

## Department Briefs

### UPMC Again in U.S. News & World Report Top 10 Rankings

UPMC is ranked No. 10 in the country for orthopaedic surgery in the 2009 *U.S. News & World Report* ranking of hospital clinical specialties — UPMC's second straight year in the top 10. In the overall "Best Hospitals" rankings, UPMC again has been named to the Honor Roll, with a ranking of number 13 in the country. Only 174 hospitals of the more than 4,800 eligible hospitals nationally were ranked in any specialty area. UPMC is ranked in 13 of 16 specialty areas, and seven specialties are in the top 10.

### 100th Anniversary Bone Bash

The Department celebrated its 100th anniversary recently with a "Bone Bash" gala in Pittsburgh sponsored by the Arthritis Foundation of Western Pennsylvania. More than 450 guests, including many former alumni, attended the event. **Dr. Albert Ferguson** (chairman, 1953-1986) was present and was recognized by **Dr. Freddie Fu** for his many contributions to the Department. Dr. Fu was honored by the Arthritis Foundation for his service to orthopaedic surgery.

### Health Affairs Editor Presents Grand Rounds at UPMC

The Department recently hosted Susan Dentzer, editor of *Health Affairs* and one of the nation's most respected health policy experts, who presented at the Department's grand rounds. Ms. Dentzer's topic of discussion was "The Obama Administration, the 111th Congress, and Health Care Reform." Ms. Dentzer has been inducted as a member of the Institute of Medicine, the highest honor for a health care journalist. Her article, "Communicating Medical News — Pitfalls of Health Care Journalism," was the lead article in the January 2009 issue of *The New England Journal of Medicine*.

### Welcome New Faculty Members

The UPMC Department of Orthopaedic Surgery is pleased to welcome:

**Lance Brunton, MD**, assistant professor of orthopaedic surgery. Dr. Brunton specializes in hand and upper extremity. He received his medical degree from the University of Pittsburgh and completed a residency in orthopaedic surgery at the University of Virginia Health System and a fellowship in hand, upper extremity, and microvascular surgery at the Curtis National Hand Center in Baltimore.

**Volker Musahl, MD**, assistant professor of orthopaedic surgery. Dr. Musahl specializes in sports medicine. He received his medical degree from Albert Ludwig University of Freiburg in Germany, and completed a residency in orthopaedic surgery at the University of Pittsburgh and a sports medicine and shoulder fellowship at the Hospital for Special Surgery in New York City.

**Peter Siska, MD**, assistant professor of orthopaedic surgery. Dr. Siska joins the Department as a specialist in orthopaedic trauma and joint reconstruction. He received his medical degree from the University of Cincinnati College of Medicine, and completed a residency in orthopaedic surgery and a fellowship in orthopaedic trauma at UPMC.

**Juan Taboas, PhD**, research assistant professor. Dr. Taboas received master's degrees in engineering from Stanford University and the University of Michigan, and his PhD in biomedical engineering from Michigan. He will work in the Department's Center for Cellular and Molecular Engineering.

### Faculty Promotions/Appointments

The Department has announced the following promotions: **Arvydas Usas, PhD**, to research assistant professor; **Nam Vo, PhD**, to assistant professor; and **Robin V. West, MD**, to associate professor. **Dane Wukich, MD**, has been appointed assistant residency director. **Ivan Tarkin, MD**, has been appointed division chief, Orthopaedic Traumatology.

### Faculty Notes

**Constance R. Chu, MD**, Albert B. Ferguson Jr., MD, Endowed Chair and vice chairman for Translational Research, has been awarded a National Institutes of Health Grand Opportunities Grant (GO) in the amount of \$1.7 million for her project, "Multicenter Cartilage Repair Preclinical Trial in Horses." It is a collaborative study with Cornell, Colorado State, and the University of California at San Diego to perform the preclinical studies needed to evaluate the suitability of new cartilage repair strategies for human clinical trials.

**Freddie H. Fu, MD**, professor and chairman, was invited by Dr. José Neves, president of the Portuguese Society of Orthopaedics and Traumatology (SPOT), to give the keynote lecture on the anatomic approach to anterior cruciate ligament (ACL) reconstruction at a round table event attended by more than 500 people, including leading orthopaedic surgeons from Brazil, Portugal, and Spain.

**Christopher Harner, MD**, Blue Cross of Western Pennsylvania Professor and medical director, UPMC Center for Sports Medicine, was the keynote speaker at the 2009 Sports Knee Surgery Conference at the University of Warwick in England. Dr. Harner was invited by the University of Warwick Department of Orthopaedics and its division chief, Dr. Tim Spalding. Approximately 125 experienced knee surgeons from the United Kingdom attended the conference. Dr. Harner addressed numerous topics, including ACL and posterior cruciate ligament reconstruction, medial meniscal root tears, meniscal transplantation, and complex revision ACL surgery.

**Rocky S. Tuan, PhD**, visiting professor and executive vice chairman for research, and director of the Center for Cellular and Molecular Engineering, recently joined the Department from the National Institutes of Health, as reported in the last issue of *Restore*. Dr. Tuan spoke this fall on stem cells, regenerative medicine, and orthopaedic science topics at the Fondazione Ri.MED Symposium in Palermo, Italy; the Formosa Association for Regenerative Medicine in Taipei, Taiwan; the Taiwan Orthopaedic Association in Taipei; and the World Congress of Regenerative Medicine in Leipzig, Germany.

**Barrett Woods, MD**, orthopaedic surgery resident, was selected as a *Pittsburgh* magazine and Pittsburgh Urban Magnet Project (PUMP) "40 Under 40" honoree. The program recognizes people under the age of 40 who have had a positive impact on Pittsburgh and have improved the image of the region. Over the past nine years, a wide variety of people have been honored, from corporate CEOs to nonprofit volunteers. Dr. Woods was honored for his community work in the Homewood and Lincoln-Lemington neighborhoods.

**Vonda Wright, MD**, assistant professor of orthopaedic surgery and director of the UPMC Center for Sports Medicine's programs for masters athletes, was elected to the International Council on Active Aging (ICAA) visioning board. ICAA supports professionals who develop wellness and fitness facilities and services for aging adults. The visioning board will drive ICAA 2020, an initiative to create a vision for the future of older people.

### In This Issue

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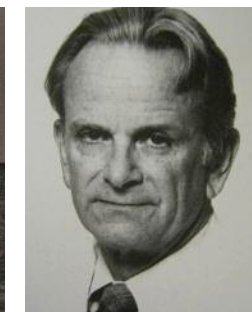
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Department Briefs

## 50 Years of Cartilage Research in Pittsburgh



Dr. Henry Mankin



Dr. William Green Jr.



Dr. Christopher Evans

Since its founding, the Department of Orthopaedic Surgery has been leading orthopaedic research in many different fields. Cartilage research is one of the fields in which the Department has been a pioneer since the creation of the Ferguson Laboratory more than 50 years ago. Many marvelous scientists and clinicians have worked here and conducted extraordinary research that still impacts cartilage research today.

### Pioneers in Tissue Engineering

Cartilage lacks regenerative capacity when compared to tissues such as bone and muscle. In the 1950s, it was not clear whether chondrocytes can divide, and how they obtain nutrition, because there are no blood vessels in cartilage. Dr. Thomas Brower, who joined the Department in 1955, was the first to show that both epiphyseal and articular cartilage chondrocytes can divide, although epiphyseal chondrocytes are younger and must have a more active metabolic rate than chondrocytes of articular cartilage. Dr. Brower also showed that the nutritional support of articular cartilage is through perfusion of intra-articular fluid, instead of through the blood vessels from the epiphysis.

Dr. Henry Mankin came to the Department in 1960, and with him the tritiated thymidine labeling method. Following the findings of Dr. Brower, Dr. Mankin investigated the mitosis of articular cartilage by injecting tritiated thymidine into a joint as a tool for the qualitative demonstration of cellular reproduction. He showed that articular cartilage appears to respond to trauma in a manner identical to the response of most other body tissues, with one major exception: the lack of vascular response of inflammation. In his study from 1964, Dr. Mankin was able to show that adult articular cartilage may continue growing, although the growth rate may be very slow. Moreover, the percentage of mitotic cells in articular cartilage was higher in newborns than in older immature



Freddie H. Fu, MD,  
DSc (Hon), DPs (Hon)  
Chairman

### Centers of Excellence

- Adult Reconstructive Surgery and Musculoskeletal Oncology
- Concussion
- Foot and Ankle Surgery
- Hand, Upper Extremity, and Microvascular Surgery
- Orthopaedic Trauma
- Pediatric Orthopaedics
- Research
  - Biomedical
  - Clinical Outcomes
  - Computer-assisted Surgery
  - Kinematics
  - Regenerative Medicine
  - Stem Cell
- Spinal Surgery
- Sports Medicine and Shoulder Surgery

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rabbits. In 1966, Dr. Mankin and his colleagues were the first to show that the intra-articular injection of cortisol caused a rapid and profound decrease of cartilage matrix synthesis with low recovery, that is, three days for lower doses and two weeks for larger doses. This breakthrough study was the basis for many studies that focus on the cytotoxicity of several drugs. Dr. Mankin also instructed the longest-standing Instructional Course Lecture (ICL) at the American Academy of Orthopaedic Surgeons (AAOS) annual meeting on articular cartilage. This ICL was offered for 29 years.

Dr. William Green Jr. was recruited in 1969. After he had finished his residency in Boston, Dr. Green went to the National Institute of Arthritis and Metabolic Diseases where, under the guidance of Dr. Leon Sakoloff, he learned how to grow chondrocytes. Although he was able to grow chondrocytes from many different types of animals, Dr. Green was the first to use rabbits as an animal model for cartilage research. In a single-layer culture, chondrocytes de-differentiate after cell passage. Dr. Green looked at the efficiency in clonal (3D) culture of chondrocytes, and found that clonal culture helps to keep chondrocytes differentiated. This finding was the fundamental principle of cartilage research for the next 30 years. Even today, the orthopaedic industry still modifies its products based on Dr. Green's principle. Dr. Green also was the first to explore cartilage tissue engineering by culturing chondrocytes on decalcified bone and transplanting them into cartilage defects. For this work, he received the Nicolas Andry Award and the prestigious Kappa Delta Award in 1976.

The Department received backup from the United Kingdom when Dr. George Bentley joined the Department as a research fellow the same year as Dr. Green. While working as senior registrar in the Nuffield Orthopaedic Centre in Oxford, Dr. Bentley had conducted research on papain-induced degenerative arthritis in the hip. In Pittsburgh, Dr. Bentley collaborated with Dr. Robert Greer, who was interested in isolating chondrocytes. Dr. Bentley's interest was in cartilage breakdown and repair. Their collaboration focused on the transplantation of isolated epiphyseal and articular cartilage chondrocytes into joint surfaces of rabbits — the first recorded successful cartilage cell joint allografts. Their breakthrough results had tremendous impact on orthopaedic-related research; Drs. Bentley and Greer truly were two of the pioneers in tissue engineering.

From that point on, cartilage research in Pittsburgh became more versatile and split into two main branches: biomechanics and biology.

### Research in Biomechanics

In the 1980s, Dr. Thomas Brown, together with Dr. Albert Ferguson Jr., conducted various biomechanical studies on cartilage contact stress using arrays of six miniature contact stress sensors that were embedded in the retropatellar cartilage of knees subjected to isometric quadriceps-extension forces. The experimental data revealed that elevation of the patellar tendon generally afforded relief of local contact stress regardless of the joint configuration. In addition, they investigated the role of load transmission by using finite element analysis.

Dr. Freddie Fu and Dr. Mark Baratz continued the work of Dr. Brower et al. with the newer technology then available. They were the first ones to use Fuji film to analyze the contact pressure and to show that the meniscus had a weight-bearing role, and that contact stresses increased in proportion to meniscus disruption and the amount of meniscus removed. The following year, Dr. Fu and Dr. Thomas Mutschler developed a dynamic shoulder model in order to investigate the anterior stability of the glenohumeral joint. This work was later refined in collaboration with Dr. Richard Debski and won the Kappa Delta Young Investigator Award in 1996. Another study on dynamics, this time focusing on the meniscus, was conducted by Dr. William Thompson and Dr. Fu using 3-D reconstruction of magnetic resonance images. Five fresh cadaveric knees were examined by magnetic resonance imaging throughout a full range of motion at 10-degree intervals, and computer-generated 3-D images of the menisci were evaluated for anteroposterior excursion and deformation.

In the 1990s and early 2000s, Dr. Savio Woo conducted robotic studies to investigate the biomechanics of the knee. Dr. Scott Tashman, director of the Biodynamics Laboratory, is now using more advanced high-speed stereography for computational evaluation of joint motion and function. This has enabled the assessment of areas of joint contact and cartilage thickness and deformation during functional loading. Dr. Christopher Harner, who has been conducting studies on meniscal injury, repair, and transplants since 1992, and Dr. Xudong Zhang have been using a computational knee model in the Knee Biomechanics Laboratory. One of their most recent studies focused on the mapping of ligament insertion sites onto bone surfaces in the knee joint by coregistration of the data acquired using digitization and computed tomography (CT). A test with four cadaveric

specimens demonstrated successful mapping of insertion sites for five ligaments. Dr. Scott Lephart and his neuromuscular laboratory also have contributed to the understanding of proprioception and neuromuscular control of the knee joint.

In researching anatomic anterior cruciate ligament (ACL) reconstruction, Dr. Fu and his team have worked with the Biodynamics Laboratory on knee kinematics projects, the Bioengineering Laboratory on biomechanics questions, and the Stem Cell Research Center and Cartilage Restoration Laboratory on histology and biological healing studies. The team, especially Dr. Sheila Ingham, also has collaborated with the Pittsburgh Zoo, Dr. Christopher Beard from the Carnegie Museum, and Dr. Owen Lovejoy from Kent State University for their expertise and facility for the "comparative ACL anatomy" project.

### Research in Biology

Dr. Christopher Evans began his research in Pittsburgh conducting studies with Dr. Dana Mears to look at wear particles and their influence on joint wear by using ferrography. Ferrography is a technique for analyzing wear by means of the magnetic separation of wear particles. It is an extremely sensitive monitor of articular erosion, with a resolution far greater than that of arthroscopy. This was particularly apparent with knees suffering from a torn ACL: Arthroscopy detected no damage to the cartilaginous surfaces, whereas ferrography detected a substantial level of "microdamage." Dr. Evans and Dr. Mears showed that wear particles played an active role in the pathophysiological progression of arthritis. Dr. Evans received the Kappa Delta Award in 1985. Together with Dr. Fu and Dr. Eric Olson, Dr. Evans also looked at the wear particles from artificial ligaments and their roles in the pathogenesis of arthritis. They found that wear particles significantly elevated enzymes and cartilage-activating factors in synovial fluid. Their research was honored with the AOSSM Cabaud Award in 1988.

In addition to his research focusing on wear particles, Dr. Evans also has been a pioneer in musculoskeletal gene therapy. Together with former chairman Dr. James Herndon and Dr. Paul Robbins, professor of molecular genetics and biochemistry at the University of Pittsburgh School of Medicine, Dr. Evans conducted the first orthopaedic gene therapy clinical trial on a rheumatoid arthritis patient, an effort to use a radically new approach to block the progress of the incurable, crippling disease. This research was featured in the *New York Times* in 1996.

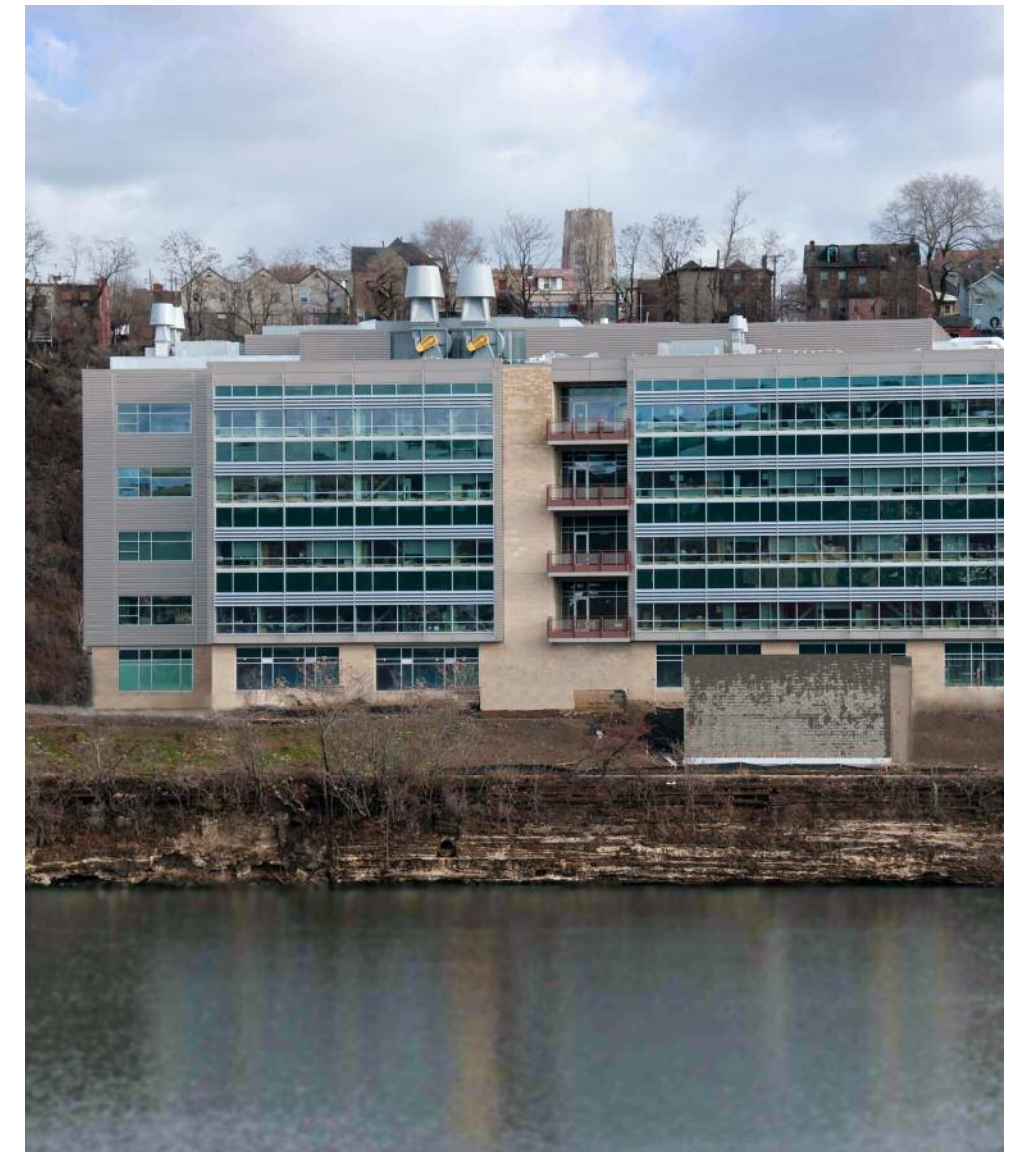
Dr. Johnny Huard joined the Department in 1996 and innovatively used muscle-derived stem cells (MDSCs) to repair cartilage tissue. His studies showed that MDSCs have multiple lineage differentiation capability and retain myogenic potential. Together with the transferred gene BMP-4, MDSC expressed the ability to repair cartilage defects. Also in 1996, Dr. James Kang began his research on intervertebral disks, with the main focus on gene therapy and stem cells. More recently, Dr. Huard demonstrated that blocking VEGF improves the chondrogenic potential of mouse MDSCs. He also has received the Kappa Delta Award (2004).

As a clinician-scientist, Dr. Constance Chu has focused on translational cartilage research, including chondroprotection, cartilage tissue engineering, and early diagnosis of articular cartilage degeneration. One of Dr. Chu's groundbreaking studies suggested that the use of lidocaine and bupivacaine could lead to chondrocytes apoptosis, and therefore articular cartilage damage. In addition, lidocaine potentiates the chondrotoxicity of methylprednisolone, a result that echoes Dr. Mankin's finding in the 1960s. Dr. Chu received the Kappa Delta Award in 2007 and recently was appointed vice chairman of translational research.

Dr. Rocky Tuan is the newest addition to the Department's active research family and the founding director of the Center for Cellular and Molecular Engineering. His research activities have focused on cartilage tissue engineering using nanoscaffolds. Dr. Tuan showed successful ex vivo development of geometrically defined cartilaginous constructs. In his experiment, human mesenchymal stem cells were seeded onto nanofibrous scaffolds, placed in custom-designed molds, and cultured in bioreactors with chondrogenesis induction by TGF-1 and IGF-1.

### Conclusion

The Department now has 14 orthopaedic laboratories of different disciplines; in today's research environment, multidisciplinary approaches are often necessary. There are more than 150 people and 30 faculty members working together efficiently and productively. One finding common to all of them is that the fine research conducted in the Department over the years still has a great impact on the field of orthopaedic surgery, and has helped to lay the foundation for the research of the future. ■



## Department of Orthopaedic Surgery Relocates Laboratory Facilities

Members of the Department of Orthopaedic Surgery recently moved into a new research facility located in the Bridgeside Point 2 building in Pittsburgh. The building includes 15,000 square feet of state-of-the-art laboratory facilities and offices overlooking the Monongahela River. It is the new home for the Center for Molecular and Cellular Engineering, directed by Dr. Rocky Tuan, and including faculty member Dr. Juan Taboas. Dr. Tuan recently relocated his laboratories to the University of Pittsburgh from the National Institutes of Health.

The Stem Cell Research Center, under the direction of Dr. Johnny Huard, and including Dr. Arvydas Usas and Dr. Burhan Gharaibeh, also has relocated to the Bridgeside facility. The Stem Cell Research Center has more than 30 staff members.

Other Department laboratory divisions located in the Bridgeside facility include the Molecular Pathology Laboratory, Dr. Yong Li, director; the Molecular Therapy Laboratory, Dr. Bing Wang, director; and the Clinical Translation and Rehabilitation Laboratory, Dr. Vonda Wright and Dr. Fabrisia Ambrosio, co-directors.