Getting acquainted: Minor looks forward to his new role as dean

By Susan Ipakchian

It's a Mac user and loves using an iPad to read several books at once, but the new leader of Stanford's School of Medicine displays a trace of cheerful regret as he mentions his imminent switch to an iPhone.

"I have to confess that I've been a BlackBerry person for mobile communications because of the keyboard. But some of my colleagues are using the voice recognition on the iPhones, so I think it would be helpful for email," Lloyd Minor, MD, said with a laugh. "Because I'm moving out here, I'm definitely making the transition to the iPhone."

Minor will become the new dean of the School of Medicine on Dec. 1. An otorhinolaryngologist who specializes in the diseases and disorders of the inner ear, he has spent the past 19 years at Johns Hopkins University, serving as provost since 2009.

And while the new leadership post will mark a much bigger transition than simply switching phones, Minor's philosophy seems similar: Rather than importing an established road map from his previous institution, he wants to thoroughly survey the School of Medicine's landscape to determine the right approach for charting the school's future.

Minor, 55, was in Palo Alto a few days after the July 18 announcement of his appointment, meeting with leaders of the school and getting a first glimpse at the home he and his wife, Lisa Keamy, MD, a primary-care physician, just purchased. (They were already schooled in the Bay Area's fast-paced real estate market. When a house in Pororua Valley had popped onto the market the previous week, Keamy quickly flew out, toured the house and snapped it up. "I saw it for the first time this morning," he said. "We both love it.

He won't be waiting until December to make the cross-country transition. He is wrapping up his duties at Johns Hopkins and will be on the Stanford campus beginning in September, spending three months getting to know the faculty, staff and students before taking over as dean.

"My goal is to add value, and to do that I first need to know the environment," Minor said. "To know what direction we should be going together, I need to get to know my colleagues in much greater depth than I do right now.

As the chief academic officer at Hopkins for the past three years, he oversaw the university's nine schools and implemented initiatives that, among other things, strengthened science education, increased interdisciplinary scholarship and bolstered diversity.

"I have experience interdisciplinary and cross-cultural collaboration as much as Johns Hopkins does, and Lloyd's talent and enthusiasm for fostering such initiatives will serve that university very well," Johns Hopkins President Ronald Daniels wrote in an email announcing Minor's departure. "So, too, will Lloyd's limitless dedication to excellence, his unflagging focus on getting the job done, and his humane, caring approach to dealing with the crises and..."

Researchers conjure up first complete computer model of whole organism

By Max McClure

In a breakthrough effort for computational biology, the world's first complete computer model of an organism has been completed, Stanford researchers report.

A team led by Markus Covert, PhD, assistant professor of bioengineering, used data from more than 900 scientific papers to account for every molecular interaction that takes place in the life cycle of Mycoplasma genitalium — the world's smallest free-living bacterium.

By encompassing the entirety of an organism in silicon, the paper fulfills a longstanding goal for the field. Not only does the model allow researchers to address questions that aren't practical to examine otherwise, it represents a stepping-stone toward the use of computer-aided design in bioengineering and medicine.

"This achievement demonstrates a transforming approach to answering questions about fundamental biological processes," said Jamie Head, associate director of the NIH Division of Program Coordination, Planning and Strategic Initiatives. "Comprehensive computer models of entire cells have the potential to advance our understanding of cellular function and, ultimately, to inform new approaches for the diagnosis and treatment of disease."

The research. See COVER, page 6

Researchers receive $40M to study potential stem cell therapies for heart failure, ‘bubble boy disease’

By Krista Conger

Robert Robbins, MD, believes that pluripotent stem cells are likely to be the ultimate cure for a broken heart. Now he and his colleagues at the School of Medicine have the financial means to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true — in the form of a $20 million, four-year investment by Stanford Medicine to investigate whether this idea is true.

A molecule widely assailed as the chief culprit in Alzheimer's disease unexpectedly reverses paralysis and inflammation in several distinct animal models of a different disorder — multiple sclerosis.

School of Medicine researchers have found this surprising discovery, reported in a study published online Aug. 1 inside Science Translational Medicine, comes on the heels of the recent failure of a large-scale clinical trial aimed at slowing the progression of Alzheimer's disease by attempting to clear the much-maligned molecule, known as A-beta, from Alzheimer's patients' bloodstream. While the findings are not necessarily applicable to the study of A-beta's role in the pathology of that disease, they may point to promising new avenues of treatment for multiple sclerosis.

The short protein snippet, or peptide, called A-beta (or beta-amyloid) is quite possibly the single most despised substance in all of brain research. It comes in their length and biochemical properties. A-beta is the chief component of the amyloid plaques that accumulate in the brains of Alzheimer's patients and serve as an identifying hallmark of the neurodegenerative disorder. A-beta deposits also build up during the normal aging process. Seeing A-beta in brain tissue is considered to be a sign of Alzheimer's disease, which afflicts more than 5 million Americans.

"This achievement demonstrates a transforming approach to answering questions about fundamental biological processes," said Jamie Head, associate director of the NIH Division of Program Coordination, Planning and Strategic Initiatives. "Comprehensive computer models of entire cells have the potential to advance our understanding of cellular function and, ultimately, to inform new approaches for the diagnosis and treatment of disease."

The research. See COVER, page 6

Reviled substance involved in Alzheimer’s can reverse paralysis in mice with multiple sclerosis

By Bruce Goldman

A molecule originally assailed as the chief villain in Alzheimer's disease unexpectedly reverses paralysis and inflammation in several distinct animal models of a different disorder — multiple sclerosis.

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The research. See COVER, page 6

Jacqueline Grant was part of the team that discovered that a molecule thought to play a key role in causing Alzheimer's disease can reverse the paralysis in mice with a form of multiple sclerosis.
Researchers first to sequence individual human sperm Variation in ‘genetic mixing’ rates and spontaneously arising mutations has implications for assessing male infertility problems

By Krista Conner

The entire genomes of 91 human sperm from one man have been sequenced by Stanford researchers. The results provide a fascinating glimpse into naturally occurring genetic variation in one individual, and are the first to report the whole-genome sequence of a human gamete — the only cells that become a child and through which parents pass on physical traits.

“Variation in ‘genetic mixing’ rates and spontaneously arising mutations has implications for assessing male infertility problems,” said Stephen Quake, PhD, a professor of bioengineering and of physics. “We now have devices that will allow us to routinely amplify and sequence to a high degree of accuracy the entire genomes of single cells, which has far-reaching implications for the study of cancer, infertility and many other disorders.”

Quake is the senior author of the research, published July 20 in Cell. Graduate student Jianbin Wang and former graduate student H. Christina Fan, PhD, share first authorship.

Sequencing sperm cells is particularly interesting because of a natural process called genetic recombination that ensures that a baby is a blend of DNA from all four of his or her grandparents.

Until now, scientists had to rely on genetic studies of populations to estimate how frequently recombination had occurred in individual sperm and egg cells, and how much genetic mixing that entailed.

“Now, the new findings bring scientists still closer to being able to generate insulin-producing cells identified

By Krista Conner

Medical school researchers have identified a molecular signaling pathway that drives the growth and maturation of young human beta cells — the insulin-producing cell type in the pancreas that malfunctions in diabetes — in mice and humans.

“The pathway, called the Cn/Nfat pathway, has been shown to be important in the growth and development of many cell types, including immune cells and neurons,” Kim said. “This is the first time it’s been shown to be involved in the development of human beta cells.”

“Now, we have a new way to approach the problem of how this process works in human embryos,” said Quake, who was not involved in the research.

The Stanford study showed that the previous, population-based estimates were, for the most part, surprisingly accurate: on average, the sperm in the sample had each undergone about 23 recombinations, or mixing events. However, individual sperm varied greatly in the degree of genetic mixing and in the number and severity of spontaneously arising genetic mutations. Two sperm were missing entire chromosomes that could result in spontaneous abortions, or miscarriages.

For the first time, we were able to generate an individual recombination map and mutation rate for each of several sperm from one person,” said study co-author Barry Behr, PhD, HCLD, professor of obstetrics and gynecology and director of Stanford’s in vitro fertilization laboratory. “Now we can look at a particular individual, make some calls about why they might contribute genetically to an embryo and perhaps even diagnose or detect potential problems.”

The researchers also identified 25 to 36 new single nucleotide mutations in each sperm cell that were not present in the subject’s diploid genome. Such random mutations are another way to generate genetic variation, but they don’t occur in points in the genome they can have deleterious effects. It’s important to note that individual sperm cells were destroyed by the sequencing process, meaning that they couldn’t go on to be fertilized. However, the single-cell sequencing described in the paper could potentially be used to diagnose male reproductive disorders and help infertile couples assess their options. It could also be used to learn more about how male fertility and sperm quality change with increasing age.

“This is likely a major step forward in our understanding of how human beta cells develop,” said Seung Kim, MD, PhD, professor of developmental biology and of pediatrics. “We have a new molecular mechanism of this genetic mixing process is unique for each sperm and egg cell,” said Quake, “and we’ve never before been able to see it with this level of detail. It’s very interesting that what happens in one person’s body mirrors the population average.”

Major problems with the recombination process can generate sperm mixing portions or even whole chromosomes, making them incapable of or unlikely to fertilize an egg. But it can be difficult for fertility researchers to identify potential problems.

“When we know that certain cellular signals, such as calcium signaling, increase in the current study, the researchers learned that the Cn/Nfat pathway (an abbreviation for calcineurin/nuclear factor of activated T cells) drives the growth and maturation of beta cells after birth in mice and humans. The pathway might be involved because 10 to 30 percent of people receiving calcineurin inhibitors (drugs used to suppress the immune system after organ transplant, for example) develop early diabetes during their treatment.

“We knew this pathway was a good one to consider, because development of cells like beta cells requires a specific message to sense the need to change and mature,” said Kim. They wondered if the Cn/Nfat pathway could generate insulin-producing beta cells. In addition, they knew that calcineurin is activated by calcium, which also signals beta cells to release insulin.

The researchers found that mice in which the pathway was genetically inactivated (in a man) or egg (in a woman) cell.

at the pancreatic islet, when all these things were still happening, so we could assess the significance of this pathway in human biology.”

Seung Kim
Research offers key for controlling the cellular fountain of youth

By Krista Conger

Telomeres are normally expressed in adult stem cells and immune cells, as well as in cells of the developing embryo. The enzyme caps off the ends of new chromosomes, allowing uninterrupted cell division and lead to diseases such as pulmonary fibrosis, aplastic anemia and a genetic condition called dyskeratosis congenita.

"The telomerase is normally expressed in adult stem cells, and it's expressed in immune cells, allowing uninterrupted cell division. Without telomerase, cells stop dividing or die when the ends — called telomeres — fall below a minimum length. Unfortunately, the enzyme is also active in nearly all cancer cells. Earlier research in Artandi's lab identified a protein called TACAI that binds to the telomerase complex (actually a large clump of many proteins) to a region in a protein called a Caja body. But no one knew how the complex was then tethered to the ends of telomeres, and research was hampered because the exact role and size, multiple components and relative scarcity. "The enzyme is extremely hard to study," Artandi said. "But we've now found that telomerase is recruited to the telomere through an interaction with a protein called TTP1 that coats the ends of chromosomes." What's more, the researchers have identified a key region that directly couples telomeres — a section called an OB-fold.

When we mutated this site in TTP1," said Artandi, "we blocked the interaction between the two proteins and prevented telomerase from going to the telomeres. And when we interfered with this interaction in human cancer cells, the telomerase began to shorten. The researchers are assessing whether the life span of the cancer cells, and their ability to divide unchecked, will be affected by the treatment.

To confirm their finding, Artandi and his colleagues used cells from patients with pulmonary fibrosis — a debilitating scarring or thickening of lung tissue associated with telomerase mutations. The disease had been troubling to researchers and clinicians, however, because the patients' mutated telomerase enzymes seemed to be fully active when tested in the laboratory. Zhong and Artandi found that the disease-associated mutations occurred in the portion of telomerase that interacted with TTP1, and interfered with their interaction with the enzyme, although active, couldn't get to where it was needed. It was impossible to even begin to understand this phenomenon unless we had access to these two molecules interact," said Artandi. "But now we can begin to think about developing inhibitors — maybe in the form of peptides or small molecules — that can mimic this disruption."

Other Stanford co-authors include postdoctoral scholar Luise Verhoef, MD, PhD, graduate student Matthew Pecel; and former graduate student Andrew Venteicher, PhD.

The researchers were supported by the Singapore Agency for Science, Technology and Research, the California Institute for Regenerative Medicine, the National Science Foundation, the Leukemia and Lymphoma Society; the Glenn Foundation for Medical Research and the NIH. Stanford's Department of Medicine also supported the work.

2012 Rosenkranz prize will aid DNA analysis of Latin Americans

By Krista Conger

Genetic mapping has led scientists to a better understanding of human disease and how genetic differences among diabetics, mental illnesses and cancer. But the information they have to work with is limited, drawing mostly from the DNA of people with European bloodlines. When it comes to figuring out how genetic disorders affect groups who don't share that ancestry or have only trace amounts of it in their family histories, researchers are often at a loss.

Andres Moreno, PhD, is changing that. Thanks to the $100,000 he is receiving as this year's recipient of the George Rosenkranz Prize for Health Care Research in Develop- ing Countries, he is working with indigenous groups and cosmopolitan populations living in Mexico, South America and the Caribbean.

The data he gathers will lay the groundwork for scientists interested in knowing how genetic diseases take hold and manifest themselves among Latin Americans — one of the most underrepresented populations in the field of genetics. Moreno can't start talking about how to deliver personalized medicine in Latin America because we still have much to learn about their genetics, says Jun Seita, MD, PhD, first author of the research, published July 18 in PLoS ONE.

"The potential analyses are very powerful," said Sahoo. "About 25,000 of the experiments had been performed with human data; 10,000 with data from mice. Individually, each data set suffered from the same drawbacks described above. But together they can be viewed as a continuum, or a stable common reference. The resulting Gene Expression Commons maps data submitted by the user on this common reference, and returns absolute expression levels that can then be compared among many combinations of samples.

To test their idea, the group performed and submitted microarray data from 39 highly purified, distinct cell types in the blood and immune system to the program. Now any researcher can explore the expression pattern of any gene in the system with just a few clicks of a computer mouse.

"The potential analyses are very powerful," said Sahoo. Microarray technology was developed at Stanford in the 1990s based on the fact that, complementary strands of nucleotides are driven to bind lengthwise to one another, like microscopic zippers. In microarrays, scientists affix thousands of tiny dots of specific nucleotide sequences, each representing a different gene — to glass slides in precise patterns, or arrays. Researchers apply a sample of interest to each slide and then can assess the relative levels of expression of each sequence across the sample.

However, because some sequences will inherently bind to their targets more or less strongly than others, it's not possible to directly compare microarray data across different experiments on the same chip. So researchers could learn that genes X and Y were both expressed at higher levels in one sample than in another. With the Gene Expression Commons, they can just type in the name of a gene and, within seconds, see the absolute expression levels that can then be compared among many combinations of samples.
The summer break can mean several weeks of hunger for children in East Palo Alto who depend on school lunches from September to June. This summer, however, the story was different — for the children as well as their families.

A lived-in community collaboration, Lucile Packard Children’s Hospital and the Ravenswood School District made sure homeless and at-risk families got a healthy lunch five days a week. “We’ve been seeing so much food insecurity over the last three years with the recession,” said Lisa Chamberlain, MD, MPH, assistant professor of pediatrics at the School of Medicine and physician lead for the Packard Children’s Pediatric Advocacy Program. “Last fall and winter it was getting so much worse. That’s when we decided to move forward with this program. We’ve never tried anything on this scale before.”

With patients from two extremes — some of the wealthiest in the state and some of the poorest — Packard Children’s is working to create a dialogue across the divide, and building relationships to heat up for children and their families.

Chamberlain worked closely with Ruth Woods, director of student services for the Ravenswood district. “I work with these kids year after year, so I know which families are really in need,” Woods said. “We started by identifying specific families, and then began including other families with children via word of mouth.”

“The schools ask for help,” said Chamberlain, “and we’ve got a lot of resources on the west side of 101. This is a time when communities need to draw together and support each other.”

Through the Ravenswood/Packard Children’s partnership, more than 500 meals a day were served to families classified as homeless, meaning they live in a shelter or double up with another family. The program ended on July 27, and served a total of 13,000 meals.

For the project, Chamberlain and her team contracted with the local nonprofit Revolution Foods to provide lunches. Revolution Foods makes healthy, locally sourced meals for kids living in poverty. The focus isn’t just on feeding the kids, but on feeding them well.

Among those who helped distribute the food nearly every day of the program were six youth girls from Willow Oaks school — Giselle Manous Ruiz, Brenda Ramirez, Briana Linares Maldonado, Yajaira Garcia, Keily Romero and Vanessa Poussa. “It feels good helping other people,” said Manous Ruiz.

Woods echoed that sentiment, noting that the experience of the volunteers helped build a stronger feeling of community.

National statistics show that more Americans than ever are on food stamps. The Department of Agriculture, which runs the National School Lunch Program, provides some funding to help keep school lunch programs for low-income children operating in the summer. However, parents or older relatives may themselves be hungry, and this can deeply impact the family’s health and well-being. “I knew this program had to be for the whole family,” said Chamberlain. “So we had to raise our own money to ensure that we could do a program that served the whole family.”

Identifying which youth to serve was easy. “I do registration for the district,” said Woods, “so I know all the homeless families and the families who are in crisis.”

Goldhaber-Fiebert on why childhood obesity doesn’t always predict adult weight problems

Instilling healthy eating and exercise habits in children may help prevent obesity later in life. But which kids most need such obesity-prevention efforts? A recent study by Jeremy Goldhaber-Fiebert, PhD, and colleagues at the School of Medicine showed that this question is harder to answer than it seems. The study, published earlier this year in Medical Decision Making, found that targeting obesity prevention to small children who are overweight might not be effective. That’s because a higher-than-normal weight at age 5 provides an accurate predictor of adult obesity only 50 percent of the time. Goldhaber-Fiebert, an assistant professor of medicine, discussed the problem with Erin Dietrich, a writer in the communications offices at the medical school and Lucile Packard Children’s Hospital.

Julie Greicius is a writer for the communications office at Packard Children’s Hospital. 5 QUESTIONS

1 What does your paper tell us about the recent focus on childhood and adolescent obesity measurements?

GOLDBAHER-FIEBERT: Our study has two take-home messages. First, while childhood obesity is an important problem, solving childhood obesity alone will not solve future adult obesity problems. Second, addressing future adult obesity will require new and more complex measures — not simply interventions focused on obese children.

2 It used to be that no one worried much if a small child was chubby; they’d say, “It’s baby fat, he’ll grow out of it.” How has that changed?

GOLDBAHER-FIEBERT: In fact, our data show that many children still do “grow out of it.” But our findings suggest that it is difficult to predict whether this will happen. In general, childhood and adolescent obesity and related health issues. Our analyses show that targeting children who are already obese is unlikely to be sufficient in addressing broad public health challenges of obesity in later childhood, adolescence and adulthood.

3 Are there more promising screening criteria for chronic adult obesity instead of using a child’s weight?

GOLDBAHER-FIEBERT: It really depends on the purpose of screening. Researchers have identified a variety of characteristics to predict a child’s future obesity status — for example, easily observed measures like the weight of a child’s parent as well as more complex measures such as their size at birth and the rapidity with which they subsequently grow and gained weight. The challenge is to have a measure that both does not miss a substantial fraction of those who become obese later on and also does not falsely identify obese for a large number of those who do not become obese as adults.

4 What are some of the best potential approaches for reducing childhood obesity if the entire population is being targeted?

GOLDBAHER-FIEBERT: Given that many health-related habits are developed in childhood, efforts to create healthy eating and exercise habits in children would seem to be beneficial. But for most potential interven-

5 What do your data tell us about the potential for screening for obesity-related conditions of childhood clearly should not be ignored. What we are concerned about is the sense that people were conflating good care for children to deal with their short-term health needs (i.e., childhood obesity management to deal with childhood health issues) and the belief that such an approach might largely solve the broader adult obesity issues.

Addressing childhood obesity is still important even if it does not fix adult obesity and its deleterious health consequences.
Developmentally delayed infants benefit from cochlear implants

By Erin Digitalle

Doctors should reconsider the common practice of avoiding the use of cochlear implants in deaf children with developmental delays, according to a new study from the School of Medicine and Lucile Packard Children’s Hospital.

While cochlear implants are now routinely given to deaf children as young as 1 year old and frequently opt not to use these devices — sometimes referred to as “bionic ears” — in babies with development delays that are indicators of probable mental retardation. The new finding suggests that the implants could significantly benefit these children’s intellectual development, if their delayed developmental milestones make it unlikely that they will ever learn to speak.

“If we can fix this deficit, it might help developmentally delayed children who are deaf from congenital heart defects, an inability to eat by mouth or serious breathing problems, for example, and doctors may not want to compromise their treatment with yet another procedure,” said John Oghalai, MD, the lead author of the study in the August issue of Otology & Neurotology. Oghalai is an associate professor of otolaryngology and director of the Packard Children’s Hearing Center.

The combination of deafness and developmental delay has become more common as increasing numbers of children survive extremely premature birth; complications of prematurity often include both cognitive delays and deafness.

Early use of cochlear implants for developmentally delayed children has often taken a back seat to their other medical issues, Oghalai said. These children may be grappling with congenital heart defects, an inability to eat by mouth or serious breathing problems, for example, and doctors may not want to compromise their treatment with yet another procedure.

Physicians have been wary of whether the implants would benefit the children. Cochlear implants send electronic signals from a microphone on the outside of the head directly to the auditory nerve, but the result is different from normal human hearing, and children typically require intensive speech and auditory therapy to learn to use and benefit from the implants.

For the study, Oghalai and his colleagues assessed use of cochlear implants in children who were cognitively normal and therefore were developmentally deaf. They used a term to characterize young children who may later meet criteria for mental retardation. The researchers reviewed records of 60 developmentally delayed and 144 cognitively normal children who received the implants, and found that the cognitively normal children got cochlear implants earlier in life (16 months of age, on average) than the developmentally delayed children (25 months, on average).

The researchers determined that later implantation had detrimental results. Not only did the delayed children start with lower intelligence, they also had slower intellectual development, perhaps because they were not able to hear for very long, researchers reported. When the team statistically adjusted for the delay in implantation, the difference in rates of development disappeared, suggesting that lack of hearing played a role in causing developmentally delayed children to fall further behind their peers.

There is synergism between different sensory inputs,” Oghalai said. “And of these kids are missing more than just hearing; they’re often having trouble with vision or touch as well. If you can fix one of the sensory problems, it might help to mitigate the effects of the other disabilities.”

Because standard scales for measuring intelligence were not appropriate for the young children being studied, part of the research team’s work was the development and validation of new methods for scoring the intelligence of these children. (For instance, some intelligence scales assess motor skills, which may be impaired if a child has physical disabilities unrelated to his or her intelligence level.)

A new study shows that early use of cochlear implants, illustrated above, can be helpful for infants with developmental delays.

Mutations that cause childhood brain tumor identified

By Erin Digitalle

Researchers at the School of Medicine and Lucile Packard Children’s Hospital have identified several gene mutations responsible for the most common childhood brain tumor called medulloblastoma, adding evidence to the theory that the diagnosis is a group of genetically distinct cancers with different prognoses. These and accompanying findings are likely to lead to less-toxic, better-targeted treatment approaches over the next two years, the researchers said.

“We tend to treat all medulloblastoma patients the same, without taking into account how heterogeneous the tumors are at the molecular level,” said Yoon-Jae Chang, MD, a pediatric neurologist and neuropsychologist at Stanford, and lead author of the new research paper. “This paper represents a finer-grained view of the genetic landscape of these tumors and provides us with new insights on how to develop new therapies.” The other senior authors are Scott Pomeroz, MD, PhD, neurologist at Stanford’s Hospital; and John Herrlinger, MD, PhD, director of developmental biology at the Broad Institute.

The research, published online in Nature Genetics (30 July) and appearing in an upcoming issue of the journal, is a more systematic evaluation of whether children with developmental delays who receive cochlear implants by 12 months of age, the minimum age approved by the FDA for use of the devices.

The study was supported by the NIH, the Stanford Department of Otolaryngology-Head and Neck Surgery also supported the research.

The research was funded by the National Institutes of Health, the St. Baldrick’s Foundation and the Children’s Health Research Institute. The work was also supported by the Pediatric Brain Tumor Consortium that guides which drugs should be moved into clinical trials next. Oghalai said that within the next one to two years we will be able to offer kids a new set of compounds that have a clear biological rationale based on our genomic studies. Cho said, “We want to make sure we’re being careful of what we move forward with, but at the same time, for some of these kids we don’t have many, if any, effective and durable treatment options.”

Several of the mutations discovered affect so-called “green signals” that switch large groups of genes on and off. “The dysregulation of these ‘epigenetic programs’ is becoming a common theme not only in medulloblastoma but across cancer,” Cho said. Such pathways may be good targets for cancer drugs, and they’re often key to signaling targeting one such pathway (histone modification) are currently in pre-clinical development, while agents against another pathway (Hedgehog signaling pathway) are entering phase-2 clinical trials for medulloblastoma.

One drawback of the current study is that the developmentally delayed children who received implants were chosen on an ad-hoc basis. The next step in the research is a more systematic evaluation of whether children who have certain genetic profiles in section of developmentally delayed deaf children. A prospective trial funded by the National Institutes of Health is now under way at Packard Children’s, Oghalai said.

The ‘issue is to catch these children early when they’re in the neonatal intensive care unit, identify their hearing loss and be aggressive in following and treating them,’” Oghalai said. Instead of asking families to return for a hearing evaluation after their child’s other health problems have stabilized, which could take several months, infants with hearing loss are being given hearing aids by 6 to 8 weeks of age, then followed regularly at the audiology clinic. When the children receive cochlear implants by 12 months of age, the minimum age approved by the FDA for use of the devices.

Managing families’ expectations of the power of the cochlear implants is also important, Oghalai noted. Cochlear implants will not make a developmentally delayed child cognitively normal but the implants can improve the children’s quality of life, make them happier and prevent them from falling further behind their peers, they may be a very worthwhile endeavor, he concluded. Co-authors include Barbara Bentley, PsyD, clinical psychologist in developmental and behavioral pediatrics; Homer Abaya, social science research assistant in otolaryngology; and Jody Winzelberg, AuD, chief of audiology and director of rehabilitation services at Packard Children’s.

The study was supported by the NIH, Stanford’s Department of Otolaryngology-Head and Neck Surgery also supported the research.

The research was funded by the National Institutes of Health, the St. Baldrick’s Foundation, Children’s Health Research Institute, Faculty Scholar endowment at Stanford University, German Cancer Aid, the BMBF KCGC-PedBrain project, the Huntington’s Disease Society of America, the Pediatric Brain Tumor Foundation, the Canadian Institutes of Health Research, the Hospital for Sick Children, and the Mullarky Research Fund. Cho said for more help to develop better drugs for the company’s clinical trials.

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Tai chi study seeks older adults who have mild memory problems

Researchers at the School of Medicine are looking for older adults to participate in a small study that will investigate whether an ancient Chinese exercise can help boost memory in seniors.

Victor Henderson, MD, professor of health research and policy and of neurology and neurological sciences, and his colleagues are seeking older adults to help answer questions about the participants' mild memory problems but in reasonably good health. They must be able to travel to Stanford for twice-a-week classes and have a study partner who will help answer questions about the participants.

Adulls with dementia or Alzheimer's disease are not eligible.

Those interested in participating or obtaining more information about the study should call 721-3308 or e-mail teem-seniors@stanford.edu.

During this trial, participants will be randomized to participate in a tai chi intervention group, current level of exercise-related activities (and not participate in the tai chi intervention group, in which the participants will be evaluated at the beginning and end of the study with tests of memory and cognition and a scan of the brain. Total involvement will occur approximately one year.

Participants will be placed in the tai chi group will be offered classes upon completion of the study.

This trial is part of a larger study, funded by the NIH that is exploring the contribution of tai chi to dementia and the Chinese exercise qigong, to prevent mental decline. General information about the rights of study participants is available by calling (866) 680-2906.
A-beta continued from page 1

Study will assess effectiveness of mobile-device app for those who suffer from PTSD

process and after brain injury. Concen-
trations of the peptide, along with those of the precursor protein from which it is carved, are found in multiple sclerosis lesions as well, said Lawrence Steinman, MD, the new study’s senior author. In a lab dish, A-beta competes with many types of cells. And when it is adminis-
terred directly to the brain, A-beta is highly inflammatory.

Yet little is known about the physi-
ological role A-beta actually plays in Al-
zheimer’s or MS, said Steinman, a profes-
sor of neurology and neuroscientifics and of pediatrics and a noted multiple-sclerosis researcher. He, first author Jacqueline Grant, PhD, and their colleagues set out to determine that role in the latter disease. (Grant was a gradu-
ate student in Steinman’s group when the work was done.)

Multiple sclerosis, an autoimmune disease, occurs when immune cells invade the brain and spinal cord and attack the insulating coatings of nerve cells’ long, cable-like extensions called axons. The myelin sheath, composed largely of a fatty substance called myelin, disrupts the transmis-
sion of nerve messages along axons, and scientists have long suspected that immune cells are behind it. Early experiments showed that when A-beta was injected into a mouse, it would destroy immune cells called B cells, rather than directly to the brain. When Steinman had Grant repeat the exper-
iment, he got different results.

The theory was being led by C. Barr

The A-beta study was featured on the cover of Science Translational Medicine.

Bickel, an assistant professor at Stanford’s Institute for Regenerative Medicine. The study was funded by the National Institutes of Health and the California Institute for Regenerative Medicine. Stanford’s Department of Pathology also supported the work.

HHMI fellowships to four international students

Four graduate students at the School of Medicine are the recipi-
ants of international predoctoral fellowships awarded by the Howard Hughes Medical Institute. Launched last year, the fellow-
ships, each worth $43,000, are designed to encourage the international students during their third to fifth years of graduate school in the United States. The four awardees and their projects are:

Fang-Chieh Chou, from Tai-
wan, who is working toward an atomically accurate structure model-
ing of protein-RNA complexes; advisor is Riju Das, PhD, assis-
tant professor of biochemistry.

Aditya Natarajan, from Can-
ada, who is working on in vitro tests of the energetics within an enzyme active site, with the goal of advancing the fundamental understanding of how catalytic interactions and the sur-
rounding enzyme environment; advisor is Daniel Herschlag, PhD, assis-
tant professor of biochemistry.

Aynul Rana, from India, who is investigating interactions be-
tween certain enzymes and their proteins to identify disease-rele-
vant signaling pathways; advisor is Ricard Torres-Aleman, MD, Ph
d Ph, professor of neurology.

And Aysel Selimbeyoglu, from Tur-
key, who is working on the optogenetic dissection of the neu-
ral circuitry underlying cognitive control; advisor is Daniel Herschlag, MD, Ph
d Ph, associate professor of bioengineering and of psychiatry and behavioral sciences.
Minor continued from page 1

to prevent the negative consequences. “When I first started going to see a psychologist, I was having a lot of trouble with my body dysmorphia and self-image issues. But after several sessions, I began to realize that it wasn’t just me and that there were other people dealing with similar challenges. It helped me to feel more normal and less isolated.”

“Even though I still have my body dysmorphia, I’ve learned to accept and love myself more,” Minor said. “I’ve also learned to be more open and honest with myself, which has helped me to make better decisions about my health and well-being.”

Minor is currently working on a new project that she hopes will help to increase awareness and understanding of body dysmorphia among young people. “I want to create a platform where young people can share their experiences and learn from each other,” she said. “I think that by doing this, we can help to reduce the stigma and shame that often come with body dysmorphia.”

Minor is also working on a new research study that she hopes will help to identify the underlying causes of body dysmorphia. “I’m hoping to recruit a diverse group of participants and use a range of research methods to gather data,” she said. “I think that by doing this, we can better understand the complex factors that contribute to body dysmorphia.”

Minor is currently in the process of applying for a grant to fund her research project. “I’m hoping to hear back from the grant agency in the next few weeks,” she said. “If I’m successful, I’ll be able to start recruiting participants and conducting the research.”

Minor is also working on a new book that she hopes will help to increase public awareness of body dysmorphia. “I’m hoping to publish the book within the next year,” she said. “I think that by doing this, we can help to reduce the stigma and shame that often come with body dysmorphia.”