn't even finished medical school, and he's already seeking funding for his first start-up. "Problem-solving and innovation is what I love," says Funahashi, who is in his third year at Pitt Med. "I'm an idea person at heart."

His big idea? Remove the walls that researchers and students build around themselves and make it possible for them to find one another and collaborate for better science and better care. Think of the project, an academic portal dubbed LabKind (a play on "humankind"), as the open-concept work space of the Internet.

"Even in a lab two doors down from you, you don't know what they're working on," Funahashi says. "Some labs don't have a Web page at all."

LabKind is conceived of as a portal that consolidates and delivers information researchers, students, and faculty seek on a daily basis. The portal helps them share what they are working on in an easily navigated space.

Through the Blast Furnace, Funahashi met undergrad business student Drew Brumbaugh and **Luca Calzoni**, an MD/PhD student in bioinformatics, to create LabKind. The team graduated from Blast Furnace in summer 2016 and received second prize from the Innovation Institute at the Startup PittBlitz Competition. They also nabbed fourth place in the Randall Family Big Idea Competition. Now the team is looking for funding to complete its prototype and run a pilot program at Pitt. *—HB*

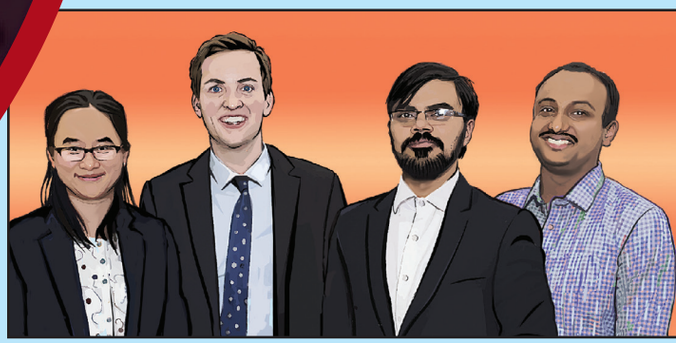
O_2 REDO

"Oxygen was discovered by Joseph Priestley in 1774. … It is therefore remarkable that oxygen treatment is still not widely available in low- and middle-income settings."

—*International Journal of Tuberculosis and Lung Disease, 2010*

The Problem: In areas without regular electricity or that have been hit by natural disasters, lack of access to supplemental oxygen can cause needless death.

The Promise: Access to supplemental oxygen can reduce the rate of children dying from pneumonia by 35 percent.



Solution, Take One: A portable hand pump that concentrates oxygen without the need for electricity, conceived by **James Newton**, a second-year Pitt Med student (shown above, in tie), along with (from left) Johns Hopkins neuroscientist Wendy Zhang, Pitt bioengineer Sushrut Bhalerao, and Carnegie Mellon engineer Ashwin Prabhu. That idea netted the team $500 for further development as third-place winner of the Blast Furnace Demo Day 2017.

But the students tried their prototype in Malawi and determined that the approach wasn't efficient in a real-world setting.

Solution, Take Two: A new design. The new idea? A solar-powered system to fill oxygen tanks at medical centers. "We are seeking funding to install the system in a health center in Malawi," Newton says, "to make observations and begin to work through logistical details." —*HB*

GOOD FOR MOM, TOO

"I guarantee you will think differently about the world once you witness the birth of a new life," says **Alysia Tucker**, a former doula (a professional who educates and assists women before, during, and after pregnancy). She birthed an app to make this blessed, though typically overwhelming, time a bit easier.

Tucker, a Graduate School of Public Health student, wants "to make sure women get connected to what they need." Hence Best4Baby, which links expectant mothers with doulas. Tucker won first place and $2,500 for the app at the spring 2017 Blast Furnace Demo Day. —*HB*

LAUNCHPADS

Pitt's Innovation Institute and other organizations at the University offer a number of programs to help biomed and biotech dreamers get their ideas off the ground.

BLAST FURNACE

Students on fire! (See p. 28.)

CHANCELLOR'S INNOVATION COMMERCIALIZATION FUNDS

Helps faculty investigators through the "derisking" stages between concept and market.

COULTER TRANSLATIONAL RESEARCH PARTNERS II PROGRAM

Each year, five $100,000 Coulter grants go to Pitt clinician-engineer teams focusing on biomedical interventions to address unmet needs. The Swanson School of Engineering–based program gets faculty boardroom ready.

MICHAEL G. WELLS ENTREPRENEURIAL SCHOLARS FUND

Awards up to $20,000 to Pitt students with ideas that could fundamentally change health care.

PITT INNOVATION CHALLENGE

A program of Pitt's Clinical and Translational Science Institute. (See "Pinch Us," right.)

PITT VENTURES FIRST GEAR

Often the first stop for students looking to figure out whether an idea has start-up potential. Pairs students with business mentors and provides $3,000 of exploratory funding via the National Science Foundation's I-Corps Site Program.

UP AND COMERS

Pitt Med students eager to contribute new ideas to medicine can now pursue the Area of Concentration in Bioengineering, Biotechnology, and Innovation.

PINCH US

The Pitt Innovation Challenge (PInCh) has been driving and rewarding innovation since 2014, granting more than half a million dollars a year to Pitt faculty and their teams to advance all manner of medical and scientific innovation.

In PInCh's very first year, Med Guardian, codeveloped by James Kaus (MD '15), won a $25,000 prize. The cell phone app is now known as Take Meds Now; it seeks to increase patient adherence to medications and to prevent some of the tens of thousands of accidental poisonings each year resulting from mismanaged medication. Take Meds Now went to market in June 2017.

These more recent PInCh hitters are also hoping to knock one out of the park.

TREATED IN UTERO

Imagine a way to prevent cerebral palsy and seizures, all in the womb and all without requiring a cesarean section of the mother at birth. That's the future Pitt's Stephanie Greene and Stephen Emery are working toward. Greene is an assistant professor of neurological surgery and a pediatric neurosurgeon at Children's Hospital of Pittsburgh of UPMC, and Emery is an associate professor of obstetrics, gynecology, and reproductive sciences and director of the Center for Innovative Fetal Intervention at Magee-Womens Hospital of UPMC.

Using technology developed to treat spina bifida in utero, they have designed a low-profile shunt that can be inserted in a fetus to drain fluid from the brain, preventing damage and, potentially, resulting conditions. It will likely be five years before they can test the shunt, called a ventriculo-amniotic shunt for fetal aqueductal stenosis (VASFAS), in humans.

NOW FEEL THIS

In his time as a neurosurgeon, Paul Gardner (MD '01), associate professor of neurological surgery, says he's "never seen anything that truly amplifies nerve healing." Mostly, he says, surgeons reconnect the nerves and hope for the best. Usually, incomplete nerve regrowth means a loss of motor control, selective weakness, and, potentially, pain.

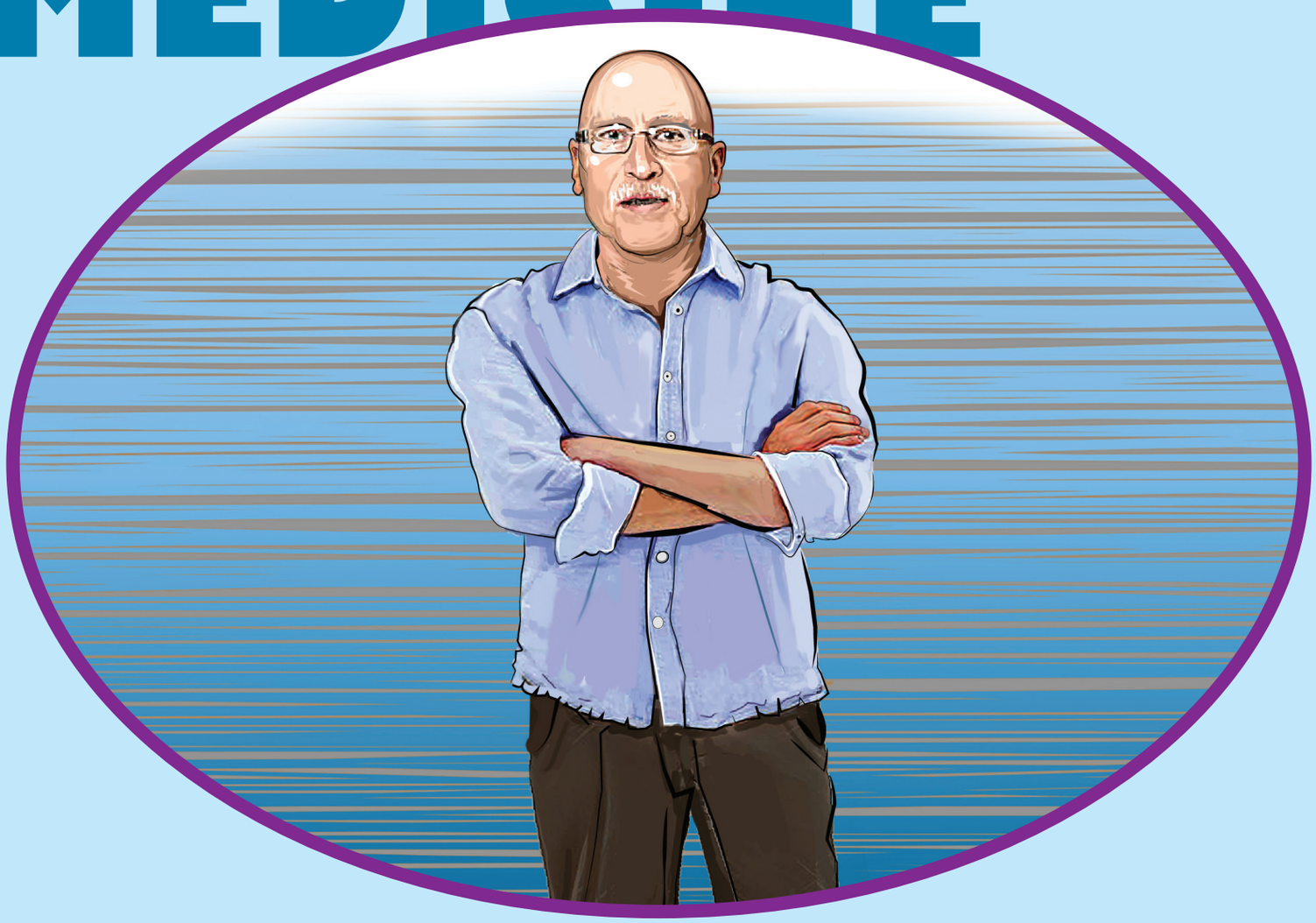
That is, Gardner never saw such a thing until he saw the solution created by Bryan Brown, PhD assistant professor of bioengineering. Brown has created a gel from porcine nerve tissue that provides scaffolding for human nerve tissue to regrow around. The gel is designed to be injected.

Brown's creation, Neurogel, won $100,000 in 2016 in the PInCh competition. Gardner and Brown have been working with the Food and Drug Administration with an eye on clinical trials.

Gardner says the PInCh prize allowed them to take their idea to the next level; a new company called Renerva is developing the technology. "To bring this to patients is a huge process that involves more studies to understand where this can be used best and a lot of regulatory work," says Gardner. *—HB*

DREAMERS

RADICAL MEDICINE



In the 1980s, Bruce Freeman, a PhD biochemist and pharmacologist, was giving a lecture in Buenos Aires; afterward, on a whim, he went to play a soccer game with a few graduate students. On his team was Rafael Radi, an MD and biochemist, who would become the first Uruguayan to be elected to the U.S. National Academy of Sciences. But back then, Radi was a new PhD student with few resources. He shared Freeman's interest in oxidants and free radicals—small, chemically reactive molecules that can start chains of dangerous reactions in the body, disrupting living cells and damaging DNA.

Freeman began to mail Radi chemicals with which to experiment. They struck up a friendship, and Radi completed a postdoctoral fellowship with Freeman in the United States (from 1989 to 1992). In 1994, Freeman returned to South America as a Fulbright Scholar at Universidad de la República in Montevideo, Uruguay.

Freeman and Radi's team was interested in a free radical called nitric oxide (NO). The molecule presented something of a puzzle to scientists, as it had contradictory properties: it was a combustion product and could react to form another molecule, nitrogen dioxide, which is "the brown gas you see in photochemical air pollution," explains Freeman, a Distinguished Professor and the UPMC-Irwin Fridovich Professor who chairs the Department of Pharmacology and Chemical Biology at the University of Pittsburgh.

High concentrations of NO also exist in blood vessels and in tissue during inflammation. Yet the gas is a critical player for the health of the immune system and for the normal functioning of the heart, lung, brain, pancreas, uterus, and liver, among other organs. NO was named "Molecule of the Year" by *Science* in 1992. It was the subject of the 1998 Nobel Prize for Physiology or Medicine; the Nobelists were honored for advancing the understanding of NO's key signaling roles in the cardiovascular system. (Many Pitt faculty, especially scientists in the Departments of Surgery and Medicine, know the molecule well. Among other things, they've helped lay out the role NO plays in organ rejection and sepsis.)

While studying NO in the late 1990s, Freeman's team deduced that the molecule transforms into nitrogen dioxide (NO_2). They found that NO_2 chemically reacts with fats and produces nitro-fatty acid derivatives with unique chemical properties—this molecule group is now called nitro-fatty acids (NO_2-FAs or NFAs). This was a wholly original discovery.

"Long story short, these nitro-fatty acids are found in insects, plants, and mammals and appear to play a central role in regulating inflammation and stress responses," says Freeman. "[They're] profoundly tissue protective and anti-inflammatory."

In the nearly 25 years since their discovery, nitro-fatty acids have been a focus in Freeman's lab. They form the basis of Complexa, a clinical-stage biopharmaceutical company that raised $62 million in its most recent funding round. Freeman is a Complexa scientific advisor and cofounder.

Nitro-fatty acids' progression from a scientific discovery to a commercial venture has been a slow burn. Freeman says it took another decade to grasp the vast potential for clinical application and for the right environment and development team to coalesce.

After the initial detection of nitro-fatty acids, Freeman and his team, anchored by Francisco Schopfer (who is a PhD and an associate professor in Freeman's group), were able to further their knowledge of the acids' molecular structure and ability to regulate gene expression. They discovered that nitro-fatty acids make up a key constituent of the Mediterranean diet—long known to be heart-healthy—rich in vegetables, legumes, fish, and other foods high in "good" unsaturated fats.

Freeman's team demystified why such a high-fat diet is beneficial. When you eat a salad doused with olive oil, for example, you increase concentrations of molecules that regulate cell behavior, including nitro-fatty acids, making your cells better able to adapt to stress and resist inflammation. (Research from Pitt's chair of medicine, Mark Gladwin, MD and Jack D. Myers Professor, has also played a key role in understanding how nitrate from foodstuffs can react to form tissue-protective fatty acids.)

Freeman began to wonder: If synthesized in their purest form, could the molecules be therapeutic? If a healthy person could reap the benefits of simply eating a nitrate-rich diet, perhaps high concentrations of nitro-fatty acids could help treat acute inflammation, even protect against it.

"In a state of delusion, I said to myself, *These could be potentially important as drugs*," says Freeman.

In 2002, while at the University of Alabama, Birmingham, Freeman began filing patents for the nitro-fatty acid class of molecules, receiving one of only four U.S. patents ever to "protect the composition of matter and methods of use" of a biomolecule, says Freeman. Ultimately, the intellectual property surrounding nitro-fatty acids make up a patent tree; the patents apply to any other molecule that has similar signaling activity. This means, essentially, no one else can patent a similar class of drug, because these patents "cover every possible atom that could be put on any possible structure to confer similar reactivity."

Freeman imagined starting a biotech company around the technology—though the overarching goal, he notes, was always to "translate [knowledge] into treating disease."

Christmas 2005: Freeman was named Pitt's pharmacology and chemical biology department chair and moved to Pittsburgh with his wife, Margaret Tarpey, MD and recently retired professor of anesthesiology. A few Christmases later, they wrote a $40,000 check out of their own pockets to synthesize the first 40 grams of CXA-10—Complexa's lead compound—and cofound the company.

"In its early years, Complexa needed to evolve, as it had encouraging lab-based data

THEY PERSISTED

It takes more than brilliance to turn a laboratory breakthrough into a new therapy. The secret formula includes inspiration, serendipity, teamwork, funding, and persistence.

1 in 10 drugs entering industry-sponsored phase 1 clinical trials between 2006 and 2015 advanced to FDA approval.

Drugs with the highest likelihood of advancing from phase 1 trials to FDA approval were in the fields of hematology, 26%, and infectious disease, 19%.

Cancer and psychiatric drugs entering phase 1 trials had the lowest likelihood of getting to patients, at 5% and 6%, respectively.

but only had a murky development and business plan," Freeman says. "We did things on our own early on just to find out if this was a crazy fantasy or if there was some substance to these molecules being truly efficacious as drug candidates."

Complexa earned its first early stage funding through local investors like the Pittsburgh Life Sciences Greenhouse (PLSG) and Innovation Works. Freeman and Schopfer took entrepreneurship classes through Pitt's Office of Technology Management (now part of the Innovation Institute). Schopfer ended up getting an MBA from Pitt's Katz School. Initially, the company was fund-raising amidst a deep recession in 2008 and 2009, when start-up investments were difficult to come by. But with help from the PLSG, Complexa was able to hire Josh Tarnoff in 2011 as its director, president, and chief executive officer.

"It was the [Pittsburgh] community coupled with the University that really enabled and gave the chance to this technology," Tarnoff says. "Without that, we would've never gotten off the launchpad."

Tarnoff and Freeman attribute both the challenges and successes of Complexa and CXA-10 to the fact that its effects are many and its applications are so broad. In Freeman's vision, nitro-fatty acids' "profound" anti-inflammatory effects could represent a new drug class because the fatty acids both *stop* acute inflammation and also *reverse* its effects in diseases like fibrosis and diabetes. Or, as Tarnoff put it, CXA-10 is a "stop and repair" technology.

"It's absolutely remarkable technology, because basically Freeman's team discovered this major reparative technology that also blocks key inflammatory mechanisms in the body," says Tarnoff.

The complexities of signaling pathway technology were less understood as recently as five years ago. Complexa produces its "stop and repair" effect by inhibiting the biological pathway NFkB, stopping inflammation, then upregulating the protective and reparative pathway Nrf2. Another Pitt pharmacology professor, Thomas Kensler, a PhD, has spent decades researching Nrf2 and the possible therapeutic effects of another molecule, sulforaphane. Found in broccoli and cruciferous vegetables, the molecule plays a cancer-preventive, detoxifying role by activating Nrf2.

One of the Freeman Lab's first animal studies gave nitro-fatty acids to obese, diabetic mice. The molecules not only lowered blood-glucose levels, helping manage diabetes, but also restored sensitivity to insulin, beginning to lessen or undo the disease's progression. The drug also produced an anti-inflammatory effect in fat cells, which could be therapeutic for obesity-related diseases. Hitting multiple targets, the molecule works through what's termed a pleiotropic signaling mechanism. (*Pleiotropy* translates to "more ways" in Greek.)

Tarnoff and Freeman say a major hurdle to CXA-10's commercialization has been pitching such a multifaceted drug to both investors and the pharmaceutical industry. "Their mindset is they like the concept of one drug, one target, one response," says Freeman. "And we've had to change their psychology."

Now, CXA-10 is on the eve of phase 2 clinical trials, scheduled to start in early 2018. After five phase 1 trials to determine safety and dosing, Complexa's leadership hopes to solidly prove efficacy. The company's strategy centers on treating two orphan diseases: focal segmental glomerulosclerosis, a renal disease affecting about 40,000 people in the United States, and pulmonary arterial hypertension, a type of high blood pressure afflicting 20,000 Americans. There's no cure or effective long-term treatment for either of these diseases.

Tarnoff predicts Complexa's approach will be a "game-changer."

Success treating these orphan diseases, Freeman hopes, would allow Complexa to go after more widespread diseases. Because so many diseases induce harmful inflammatory responses, Freeman's lab is exploring even broader applications of nitro-fatty acids: the potential to treat asthma, sickle-cell anemia ("fundamentally a vascular inflammatory condition," says Freeman), even acute lung injury from viral infections.

Funders in Complexa's most recent round included international investors like NEA and Edmond de Rothschild Investment Partners, two of the world's largest financial advisory groups, and JAFCO, a Japanese venture firm, as well as U.S.-based Pfizer. And there's interest in Complexa among several other major pharmaceutical companies.

Successful phase 2 trials may lead to a buyout by a pharmaceutical company, an initial public offering (IPO), or another round of fund-raising for phase 3 trials.

Freeman likens seeing Complexa take off to watching a child go off to college. But his goal was always larger than starting a company. He estimates even with a small marketplace penetration, CXA-10 could save tens of thousands of lives.

"My team and I want to make a transformative difference," he says. —*RW*

VIRUSES FOR GOOD

Among the 102 patents issued to Pitt inventors in the past fiscal year, one was based on the work of Joseph Glorioso, a PhD professor of microbiology and molecular genetics, and Paola Grandi, PhD assistant professor of neurological surgery and of microbiology and molecular genetics. The researchers modified the herpes simplex virus to target highly malignant forms of cancer, including the most aggressive brain cancer, glioblastoma, by activating the body's immune response. This experimental approach is known as an "oncolytic virus."

The herpes technology was partially licensed from Glorioso and Grandi by Cambridge, Mass.–based Oncorus. In July 2016, Oncorus raised $61.4 million to support phase 1 clinical trials. The company was featured in the *Wall Street Journal*, and the industry site BioSpace put Oncorus among the "Top 20 Life Science Startups to Watch in 2017."

"As far as an unmet medical need, it's gigantic," says Glorioso.

Another oncolytic virus, invented by Pitt's Stephen Thorne, a PhD assistant professor of cell biology, immunology, and surgery, has also resulted in a spin-off company, Western Oncolytics. The company struck a deal with Pfizer to codevelop the virus WO-12. In mouse models, WO-12 cleared several types of solid tumors up to 100 percent of the time. The technology will soon go into clinical trials. —*RW*

DATA, IT'S BIG

• In fall 2012, UPMC announced it would invest $100 million throughout the next five years in a data warehousing, integration, and analysis project that would bring together clinical, financial, genomic, and other information to improve patient care. UPMC is partnering with Oracle, IBM, Informatica, and dbMotion to make this happen. Pitt faculty lead the research efforts.

• In January 2014, Pitt established its Institute for Precision Medicine, which harnesses the power of data analytics to understand complex biology at the level of the individual.

• In 2014, the National Institutes of Health awarded Pitt's School of Medicine $11 million to lead the Big Data to Knowledge Center of Excellence.

• In 2015, Pitt, UPMC Enterprises, and Carnegie Mellon partnered to create the Pittsburgh Health Data Alliance to move knowledge acquired from data into solutions for patients. The Alliance expects to attract hundreds of companies and entrepreneurs to Pittsburgh.

• In June 2017, NIH and Pitt announced the initial recruitment phase for the All of Us campaign to inform advances in precision medicine. In Western Pennsylvania the study is called PA Cares for Us; and over five years, Pitt will recruit 150,000 participants of the expected 1 million total nationwide. Pitt's was the first site to open nationally.

• Just this year, Dean Arthur S. Levine, senior vice chancellor for the health sciences, was asked by the National Library of Medicine to chair a working group charged with determining how to advance biomedical discovery and translational research in this data-driven era.

SAVING THE THYROID

1 in 4 thyroid cancer screens come up inconclusive.

20% of inconclusive nodules turn out to be cancer.

Old standard of care: If any suspicious nodules were found, the whole, or part of, the thyroid was removed, necessitating lifelong thyroid hormone replacement therapy for many.

Current approach: Pitt-developed molecular marker panel, ThryoSeq, helps UPMC doctors be more accurate and judicious in evaluating nodules. ThyroSeq was developed by Yuri Nikiforov, MD/PhD professor and vice chair of pathology.

Better yet: A new two-year trial includes patients who have a biopsy that is positive or suspicious for cancer. Some patients may be adequately treated with partial removal of the thyroid and not require follow-up medication. The current trial will see if ThryoSeq can offer doctors that important preoperative information.

"We want to do the right operation the first time around," says Linwah Yip, MD associate professor of surgery and principal investigator on the trial. —*HB*

DRIVER, ID PLEASE

Excuse me, cell. Do you know how fast you were multiplying? You're going to need to show me some ID.

"Cells accumulate genetic mutations every time they divide," Xinghua Lu, MD/PhD professor of biomedical informatics, says. "Some of these drive cells into uncontrolled proliferation and migration and eventually lead to cancer. And some are nonconsequential events. We need to differentiate between the driver and the passenger."

Hence the Tumor-specific Driver Identification (TDI) algorithm and software being developed and tested at Pitt by Lu and Gregory Cooper, MD/PhD professor and vice chair of biomedical informatics. TDI is designed to reveal, in a given tumor, mutations that might cause cancer.

At this point, Lu and colleagues are still sorting out the mutational noise from the significant events and fine-tuning parameters. "Most others are working out this issue from the population level—watching for mutations in a cohort of, say, 10,000 people," he says. "We are doing it at an individual tumor level." —*HB*

CRASHES PREDICTED, COURSE CORRECTED

Your blood pressure can keep going up and still stay in the normal range.

So when is that safe and when should it raise a red flag? That's what Ricardo Muñoz, MD professor of critical care medicine, pediatrics, and surgery, found himself wondering after witnessing cardiac events in children.

"We don't want to treat an event; by then, it's too late," he says. "You've already crashed. . . . When a plane crashes, and you have survivors, that's lucky. It's preventing it before it happens" that's the real trick, he says.

To do that, Muñoz is harnessing retrospective data from Children's Hospital to train a computer algorithm to recognize and flag warning signs of cardiac events before they happen.

That's where Rich Tsui, PhD associate professor of biomedical informatics, comes into the picture. Tsui had already been working on predictive technology to identify whether patients were likely to be readmitted to a hospital after discharge when he met Muñoz. Then the two men started brainstorming how to teach a computer to identify negative trends and flag them so providers can take action. And, ideally, they would prevent crashes.

The resulting algorithm, now being tested in a partnership between Pitt and Children's, has shown that, using retrospective data, it can predict cardiac events in patients. The next step is to sift through real-time hospital data and identify trends. That part of the project should begin in 2018, says Muñoz. If successful, it could be rolled out beyond UPMC to other hospital systems.

And while the team has already applied for a patent for their system, Muñoz said that's not the point. "My interest isn't in money," he says. "If we can make a really effective machine, it could make a tremendous difference for patients and for health care spending." —*HB*

PIVOTS

While an undergrad at Carnegie Mellon University, Shivdev Rao was a skateboarder and social history major, interested in philosophy and headed toward an academic career in the humanities.

Then he went to a lecture by architect William McDonough.

McDonough told the story of Govindappa Venkataswamy, an Indian eye doctor who founded one of the largest ophthalmology hospital networks in the world and restored more than two million people's sight for free. Venkataswamy achieved this by designing a swiveling surgical room resembling an assembly line, where he and his team could perform a cataract operation in 10 to 20 minutes, then quickly move to the next prepped patient.

McDonough's philosophy, that "design is the first signal of human intention," spoke deeply to Rao."He inspired me to think about how I want to impact people," says Rao, who then "pivoted" toward medicine. Rao (MD '07) is now a clinical instructor of medicine at Pitt and executive vice president for UPMC Enterprises, the commercialization arm of the medical center.

Rao carries his ethos of influencing the world through design to his work at UPMC Enterprises. The unit invests in and builds technologies that do what Rao calls the "three As": assist, augment, or automate aspects of health care delivery, with an immediate focus on UPMC's $16 billion health care system.

This mission is newly evolved, says Rao. Enterprises—which has its colorful open-concept offices in Bakery Square—was originally called the Technology Development Center and focused largely on software-centered solutions for UPMC and elsewhere. The vision has broadened in recent years to include solutions based on everything from basic science to advanced analytics.

Rao says Enterprises' "secret sauce" is access to UPMC's more than 30 hospitals, 600 doctor offices, and 3,800 physicians, as well as its insurance plan; UPMC's massive system constantly generates data and can function as a real-time feedback mechanism.

Still a practicing cardiologist, Rao takes weekly appointments at Magee-Womens Hospital of UPMC and performs rounds at UPMC Presbyterian.

"Seeing patients always . . . informs me about some new nuance that I can bring here [to Enterprises]," he says.

At Enterprises, Rao focuses on solutions that "work backwards" from patient care. Rao says the goal is to embrace higher-level ideas that would affect patient and provider experiences. These include artificial intelligence and its subsets like deep learning (wherein networks, with designs inspired by the structure of the brain, are capable of learning and sometimes making decisions from large datasets).

"Deep learning really sings in the imaging space, more than any other domain. Radiology, pathology, aspects of ophthalmology and cardiology" will all benefit, says Rao.

For instance, a pathology system might filter for images with abnormalities and even make diagnostic suggestions based on the data to create an entirely new workflow. For perpetually overworked clinicians, Rao believes such technology would improve efficiency and help with decision-making. He emphasizes he doesn't believe in "push-button" technology for diagnosis in the near future. Instead, he believes that "we can help doctors do better." Through a partnership with Microsoft's artificial intelligence labs, he envisions leveraging "technology to transform clinicians from overwhelmed and time scarce, to nearly omniscient and omnipresent healers."

He says Enterprises is walking a path toward wholly person-centered health care, where every patient controls his or her own data over vastly interconnected systems.

"We're far from that," says Rao. "But we have all the ingredients." —*RW*