Egg growth induced in infertile women

By Krista Conger

Researchers at the School of Medicine have identified a way to induce the ovaries of some infertile women to produce eggs.

Using the technique, clinicians at the St. Marianna University School of Medicine in Kawasaki, Japan, collected viable eggs from five women with a condition called primary ovarian insufficiency. One of these women has given birth to a healthy baby.

Twenty-seven women in Japan took part in the experimental study. The researchers were able to collect mature eggs for in vitro fertilization from five of them. Although it has not yet been tested in women with other causes of infertility, the researchers plan to investigate whether the technique can also help women with early menopause caused by cancer chemotherapy or radiation, and infertile women between the ages of 40 and 45.

The research was published online Sept. 30 in the Proceedings of the National Academy of Sciences.

The technique, which the researchers refer to as "in vitro activation," or IVA, requires an ovary (or a portion of an ovary) to be removed from the woman, treated outside the body and then re-implanted near her fallopian tubes. The woman is then treated with hormones to stimulate the growth of specialized structures in the ovaries called follicles, in which eggs develop.

"Women with primary ovarian insufficiency enter menopause quite early in life, before they turn 40," said Aaron Hsueh, PhD, professor of obstetrics and gynecology at Stanford and senior author of the study. "Previous research has suggested that these women still have very tiny primordial, primary and secondary follicles, and that even though they are no longer having menstrual cycles they may still be able to substantially improve its clinical research support infrastructure, expanding innovation-training programs in medical

For new grad students, counterintuitive advice

By Tracie White

For newly arrived graduate students in the biosciences, here’s a surprising key to future success: Be comfortable with that adventure.

This was the overriding message imparted to the students at their orientation dinner Sept. 24.

"The importance of succeeding in science is the ability to embrace your stupidity," said Dan Herschlag, PhD, senior associate dean for graduate education and postdoctoral affairs, speaking to the crowd of about 120 diners in the Li Ka Shing Center for Learning and Knowledge. "And being comfortable with that adventure."

Each student

See STUDENTS, page 6

Stanford awarded more than $45 million to spur translational research in medicine

By Kris Newby

A Stanford center focused on accelerating the translation of medical research from bench to bedside will receive $45.3 million over four and a half years from the National Institutes of Health.

The Stanford Center for Clinical and Translational Science (Spectrum), is among 15 institutions to receive Clinical and Translational Science Awards from the NIH. Spectrum earned the top peer-review score on its proposal for the new funding. The dollar amount is 70 percent more, on an annual basis, than that of its previous Clinical and Translational Science Award.

"The award is a strong vote of confidence for our work in translational discovery," said Lloyd Minor, MD, dean of the School of Medicine. "This new funding will help fuel the efforts of our physicians and scientists working to translate medical discoveries into better patient care and to train the medical innovators of tomorrow."

Spectrum’s director, Harry Greenberg, MD, said he is pleased with the award in light of recent cutbacks in government-funded research. "We’re facing major paradigm shifts in medicine, and I believe that the CTSA funding will make an enormous difference in addressing what is certainly one of our nation’s biggest challenges: providing better, safer and less costly health care to our entire population," said Greenberg, who is also senior associate dean for research at the medical school and professor of medicine and of microbiology and immunology.

This new award marks Stanford’s sixth year as a member of the CTSA consortium, a group of 60-plus institutions working together to improve human health through innovations in clinical and translational research and education.

The NIH launched the CTSA program in 2006 to help meet the nation’s urgent need to provide better health care to more people for less money. This motivated the NIH to incentivize research institutions to more rapidly move breakthroughs in basic research to breakthroughs in patient care.

The CTSA program tackles this problem on three fronts: It catalyzes innovation by encouraging collaborations across departments and institutions; it underwrites the modernization and streamlining of research infrastructure and processes; and it finances the training of more researchers skilled at ‘translational medicine,’ the art and science of turning biological discoveries into therapeutics, devices and preventive measures that improve patient health.

During its first round of CTSA funding, Stanford was able to substantially improve its clinical research support infrastructure, expanding innovation-training programs in medical
Technique created for high-speed, low-cost epigenomic mapping

By Bruce Goldman

A new technique developed by researchers at the School of Medicine could pave the way to an era of personalized epigenomics. The technique, described in a study published online on Oct. 6 in Nature Methods, could quickly yield huge amounts of useful information about which genes are active in particular cells. The technology is relatively cheap, fast and easy to use, and all that would be needed from the patient is a blood sample or needle biopsy.

As word of the new technique has leaked, dozens of researchers around the world have begun putting it to work in their labs, said Howard Chang, MD, PhD, professor of dermatology and associate professor of pediatrics at Howard Hughes Medical Institute early-career scientist. Chang shared senior authorship of the study with William Greenleaf, PhD, assistant professor of genetics. The lead author is graduate student Jason Buenrostro.

Genes are recipes for the production of proteins, which do almost all the work in every living cell. The biological field of genomics focuses on describing which genes an organism has. The newer field of epigenomics aims to discern which genes are actually used by various tissues within an organism — or, in the case of disease, misused. Virtually every cell in a person's body contains the same genes. Yet cells from different tissues — liver, blood, muscle — do very different things because they use different genes, as do otherwise identical cells in different biochemical environments, developmental stages or states of health.

For a gene to give rise to the specific protein it codes for, the gene must be read and copied (or "transcribed") by complex molecular machines. The genes of simple, single-celled life forms, such as bacteria, are all available for transcription because those microbes' DNA floats around as a flexible, circular chromosome within the cell.

But in complex organisms from yeast and amoeba to orchids and people, few of any cell's genes are expressed at any one time. Instead, only a small fraction of a cell's genome is transcribed, and the vast majority of DNA, much of which is devoted to regulating the timing and extent of each gene's activation rather than encoding proteins. Human DNA, as well as that of other advanced life forms, is confined within a tiny cellular compartment known as the nucleus.

"If you could stitch together all 46 chromosomes in one of your cells and stretch the resulting, single string of DNA full-length, it would be about 2 meters long," said Greenleaf. "But in real life, all that DNA is scraped up inside the cell's nucleus, which is about one two-hundred-thousandth of a meter in diameter." The Stanford researchers, including Buenrostro, are tapping into a phone line that stretches from New York City to Los Angeles and stuffing it into a two-bedroom house.

Most of a chromosome's DNA is tightly spooled around ball-shaped protein assemblies called nucleosomes, rendering it inaccessible for transcription. Much of the genome is blocked this way. Elsewhere, various enzymes within the cell are capable of chemically reacting some nucleosomes' grip, unleashing erasable and - thus - inaccessible DNA from transcription by altering the cell's gene-expression patterns.

Some of the current methods of determining the epigenomic state of a cell are so complex that only a handful of laboratories are equipped to carry them out. These procedures require dozens of separate technical steps, start-to-finish timescales of several days or more, and millions to tens of millions of cells from the same tissue.

In order to study relatively rare cell types using these methods, you have to do one of two things, said Chang. "You can force those cells to copy themselves repeatedly in the artificial environment of a laboratory dish or flasks, driving their replication with biochemical sleight of hand. Or you can use the time you get enough cells for analysis, their epigenomic state may have changed wildly from its original condition, if you had a replicating cell line." Alternatively, he said, you can pool biological samples from numerous different individuals. But this wipes out any possibility of meaningful personalized analyses.

The new method requires only 500 to 50,000 cells, which can easily be provided by one individual, Chang said. It involves about 15 minutes of hands-on technique and some automation starting from the sample and finishing. Samples obtained on a daily basis from, say, a hospitalized patient or a subject in a clinical trial meant to measure a drug's effect, can be processed in a clinically relevant timeframe.

The insight that opened the door to this new technique came a year ago when the study's lead author, Buenrostro, proposed that a bacterial enzyme could be used to "spray paint" the regions of the genome that are accessible to the molecular machines employed by cells to read genetic information.

Transposases — the kind of enzyme the Stanford scientists borrowed from bacteria — are found in all organisms. These enzymes insert copies of a particular DNA sequence into the genome known to be regulatory. These small, tag-free "footprint" they'd left. This was an important finding: Tagging DNA-specific regulatory DNA sequences in a test tube, along with the modified transposase.

But because bacteria lack barriers such as nucleosomes, bacterial transposases haven't evolved ways of inscribing their DNA "tags" on nucleosomally or otherwise blocked DNA.

In a major breakthrough, investigators used a bacterial transposase modified so that, instead of inserting its usual DNA tag at any part of the genome, it inserted special DNA sequence only in those DNA stretches that traditionally stood in the way. These DNA sequences were chosen to facilitate a high-throughput, laboratory-based, DNA-copying procedure. Incubating myriad copies of these sequences in a test tube, along with the modified transposase and a line of well-studied immune cells, yielded tags on whatever parts of the genome weren't 'spotted' around a nucleosome or occupied by one or another DNA-binding protein.

A single nucleosome ties up just under 150 chemical units of DNA. Tag-free DNA stretches of just that length designated nucleosome-blocked regions at numerous spots along the genome. Much shorter tag-free zones, numbering between eight and 10 DNA chemical units, occurred at specific sites along open areas of the genome known to be regulatory. These small, tag-free stretches, the Stanford team reasoned, had been occupied by DNA-binding proteins whose exact identities could be inferred from the size and sequence of the tag-free "footprint" they'd left. This was an important finding: As DNA-binding proteins either facilitate or impede gene transcription.

To demonstrate the method's clinical potential, the investigators drew blood from a healthy volunteer on three consecutive days, performing their analytic procedures each day. They were able to show, for this volunteer, which of three different regulatory DNA sites on a particular gene had been engaged by a DNA-binding protein. This regulatory-site pinpointing could guide clinical decisions about which drug would be best for changing a gene's activity level with minimal side effects.

Other Stanford co-authors of the study were post-doctoral scholars Paul Giresi, PhD, and Lisa Zaba, MD, PhD.

The study was funded by the National Institutes of Health, the California Institute for Regenerative Medicine, the Department of Dermatology and Department of Genetics also supported this work.

Send letters, comments and story ideas to John Sanford at 723-8309 or at johnanford@stanford.edu. Please also contact him to receive an e-mail version of Inside Stanford Medicine.

October 7, 2013 INSIDE STANFORD MEDICINE
Antidepressant could combat deadly form of lung cancer

By Krista Conger

A little-used class of antidepressants appears potentially effective in combating a particularly deadly form of lung cancer, according to a new study from researchers at the School of Medicine.

And because the drugs have already been approved by the U.S. Food and Drug Administration for use in humans, the researchers have been able to quickly launch a clinical trial to test their theory in patients.

The phase-2 trial is now recruiting participants with small-cell lung cancer and other, similar conditions like aggressive gastrointestinal neuroendocrine cancers, an aggressive skin cancer called Merkel cell carcinoma, and a pediatric cancer called neuroblastoma. (Neuroendocrine cells receive signals from the nervous system and secret hormones like adrenaline into the blood to affect the body’s function.)

Further investigation showed that the drugs appear to work through a class of molecule on the cancer cells’ surfaces called G-protein-coupled receptors, but the receptors are not the same in healthy and malignant cells.

“The repositioning of an existing drug to treat a disorder other than the one for which it was originally approved enables us to identify a large genetic and biological databases are changing the face of medicine.”

“After turning down the decade and more than the $1 billion it can typically take to translate a laboratory finding into a successful drug treatment to about one to two years and spending about $100,000,” said Atul Butte, MD, PhD, associate professor of pediatrics.

Butte is the division chief of systems medicine and director of the Center for Pediatric Bioinformatics at Lucile Packard Children’s Hospital at Stanford. He is a co-senior author of the study, which was published online Sept. 27 in Cancer Discovery. Julien Sage, PhD, associate professor of pediatrics and senior author of the study’s lead author is postdoctoral scholar Nadine Jahchan, PhD. Joel Neal, MD, PhD, an assistant professor of medicine, is the principal investigator for the clinical trial.

Small-cell lung cancers account for only about 15 percent of all lung cancers, but they are particularly deadly. “The survival rate for small lung cancer is only 5 percent,” said Sage. “There has not been a single efficient therapy developed in the last 30 years. But when we began to test these drugs in human cancer cells grown in a dish and in a mouse model, they worked, and they worked, and they worked.”

Specifically, these drugs activated a cellular self-destruct pathway, called imipramine on human small-cell lung cancer cells and that an anti-seizure drug could be a new way to treat inflammatory bowel disease.

This time around, Jahchan was interested in small-cell lung cancer. When researchers in the Butte lab used the computerized algorithm to identify possible drug candidates, tricyclic antidepressants like imipramine were at the top of the list. These drugs are approved to treat depression, but have since been supplanted by newer antidepressants with fewer side effects.

Jahchan tested the effect of a tricyclic antidepressant called imipramine on human small-cell lung cancer cells and found that the drug was able to potentiate a self-destruction pathway in the cancer cells and to reduce metastases in animals. The drug maintained its effectiveness regardless of whether the cancer cells had previously been exposed, and became resistant, to traditional chemotherapy treatments. Another drug, called tricomine, was also identified by the bioinformatics screen, also exhibited cancer-cell-killing abilities.

Although imipramine did not affect cells from another main type of lung cancer called small-cell lung adenocarcinoma, it did inhibit the growth of cells from other neuroendocrine cancers, an aggressive skin cancer called Merkel cell carcinoma, and a pediatric cancer called neuroblastoma. (Neuroendocrine cells receive signals from the nervous system and secrete hormones like adrenaline into the blood to affect the body’s function.)

Butte and Sage have had success with this approach before. In 2011, they reported in Science Translational Medicine that an anti-convulsant drug might be effective against a different subtype of lung cancer, and that an anti-seizure drug could be a new way to treat inflammatory bowel disease.

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Sage said. “It was less than 20 months from the time of our first discussion about whether the bioinformatics approach had been established and the drugs are FDA-approved. By focusing on diseases with little hope for the patient, it’s easier to go forward fast.”

For more information about the ongoing clinical trial, which uses a molecule related to imipramine called desipramine, contact the Stanford Cancer Clinical Trials Office at (650) 498-7061 or email ccito- office@stanford.edu.

Additional Stanford researchers involved in the study were postdoctoral scholars Pawel Mazur and Kwon Park, PA. McKee also will speak. Additional Stanford researchers involved in the study were postdoctoral scholars Pawel Mazur and Kwon Park, PA.

The research was supported by the Lucile Packard Foundation for Children’s Health, the Department of Veterans Affairs, the National Library of Medicine Biomedical Informatics Training Grant, the National Cancer Institute, the National Institute of General Medical Sciences, a Starna Endowment, the National Radiology Society of America, the Tobacco-Related Disease Research Program and the Stanford Cancer Institute. Sage is also supported by Harriet and Mary Zemek.

Information about Stanford’s Department of Pediatrics, which also supported the work, is available at http://pediatrics.stanford.edu.

School of Medicine faculty senate to meet Oct. 15

The next meeting of the medical school’s faculty senate is scheduled from 5:15 to 6:05 p.m. Oct. 15 in the Bulletin Room at Stanford’s School of Medicine.

James Chen, president of the Stanford Medical Student Association and a medical student, was elected as a member-at-large on the senate by the faculty. Chen said he plans to work primarily on issues related to medical education and patient care.

Chen, a first-year medical student, was elected as a member-at-large on the senate by the faculty. He is working primarily on issues related to medical education and patient care.

Lloyd Minor, who is currently serving his third term on the faculty senate, is encouraging his colleagues to consider running for office.

Minor called the 21st century “the century of biology,” particularly with Stanford’s efforts focused on the biological revolution now underway. He cited the recruitment of distinguished physician Steven Chu, PhD, former U.S. Secretary of Energy, as an example of how the university is working to align with the changing needs of society.

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A cauldron of creativity, boiling now for a decade

By Robin Wander

Created as a social experiment in collaboration and described as both a cauldron of creativity and Noah's ark, the James H. Clark Center, home to Bio-X, turns 10 this month. The three-story, 146,000-square-foot research center brings together a variety of disciplines, including biology, medicine, chemistry, physics and engineering, under one roof. That's why it's an ark: It houses a menagerie of disciplines and specialties that co-exist side by side. But it's also a cauldron: Ideas and discoveries are always brewing and mixing inside it.

The building that has inspired these metaphors was designed by Foster and Partners in collaboration with MBT Architecture. Construction began in 2001; it opened in 2003.

The building features three wings enfolding a courtyard, at the center of which is a circular stage for events such as concerts. Beneath the stage, under the world of parts’ that has established a strong communication for University Communications. The Clark Center opened its doors 10 years ago this month. The three-story, 146,000-square-foot research center brings together a variety of disciplines, including biology, medicine, chemistry, physics and engineering, under one roof. Glass walls, bridges linking wings, and exposed staircases and balconies all contribute to the open design that supports connections.

...
Bio-X in Focus

By Bjorn Carey

Microscope may be able to spot the seeds of cancer

One of the crueltiest truths about cancer is that even after you beat the disease, it can still come back to kill you.

A tumor growing in the prostate gland, breast or any other organ can shed cancerous cells into the blood. These cancerous seeds travel the body and can take root nearly anywhere, growing into a new cancer threat even after the initial cancer is treated.

The rule of thumb with cancer is that the earlier you can detect the disease, the more effective the treatment and increased likelihood of better outcomes.

Currently, doctors draw a patient’s blood and analyze it using special antibodies to detect the presence of the seeds, called circulating tumor cells. This works well if CTCs are present in large numbers, but may fail to detect smaller numbers released by earlier tumors.

Now, a team of engineers, scientists and doctors from Stanford is developing a miniature microscope that can detect circulating tumor cells more readily than ever, allowing for earlier interventions.

“There has been a huge push to increase sensitivity,” said Bonnie King, PhD, an instructor in neurobiology and of biology, discusses the Clark Center and how the building embodies the spirit of the Bio-X initiative, which began 15 years ago. To listen to the podcast, visit http://med.stanford.edu/121.

A major advantage with the microscopic technique, King said, is the ability to screen much larger volumes of blood, rather than just a small vial collected from a patient. This allows hundreds of scientific publications, dozens of patents and more than a tenfold return on research funds to Stanford. The following article by Bjorn Carey, a science writer at the Stanford News Service, highlight a few of the projects that have received Bio-X seed funding.

A way to combat viruses by targeting host-cell proteins

When a virus infects a person, it hijacks the body’s natural processes in order to fuel its rampage.

A pair of Stanford scientists aims to turn this strength into a weakness and develop what could become a broad-spectrum antiviral drug.

Most antiviral drugs are concocted to act against a specific viral protein. As such, they usually provide a “one drug/one bug” approach.

“Penicillin can kill many types of bacteria, but most antiviral drugs work only against one virus, and sometimes a single subtype of a virus,” said Shirin Einav, MD, an assistant professor of medicine and of microbiology and immunology.

Additionally, targeting viral proteins is problematic; viruses can mutate quickly, and a single change in the viral sequence can render it fully resistant to the drug.

With the exception of HIV, we still have very few antiviral drugs to offer patients with viral infections, and even those are often quite limited,” Einav said.

“No approved antiviral drugs or vaccines are available for emerging viruses, such as dengue, which pose major challenges to global health.”

Viruses live within our cells and rely upon host cell machineries in order to replicate. Instead of targeting the virus directly, the solution, Einav said, may be to instead interfere with host cell proteins that are utilized by multiple viruses.

“We treat diabetes and hypertension by targeting host proteins, so why not viral infections?” Einav said.

With support from Stanford’s Bio-X Interdisciplinary Initiatives Program, Einav and Stephen Quake, PhD, professor of bioengineering and of applied physics, have developed a process of identifying host proteins that wide families of viruses depend on for their success.

The initial focus of the work has involved identifying host proteins that, if knocked out, could inhibit both hepatitis C virus and HIV. This requires combing through incredibly large libraries of thousands of proteins, and a careful

‘Brain stethoscope’ turns seizures into music

Josef Parvizi was enjoying a performance by the Kronos Quartet when the idea struck.

The ensemble was midway through a piece in which the melodies were based on radio signals from outer space, and Parvizi, MD, an associate professor of neurology at the School of Medicine, began wondering what the brain’s electrical activity might sound like set to music.

He didn’t have to look far for help. Chris Chafe, DMA, a professor of music research at Stanford, is one of the world’s foremost experts in “musification,” the process of converting natural signals into music.

One of his previous works involved measuring the changing carbon dioxide levels near ripening tomatoes and converting those changing levels into electronic performances.

Parvizi specializes in treating patients suffering from intractable seizures. To locate the source of a seizure, he places electrodes in patients’ brains to create electroencephalogram recordings of both normal brain activity and a seizure state.

He shared a consenting patient’s EEG data with Chafe, who began setting the electrical spikes of the rapidly firing neurons to music. Chafe used a tone close to a human’s voice, with the aim of giving listeners an empathetic and intuitive understanding of the neural activity.

Upon a first listen, the duo realized they had done more than create an interesting piece of music. “My initial interest was an artistic one at heart, but, surprisingly, we could instantly differentiate seizure activity from nonseizure states with just our ears,” Chafe said. “It was like turning a radio dial from a static-filled station to a clear one.”

If they could achieve the same result with real-time brain activity data, they might be able to develop a tool to allow caregivers for people with epilepsy to quickly listen to the patient’s brain waves to hear whether an undetected seizure might be occurring.

Parvizi and Chafe dubbed the device a “brain stethoscope.”

See MUSIC, page 6
The 126 new students in the 13 bio-
science programs came from 19 coun-
tries and R2 undergraduate institutions.
Sixty are women, 66 are men and 15 hold advanced degrees. The top under-
graduate alma mater for the new class is
the University of California—Berkeley.
Bioscience students were drawn from
an applicant pool of 1,858. The admis-
sion rate was just 8.5 percent. The yield
of students who accepted Stanford offers
into the biosciences increased this year
from 51 to 61 percent, according to Ter-
rance Mayes, assistant dean for graduate
education. "Stanford biosciences con-
tinues to be one of the most attractive
programs in the world for graduate stu-
dents," Mayes said.

Herschlag was joined by Lloyd Minor,
MD, dean of the medical school, and
Omm Brandman, PhD, assistant profes-
sor of biochemistry, in welcoming mem-
bers of the new class, which is composed
of 126 graduate students in bioscience
programs and 30 in the stem cell and
bioengineering programs. About 60 fac-
ulty members joined the students in dis-
cussions at each table.
"This is the best of the best," Minor
said. "We are so honored that you chose
to be here. Your success is our success.
We're going to set the standards high;
your success is going to set them even higher.
Scientifically, there's never been a more
exciting time, and there's no better place
in the world to pursue your careers than
right here at Stanford."

The graduate students represent a va-
rity of scientific disciplines, balancing from
programs in the School of Medicine, the
School of Humanities and Sciences, and the
School of Engineering. They are en-
tering 15 different graduate programs.

The EEGs Parvizi conducts register brain activity from more than 100 electrodes placed inside the brain; Chafe selects certain electrode/neuron pairings and al-
 lows them to modulate notes sung by a female singer. As the electrode captures increased activity, it changes the pitch and inflection of the singer's voice.
Before a seizure begins — during the so-called pre-
ictal stage — the peeps and pops from each "singer"
 almost synchronize and fall into a clear rhythm, as if
they're following a conductor, Chafe said.
In the moments leading up to the seizure event, though, each of the singers begins to improvise. The
 notes become progressively louder and more scattered, as the full seizure event occurs — the ictal state. The
way Chafe has orchestrated his singers, one can hear the electrical storm originate on one side of the brain and eventually cross over into the other hemisphere, creating a sort of sing-off between the two sides of the brain.
After about 30 seconds of full-on chaos, the singers begin to calm, trailing off into their post-ictal rhythm.
Occasionally, one or two will pipe up erratically, but on the whole, the choir sounds extremely fatigued.
It's the perfect representation of the three phases of a seizure event, Parvizi said.
Posterior to the seizure, some of the electrical activity can be very difficult, as not all seizure activity manifests itself with behavioral cues. It's often impossible to know whether a person with epilepsy is acting confused because they are hav-
ing a seizure or because they are experiencing epileptiform activity — a marker of the post-seizure phase.
To that end, Parvizi and Chafe hope to apply their work to test the so-called neural signatures of an ongoing seizure or a post-ictal fatigue brain state. "Someone — perhaps a mother caring for a child with epilepsy — who hasn't received training in interpreting their EEGs can hear the seizure rhythms and easily ap-
 preciate that there is a pathological brain phenomenon taking place," Parvizi said.

The device can also offer biofeedback to non epileptic patients who want to hear the music their own brain waves create. From a clinical perspective, the work is still very experimental.

"We've really just stuck our finger in there," Chafe said. "We know that the music is fascinating and that we can hear important dynamics, but there are still quite a few hurdles we need to make.
Next year, Chafe and Parvizi plan to unveil a version of the system at the Cantor Arts Center. Visitors will wear a headset that will transmit EEG of their brain activity to their handheld device, which will convert it into music in real time.
"We're not there yet," Chafe said. "After Stanford," Parvizi said. "It nurtures collaboration between fields that are seemingly
light-years apart — we're neurology and music profes-
sors! — and our work together will hopefully make a
positive impact on the world we live in."

Chris Chafe and undergraduate Michael Iorga discuss the patterns of brain activity to their handheld device, which will convert it into music in real time.

"We're here to celebrate your embark-
ing on this journey," Herschlag said. "We are so honored that you chose
to be here. Your success is our success.
Do not feel stupid that things we're not really trying," he adds.

The experimental biology course and much of what we do in the fall quarter is geared to help transform students from consumers of knowledge into producers of knowledge," Myers said. "It's geared toward helping students make that men-
tual switch to being more independent and to help students focus on future careers."

Christopher Contrag, PhD, professor of pediatrics and of microbiology and immunology, envisioned a doctor who would interact with a patient with a dye that will cause the CTCs to fluoresce. The doctor would then use the pen-size microscope to focus a low-power laser light on a blood vessel just a few hair-widths below the patient's skin.
As the dried cancer cells pass through the laser, the light excites them and causes them to stand out from normal cells. The microscope registers each of these cells and a computer logs each observation. The im-
proved sensitivity of the technology should allow noninvasively scan blood for long periods will help
create a fuller picture of the number of CTCs in a per-
son's body.
At present we will not screen all of a person's blood [with the microscope], but we are aiming to increase the amount of blood screened compared to a 7-mil-
limeter blood draw," Contrag said.
The work is a collaborative effort of Olav Solgaard, PhD, professor of electrical engineering; Geoffrey Gurtner, MD, a professor of surgery; and Michael Clarke, MD, a professor of oncology. It began last fall, when the proposed project was awarded a seed grant by Stanford's Bio-X Interdisciplinary Initiatives Program.

To date, the blood-scan group has focused on de-
veloping the method in mice, taking advantage of the thin transparent tissue of the ear to image fluorescent cells traversing the small blood vessels below the skin. Soon the researchers will move the microscope to a clinical setting to conduct a proof-of-principle test of the technique in humans. Gurtner is currently con-
ducting a clinical trial to evaluate the Food and Drug Administration-approved green dye for defining skin
vasculature during postmortem breast reconstruc-
tion surgeries. The researchers are piggybacking on this trial to test the miniature microscope's ability to detect blood vessels and circulating cells.

Diya Li and Max Segreli attended the biosciences orientation and welcome dinner on Sept. 24.
News Briefs: Stanford Medicine and the World

Inside Stanford Medicine
October 7, 2013
Stanford scientists awarded grants for innovative research

Eight Stanford University scientists have received more than $17 million from the National Institutes of Health that will enable them to pursue innovative research in biomedicine.

The following are the recipients of 78 Pioneer, New Innovator, Transformative Research and Early Independence Awards presented by the NIH in 2013, the awards, which were announced Sept. 30, aim to encourage high-risk, high-reward approaches to biomedical and behavioral research.

“arztheses reward and support the kind of creative research that is a hallmark of Stanford as the epicenter of innovation,” said Lloyd Minor, MD, dean of the School of Medicine. “I would like to extend my congratulations to these eight investigators whose unconventional ideas are changing biomedicine.”

This year, the NIH awarded approximately $123 million in grants.

New Innovator Awards, 10 Transformative Research Awards and 15 Early Independence Awards (the only category in which Stanford is not represented).

“NIH is excited to continue support of visionary investigators, among all career stages, pursuing science with the potential to transform scientific fields and accelerate the translation of scientific research into improved health,” said NIH director Francis Collins, MD, PhD.

Following are the names of the award recipients and descriptions of their research projects.

PIONEER AWARD

The NIH Director’s Pioneer Award, now in its 10th year, carries a five-year, $2.5 million grant to be used in high-risk, high-reward research with the potential to affect a broad area of biomedical or behavioral research.

MICHAEL LIN, MD, PhD, assistant professor of pediatrics, will use his award to enhance the bioengineering of novel proteins to improve drug delivery by targeting the proteins to specific locations within the body.

Lin’s research group recently discovered a light-controllable, protein-protein interaction involving a protein called Dronpa, which changes shape on exposure to cyan (greenish-blue) light. Using basic genetic manipulation, Lin’s team creates a FLIP by fusing Dronpa to both ends of another protein, then reach across the center protein to bind each other, blocking binding sites on the center protein, rendering it inert. But shine cyan light on the FLIP and the shape-shifting Dronpas go on each other, opening the binding sites on the sandwiched protein for chemical activity.

FLIPs could be used for precisely controlling protein activities in time and space in a wide range of applications.

NEW INNOVATOR AWARDS

Three Stanford faculty members will receive New Innovator awards, which are designed to support innovative research projects by investigators who are within 10 years of having completed their education or clinical residency, but who have not yet received an R01 grant, which is the most common mode of NIH funding, or another equivalent type of NIH support. Each award provides $1.5 million over five years.

CATHERINE BLISH, MD, PhD, assistant professor of medicine, will use her New Innovator Award to explore ways of harnessing the immune system’s natural-killer cell’s role in fight viruses.

While vaccination has clearly been one of medicine’s greatest success stories, many viral infections such as HIV, SARS and Ebola have eluded efforts to control them with vaccines — in great part because these pathogens can mutate quickly and evade the immune system’s efforts to fight them. Natural-killer cells, which are a type of lymphocyte, can mount a rapid response to virus-infected cells and, like other immune system weapons, can mutate quickly and evade the immune system’s efforts to fight them.

The investigators will monitor the microbial ecosystems of healthy humans before, during and after several types of planned disturbances, such as changes in diet or antibiotic administration. They will apply novel mathematical methods to the data generated from these clinical experiments and identify features associated with recovery and recovery from these disturbances, with the goal of predicting disease and restoring health.

State of mental health care, policy will be focus of upcoming forum

Mental health care and policy will be the subject of a panel discussion scheduled from 11:30 a.m. to 1 p.m. Oct. 10 at the Li Ka Shing Center for Learning and Knowledge.

The event, “Serious Mental Illness: How Can We Promote Public Health and Public Safety?” is free and open to the public.

The panelists will be Laura Roberts, MD, professor and chair of psychiatry and behavioral science at Stanford; Harold Pollack, PhD, co-director of the University of Chicago Crime Lab and a professor at the university’s School of Social Service Administration; and Leroy Baca, sheriff of Los Angeles County.

They will discuss what the health-care system and public policymakers can do to promote the well-being of families with loved ones who are mentally ill, and why so many people with mental illnesses are incarcerated.

They will also address how society should respond to the small fraction of mentally ill people who commit extreme acts of violence.

The event will be moderated by Paul Castello, chief communications officer for the School of Medicine. It is part of the Stanford Health Policy Forum, an ongoing series of discussions and presentations designed to inform public debate about major health policy issues. For more information, visit http://healthpolicyforum.stanford.edu.

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