What makes us human?

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Ultrasound can help determine risk of heart attack

Physicians at the University of Chicago Medical Center are now offering a screening test using ultrasound images of arteries in the neck to assess the future risk of heart attack or stroke.

Heart specialists have used the test, known as carotid intima-media thickness, or CIMT, for more than a decade in research to monitor the effects of exercise, diet or medications on the progression of atherosclerosis (hardening of the arteries). Now, using data gathered from thousands of patients in such studies, physicians can estimate the risk of a major cardiovascular event—such as a heart attack or stroke—by taking precise measurements of the thickening of the easily accessible carotid arteries that pass near the surface of the neck.

“The standard risk factors—increased age, smoking, cholesterol levels, high blood pressure, diabetes—affect the arteries throughout your body in much the same way as they affect those that supply your heart,” said cardiologist Parker Ward, MD, assistant professor of medicine at the University of Chicago. “By measuring the thickness of the first two layers of your carotid artery, we can get a pretty accurate estimate of your risk of cardiovascular disease.”

“This ultrasound image shows (in red) the thickness of the first two layers of the far wall of the carotid artery, called the carotid intima-media thickness (CIMT). A patient’s CIMT can be used to estimate the risk of future heart attack and stroke. It also can be used to determine a surrogate ‘age’ of the patient’s blood vessels.”

CIMT is appropriate for patients without symptoms but with traditional risk factors for heart disease—such as a family history of cardiovascular disease, high blood pressure or high cholesterol levels—to prompt lifestyle changes or possibly medications to modify these risks. Among patients with existing cardiovascular disease, serial studies can be used to monitor the blood vessels’ response to lifestyle and medication changes.

“Atherosclerosis often remains ‘silent’ for many years,” Ward said. “In about half of patients who present with heart disease, the first clinical manifestation is a heart attack or sudden cardiac death. Traditional risk factors should always be the first step in identifying patients at risk, but among those with risk factors, clinical CIMT testing may provide an additional option to patients and physicians to identify those patients at the highest risk.”

While CIMT is recognized as a valid, safe and non-invasive means for assessing cardiovascular disease, the test only recently has begun to move from research to clinical application. It is not yet widely recommended to patients for screening. Medicare and most private insurance will not routinely pay for the CIMT test at this time.

Conscience, religion alter physicians’ treatments

Many physicians feel no obligation to tell patients about legal but morally controversial medical treatments or to refer patients to doctors who do not object to those treatments, researchers from the University of Chicago reported in the Feb. 8, 2007, issue of the New England Journal of Medicine.

The medical profession appears to be divided, the researchers wrote, not just in its attitudes about providing controversial practices such as terminal sedation, abortion or birth control for teens, but also in its judgments about what doctors should do when patients request a legal procedure to which their doctor objects.
The study found that although 86 percent of doctors did feel obliged to present all options in such cases, only 71 percent said they would feel obligated to refer the patient to a doctor who did not object to the requested procedure, and 63 percent believed it is ethically permissible for a doctor to describe his or her objection to the patient.

“If physicians’ ideas translate into their practices, then 14 percent of patients—more than 40 million Americans—may be cared for by physicians who do not believe they are obligated to disclose information about medically available treatments they consider objectionable,” the authors wrote. “In addition, 29 percent of patients—or nearly 100 million Americans—may be cared for by physicians who do not believe they have an obligation to refer the patient to another provider for such treatments.”

“Our survey data point to a basic dilemma facing patients and physicians in our plural democracy,” said study author Farr Curlin, MD, assistant professor of medicine and a member of the MacLean Center for Clinical Medical Ethics at the University of Chicago. “Because patients and physicians come from many different moral traditions, religious and secular, they will sometimes disagree about whether a particular medical intervention is morally permissible.”

—Farr Curlin, MD, Assistant Professor of Medicine

Illustration by Nora Morales
Two-step process filters evolution of genes

Although the human and chimpanzee genomes are distinguished by 35 million differences in individual DNA “letters,” only about 50,000 of those differences alter the sequences of proteins. Of those 50,000 differences, an estimated 5,000 may have adaptive consequences in the evolutionary divergence between these two species, according to a study published in the March 6, 2007, issue of the Proceedings of the National Academy of Sciences.

Before a new and beneficial mutation can take its place in the human genome it has to pass through a rigorous two-step—negative and positive—screening process, say the study authors, evolutionary geneticists from the universities of Chicago, Tokyo and Washington. Both steps focus on the most radical changes.

In step one, mutations, the genetic equivalent of typographical errors, are randomly introduced. When these mutations are still rare in the population, only the strongly deleterious ones get weeded out through negative selection. The more radical mutations are more likely to be harmful and quickly removed. For those that are only slightly harmful, neutral or beneficial, the selective forces are weak and luck determines their fates.

In step two, mutations that survive the initial elimination process and confer some benefit can then spread quickly through positive selection. The more radical the mutation, at this point, the faster it is likely to spread.

“We found that the same genetic changes that are unlikely to survive early negative selection are the ones that spread most quickly once they gain a foothold.”

—Chung-I Wu, PhD, Professor of Ecology and Evolution

For their analysis, the researchers used the large survey of human genetic variation called HapMap, which compared human variations with the chimpanzee genome. They focused on the simplest and most common mutations: those that alter just one letter, a single base pair, of DNA.

DNA uses a three-letter code to designate the 20 types of amino acids that are strung together in specific order to create a protein. Some mutations alter just one letter of the code, replacing one link in a protein’s amino-acid chain with a different amino acid. While some of those substitutions make only a moderate difference in a protein’s structure or function, others have radical impact on its shape and performance.

Radical amino acid changes alter protein function. Most of those are deleterious and get removed, but “when a mutation is beneficial, we do not know whether they tend to be the radical or moderate kind of amino acid changes,” Wu said. “Since beneficial changes are the ones that fuel evolution, we wanted to find out if these improvements are smooth or jerky.”

When Wu and colleagues sorted these changes according to their evolutionary success, they found that radical changes were more harshly screened—negatively and positively—by the forces of evolution.

In rare cases, radical mutations escaped elimination by negative selection. Once they had established a beach head, occurring in as little as 5 percent of a population, these radical mutations tended to spread quickly throughout the species, their survival or reproductive advantage allowing them to gain ground over multiple generations.

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When they multiplied that result times current estimates of the number of functional genes, it came to about 3,000 to 7,000.

“These are the genetic changes that are possibly adaptive,” Wu said. “Out of those differences, we suspect that some, and perhaps most, are responsible for the most significant changes between human and chimpanzee.”

The National Institutes of Health funded the study. Additional authors were Jun Gojobori of the University of Tokyo, Hua Tang of the University of Chicago, and Joshua Akey of the University of Washington.

—JE

Parents part of the solution, not the problem

Common practice in the treatment of adolescent eating disorder patients has been to exclude the parents. Many experts consider parents part of the problem and thus keep them away during therapy.

Two U.S.-based clinicians disagree and have written a “how to” book that includes family in the treatment of these patients. They say parents are well poised to help their children overcome bulimia nervosa, a disorder characterized by binging and purging.

“We don’t see parents as the culprit,” said co-author Daniel le Grange, PhD, associate professor of psychiatry and director of the

Hypertension connected to vertebra

A study of 50 hypertensive patients with a misaligned C1 (or Atlas) vertebra showed significant blood pressure decrease after a one-time adjustment of that vertebra. The decrease was equal to taking two blood pressure drugs at once. Located high in the neck, the Atlas is uniquely vulnerable to displacement because unlike other vertebrae it relies solely upon muscles and ligaments to maintain alignment, said lead author George Bakris, director of the hypertension center at the University of Chicago Medical Center. Half the patients enrolled in the study received tailor-made adjustments based on a prior cervical assessment; half received a “sham intervention.” Assessment after eight weeks showed continued reduction in blood pressure after correction of Atlas misalignment but no significant change in heart rate.

The study, however, was unable to determine what caused the blood pressure drop. A larger trial involving multiple practitioners is planned to address such questions as whether there is a cause-and-effect relationship between C1 misalignment and hypertension.

Million-dollar boost for lung disease

Two University of Chicago researchers have received a three-year, $1 million grant to develop a Center for Excellence in Pulmonary Fibrosis. There is no known cause or effective treatment for the lung-scarring disease, which affects about 5 million people worldwide—including 200,000 patients in the United States, more than 40,000 of whom die each year. Joe G.N. Garcia, chairman of medicine, and Imre Noth, director of the pulmonary fibrosis program, plan to work with the program’s team of clinicians, physician-scientists, geneticists and information specialists to conduct laboratory and clinical research to understand the disease at the molecular level and to improve treatment for patients, including those who require lung transplant. “This is a fairly common and potentially devastating disease that we know very little about and have only limited funds to study,” Noth said. “This [grant] should make a real difference in our ability to understand this disease and ultimately to find the tools to treat it.”

Brittany Goodrich (front), with parents Brian and Sue Goodrich, has been getting treatment for bulimia nervosa at the University of Chicago’s eating disorders program for about three years. Using the family-based Maudsley approach, they have seen success with her treatment.

Photo by Dan Dry
eating disorders program at the University of Chicago. “We see them as a valuable resource in the treatment of these adolescents. Our goal is to empower parents to feed their kids. Feeding kids is something they do well.”

*Treating Bulimia in Adolescents*, published in February, is the third in a trilogy written by le Grange and James Lock, MD, PhD, professor of child psychiatry and pediatrics at Stanford University. The duo also wrote the parents guide *Help Your Teenager Beat an Eating Disorder* in 2005 and collaborated with two colleagues to write *Treatment Manual for Anorexia Nervosa*, a clinical guide for clinicians, published in 2001.

“We found many parents using the *Treatment Manual for Anorexia Nervosa*, even though it was designed for clinicians, simply because it gave them step-by-step advice on what should be done. We think we’ll find the same thing with the bulimia book,” le Grange said. “And because bulimia affects more adolescents than does anorexia nervosa, there might be greater demand for it.”

Le Grange learned this approach at the Maudsley Hospital in London, known for its family-based approach. It has proven effective in treatment of anorexic adolescents and is being studied for efficacy with bulimic adolescents, he said. But to date, no one has written a manual for practitioners.

“Something else quite different about this approach is that it takes place in an outpatient setting, in 15 to 20 50-minute visits,” le Grange said. “Other methods to treat bulimia entail hospitalization or day-long visits. The Maudsley approach is truly minimalistic.”

The Maudsley approach has parents supervising the adolescent’s every meal, making sure an appropriate amount of food is consumed and that they remain with their child for a while after the meal to prevent purging. This requires parents to be home for every meal, at least at the outset of treatment, and that the adolescent understand there is relatively little room for negotiation.

“Adolescents with bulimia are ill,” le Grange said. “If a child required chemotherapy or dialysis or was in a horrendous car accident, the parents would take whatever time off from work was necessary to deal with this emergency. Dealing with an adolescent who has bulimia can be just as critical.”

The authors also discuss the need for parents to take a unified approach in dealing with a child's bulimia. They say both parents must equally support the same strategies and restrictions for the treatment to be successful.

Treatment plans for bulimia that neglect making use of the family unit miss a golden opportunity for reinforcement and are at risk for recidivism, they said.

—Scott Roskelley

**Researchers looking for alien invaders**

Alien invaders exist in Chicago. They’re little and green, and for the past four decades they’ve surveyed human life in the city from on high.

Now, though, one University of Chicago scientist wants to turn the tables. Stephen Pruett-Jones, associate professor of ecology and evolution, is initiating a year-long Chicago-area survey, encouraging locals to turn their eyes to the skies in search of these foreign creatures—in this case, monk parakeets.

Pruett-Jones and research partner Christopher Appelt at Saint Xavier University want to generate a map of all active monk parakeet nests stretching from Northwest Indiana into southern Wisconsin.

Hyde Park residents first reported sightings of the alien species—indigenous to Central and South America—in the late 1960s. Though people kept and continue to keep parakeets as pets, these sightings were of feral parakeets perched in treetops or on massive nests made primarily of sticks.

Researchers believe that the original feral parakeets in Hyde Park were pets that escaped their owners. In the wilds of this South Side Chicago neighborhood, they formed colonies, and by the ’90s their population had expanded to an estimated 400.

They’re expanding again—this time geographically. During the past eight years, “their numbers in Hyde Park have declined, whereas in surrounding communities their numbers have skyrocketed,” Pruett-Jones said.

“This work will help better understand the biology of this interesting species and the reasons for its moving out of the city as well as nest site preferences,” he said.

After an initial study, Pruett-Jones concluded that the parakeets were moving away from the city via corridors along train lines and utility structures. They also have switched their dwellings from oak and elm trees to conifers and utility poles, which prove hazardous because “when the nests get wet during rain and snow storms they can cause electrical shorts, power outages and electrical fires.”

Those hazards are no shock to Hyde Park residents who watched electrical power supplier ComEd remove a 10-foot-wide nest from a utility pole in ’97. A debate erupted between the alien species’ advocates and residents who feared for their safety and property values.

“Understanding the present distribution of nests and how corridors of open space facilitate a change in that distribution may help minimize this danger,” Pruett-Jones said.
People who have spotted the feral green-and-gray creatures and know locations of active nests should send a description of the nests’ exact locations and any other information regarding the parakeets to the researchers at pruett-jones@uchicago.edu and appel@sxu.edu or call (773) 702-3115.

—Katie Scarlett Brandt

Cancer study provides data about long-term prognosis

Childhood cancer survivors are nine times as likely as the general population to develop a sarcoma—a cancer of connective or supportive tissue such as bone, fat, or muscle—but indicators can help physicians in knowing who’s at most risk, according to a study published Feb. 21, 2007, by the Journal of the National Cancer Institute.

With data from more than 14,000 childhood cancer survivors treated between 1970 and 1986, the Childhood Cancer Survivor Study (CCSS) is believed to be the largest of its kind. Tara Henderson, a pediatric oncologist/hematologist at the University of Chicago Comer Children’s Hospital, led a study investigating the risk factors associated with developing second sarcomas among the participants of the CCSS.

Today the cure rate for childhood cancer is approaching 80 percent. The survival rate for childhood acute lymphoblastic leukemia alone approaches 90 percent. When deciding upon therapies, physicians need a better understanding of the long-term effects of cancer treatments.

“A generation ago, a pediatric cancer diagnosis was a death sentence,” Henderson said. “A new generation is coming of age. Finally, we can see the effects of therapy on growing bodies.

“The hope with this study is that we can learn which patients are predisposed to secondary cancers,” she said.

The researchers identified factors that increased the risk of developing secondary sarcoma. Those factors include: high doses of anthracyclines or alkylators (two types of chemotherapy); previous radiation exposure; age at the time of primary diagnosis; and type of cancer.

Cancer survivors who are at highest risk for secondary sarcoma are those who were first diagnosed with soft tissue or bone sarcomas, renal tumors or Hodgkin lymphoma, Henderson said.

The study combined data from 26 U.S. and Canadian institutions. From the 14,372 participants, medical records and pathologic reviews identified 104 independent secondary sarcomas. Four of the 104 developed tertiary sarcomas.

The median age of secondary sarcoma diagnosis was 20 years with a median age for primary diagnosis at 11 years.

Doctors should be vigilant when caring for a childhood cancer survivor, Henderson said. “They should investigate [a complaint] more quickly—order imaging or blood work as appropriate,” she said.

The study confirmed a direct correlation between radiation therapy and the development of secondary sarcomas, although researchers found that some survivors who did not have radiotherapy also developed them.

Sarcomas are more difficult to detect than other cancers because they can occur anywhere in the body. Secondary cancers are the second leading cause of death among five-year childhood cancer survivors. And the leading cause of death among cancer survivors is a relapse of the primary cancer.

Henderson emphasized the importance of early screening for survivors of pediatric cancer. “It’s important for childhood cancer survivors to have regular follow-up appointments with physicians who have knowledge of childhood cancer and its late effects so the patients can be appropriately screened,” she said.

—Theresa Carson

Arsenic compound improves survival rates for leukemia patients

A phase III cancer clinical trial indicates that adult patients with previously untreated acute promyelocytic leukemia (APL) who had standard chemotherapy to induce remission of their disease, and then received the chemotherapy drug arsenic trioxide to maintain remission, had a significantly better event-free survival (more patients free of leukemia) and better overall survival than those who received only standard chemotherapy.

Chicago gets high marks

The University of Chicago’s paleontology and ecology/evolutionary biology programs were rated best in the United States in the latest U.S. News & World Report ranking of the nation’s graduate schools. The Pritzker School of Medicine climbed from a two-way tie for 17th to a three-way tie for 15th. Graduate biosciences programs overall moved from a tie for 19th to a tie for 18th in the magazine’s “Best Graduate Schools.” Though Pritzker is relatively small and disadvantaged in terms of total research funding from the National Institutes of Health, its fifth-place national ranking in research funding per faculty member helped its overall position. Funding for biomedical research increased more than 9 percent, the largest overall gain for any medical school in the top 25.

The magazine also selected the University of Chicago Medical Center as one of the 18 best hospitals in the United States. In the 2007 “Best Hospitals” issue, the magazine ranked the Medical Center at 17th, tied with Cedars-Sinai of Los Angeles, out of America’s 5,462 hospitals. Because the Medical Center scored highly in so many areas it is featured in the magazine’s elite list of Honor Roll hospitals. The only Illinois hospital ever to be included in the honor roll, the Medical Center has appeared on this sought-after list 10 times since 1995.

Adding to that, Chicago’s graduate programs made an impressive jump in The Scientist’s list of the best places to be a postdoc. In the March 2007 issue, “Top 40 North American Institutions” shows the University of Chicago moving from 56th in ’06 to 37th place in ’07.

Big improvement at low cost

A University of Chicago-based research team has found that relatively inexpensive improvements in diabetes care can reduce patients’ lifetime risk of common diabetic complications such as blindness, end-stage kidney disease and coronary artery disease. The four-year study was conducted at selected clinics by the Centers for Disease Control and Prevention’s Health Disparities Collaboratives. It found that at a cost of less than $500 per patient per year, the changes could reduce incidence of major complications such as end-stage renal disease that can cost $44,000 per patient per year. Internist Elbert Huang is the study’s author.
“The positive result in a clinical trial of a common element holding an uncommon disease in remission for a significant period of time is very encouraging,” said NIH Director Elias A. Zerhouni, MD.

“It is fair to say that arsenic trioxide has now become part of the standard of care for initial treatment of acute promyelocytic leukemia,” said Richard Larson, MD, professor of medicine at the University of Chicago and a co-investigator of the study.

The trial was sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health, and was led by one of its Cooperative Clinical Trials Groups—the Cancer and Leukemia Group B (CALGB), directed by University of Chicago's Richard Schilsky, MD.

Acute promyelocytic leukemia, an uncommon subtype of acute myeloid leukemia (AML), accounts for about 10 percent of AML cases, or about 1,500 cases per year, in the United States. It is most often diagnosed in young and middle-aged adults, but also occurs in children and older adults. Standard chemotherapy regimens produce complete remission rates of about 70 percent and show a five-year survival without the recurrence of disease in 35 to 45 percent of patients.

“Achieving success in a clinical trial for a rare cancer is a difficult task due to the limited number of patients eligible to enroll in the trial, so this is very encouraging news for all patients with this form of leukemia,” said NCI Director John E. Niederhuber. “This positive outcome demonstrates, yet again, the benefits of clinical trials and will hopefully serve as encouragement for others to join such trials.”

This particular type of leukemia is often accompanied by life-threatening bleeding at diagnosis that typically worsens, even as initial treatment is administered. Treatment has improved dramatically in recent years with the addition of all-trans retinoic acid (ATRA, or tretinoin) to chemotherapy. More recently, arsenic trioxide (Trisenox) was shown to be an effective drug for producing a second remission in patients who had a relapse or recurrence of their APL after initial treatment.

The CALGB-coordinated study, which involved 582 patients in a six-year period ending in 2005, tested the effectiveness and side effects from adding two 25-day courses of intravenous arsenic trioxide to the combination of ATRA and chemotherapy.

The percentage of adult patients who remained alive and in remission three years after diagnosis was 77 percent among those who received arsenic trioxide compared with 59 percent on the standard treatment. The greater effectiveness of the experimental combination also resulted in better overall survival after three years of 86 percent for the patients who received the arsenic trioxide, compared with 77 percent for patients on the standard treatment.

“The willingness of patients with leukemia and their physicians to participate in this important clinical trial has markedly improved the outcome for these and future patients with APL,” said Bayard Powell, MD, Wake Forest University, Winston-Salem, N.C., principal investigator of the study.

The side effects from treatment were reported at the annual meeting of the American Society of Hematology in Orlando, Fla., in December 2006. There was no difference in hematologic (blood count) toxicities between the group who received arsenic trioxide and those who did not, but there was a slightly higher incidence of headache and infection in the group who received arsenic trioxide.

The full study was presented at the annual meeting of the American Society of Clinical Oncology in Chicago this past June.

The study was sponsored by the Division of Cancer Treatment and Diagnosis (DCTD), NCI (under a Clinical Trials Agreement between DCTD), NCI and Cephalon (marketers and sellers of Trisenox), and monitored by an independent Data and Safety Monitoring Board that recommended release of the results.

CALGB is a national clinical research group sponsored by the National Cancer Institute, with its central office headquartered at the University of Chicago and its statistical center located at Duke University. —JE

Fishing for old genes

Long before animals with limbs (tetrapods) emerged on the scene about 365 million years ago, fish already possessed genes associated with helping to grow hands and feet (autopods), researchers reported in the May 24, 2007, issue of Nature.

This finding overturns a long-held, but much-debated, theory that acquiring limbs was a novel evolutionary event in which the descendants of lobed-fin fish dramatically altered their genes to adapt to new environments.

According to the new research, the genetic and developmental toolkit that builds limbs with fingers and toes existed in some primitive form much earlier—before the limbs themselves.

“We found that the genetic capability seen in tetrapods to build limbs is present in even more primitive fish,” said Marcus Davis, PhD, a postdoctoral fellow in Neil Shubin’s lab at the University of Chicago and lead author of “An autopodial-like pattern of Hox expression in the fins of a basal actinopterygian fish.”

Instead of using zebrafish—the hallmark animal for laboratory development studies—the Chicago team used paddlefish as a proxy for a more primitive ancestor.
They examined Hox genes, which play a vital role in limb development, in the pectoral fins of the paddlefish.

Unlike the simple fins of zebrafish, paddlefish have an elaborate fin skeletal pattern similar to that seen in more primitive vertebrates such as sharks. This sturgeon-type fish is farm-raised for caviar, which gives scientists relatively easy access to the animal for study.

The fin of paddlefish resembles that of zebrafish. The interior arrangement is the same, but the back part of the paddlefish fin has longer elements. Accepted theory among scientists has been that the pattern of Hox gene expression seen in zebrafish represents the primitive condition for the fin in any vertebrate, and the group leading to tetrapods elaborated on this Hox expression and added to the skeletal structure.

The scientists studied the development of paddlefish fins to test whether the genes activated to make hands and feet in tetrapods were different from the genes activated to make fish fins.

This is the first molecular support for the theory that the genes to help make fingers and toes have been around for a long time—well before the 375-million-year-old *Tiktaalik roseae*, the newly found species discovered in 2004 by Shubin and colleagues. Tiktaalik provided a missing evolutionary link between fish and tetrapods and was among the first creatures to walk out of water onto land.

By examining Hox genes, scientists found that the genetic capability seen in land vertebrates to build limbs also is present in primitive fish. Illustration courtesy of M.C. Davis

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**Five-year grant aids research**

A five-year, $4.6 million grant will expand research into the causes, prevention and treatment of mental retardation and developmental disabilities. Awarded by the National Institute of Child Health and Human Development to the University of Chicago’s Joseph P. Kennedy Mental Retardation and Developmental Disabilities Center, the P01 grant will help support the work of 47 Kennedy Center biological and social scientists from the University of Chicago, Northwestern University and the University of Illinois at Chicago. The center’s researchers focus on neuroscience, model organisms, and genomics and bioinformatics with the aim of better understanding the causes of retarded development and behavioral disabilities.

**Nurses get Magna Carta status**

The American Nurses Credentialing Center (ANCC) has awarded Magnet Recognition status to the University of Chicago Medical Center. The Magnet Recognition Program, established by the ANCC in 1993, recognizes health care organizations that demonstrate excellence in nursing practice and adherence to national standards for the organization and delivery of nursing services. UCMC is now one of only 235 hospitals nationwide—fewer than 5 percent of all U.S. hospitals—designated Magnet facilities. The level of nursing care required to earn Magnet status “has been associated with direct benefits to patients,” said Jamie O’Malley, chief nursing officer at the medical center.

**Immunity, lipids connected**

A University of Chicago team found an unsuspected link in mice between the immune system and high plasma lipid levels (blood cholesterol and triglycerides). Using an assortment of engineered and non-engineered mice, they looked at the role of T cells: white blood cells that play a key role in immunity. When T cells expressing LIGHT (a specific type of molecule that binds to a receptor site of another cell) were introduced into the mice, lipid levels rose despite the mice’s dietary fat levels. However, when LIGHT signaling was blocked using an engineered protein (LTXRIg), lipid levels lowered again. The livers of mice with T cells expressing LIGHT made and secreted much less hepatic lipase (which plays a key role in lipid metabolism) and consequently had higher plasma lipid levels. The study was led by James C. Lo, an MD/PhD student in the laboratory of pathologist Yang-Xin Fu.
Prior to this find, scientists had little evidence of where the wrist came from. A popular theory, one Shubin himself subscribed to, was that it was a novel development—that genetic variance gave rise to an entirely new function.

What Tiktaalik revealed morphologically, Shubin, Davis and Dahn proved genetically.

Scientists have attacked the evolutionary quandary of limb development on two fronts: the direct evidence of the fossil record and the morphology, and its relationship with specific genetic mechanisms. What they needed, Davis said, was an animal “unmolested by time.”

“When you try to directly compare zebrafish fins and tetrapod limbs, it’s like comparing apples to oranges because each retains portions of the skeleton lost by the other,” he said. “Just as tetrapods went off and did something crazy with their fin by adding to it, zebrafish went off and did something crazy by losing part of their fin.

“So the innovation here is about a pattern of loss of gene activity [for the zebrafish] and not a pattern of acquisition [for tetrapods],” he said.

Although this pattern of genes clearly helps to make hands and feet today in tetrapods, that may not be their original intent. “Here’s a fish that doesn’t have an autopod but is still using those genes in a second phase to help pattern out a fin that doesn’t have fingers, never did, and is very far removed from tetrapods,” Shubin said.

The capability of building limbs with fingers and toes existed for a long time, but it took a set of environmental triggers to make use of that capability, he said.

According to Shubin, in the Late Devonian period, animals like Tiktaalik and its descendants acquired limbs with fingers using this primitive design largely because their ecosystem—small streams—was new.

“\[\text{Noteworthy}\]

Jean-Luc Benoit, MD, assistant professor of medicine, section of infectious diseases, won the Leonard Tow Humanism in Medicine award for his “sincere compassion and bedside manner.”

Jerry Coyne, PhD, professor of ecology and evolution, has been elected a 2007 Fellow of the American Association for the Advancement of Science.

Michelle Obama, vice president for community and external affairs, is the inaugural recipient of Ebony magazine’s Visionary Award for Community Affairs. Ebony created the award to recognize women who “intertwine their remarkable communications skills with a love and commitment to the community they serve—going above and beyond the duties of the job to make a difference in someone’s life.”

Olufunmilayo Olopade, MD, the Walter L. Palmer Distinguished Service Professor, director of the hematology/oncology fellowship program and director of the Center for Clinical Cancer Genetics, was elected to the board of the American Society of Breast Disease.

Monica Peek, MD, MPH, assistant professor of medicine, has been named to the African American National Advisory Council of Susan G. Komen for the Cure, a grassroots network of breast cancer survivors and activists.

Lou Philipson, MD, PhD, professor of medicine, received the Outstanding Scientist Award 2007 from the National Disease Research Interchange. The group recognized Philipson for his contributions to research of genetics of neonatal and monogenic diabetes subtypes.

Robert Rosenfield, MD, professor of pediatrics and medicine, was named president of the Lawson Wilkins Pediatric Endocrine Society at its meeting this past May.

Donald Steiner, MD, the A.N. Pritzker Distinguished Service Professor, received the American Diabetes Association’s Albert Renold Award at the group’s Scientific Sessions in Chicago June 25, 2007.

Michael Thirman, MD, associate professor of medicine, received a $5.25 million Specialized Center of Research (SCOR) grant to support his efforts to understand the genetic changes that cause leukemia and to use that knowledge to design precisely targeted, potent and minimally toxic therapies.

Eve Van Cauter, PhD, professor of medicine, won the 2007 Gerald D. Aurbach Award Lecture for her endocrinology research.

“It had the tools,” he said, “but it needed the opportunity as well.”

The Shubin lab has expanded its studies to see if the Hox gene expression is present in yet older common ancestors. The research team now is studying the primitive fin development of sharks.

—Catherine Gianaro
Beyond biology
In the 1990s, dubbed by Congress “the decade of the brain,” many top-tier universities—Johns Hopkins, Columbia, Berkeley, Yale and Harvard among them—gained significant recognition for their neuroscience programs.

At the same time, the National Research Council’s report of research-doctorate programs ranked neurosciences at the University of Chicago—not as an official program but based on a series of characteristics—No. 22 of 102 schools.

“The University of Chicago is famous for doing things last, but doing them exceedingly well,” said Daniel Margoliash, PhD, professor of organismal biology and anatomy. “I believe we’re poised to make major advancements in the neurosciences community.”

“No discipline is more interdisciplinary in nature than neuroscience, and so strengthening it here will serve to bind large segments of the university together in complementary and symbiotic scholarly research.”  
—University of Chicago Neurosciences Taskforce Report

Margoliash can speak with some authority on the subject. He served as co-chairman of Chicago’s neurosciences taskforce, whose findings have now yielded an official change on the academic landscape: A new Neurosciences Institute, created to increase cooperation and to improve strategic planning across the campus in basic, translational and clinical research, is now an official legal entity at the university. Though the task force has accomplished its main goal—establishing the institute—it still seeks more support and a better-unified voice and structure.

The Neurosciences Institute isn’t the university’s first brain-related organization. In 1964, the university co-founded the Brain Research Institute with the Brain Research Foundation. The former differs from the latter in that the BRI focuses solely on the most debilitating and prevalent diseases. Meanwhile, the Neurosciences Institute will be all encompassing, potentially studying anything that relates to the brain and nervous system.

A new Department of Neurobiology, dedicated to the biology of the brain and nervous system, also has been formed. Many of the faculty formerly in the Department of Neurobiology, Pharmacology & Physiology joined the new department, while others transferred to different departments. Vinay Kumar, MD, vice dean of the Biological Sciences Division, oversaw NPP faculty transitions. The new department will coordinate its efforts with the Neurosciences Institute.

“One of the enduring strengths of the University of Chicago is its embracing of interdisciplinary approaches to scholarship,” the task force wrote in its concluding report. “No discipline is more interdisciplinary in nature than neuroscience, and so strengthening it here will serve to bind large segments of the university together in complementary and symbiotic scholarly research.”

A cornerstone of the new institute is collaboration. “The University of Chicago is in a unique position to str...
The geographic integration combined with the administration’s increased support of cross-disciplinary research have helped get the new institute as far as it is today. Additional goals are to launch a neurosciences educational program, identify new research opportunities and generate a new fundraising model for the neurosciences that incorporates both existing assets and new resources. Sherman said that he sees promise in their progress, adding, “I know we can be in the top 10.”

—KSB

**Grouping chimps**

The largest study to date of genetic variation among chimpanzees has found that the traditional, geography-based sorting of chimps into three populations—western, central and eastern—is underpinned by significant genetic differences, two to three times greater than the variation between the most different human populations.

In the April 2007 issue of the journal *PLoS Genetics*, researchers from the University of Chicago, Harvard, the Broad Institute and Arizona State show that there has been very little detectable admixture between the different populations and that chimps from the central and eastern populations are more closely related to each other than they are to the western “subspecies.” They also devised a simplified set of about 30 DNA markers that zookeepers or primatologists could use to determine the origins of a chimpanzee with uncertain heritage.

“Finding such a marked difference between the three groups has important implications for conservation,” said Molly Przeworski, PhD, assistant professor of human genetics at the University of Chicago and a senior author of the study. “It means we have to protect three separate habitats, all threatened, instead of just one.”

To unravel the evolutionary history to chimpanzees, the research team collected DNA from 78 common chimpanzees and six bonobos, a separate species of chimpanzee, and examined 310 DNA markers from each.

They found four “discontinuous populations,” three of common chimps plus the bonobos. Hybrids, those with at least 5 percent of their DNA from more than one common chimpanzee population, were rare. Most of the hybrid chimps were born in captivity.

“We saw little evidence of migration between groups in the wild,” said Celine Becquet, first author of the paper and a graduate student in Przeworski’s laboratory. “Part of that could stem from the gaps in our samples, but we think most of this separation is genuine, a long-term consequence of geographic isolation.”

The original boundaries between groups may have been the emergence and growth of rivers, such as the Congo River, which is thought to be about 1.5 million years old. “Chimps don’t swim,” Becquet said. “For them, water provides a very effective border.” Ongoing loss of habitat has increased the physical separation between the three groups.

The extent of accumulated genetic difference enabled the researchers to speculate about when the different populations separated. They estimate that bonobos, which live south of the Congo River, split off from the ancestors of modern chimpanzees about 800,000 years ago. Western chimps appear to have separated from central and eastern chimpanzees about 500,000 years ago and central and eastern chimps divided about 250,000 years ago.

“Even though the chimp genome has been sequenced, it’s amazing how little we know about their evolution and the level of variation within chimpanzees,” Przeworski said. “These are our nearest relatives, closer to humans than they are to gorillas, yet we know so little about them, and even less about gorillas and orangutans.”

The chimpanzee genome differs from the bonobo genome by about 0.3 percent, which is one-fourth the distance between humans and chimps. Yet chimps and bonobos have radically different social systems, cultures, diets and mating systems.

On the other hand, in this study, looking at three “subspecies” of common chimpanzees, “we found significant genetic variation,” said Przeworski, “but there’s very little detectable difference between the populations in terms of appearance or behavior.”

—JE
This book fills a need for evidence-based treatment guidelines for adolescent bulimia. Its authors apply the principles of the Maudsley approach to treating anorexia, demonstrated effective in a controlled clinical trial at the University of Chicago. They review current knowledge on bulimia and its treatment, compare and contrast it to anorexia, and discuss the adaptation of the Maudsley approach to meet the unique needs of this population. They also walk clinicans through three recommended phases of therapy, offering workable strategies for involving families in treatment. Co-author Le Grange is associate professor of psychiatry and director of the eating disorders program at the University of Chicago.

The JNK Signaling Pathway
Anning Lin, PhD, ed. Landes Bioscience, 2006

Authors from various biomedical disciplines review the c-Jun amino-terminal kinases (JNKs) pathway—one by which membranes transmit signals to the nucleus to change cell function. Chapters range from pathway discovery to its use as a therapeutic target, focusing on biological function, physiological roles of JNKs and the signal transduction pathway in Drosophilia. Lin is a professor in the Ben May Department for Cancer Research at the University of Chicago.

The Chicago River: A History in Photographs
Jonathan Genzen, PhD ‘02, MD ‘04 Westcliff Publishers, 2007

Genzen, who kayaks the Chicago River regularly, takes readers on a pictorial journey that begins before the river’s birth, during a time 400 million years ago when an ocean submerged all of present-day Chicago. Continents shifted, glaciers melted and eventually the Chicago River evolved into a severely polluted waterway. By the mid-1800s, a city of 12,000 was forming along its banks, and with it came sewage from inhabitants and stockyards. Through photographs and illustrations, readers see the Great Chicago Fire, follow construction of channels and bridges, bear witness to the Eastland disaster and learn about the sanitation of the river. They also look at Chicago’s present-day skyline.

Difficult Decisions in Thoracic Surgery: An Evidence-Based Approach
Mark K. Ferguson, MD, ed. Springer, 2006

A resource for surgeons in training, educators and practicing surgeons, this text goes beyond customary care to describe a recommended, ideal approach to thoracic surgery. Its authors analyze questions according to the level of supporting evidence available, offering readers both evidence- and experience-based recommendations and descriptions of surgeons’ personal practices and published literature. The book also reviews available evidence and offers a general discussion of recommended practice. Ferguson is professor of surgery at the University of Chicago.

Chronic Rhinosinusitis: Clinical Patterns of Illness and Medical Management
Daniel Hamilos, MD, and Fuad Baroody, MD, eds. Informa Health Care USA, 2007

Written for allergists, otolaryngologists, immunologists and residents, this text is a comprehensive, interdisciplinary reference. It includes recommendations for optimal treatment for chronic rhinosinusitis, an ailment that affects about 31 million Americans annually. The authors explore advances in the understanding of the pathophysiology of the diseases, diagnostic tools for the assessment of chronic rhinosinusitis and pathways for new research in the field, and summarize published studies of chronic rhinosinusitis management. Baroody is associate professor of surgery and director of pediatric otolaryngology at the University of Chicago.

Reluctant Warriors: Israelis Suspended Between Rome and Jerusalem
Nathan Szajnberg, MD ‘74 Xlibris Corporation, 2006

These are stories about the courage and humility of elite combat soldiers in a democratic society: soldiers who were born in kibbutz and bred in battle. “My work is a kind of soul spelunking, exploring carefully in dark caves, prodding gently, following caverns to see where they lead,” Szajnberg wrote about his subjects—the last cohort from the communal child-rearing kibbutz who have faced the Intifada as soldiers only to return to civilian life in Israel. Szajnberg offers a map of these young men’s struggles to come to terms with the roles of humane citizen versus effective soldier. A clinical professor of psychiatry at the University of California School of Medicine, Szajnberg addresses the question of how to facilitate the transition from the adolescent task of establishing intimacy and isolation. Born in a German D.P. (displaced persons) camp in 1949, Szajnberg studied with Bruno Bettelheim and Saul Bellow while at the University of Chicago. He is the Wallerstein Research Fellow in psychoanalysis, and now lives in Jerusalem.

Pediatric Examinations & Board Review (McGraw-Hill Specialty Board Review Series)
Robert Daum, MD, and Jason Canell, MD McGraw-Hill, 2006

Those preparing for certification and re-certification (especially for the USMLE3) will find this text helpful. Daum and Canell take a case-based, step-by-step approach that covers the best cases and best questions that comprise the most comprehensive review for pediatric examinations and boards. They cover all recent advances of clinical importance. Included are more than 1,000 board-style questions with detailed explanations for correct or incorrect answers, progressive cases with additional clinical information revealed after the initial question-sets, color photographs that illustrate dermatologic and ophthalmic conditions, and coverage of developments in such areas as genetics, infectious diseases and oncology. Co-author Daum is professor of pediatrics at the University of Chicago.