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News from the UPMC Department of Orthopaedic Surgery

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Limb Lengthening and Reconstruction Center Treats Complex Orthopaedic Problems

The Limb Lengthening and Reconstruction Center (LLRC) at the UPMC Department of Orthopaedic Surgery provides innovative treatment of complex orthopaedic problems and showcases the latest in orthopaedic technology.

Figure 1. Patient undergoing cosmetic bilateral tibia lengthening for height increase.

The LLRC was founded by Anton Plakseychuk, MD, PhD, who first brought Soviet-born Professor Gavriil A. Ilizarov's limb-lengthening techniques to UPMC in 1995. Dr. Plakseychuk worked under guidance of Prof. Ilizarov in Russia, and for the past 20 years has dedicated his career to improving the lives of patients with limb disorders. He has performed many thousands of limb reconstruction surgeries and developed some of the most advanced surgical methods for limb lengthening and deformity correction for children and adults with upper and lower limb-length discrepancies, limb deformities, nonunions, bone defects, bone infections, joint contractures, foot deformities, and short stature. The LLRC provides limb lengthening for variety of medical problems, as well as for cosmetic height increase, and also offeres innovative treatments for Perthes disease, avascular necrosis, and hip dysplasia, including arthroscopic labral and impingement repair, as well as resurfacing and joint replacement.

Limb Lengthening: How Does It Work?

Limb lengthening has been performed successfully for about 50 years in Kurgan, Russia. Prof. Ilizarov initially developed the process, which works on the principle of distraction osteogenesis. This was a revolutionary concept that reversed the long-held belief that bone cannot be regenerated. In the process, a bone that has been cut during surgery can be gradually distracted, leading to new bone formation (osteogenesis) at the site of the lengthening. Bone and soft tissue regenerate when they are pulled apart at a very slow rate of approximately 1 mm per day. In this way, bone segments can be lengthened by 1 to 5 inches (Figure 1). There are many different lengthening devices used. The most common are external fixators, which are devices that attach to the bone by means of thin wires or thicker pins that have a screw threading at their attachment to the bone. When only an external fixator is used, the fixator needs to remain in place for both the distraction and consolidation phases. The total time in the external fixator is approximately one month for each centimeter of lengthening in children and 1.5 months per centimeter in adults (Figure 2a–2d, Page 2).

The original process was very reliable, but was lengthy and difficult for the patients. In order to shorten treatment, automatic distraction was developed. Instead of manual

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lengthening by 1 mm a day, small motors lengthen the bone up to 60 times a day, enabling a gain of 2 to 3 mm a day, thus reducing the total time of treatment. Also, to decrease the external fixator treatment time, a new technique was developed, called lengthening over nail (LON). With LON, a metal rod is inserted into the bone and the external fixator removed when the required lengthening has been achieved. The total external fixation treatment time is reduced by a factor of three. The most recent development is a fully implantable device that can lengthen the limb from within, without the need for an external fixator (Figure 3, Page 5). This has many advantages, including no risk of pin infection, no muscle tethering by the pins, less pain, and better comfort. This method is mostly used in skeletally mature children and adults.

Ilizarov Method in Fracture Care

When Prof. Ilizarov developed his method, his goals were to stabilize long-bone fractures and improve treatment of malunions and nonunions. Many years later, Ilizarov frames continue to be the best devices for the treatment of the most complicated fractures of the distal femur, proximal and distal tibia, and calcaneus. Dr. Plakseychuk has developed a new technique for the treatment of intra-articular fractures of the lower extremity with questionable soft tissue integrity by utilizing a new arrangement of an Ilizarov frame in combination with a mini-open reduction technique. The Ilizarov fixator, by virtue of its use of percutaneous small diameter wires, does not violate the soft tissues, and the use of olive wires helps to reduce the major fracture fragments. Patients are allowed to bear weight almost immediately after surgery, and at the end of treatment all metal is removed from the extremity in the office setting. Prospective study of Ilizarov treatment of complex tibial pilon fractures is under way, with more than 100 patients treated with great success at LLRC. Dr. Plakseychuk utilizes the Ilizarov method in most complex trauma cases. He introduced the two-stage technique of Ilizarov frame application for bone transport and simultaneous free-flap coverage. Simultaneous flap coverage and bone transport shortens a patient's total hospitalization time, reduces the number of surgeries, and shortens consolidation time.

Reconstructive Surgery

Another clinical avenue for the LLRC is the development of new techniques for total hip replacement, hip resurfacing, and arthroscopic hip surgery. The direct anterior approach (DAA) to hip replacement was introduced to the United States by Dr. Joel Matta in 1996, as tissue-sparing surgery. The DAA enables the surgeon to reach the hip joint from the front of the hip, as opposed to the lateral or the posterior approach. The DAA is the only approach that is both internervous and intermuscular, so the surgeon can simply work through the natural interval between the muscles and replace the hip with minimal trauma. Conventional lateral or posterior surgery typically requires strict precautions for patients. They must limit the flexing of the hip to no more than 90 degrees, which complicates normal activities such as sitting in a chair, putting on shoes, or getting into a car. DAA hip replacement allows patients to immediately bend their hip freely and bear full weight when comfortable,

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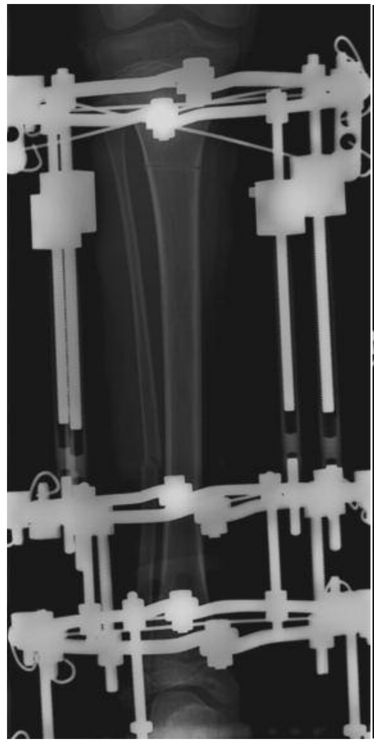

Figure 2a — Day of surgery (July 5).

Figure 2b — Lengthening in progress (July 27).

Figure 2c — 5 cm of lengthening (Aug. 27).

Figure 2d — Day of frame removal; new bone is mature (Nov. 12).

A Useful Genetic Mouse Model to Explore How Aging Contributes to Intervertebral Disk Degeneration

One could argue that back pain is a biological phenomenon that owes its existence to an epic evolutionary explosion that occurred during the Cambrian period over half a billion years ago. It was during this geological time that a group of organisms diversified by adding a new body part — a spinal column running the length of their bodies. The vertebrates have since evolved into various living forms, including fish, amphibians, reptiles, birds, and mammals. While the spine imparts greater mobility and strength, this body part unfortunately also gives its owner considerable grief when it fails. This is most evident among the humans, which might be a result of inferior "design" of our spine or high axial loads because of our bipedal nature. Whatever the reasons, spinal disorders and associated back pain are particularly widespread among people living in highly developed countries. Back pain is responsible for an estimated 149 million lost work days and an overall economic loss of $90 billion each year in the United States alone. Hence, back pain is a major public health concern with long-term socioeconomic consequences.

Low back pain is often diskogenic and associated with intervertebral disk degeneration (IDD). Situated between the bony vertebrae, intervertebral disks (IVDs) are elastic pads that provide support and flexibility to the otherwise rigid vertebral column. IVDs consist of the annulus fibrosus (AF) surrounding the central nucleus pulposus (NP). AF tissue, composed of highly organized lamellae or sheets of collagen fibrils, functions primarily to bear tensile forces generated during bending or twisting. NP tissue, on the other hand, serves to counteract compressive loads and is made up of loosely organized networks of collagen type II and elastin fibers that enclose a gel-like substance of proteoglycan and water. IVDs are built to withstand continuous compressive pressure and tensile forces years on end. For example, a lumbar disk two inches in diameter in a 150-lb. person is subjected to a weight of about 220 lbs. of compression if he stands still, and 450 to 750 lbs. if he runs or lifts. This is in addition to the constant shears and torsion stresses of normal living activities. The lumbar disks of an individual surviving 50 years of adulthood would have endured continual mechanical pounding for 300,000 hours, sleeping time not included. In light of such persistent physical assault, it is not shocking that this marvelous biological structure experiences occasional breakdowns.

The etiology of IDD is complex and the causes unclear; however, aging clearly plays a key role, because the incidence of disk degeneration markedly increases with age. Aging of biological structures, not unlike that of man-made structures such as bridges and buildings, comes about as a result of time-dependent accumulation of stochastic damage to cellular macromolecules. Damaged DNA, unlike damaged proteins or other macromolecules that generally can be degraded and replaced by new synthesis, is particularly harmful and requires repair in order to maintain normal cellular function. Each cell in an organism is subjected to tens of thousands of individual DNA lesions each day due to the inherent chemical instability of DNA structure, metabolic byproducts, and environmental exposure to tobacco smoke, UV light, radiation, and so forth. Cells, as a consequence, have evolved elaborate mechanisms to repair DNA damage, but even so, they still amass DNA damage over time due to incomplete or imperfect repair. Accumulation of DNA damage is a major driving force behind aging, evidenced by the fact that inherited defects in DNA genome maintenance mechanisms invariably lead to a variety of diseases characterized by accelerated aging of one or more organ systems. For example, deficiency in humans of certain genes involved in repair of DNA damage, such as ERCC1-XPF, leads to dramatic progeroid, or accelerated aging, symptoms.

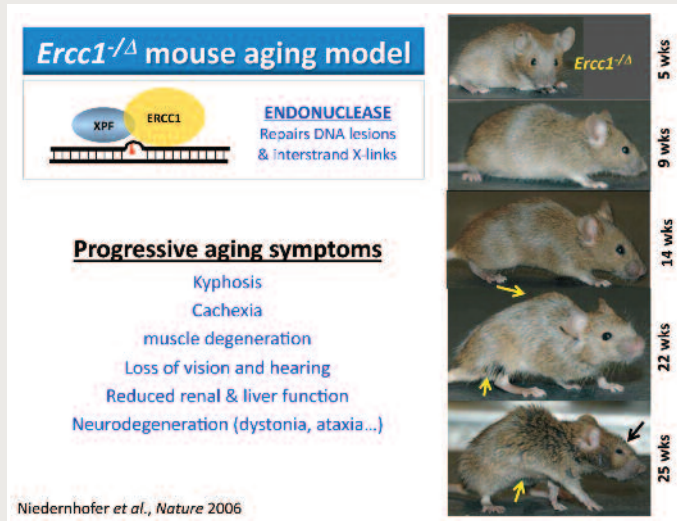

Figure 1

Significant progress has been made in intervertebral disk research using animal models. However, there are currently no rapid models of IDD for analysis of the age-dependent biologic changes in the disks or for determining how aging induces these changes. The sand rat and chondrodystrophoid dog represent spontaneous models of IDD, but have undefined genetic causes. Thus, the availability of small economical animal models of age-associated IDD would guide the development of effective therapeutics to improve the health of disks in aged individuals. Laura Niedernhofer, a faculty member of UPMC's Hillman Cancer Center and the Department of Microbiology and Molecular Genetics, has together with her co-workers created a mouse strain modeled after human progeria by deleting the gene ERCC1. Without ERCC1, a key

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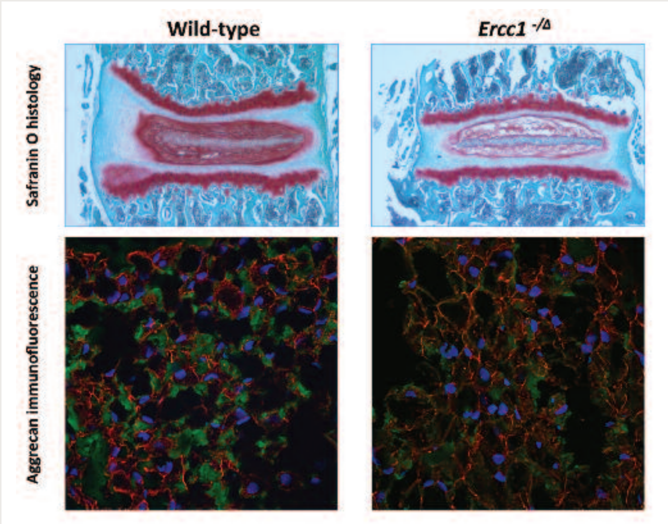

Figure 2

component of the cellular DNA repair machinery, the mice age rapidly and exhibit a number of age-related pathologies, including epidermal atrophy, visual impairment, cerebellar degeneration, renal insufficiency, decreased liver function, osteoporosis, cachexia, and others (Figure 1). Compared to their wild-type counterparts, which have an average lifespan of 2.5 to 3 years, the progeroid ERCC1-deficient mice have a much shorter lifespan (4 to 25 weeks, depending on the types of ERCC1 deletion) but still mimic natural aging, as confirmed by various comparative profiling techniques. These features make the ERCC1-deficient mice an exceptionally useful model to explore and dissect the many complex biochemical processes of aging in a much shorter time period, saving vital research time and money.

The Ferguson Laboratory for Orthopaedic and Spine Research has been investigating the molecular and cellular processes of age-dependent disk degeneration using the ERCC1-deficient mice in collaboration with Dr. Niedernhofer. ERCC1-deficient mice offer several advantages as a model for human disk aging, because the molecular machineries responsible for many aging processes are highly conserved between the two species, allowing extrapolation from mouse to human. Mouse lumbar disks were recently demonstrated to be proportionally and geometrically most similar to human disks among the tested animal models. Mouse lumbar motion segments also exhibit mechanical properties, such as compression and torsion stiffness, similar to those of humans, providing further validation for the mouse disk as a mechanical model of the human disk. Other obvious benefits of using mice include the availability of commercial research reagents and well-established methods, and mouse genome and genetic resources and extensive biologic literature. The genetic purity of laboratory-bred mice and the controlled environment in which they are housed also eliminates the experimental variability that has plagued intervertebral research using human specimens, where normal tissue availability is limited and genetics and environmental factors cannot be controlled.

Recent research from the Ferguson Laboratory revealed that ERCC1-deficient mice also undergo accelerated progression of IDD similar to that seen in naturally aged mice, including reduced disk height, disk matrix loss, and apoptosis (Figure 2). Therefore, the mouse model of human progeria could represent a model of rapid, progressive, age-dependent IDD that is potentially useful for exploring disk-aging mechanisms and therapeutic testing. The timely arrival of this new model complements the previously established rabbit disk injury-induced model of IDD in the Ferguson Laboratory. These models, along with other existing research tools developed in the Ferguson Laboratory, are vital to the Ferguson research program. Under the strong leadership of its director, Dr. James Kang, and co-director, Dr. Gwen Sowa, that program encompasses several distinct but related areas of interest: biology of disk degeneration, mechanobiology, biomechanics, and gene- and cell-based therapy, all directed toward the mission of understanding the basic science behind disk degeneration and developing therapeutic strategies to treat it.

The biology of disk degeneration group, led by Dr. Nam Vo, Dr. Rebecca Studer (who recently retired after a long and productive career), and Dr. Joon Lee, aims at dissecting the molecular pathways involved in disk aging and injury-associated inflammation to identify potential molecular therapeutic targets. Dr. Sowa is leading the effort in the mechanobiology group to explore the effects of time, magnitude, and frequency of mechanical forces on disk cell matrix homeostasis, with the goal of defining the mechanical forces experienced by disk cells in vitro and how they relate to motion-based exercise therapy and rehabilitation. Kevin Bell directs the biomechanics research using a robot-based spinal in vitro testing system, as well as a virtual-reality-controlled cervical kinematics system for in vivo studies. The knowledge derived from these areas of basic research is being used to guide our effort to test and develop gene- and cell-based therapies to treat disk degeneration, an endeavor initiated more than 10 years ago by Dr. James Kang. Obviously, none of these exciting research endeavors would be possible without the Ferguson team of dedicated and talented technicians, students, residents, postdoctoral fellows, administrators, and the unwavering support from the Department of Orthopaedic Surgery and its chairman, Dr. Freddie Fu.

The multidisciplinary nature of the Ferguson research program also has spurred a large and growing number of productive collaborations within the Department and beyond. In a fertile UPMC research environment, the Ferguson team is favorably poised to tackle the challenges of spine research, understanding its structure and function, how it breaks down, and how to fix it.

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resulting in a more rapid return to normal function. After surgery, patients are instructed to use their hip normally without cumbersome restrictions. Dr. Plakseychuk has advanced the technique even further by performing surgery in the lateral position on a special surgical table, enabling him to perform the replacement through a 4-to-5-inch incision without muscle detachment or trauma. Dr. Plakseychuk has performed more than 200 DAA hip replacements since 2008, when the improved technique was developed.

Hip resurfacing (HR) is an important alternative to total hip replacement, and has been performed at the LLRC since 2008. After resurfacing, patients have virtually no athletic limitations. HR is intended for younger, active adults who are under 60 years of age and in need of a hip replacement. Adults over 60 who are living nonsedentary lifestyles also may be considered for this procedure. Small-framed women and women of childbearing age should not be considered for this procedure. The ideal candidate would be an active, middle-aged man intent on returning to sports like running or to heavy labor. The potential advantages of HR include less bone removal (bone preservation), a reduced possibility of future hip dislocations thanks to the relatively larger femoral head size, and a potentially easier subsequent total hip replacement because a surgeon could have more bone stock available with which to work.

Traditional HR techniques involve operating through the posterior approach to the hip, which requires a significant disturbance of the blood supply to the femoral head and an incision approximately 8 to 12 inches long. Dr. Plakseychuk prefers using an anterolateral approach to preserve the blood supply to the femoral head. He also is working on the development of a direct anterior approach to HR, involving an incision of only 5 to 6 inches in length, which would allow for a more natural return to normal function and activity.

Hip arthroscopy is a cutting-edge technology utilized at LLRC for the treatment of young patients with soft tissue injury to the hip and mechanical problems, such as femoro-acetabular impingement (FAI). An area of future research for the LLRC is the development of a computer-assisted optical tracking system for the arthroscopic reshaping of the hip in the treatment of FAI and Perthes disease. ■

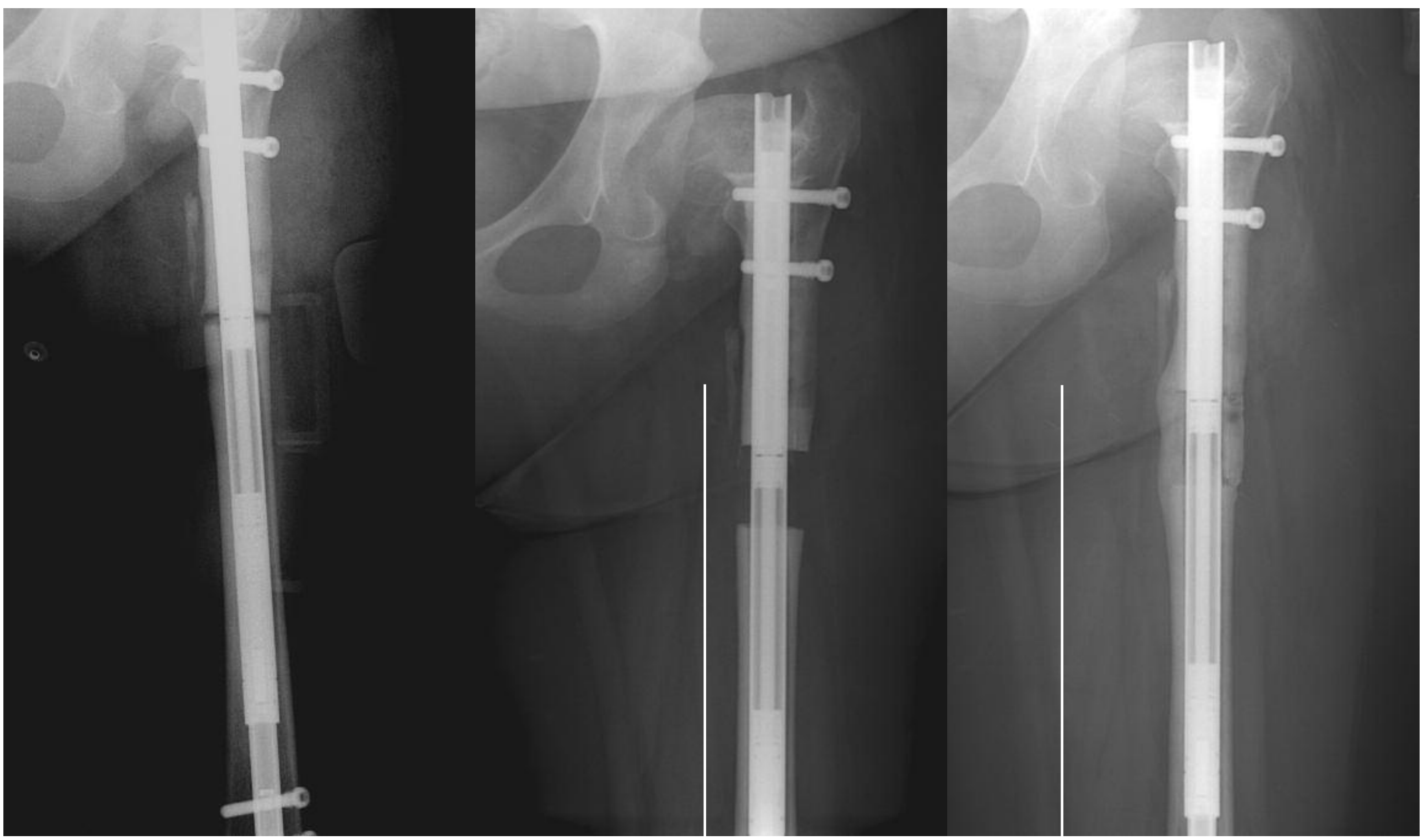

Figure 3. Patient undergoing femur lengthening with ISKD implantable device.

Department Briefs

UPMC Honored by *U.S. News & World Report*

UPMC is ranked No. 8 for orthopaedic surgery in the 2010 *U.S. News & World Report* "America's Best Hospitals" survey. This is the highest ranking ever achieved by UPMC for orthopaedic surgery in this annual survey.

Department Featured in Two Prestigious Journals

The outstanding, 100-year history of the Department was featured in the January 2010 issue of *Orthopaedics Today*. The article highlighted the fact that in its entire history, the Department has only had five chairmen, and has trained dozens of top leaders who have gone on to lead other strong orthopaedic programs across the country.

Dr. Freddie H. Fu's American Orthopaedic Society for Sports Medicine (AOSSM) presidential address, "Credibility, Integrity, and the Terrible Towel," was featured in the December 2009 issue of the *American Journal of Sports Medicine*. This address was initially presented to more than 1,000 people at the 35th annual meeting of the AOSSM. The address focuses on the three values of credibility, integrity, and giving back, which provide the foundation on which to build a profession.

Faculty Appointments and Promotions

The Department of Orthopaedic Surgery is pleased to welcome the following new faculty members:

James Roach, MD, professor of orthopaedic surgery. Dr. Roach received his medical degree from Duke University and completed his orthopaedic residency at Tripler Army Medical Center. Dr. Roach most recently served as chief of staff for Shriners Hospital in Salt Lake City, Utah. He is the current president of the Pediatric Orthopaedic Society of North America.

Lisa Blackrick, MD, assistant professor of orthopaedic surgery. Dr. Blackrick received her medical degree from Case Western Reserve University. She completed a residency in orthopaedic surgery at UPMC and a fellowship in orthopaedic trauma at Case Western.

Patrick Bosch, MD, assistant professor of orthopaedic surgery. Dr. Bosch received his medical degree from the University of Iowa College of Medicine. He completed a residency in orthopaedic surgery at UPMC and a pediatric orthopaedic fellowship at Starship Hospital in Auckland, New Zealand.

Anthony Kontos, PhD, assistant professor of orthopaedic surgery. Dr. Kontos received his doctorate from Michigan State University. He will participate in concussion research.

Kurt Weiss, MD, assistant professor of orthopaedic surgery. Dr. Weiss received his medical degree from Jefferson Medical College of Thomas Jefferson University. He completed a residency in orthopaedic surgery at UPMC and a musculoskeletal oncology fellowship at the University of Toronto.

Eric Johnson, PsyD, instructor of orthopaedic surgery. Dr. Johnson received his doctorate from the Arizona School of Professional Psychology at Argosy University. He also completed a two-year, postdoctoral fellowship with the UPMC Sports Medicine Concussion Program.

Other faculty announcements and promotions:

Freddie H. Fu, MD, David Silver Professor and chairman, has been appointed by the University of Pittsburgh to the rank of Distinguished Service Professor. This appointment is the highest honor that the University can bestow on a faculty member for distinguished service to the University, as well as performance excellence and national stature in his field. Only seven other University of Pittsburgh School of Medicine faculty members have received this honor, and Dr. Fu is the first Distinguished Service Professor in the Department of Orthopaedic Surgery.

Rocky S. Tuan, PhD, has been appointed professor of orthopaedic surgery with tenure and also has been appointed to the Arthur J. Rooney Sr. Chair in Sports Medicine. Dr. Tuan serves as the Department's executive vice chairman for Orthopaedic Research and director of the Center for Cellular and Molecular Engineering.

Constance R. Chu, MD, has been promoted to professor with tenure. Dr. Chu also holds the Albert B. Ferguson Jr. Endowed Chair in Orthopaedic Surgery.

Jianying Zhang, PhD, has been promoted to research assistant professor. Dr. Zhang is a member of the Mechanobiology Laboratory.

Faculty Notes

Lance Brunton, MD, and ***Susan S. Jordan, MD,*** both assistant professors of orthopaedic surgery, have been accepted to participate in the U.S. Bone and Joint Decade's Young Investigators Initiative Fall 2010 Workshop in Toronto.

Constance R. Chu, MD, professor of orthopaedic surgery and Albert B. Ferguson Jr. Endowed Chair in Orthopaedic Surgery, was featured in a *Wall Street Journal* article entitled, "The Latest Front in the War on Arthritis," by Shirley S. Wang. She also was featured in a *New York Times* article, "Phys Ed: What Causes Early Arthritis in Knees?" by Tara Parker-Pope. Dr. Chu is researching better ways for surgeons to treat cartilage damage in humans.

Freddie H. Fu, MD, Christopher Harner, MD, and ***James Kang, MD,*** are among the first class of Achievement Award winners of the American Academy of Orthopaedic Surgeons (AAOS), for their dedicated volunteer work. The AAOS established the Achievement Award program to encourage and enhance individual growth of academy members, and to thank them for their many contributions to education, research, and advocacy in orthopaedics.

Indiana University School of Medicine also has awarded ***Dr. Freddie Fu*** the 2010 Mark Brothers of South Bend Lectureship Award, which recognizes nationally and internationally renowned medical scientists of Asian descent. Previous recipients of this prestigious award include AIDS researcher Dr. David D. Ho, CEO and professor of the Aaron Diamond AIDS Research Center at The Rockefeller University.

Christopher Harner, MD, is the newly appointed secretary of the prestigious sports medicine organization, the Herodicus Society. Following his term as secretary, he will serve as vice president and then president.

Johnny Huard, PhD, Henry J. Mankin Professor and vice chair for Musculoskeletal Cellular Therapeutics, has been invited to become a member of the College of CSR Reviewers for a two-year period. Dr. Huard recently completed service as a standing member of the Center for Scientific Review (CSR) for the Skeletal Muscle and Exercise Physiology Study Section from 2006 to 2009.

Robert Kaufmann, MD, assistant professor of orthopaedic surgery, has been named associate editor for the Review/Technique section of the A*merican Journal of Hand Surgery*.

Congratulations are extended to ***Marc Philippon, MD,*** adjunct associate professor of orthopaedic surgery, on the newly renamed Steadman Philippon Research Institute in Vail, Colorado. Dr. Philippon is known worldwide in sports for innovative contributions to the treatment and rehabilitation of hip injuries. Dr. Philippon was a full-time faculty member with the Department until 2005 before moving to Vail.

Ivan Tarkin, MD, assistant professor of orthopaedic surgery, and chief of the Division of Orthopaedic Traumatology, was elected as an active member of the Orthopaedic Trauma Association (OTA).

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