The California Tech

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SpaceX COO Envisions Road to Mars

Maitreyi Nair
Page Editor

Since its inception in 2002, SpaceX has continually demonstrated itself to be a company with high aspirations, specializing in manufacturing and launching advanced rockets and spacecraft. This past Friday, May 19, SpaceX's current President and Chief Operating Officer, Gwynne Shotwell, visited Caltech to deliver the Division of Engineering and Applied Science's 2017 Wouk Lecture, aimed at providing an overview of the technology development and business plans for what is shaping up to be SpaceX's loftiest goal yet - the human colonization of Mars.

Gwynne Shotwell, who graduated with degrees in Mechanical Engineering and Applied Mathematics from Northwestern University, started at SpaceX as the Vice President of Business Development and is currently the woman in charge of managing all day-to-day operations, strategic relations, and customer relations for the company. Addressing a large crowd of students, faculty, alumni, and community members in Cahill's Hameetman Auditorium, she expanded on the company mission presented by SpaceX founder, CEO, and CTO Elon Musk at last September's International Astronautical Conference, where he first presented his vision for the future in a similar talk titled "Making Humans a Multiplanetary Species".

Beginning with a brief synopsis of SpaceX's operational history, Shotwell gave descriptions of Dragon cargo capsules and the Falcon vehicle family, both of which are currently used to deliver payloads into Earth orbit, speaking frankly and, at times, with humor about the often bumpy road to their current launch and landing capabilities. Looking to the near future of advanced vehicle technology, SpaceX has several projects on the books: for one, they are currently in the late testing stages of implementing crew transport capabilities in the Dragon capsules as a part of their 2011 NASA contract, the timeline for which Shotwell said involves sending US astronauts back to the International Space Station sometime early next year, with private commercial spaceflights expected as well. In addition, the first demonstration of the multicore Falcon Heavy rocket is slated for October of this year, at which point it is set to become "the most powerful operational rocket in the world by a factor of two", with a maximum payload capability of 54 metric tons. By placing much of their technological impetus on the "recoverability and reusability" of their spacecraft and refining their technology through repeated testing, SpaceX has come an impressively long way towards achieving one of their earliest goals of improving the cost and reliability of access to space; through this learning process, Shotwell said, came the building blocks for the ultimate goal of creating a human civilization on Mars.

In her presentation, Shotwell primarily focused on the vehicular components and timeline necessary for the journey: Raptor engines, which run on methane and are currently in use at a scale roughly 2/3 of the required size, will propel the "Interplanetary Transport System" (ITS) into Earth orbit, where it will await refueling by the same booster rocket that delivered it to orbit; once that is complete, two 200-kW solar arrays will deploy, and the ITS and its cargo will be en route to Mars. The timeline for testing, as described at Friday's talk, involves having the full-scale Raptor engines developed by the end of 2018 and starting preliminary launch and flight tests by the end of 2018, with an optimistic date of getting an initial ship landing on Mars in 10 years.

The very notion of reaching Mars, let alone colonizing it, is one of extraordinary magnitude, and, obviously, any serious plans to successfully pursue such an endeavor face significant challenges. In the interactive discussion portion of the afternoon, Shotwell took audience questions discussing such challenges, in one case bringing up the point that, as a private company, one of the greatest obstacles is that the equity necessary to fund a slow-return project such as this Mars colonization mission is on the order of tens of billions of dollars for each flight, though the cost should go down after the initial missions, and the rate of progress in this respect is slowed largely by economic obstacles. To alleviate this financial burden in the long run, Shotwell also described SpaceX's plans for the development of a global broadband internet network operated using a "Satellite Constellation" to provide low-cost, reliable internet access through a space-based internet communication system - this plan was proposed by Elon Musk to address consumer and technological issues with the current internet provider system, practice for an extension of a similar system to a Martian colony, and tap into the global internet market, providing capital for future Mars missions. Although the viability of such a venture is unknown, test satellites are slated to go up in the next year or so, and initial operation of the array could begin in 2020.

Apart from the purely economic challenges, there are still larger questions up in the air regarding manned missions to Mars that will need to be addressed and solved before any kind of colonization can happen at all, of considerable technical, financial, and cultural significance. SpaceX's role in implementing a full colonization of Mars is necessarily limited by their niche as a manufacturer of spacecraft and launch vehicles, while other companies and governmental entities such as NASA have demonstrated interest and are actively preparing for similar missions, with NASA's multi-stage "Journey to Mars" culminating in sending humans to low-Mars orbit in the early 2030s. In the end, as this project is only in its nascency, we can only wait and see what the next few years bring, keeping in mind Gwynne Shotwell's words from the conclusion of Friday's lecture: "[t]his is not just a project for SpaceX - this is a project for humankind."

SAFE Review: "Did My Neurons Make Me Do It?"

Rona Yu
Page Editor

Can our decisions be reduced to the "mindless motion of molecules"? Does our creativity emerge from a set of rigid rules?

Dr. Warren S. Brown, a Psychology professor at the Travis Research Institute of the Fuller Theological Seminary, discussed determinism and reductionism at the May Science and Faith Examined (SAFE) event.

Brown introduced himself with a brief overview of his neuroscience research in corpus callosum agenesis (ACC) and involvement with the National Organization for Disorders of the Corpus Callosum.

Afterwards, Brown defined technical terms from his work with philosopher Nancey Murphey. Cartesian dualism, a view Brown personally disagrees with, is the belief that the body is merely a material reflection of what there is. On the other hand, eliminative materialism is the belief that physical processes are subject to the deterministic laws of physics. Under this theory, the brain, a physical object, is based on deterministic laws. Thus, conscious mental life is epiphenomenal, and our decisions are results of deterministic physical processes.

Disagreeing with both views, Brown introduced emergence through nonreductive physicalism: an alternative to eliminative materialism and Cartesian dualism that is consistent with modern neuroscience, involves mental life as a causal role, and allows human beings to have genuine interpersonal relationships, moral agency, and religious experiences. Unlike eliminative materialism, emergence relies on the higher-level causal properties which emerge from the complexity, interconnectivity, and two-way interactions of neurons and cannot be explained by analyzing the parts (individual neurons) alone.

Brown claimed the mind is physically embodied in the body and brain, embedded in the contextualized action of the world, emergent from patterns of interaction, and extended by incorporating things outside the body. For this presentation, Brown focused on embodiment and emergence.

Embodiment was illustrated by hypothesizing an elephant with a human brain. Brown argued that despite having the same brain, the elephant would have a very different mind that resulted from different bodily interactions with the world.

Emergence was illustrated by comparing an ant colony, a complex dynamical system which is self-organizing and responds to the environment to display interaction patterns, to an ant aggregate. Assuming a passive queen ant and no strongly commanding individual ants, the colony's actions and characteristics were not due to the actions of individual ants. Like chess or neural networks, complex patterns arose from very simple rules. Generally, emergent properties were described to result from a qualitatively different repertoire of states and greater degrees of freedom as a system reorganizes. Under Brown's definition of determinism, the ant colony is not deterministic.

Ultimately, Brown argued that the neurons "did not make me do it." I was defined as a whole integration of the body and the brain. Mental and behavioral patterns are emergent properties based on the patterns of organizations of all parts of the body, and individuals are formed by their interactions with the outside world.

Like other SAFE events, Brown's presentation was followed by a general question and answer session, and small group discussions consisting of undergrads, graduate students, and faculty members. This was the sixth and final event for the academic year.

IN THIS ISSUE

Caltech Y Column

CALTECH Y

Upcoming Events

Eastern Sierras Backpacking: Lake Sabrina

Friday 5:30pm - Sunday evening | June 2nd-4th | $40

Ever feel like backpacking in the snowy mountains in June? Join in a backpacking trip out to the beautiful Sierra Nevadas. We'll drive up to the mountains Friday and spend the night near the trailhead. On Saturday, we'll hike or snowshoe past Lake Sabrina in around 10 miles and explore the high lakes region. We'll camp in the snow, and get back late Sunday evening. It'll be a cold intense backpacking trip up around 10,000 feet in elevation. The mountains will be majestic, and the trip should be a blast!

Please contact jbrouill@caltech.edu if you have any questions.

Caltech Y Memorial Weekend Office Hours

Due to the Memorial Day Holiday we will be closing at 2:00 PM on Friday May 26th and closed on Monday May 29th. We will re-open with regular hours on Tuesday May 30th. Please contact us at caltechy@caltech.edu for any inquiries.

Caltech Y Photo Contest

Choose Your Favorites in the Caltech Y Photo Contest!

Wednesday | May 31st | 12 Noon

The Caltech Y Photo Contest is back. Vote for your favorite photos in our 2nd annual photo contest.

Like us on Facebook—then "like" your favorite photo(s) in each category.

Perspective
Adventure
Service
Civic Engagement
Leadership

Voting will end at 12 p.m. (noon) on Wednesday, May 31. If you don't have a Facebook account send us your votes by email.

We can't wait to see which ones you pick!

Hathaway Sycamores

Every Wednesday | 6:00 - 8:00 PM | Highland Park

Volunteer at Hathaway Sycamores, a group that supports local underprivileged but motivated high school students. There are a variety of ages and subjects being tutored. The service trip includes about an hour of travel time and 1.5 hours of tutoring. Transportation is included.

For more info and to RSVP email Sherwood Richers at srichers@tapir.caltech.edu. Eligible for Federal Work Study.

Pasadena LEARNS

Every Friday | 3:00 - 5:00 PM | Pasadena

Come volunteer at Madison and Jackson Elementary School! We are partnered with the Pasadena LEARNs program and work with their Science Olympiad team or do regular tutoring along with occasional hands-on science experiments. Transportation is provided. For more information and to RSVP, contact azhai@caltech.edu. Eligible for Federal Work Study.

Mentoring For Life

Every Monday | 3:30pm | Wilson Middle School Pasadena

Stressed out by college life? Step outside the Caltech bubble and mentor tweens who've never even thought about college. Things you could do: Build a baking soda and vinegar volcano, read a book aloud, play sports or board games, teach the alphabet of another language, do a craft. Having a mentor makes an at-risk student 55% more likely to attend college, 78% more likely to volunteer regularly, and 130% more likely to hold a leadership position. Interested? If you have 180 seconds, you can watch this video and be inspired. If you have an hour a week, you can mentor someone and be their inspiration. If you feel unqualified, don't worry. Ultimately, mentoring is about being a consistent, dependable friend—not a surrogate parent or psychiatrist. To get started, contact noelle@caltech.edu.

VICE PROVOST'S OFFICE HOURS

Vice Provost, Chief Diversity Officer, and Professor of English Cindy Weinstein holds regular office hours as an opportunity for undergraduate students, graduate students, and postdocs to meet for discussions pertaining to the Council on Undergraduate Education; Caltech accreditation; the Staff and Faculty Consultation Center; Student-Faculty Programs; the Center for Teaching, Learning and Outreach; the Caltech Diversity Center; and the Caltech Libraries.

There are four 15-minute appointments available per office hour. Sign up in the Office of the Vice Provost, Parsons-Gates room 104, ext. 6339 or by sending an email to dlewis@caltech.edu. We look forward to hearing from you!

Student Office Hours for Spring Term 2017:

5/24/17 Wednesday 11:00 a.m.-12:00 p.m.
5/31/17 Wednesday 11:00 a.m.-12:00 p.m.
6/8/17 Thursday 11:00 a.m.-12:00 p.m.

Undergraduate Due Time Preferences

Cody Lim
ARC Rep

In August 2016, the ARC surveyed undergraduates to determine their preferred time of day for sets to be due. Undergraduates could rank four time ranges: 12 – 2 AM, 8 – 10 AM,

12 – 2 PM, and 4 – 6 PM. In addition, they could write-in a time range under "other," as well as provide reasons for their preferences in a comment box. A method based on instant runoff voting was used to determine students' preferences. In the first round, the number of votes was counted to determine the most preferred time range. After this, the most popular time range was eliminated. People whose first choice votes were eliminated had their votes transferred to their next ranked choice. This yields a ranking of time ranges based on preference.

From the survey, it was determined that the most preferred time range was 4 – 6 PM, with over half of the first-choice votes in the first round (Figure 1). After eliminating this choice, the next most popular time range was 12 – 2 PM (Figure 2). In the final round, 8 – 10 AM narrowly beat out 12 – 2 AM (Figure 3). This shows that students greatly prefer for sets to be due in the middle of the day/ late afternoon.

When prompted for a reason, students preferred 4 – 6 PM because they were allowed to have the early hours of the day to work on sets. This could allow for students to have more time available in the evening. Students could have more time for activities such as dinner, intercollegiate sports, and spending time with friends. In addition, students can attend evening office hours for a class the evening before a set is due, and work on the set the next day. Finally, a mid-day due time could prevent students from rushing to complete a set during the evening before going to bed.

Despite its popularity, the 4 – 6 PM time range has some drawbacks. To begin with, this time range can negatively affect attendance for morning classes, as students can skip class to work on a set. Because of this, more professors are implementing 12 – 2 AM due times in order to discourage students from staying up late and skipping class to work on sets. The 4 – 6 PM time range also coincides with athletes' practices, forcing athletes to turn in sets earlier and potentially miss out on last minute corrections.

Student preferences are important for professors to consider when deciding a time of day for sets to be due. However, professors must also consider factors such as the potential for all-nighters, effects on course attendance, and conflicts with athletic practice and other extracurricular activities. These factors may result in a professor choosing a due time that is unpopular with students taking the course. Because of this divide in the preferences of students and professors, professors can often struggle to find a set due time that works well.

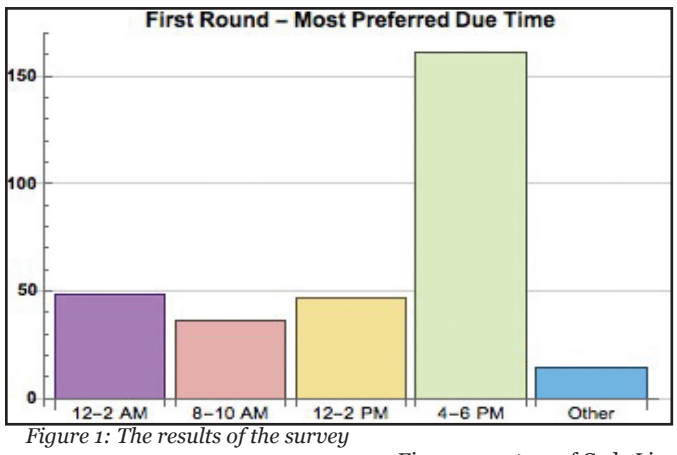


Figure 1: The results of the survey

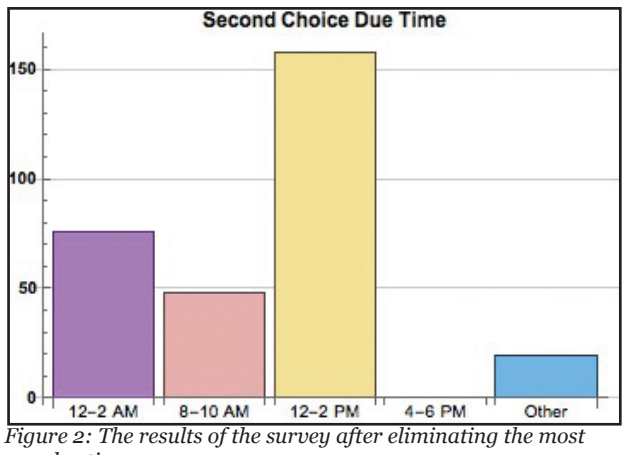


Figure 2: The results of the survey after eliminating the most popular time

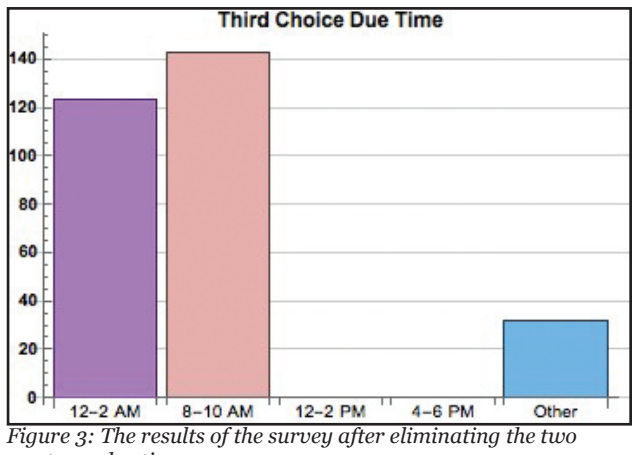


Figure 3: The results of the survey after eliminating the two most popular times

Figures courtesy of Cody Lim

Cutting Down on Cancer Surgeries

ROBERT PERKINS
Caltech Media Relations

This article is adapted from a story that was originally published online at caltech.edu.

Engineers at the Optical Imaging Laboratory led by Caltech's Lihong Wang have developed an imaging technology that could help surgeons removing breast cancer lumps confirm that they have cut out the entire tumor—reducing the need for additional surgeries.

About 300,000 new cases of invasive breast cancer are discovered annually. Of these, 60 to 75 percent of patients underwent breast-conserving surgery.

Breast-conserving surgeries, or lumpectomies, attempt to remove the entire tumor while retaining as much of the undamaged breast tissue as possible. (In contrast, a mastectomy removes the entire breast.) The extracted tissue is then sent to a lab where it is rendered into thin slices, stained with a dye to highlight key features, and then analyzed. If tumor cells are found on the surface of the tissue sample, it indicates that the surgeon has cut through, not around, the tumor—meaning that a portion of the tumor remains inside the patient, who will then need a follow-up surgery to have more tissue removed.

After a week or two waiting for lab results, 20 to 60 percent of patients find out that they must return for a second surgery to have more tissue removed. But, asks Wang, "what if we could get rid of the waiting? With 3D photoacoustic microscopy, we could analyze the tumor right in the operating room, and know immediately whether more tissue needs to be removed." Wang is a Bren Professor of Medical Engineering and Electrical Engineering in Caltech's Division of Engineering and Applied Science. His lab invented 3D photoacoustic microscopy.

Photoacoustic microscopy, or PAM, excites a tissue sample with a low-energy laser, which causes the tissue to vibrate. The system measures the ultrasonic waves emitted by the vibrating tissue. Because nuclei vibrate more strongly than surrounding material, PAM reveals the size of nuclei and the packing density of cells. Cancerous tissue tends to have larger nuclei and more densely packed cells.

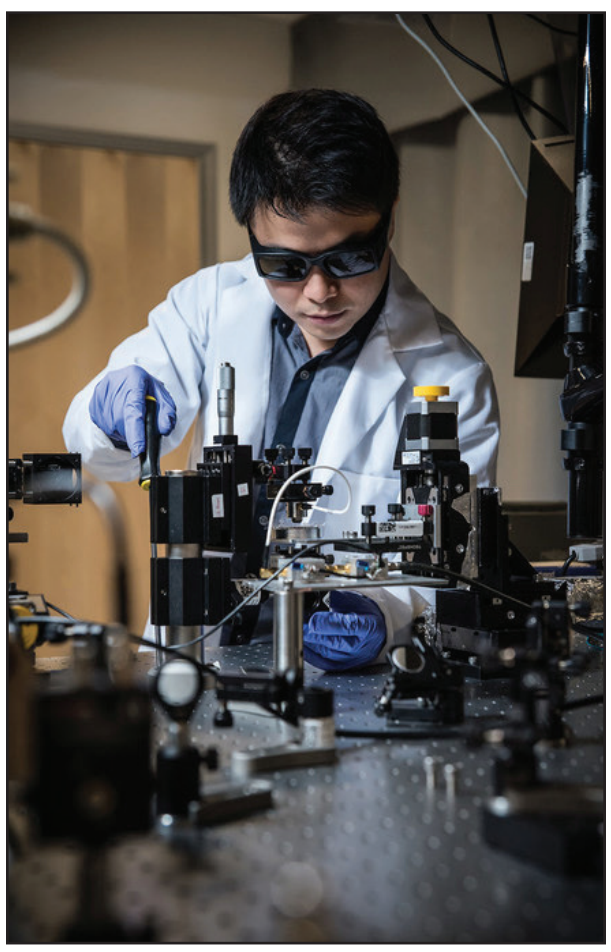
Indeed, as described by Wang and his team in a paper published in the journal Science Advances on May 17, PAM produces images capable of highlighting cancerous features, with no slicing or staining required.

Wang conducted this research while the Optical Imaging Laboratory was located at Washington University in St. Louis. He moved the lab to Caltech's Andrew and Peggy Cherng Department of Medical Engineering in January 2017.

Although Wang's team has focused primarily on breast cancer tumors, his work has potential applications for any analysis of excised tumors—from melanoma to pancreatic cancer. In a proof-of-concept scan described in the new paper, PAM analyzed a sample in about three hours. Comparable traditional microscopy takes about seven hours to achieve the same results. However, Wang says that PAM's analysis time could be cut down to 10 minutes or less with the addition of faster laser pulse repetition and parallel imaging. This would make the technology useful for clinical applications.

"Because the device never directly touches a patient, there will be fewer regulatory hurdles to overcome before gaining FDA approval for use by surgeons," Wang says. "Potentially, we could make this tool available to surgeons within several years."

The Science Advances paper is titled "Fast Label-free Multi-layered Histology-like Imaging of Human Breast Cancer by Photoacoustic Microscopy." Among the coauthors are Terence Wong, Ruiying Zhang, Pengfei Hai, Chi Zhang, and Miguel Pleitez, who are current or former members of the Optical Imaging Laboratory, and Rebecca Aft and Deborah Novack, who are clinical collaborators at Washington University. This research was funded by the National Institutes of Health and the Siteman Cancer Center.



Terence T. W. Wong, first author of the May 17 Science Advances paper, adjusts a photoacoustic microscope at the Caltech Optical Imaging Laboratory.

Photo Courtesy of Caltech

Chemistry Professor Awarded Feynman Teaching Prize

LORI DAJOSE
Caltech Media Relations

This article is adapted from a story that was originally published online at caltech.edu.

This year, the Richard P. Feynman Prize for Excellence in Teaching has been awarded to Professor of Chemistry Brian Stoltz, who has taught at Caltech for 17 years.

Stoltz was nominated for the Feynman Prize by undergraduate and graduate students, alumni, and fellow faculty members, who praised his dedication and passion for teaching as well as his commitment to diversity and an individually tailored approach to mentorship. Many who have taken his courses credited Stoltz with their renewed enthusiasm for the subject. His teaching evaluations are "uniformly outstanding," according to the citation.

Stoltz previously was awarded the ASCIT (Associated Students of the California Institute of Technology) teaching award and the Caltech Graduate Student Council Teaching Award, was named a professor of the month by the undergraduate-run Academics and Research Committee (ARC), and was awarded a Camille Dreyfus Teacher-Scholar Award. In addition, Stoltz has served for several years as the graduate and undergraduate chemistry option representative. He also has been engaged with pre-college education and outreach, working with local schools as well as the Caltech preschool through on- and off-campus educational activities.

"I am so excited to have been nominated by my former students and colleagues, and to receive this amazing recognition from Caltech," Stoltz says. "To be associated in this way with the most outstanding educators at the Institute and with Feynman himself is truly humbling. It is an honor to work with such exceptional people on a daily basis and incredibly gratifying to know that I have had some impact on them as well."

The Feynman Prize has been endowed through the generosity of Ione and Robert E. Paradise and an anonymous local couple. Some of the most recent winners of the Feynman Prize include Ellen Rothenberg, Albert Billings Ruddock Professor of Biology; Kevin Gilmartin, professor of English; Steven Frautschi, professor of theoretical physics, emeritus; and Paul Asimow, the Eleanor and John R. McMillan Professor of Geology and Geochemistry.

The prize was established in 1993 to honor annually a professor who demonstrates, in the broadest sense, unusual ability, creativity, and innovation in undergraduate and graduate classroom or laboratory teaching. Nominations for next year's Feynman Prize for Excellence in Teaching will be solicited in the fall. Further information about the prize and a full list of past recipients can be found on the Provost's Office website.

Brian Stolz

Photo Courtesy of Caltech

Small-Molecule Talk with Alison Ondrus

WHITNEY CLAVIN
Caltech Media Relations

This article is adapted from a story that was originally published online at caltech.edu.

New Caltech professor talks about the intersection between chemistry and biology

New assistant professor of chemistry Alison Ondrus says she's excited to apply the tools of traditional chemistry to the study of biological problems and thinks Caltech, with its small, interdisciplinary environment, is the perfect place to do it.

Ondrus received her PhD in organic chemistry in 2009 from MIT, where she learned to synthesize structurally complex molecules. From there, she became interested in biology and began studying the Hedgehog signaling pathway as a postdoctoral scholar at the Stanford University School of Medicine. The Hedgehog family of proteins is responsible for many basic functions in animals, including development and organization of the overall body plan. Mutations in Hedgehog pathway genes can lead to congenital deformities as well as both juvenile and adult cancers.

At Caltech, Ondrus plans to use her chemistry background to continue studying the Hedgehog signaling pathway and address mysteries about how essential small molecules, such as cholesterol, control Hedgehog activity during the development of embryos, a process known as embryogenesis.

Your PhD was in synthetic chemistry. What does this involve?

In synthetic organic chemistry, you build complex molecules from scratch. You start with a hypothesis for how to make an interesting molecular structure in the most convergent, elegant, efficient way possible based on the reactions that you choose. From there, you go to the lab and try to build the molecule.

How did you go from synthesizing chemicals to studying biological pathways?

I'd spent a lot of time just looking at the structures of molecules and appreciating the richness of structure, so when I had an opportunity to see how the same principles translated to biological activity, a new world opened up. I started finding myself thinking more and more about all of the small molecules that are already present in our own bodies. I've always been fascinated by human health and human development, and I started to question how these molecules participate in normal physiology and disease. I started reading to try to find examples of where people had at least circumstantial evidence that small molecules played key roles in regulating a biological pathway, in particular in human health.

Through my reading, I came across the really fascinating pathway that I now study—the Hedgehog signaling pathway.

Why is the Hedgehog signaling pathway important?

Hedgehog is important in almost every aspect of how an embryo becomes a human form, and its deficiencies showcase its importance. It's responsible for establishing our body plan, from our left-right symmetry to how many digits we have. As you can imagine, defects in the pathway lead to really acute phenotypes because it's so fundamental in these early processes. The pathway also plays a role in various cancers, most notably basal cell carcinoma—skin cancer—the most prevalent form of cancer in humans.

We know that certain small molecules that are based on cholesterol can turn the pathway on or off, but we don't know what enzymes produce these molecules, where they're localized, or how they interact with the Hedgehog pathway. Elucidating these cellular processes is essential to understanding how the pathway controls things like body patterning and brain development, and how that can go wrong and lead to cancer.

If we can understand what components of cholesterol metabolism are necessary for Hedgehog activity, then we can start to address much more specifically some of these medical conditions and intervene in ways that we haven't yet considered.

How will you go about studying cholesterol in the Hedgehog pathway?

I'm going to merge the synthesis part of my background with my understanding of signal transduction to ask questions about cholesterol and related molecules, and their role in regulating the Hedgehog pathway. Small molecules are often the missing link in hypotheses regarding Hedgehog pathway signal transduction. You may have two proteins in the pathway that communicate via these very specific small molecules, but without having chemical tools to ask questions in a precise way, the mechanism remains unknown. What are the exact structures of these molecules? How do they perform this communication? Something that's unique about our lab is that we can synthesize the specific cholesterol molecules needed to answer these questions.

Alison Ondrus

Photo Courtesy of Caltech

What do you like about Caltech?

At Caltech, there are really no barriers. Nobody says you can't do something or that an idea is too unprecedented. There's a cultural acceptance that doing new things is fundamentally exciting and valuable. That's what I really appreciate about Caltech.

What do you like to do in your spare time?

I love yoga and riding my bike, and reading both Eastern and Western philosophy. I just finished listening to the audiobook of The Structure of Scientific Revolutions by Thomas Kuhn, which I recommend to anyone.

Taking a Closer Look at Genetic Switches in Cancer

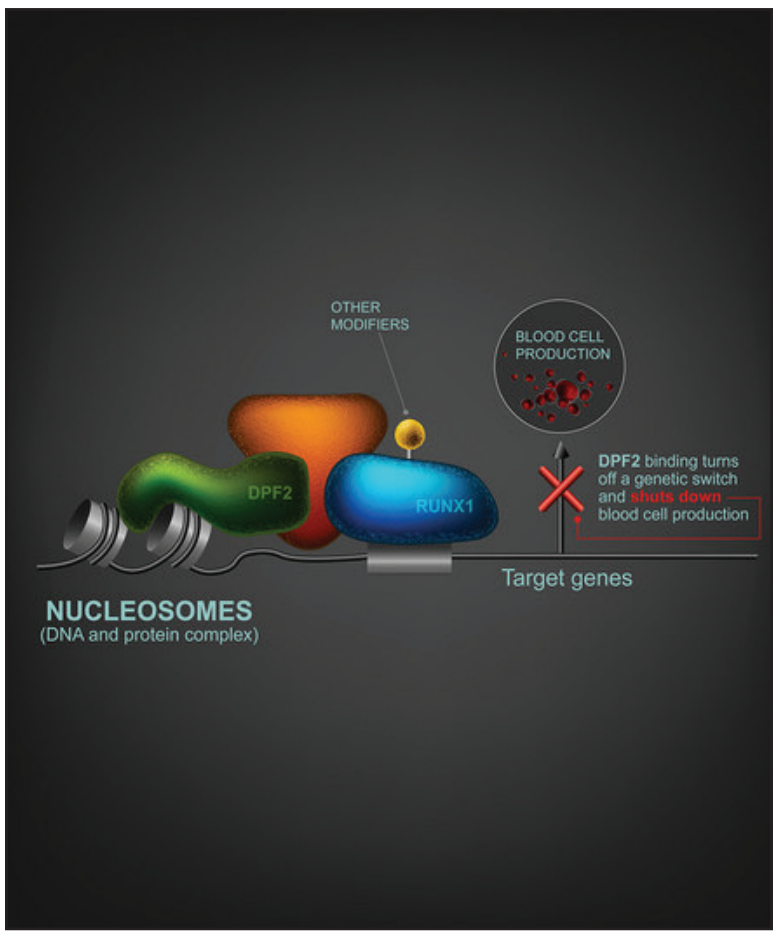
WHITNEY CLAVIN
Caltech Media Relations

This article is adapted from a story that was originally published online at caltech.edu.

Many things go wrong in cells during the development of cancer. At the heart of the chaos are often genetic switches that control the production of new cells. In a particularly aggressive form of leukemia, called acute myeloid leukemia, a genetic switch that regulates the maturation of blood stem cells into red and white blood cells goes awry. Normally, this switch leads to appropriate numbers of white and red blood cells. But patients with acute myeloid leukemia end up with a dangerous accumulation of blood stem cells and a lack of red and white blood cells—cells that are needed to supply the body with oxygen and fight infections.

Now, researchers at Caltech and the Sylvester Comprehensive Cancer Center at the University of Miami are narrowing in on a protein that helps control this genetic switch. In healthy individuals, the protein, called DPF2, stops the production of red and white blood cells when they do not need to be replaced. That is, it turns the switch off. But the protein can be overproduced in acute myeloid leukemia patients. The protein basically sits on the switch, preventing it from turning back on to make the blood cells as needed. Patients who overproduce DPF2 have a particularly poor prognosis.

In a new study, to be published the week of May 22, 2017, in the journal Proceedings of the National Academy of Sciences, the researchers demonstrate new ways to impede DPF2, potentially rendering acute myeloid leukemia more treatable. They report new structural and functional details about a fragment of DPF2. This new information reveals targets for the development of drugs that would block the protein's function.



The DPF2 protein controls a genetic switch that tells blood stem cells when to become red and white blood cells. When DPF2 is bound to DNA-protein complexes called nucleosomes at specific regions in the genome, it blocks the activation of genes that promote red and white blood cell production. When DPF2 is not bound, the switch is flipped on and blood cells are made. In some patients with acute myeloid leukemia, DPF2 is overproduced, blocking cell differentiation and indicating a poor prognosis.

Photo Courtesy of Hoelz group/Caltech

"Many human diseases, including cancers, arise because of malfunctioning genetic switches," says André Hoelz, the corresponding author of the study. Hoelz is a professor of chemistry at Caltech, a Heritage Medical Research Institute (HMRI) Investigator, and a Howard Hughes Medical Institute (HHMI) Faculty Scholar. "Elucidating how they work at atomic detail allows us to begin the process of custom tailoring drugs to inactivate them and in many cases that is a significant step towards a cure."

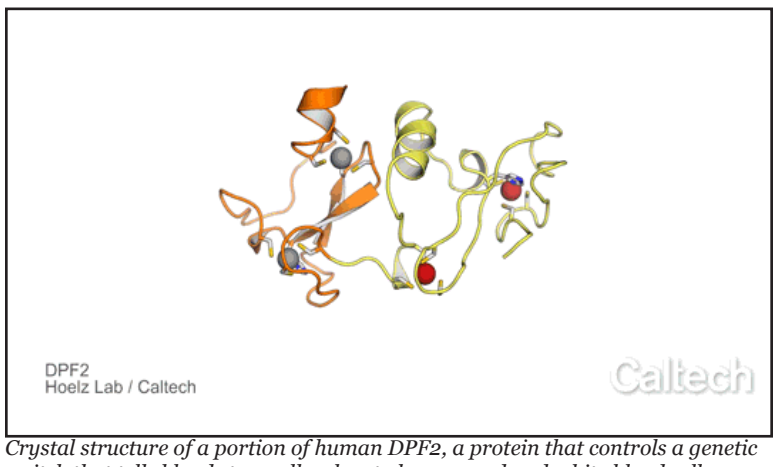
Red and white blood cells are constantly regenerated from blood stem cells, which reside in our bone marrow. Like other stem cells, blood stem cells can live forever. It is only when they become differentiated into specific cell types, such as red and white blood cells, that they then become mortal, or acquire the ability to die after a certain period of time.

"Our bodies use a complex series of genetic switches to differentiate a blood stem cell into many different cell types. These differentiated cells then circulate in the blood and serve a variety of different functions. When these cells reach the end of their lifespan they need to be replaced," says Hoelz. "This is somewhat like replacing used tires on a car."

To investigate the role of DPF2 and learn more about how it controls the genetic switch for making blood cells, the Hoelz group partnered with Stephen D. Nimer, co-corresponding author of the paper and director of the Sylvester Comprehensive Cancer Center, and his team. First, Ferdinand Huber and Andrew Davenport—both graduate students at Caltech in the Hoelz group and co-first-authors of the new study—obtained crystals of a portion of the DPF2 protein containing a domain known as a PHD finger, which stands for planet homeodomain. They then used X-ray crystallography, a process that involves exposing protein crystals to high-energy X-rays, to solve the structure of the PHD finger domain. The technique was performed at the Stanford Synchrotron Radiation Lightsource, using a dedicated beamline of Caltech's Molecular Observatory.

The results revealed how DPF2 binds to a DNA-protein complex, called the nucleosome, to block the production of red and white blood cells. The protein "reads" various signals displayed on the nucleosome surface by adopting a shape that fits various modifications on the nucleosome complex, like the different shaped pieces of a jigsaw puzzle. Once the protein binds to this DNA locus, DPF2 turns off the switch that regulates blood cell differentiation.

The next step was to see if DPF2 could be blocked in human blood stem cells in the lab. Sarah Greenblatt, a postdoctoral associate in Nimer's group and co-first author of the study, used the structural information from Hoelz's group to create a mutated version of the protein. The Nimer group then introduced the mutated protein in blood stem cells, and found that the mutated DPF2 could no longer bind to the nucleosome. In other words, DPF2 could no longer inactivate the switch for making blood cells.



Crystal structure of a portion of human DPF2, a protein that controls a genetic switch that tells blood stem cells when to become red and white blood cells. Orange and yellow regions illustrate the DPF2 "reader" domain, which is stabilized by zinc ions, represented as red and grey spheres.

Photo Courtesy of Hoelz group/Caltech

"The mutated DPF2 was unable to bind to specific regions in the genome and could not halt blood stem cell differentiation," says Huber. "Whether DPF2 can also be blocked in the cancer patients themselves remains to be seen." The researchers say a structural socket in DPF2, one of the puzzle-piece-like regions identified in the new study, is a good target for candidate drugs.

The study, titled "Histone-Binding of DPF2 Mediates Its Repressive Role in Myeloid Differentiation," was funded by a PhD fellowship of the Boehringer Ingelheim Fonds, a National Institutes of Health Research Service Award, the National Cancer Institute of the National Institutes of Health, a Faculty Scholar Award of the Howard Hughes Medical Research Institute, the Heritage Medical Research Institute, Caltech startup funds, the Albert Wyrick V Scholar Award of the V Foundation for Cancer Research, a Kimmel Scholar Award of the Sidney Kimmel Foundation for Cancer Research, and a Teacher–Scholar Award of the Camille & Henry Dreyfus Foundation. Other authors are Concepcion Martinez and Ye Xu of the University of Miami and Ly P. Vu of the Memorial Sloan Kettering Cancer Center.

Join the Meditation Mob!

Tuesdays, 12:00 - 12:50

Want to learn more about mindfulness meditation? It's a great way to improve your attention and to become more grounded in the present moment.

There's no religious component. We use secular, evidence-based meditation techniques.

We meet in the small room just off the lounge in Winnett. All students are welcome, from total beginners to more experienced meditators.

Mailing list and MP3 archive:
counseling.caltech.edu/students/meditation

ASCIT Minutes

Meetings are every week in SAC 13

ASCIT Board of Directors Meeting
Minutes for 19 May 2017. Taken by Dana He.
Officers Present: Sakthi Vetrivel, Kavya Sreedhar, Rachael Morton, Sara Adams, Sarah Crucilla, Alice Zhai, Dana He
Guests: David Berger
Call to Order: 1:01 pm

President's Report (Sakthi):

- Midnight donuts will be the night of Thursday, June 1.
- ASCIT Alumni party tonight. Transition dinner next Wednesday.
- Proposal to publish budget in public location.
- Would like ASCIT to become more mission-oriented and develop specific goals for third term.

Officer's Reports:
V.P. of Academic Affairs (Kavya):

- Ma13 – Vector Calculus Bootcamp course has been approved by Curriculum Committee. Class details are being finalized, but the plan is to have this class run for 5 weeks 2nd term starting next year to teach multivariable concepts needed in the analytical track of Ph1b that aren't taught until Ma1c. Class should be taken concurrently with Ph1b but will be optional for students.
- Plan to resume recording courses during fall term and finalize classes and students who will be doing the recording this term after registration. MHF to buy a new camera approved; need to buy camera.
- Student Faculty Lunches coming up twice this term due to popular demand. First is on Monday, May 22 at noon, Lloyd House Dining Hall. Second is on Thursday, June 1 at noon, Ruddock House Dining Hall.
- Drop Day is next Wednesday, May 24, and registration is next Thursday, May 25. Peer Advising should be happening before registration in all the houses.
- Academic Advising Survey results are available at https://goo.gl/Gyx8up.
- EE5x sequence will no longer be required and the elective version of that track will be called EE110abc and will be offered starting the 2019 to 2020 school year. This requirement will be replaced with EE10ab offered 2nd and 3rd term and overall, the requirements for the EE major will have increased by 3 units due to other changes.
- ASCIT Teaching Awards have been award to TAs Chinmay Nirkhe, Dylan Freas, Eugene Tang, and Todd Norton, and professors Adam Wierman, Evan Kirby, Rob Phillips, and Paul Asimow.

V.P. of Non-Academic Affairs (Rachael):

- Bechtel focus groups and group leaders have been decided.
- IHC is generally against Big I, so it probably will not happen. Would be in favor of doing joint party with Harvey Mudd at Mudd, but need to ask Mudd.
- Proposal to do house-associated campus-wide events. Possible events include Blackerathon and/or a Dabney tie-dye event.
- Proposal for ASCIT events such as campus-wide lasertag or paintball. Could get funding from the Student Investment Fund.
- Proposal to bring back the Mudeo mud-pit tradition now that the drought is over.
- Will send out survey to gauge interest in proposed events.

Director of Operations (Sara):

- Blacker may still have cords for ASCIT lights, will ask Blacker.

Treasurer (Sarah):

- Refunded $600 to each house for ditch day, $400 to Caltech Hip-Hop Troupe, and $175 to Out of Context for concert.
- Will reimburse $400 for Ricketts and Blacker.
- Voted and approved request to reimburse $1,000 (in addition to $1,500 already given) for Techstock, which was needed for food for about 500-600 attendees.
- Proposal to raise dues starting January 2018, and to combine yearbook dues, which are currently around $19, and ASCIT dues.

Social Director (Alice):

- Plan to create general social calendar.
- Will talk to Tom Mannion and Harvey Mudd about possible joint party between Caltech and Mudd.
- Will send out email to get volunteers for ASCIT social team.
- Plan to organize Dodgers game on tentative date Sunday, June 11. Will send out survey to gauge interest. Needs to get funding from Marsh Fund.
- Need to order ASCIT plaques.

Secretary (Dana):

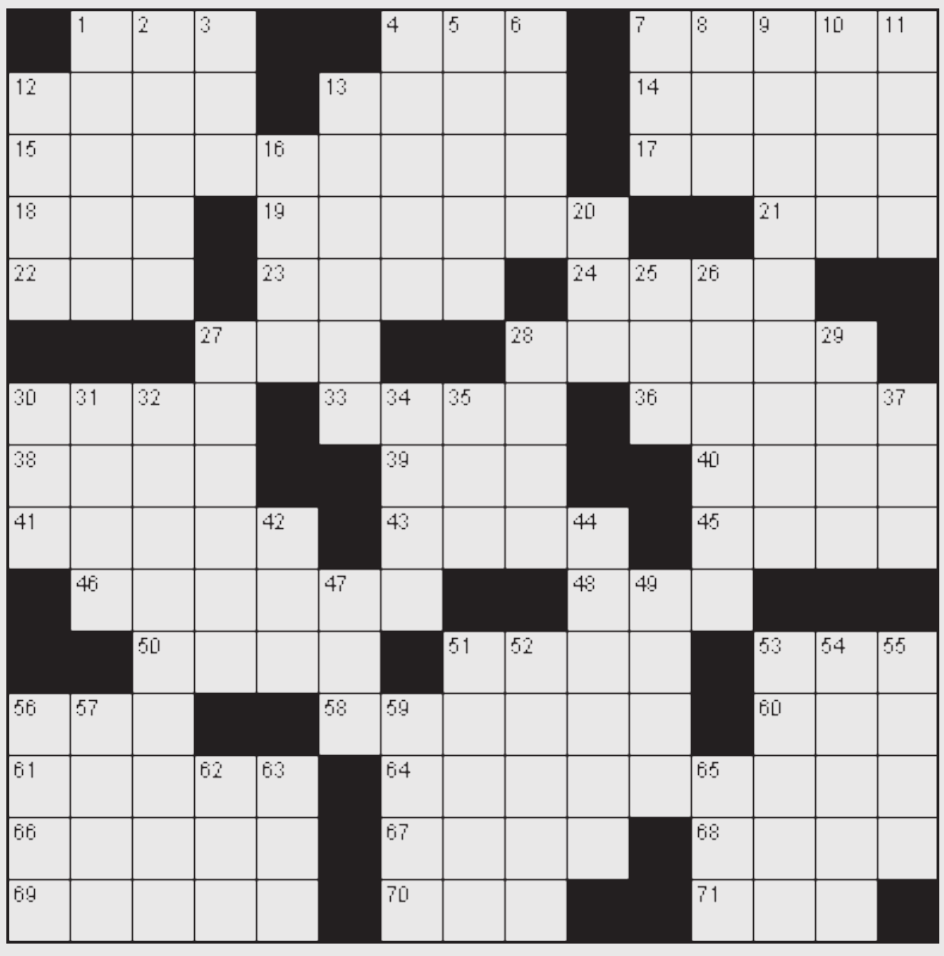
- Nothing to report.

<u>If anyone has any questions or concerns about a section of the minutes please email the appropriate officer. We are happy to answer any questions.</u>
Meeting Adjourned: 1:46 pm

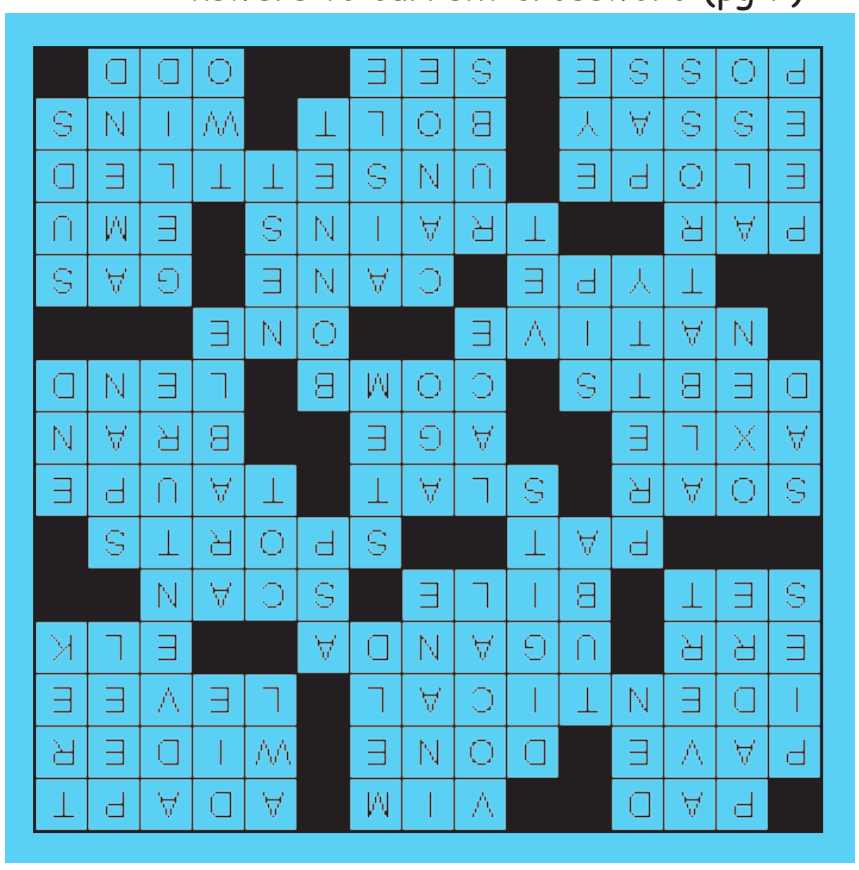
Crossword

Across
1. Launch area
4. Vitality
7. Adjust
12. Cover with stone or concrete
13. Finished
14. Broader
15. Indistinguishable
17. River embankment
18. Make a mistake
19. Landlocked African country
21. Moose
22. Series of exercises
23. Digestive juice
24. Wide sweeping search
27. Hit lightly
28. Competitive activities
30. Rise rapidly
33. Spline
36. Fuscous
38. Wheel shaft
39. Era of history
40. Husks of cereal grains
41. Financial obligations
43. Search thoroughly
45. Give temporarily
46. Indigenous person
48. Single
50. Printed characters
51. Bamboo stick
53. Fuel
56. Golfing term
58. Coaches
60. Flightless bird
61. Run away to marry
64. Changeable
66. Composition
67. Part of a lock
68. Is victorious
69. Temporary police force
70. Understand
71. Peculiar

Down
1. Military chaplain
2. Obviate
3. Lair
4. Outspoken
5. Vacuous
6. Blend gradually
7. Hole punch
8. Device used for shaping metal
9. Escapade
10. Rind
11. Long and difficult trip
12. Pastries
13. Fingers or toes
16. Brass instrument
20. Small snake
25. Crib
26. Tillable
27. Having delicacy or grace
28. Stalk
29. Distance between two points
30. Lamentable
31. Domesticated bovine animals
32. Large web-footed bird
34. Decorative woven fabric
35. In the past
37. Conclusion
42. Take a small amount of liquid
44. Kind of hat
47. Examine carefully
49. Bird shelter
51. Small boat
52. Part of a church
53. Extremely cold
54. Rectify
55. Froth
56. Secret look
57. In addition
59. Chafes
62. Ballet step
63. Oculus
65. Pair



Answers to current crossword (pg 7)



-http://puzzlechoice.com

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