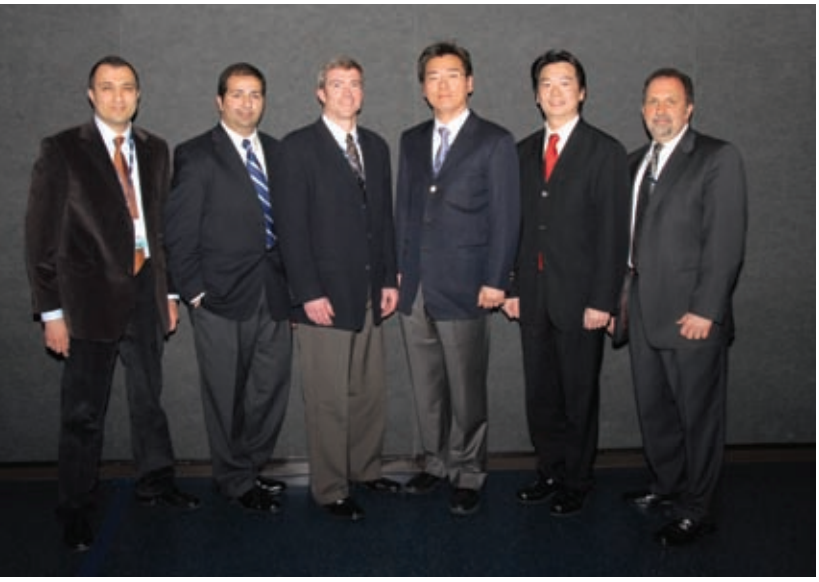
New Travel Awards recognize quality research, promote professional growth

ORS & OREF: STILL MORE IN COMMON



▲ ORS/OREF Travel Award recipients with George R. Dodge, PhD, chair, ORS Special Projects Committee (far right): (l-r) Kivanc I. Atesok, MD; Asheesh Bedi, MD; Robert H. Brophy, MD; Ilkyu Han, MD; and Jia-Lin Wu, MD

The first recipients of the newly created ORS/OREF Travel Awards presented their winning studies at the 56th annual meeting of the Orthopaedic Research Society (ORS) in March 2010. The ORS Special Projects Committee and Program Committee selected this year's five honorees from a pool of 13 applicants based on the quality of the studies.

The ORS/OREF Travel Awards in Orthopaedic Research Translation recognize clinician scientists and clinical investigators who have played a leading role in an original research project in clinical or translational medicine. Recipients can be no more than five years past completion of a clinical residency or fellowship program.

In addition to the opportunity to present their research, the recipients received a modest honorarium and travel stipend to attend the 2010 ORS Annual Meeting. Recipient **Kivanc I. Atesok, MD**, commented, "The best part of this award was the prestige, but financially it helps me a lot as I'm just starting my PhD studies."

The Travel Award is designed not only to recognize the accomplishments of the recipients but also to foster their relationship with other clinician scientists and the orthopaedic research community. To that end, the travel award includes a waiver of registration fees for the next two ORS Annual Meetings. These waivers will help the recipients remain engaged in discussions of current research and maintain networks within the professional community.

Travel Award fellow **Robert H. Brophy, MD**, described how attendance at the 2010 ORS Annual Meeting provided

many important opportunities for him professionally. "It's very interesting to hear what's going on — what new things are out there, where the body of knowledge is moving. It helps me in terms of thinking about my own research. What questions are other people asking? What methodology are they using to look into those questions?"

Dr. Brophy added that the experience is also important for his clinical work. "When I go back and talk to patients, I'm aware of what's out there and what's potentially coming," he said.

The Travel Award promises to be a valuable tool to advance the goal of both ORS and OREF to promote the role of emerging clinician scientists in translating research into quality patient care and improved clinical outcomes. Recipient **Asheesh Bedi, MD**, described his view on being a part of this effort: "I feel privileged to be coming into the field as a young faculty member when there is such a great opportunity to improve clinical care. I think the future of orthopaedics, whether it be in the world of trauma or joint replacement or sports medicine, will be improving the biologic aspects of healing — enabling us to combine surgical prowess with our improved knowledge of basic science."

THE 2010 TRAVEL AWARD FELLOWS

Jia-Lin Wu, MD

NATIONAL DEFENSE MEDICAL CENTER
Taipei, Taiwan

In-Situ Forces in the Anteromedial and Posterolateral Bundles of the Anterior Cruciate Ligament Under Simulated Functional Loading Conditions

The fibers of the anterior cruciate ligament (ACL) in the knee joint are organized primarily into two bundles: the anteromedial (AM) and posterolateral (PL). **Jia-Lin Wu, MD**, investigated the distribution of force on these bundles using robotic devices that simulate muscle load.

▲ Dr. Wu (right) in the operating room at Massachusetts General Hospital with **Thomas J. Gill IV, MD**, Chief of Sports Medicine

THE TRAVEL AWARD AT A GLANCE

Travel Award recipients receive:

- A presentation opportunity at the ORS Annual Meeting
- $500 honorarium
- Reimbursement for travel expenses up to $1,000
- Free registration for two additional ORS Annual Meetings

ORS AND OREF: WORKING TOGETHER

The ORS/OREF Travel Awards represent only one of several ways in which ORS and OREF partner to support orthopaedic research and education. Additional programs include:

- **Distinguished Investigator Award**: Since being introduced in 2008, the ORS/OREF Distinguished Investigator Award has honored the work of **Drs. Victor M. Goldberg**, **Carl T. Brighton**, and **Henry J. Mankin**, and has celebrated the many ORS MD and PhD members who, assisted by OREF grants and awards, have advanced the science and practice of orthopaedics.
- **ORS/OREF Grant Recipient Recognition Breakfasts:** These gatherings celebrate how ORS and OREF have collaborated to improve orthopaedics. The ORS/OREF Distinguished Investigator Award is presented during the program.
- **OREF/ORS Resident Research Symposia:** In 2010 ORS joined OREF in encouraging young scientists through these symposia that give orthopaedic residents at area training programs an opportunity to present research papers to a panel of experienced investigators and clinicians. (See story, p. 4)

"The load sharing of the AM and PL bundles may have important clinical relevance in ACL reconstruction," Dr. Wu said.

Most surgical reconstructions of a torn ACL use a single ligament graft such as a bone-patellar tendon-bone or hamstring tendon graft. An alternative and still relatively new procedure uses two narrower grafts to reproduce more closely the double-bundle anatomy of the ACL. A better understanding of force distribution during normal ACL function may be instrumental in improving this procedure, called double-bundle ACL reconstruction.

Dr. Wu and colleagues conducted their study with a robotic system and cadaveric knee joints to simulate functional load. They tested three conditions: an anterior tibial load, a combined rotational load, and a quadriceps muscle load at five different flexion angles.

They found that the AM and PL bundles carried similar loads, but that on average, the loads of the AM bundle were higher. The data support the concept that bundles function in a complementary rather than reciprocal manner. Dr. Wu noted that these findings lay the groundwork for investigating and refining methods to recreate the two-bundle functions in ACL reconstruction.

Asheesh Bedi, MD

UNIVERSITY OF MICHIGAN
HEALTH SYSTEM
Ann Arbor, Michigan

Dynamic Contact Mechanics of Radial Tears of the Medial and Lateral Meniscus: Implications for Treatment

Damage to a meniscus compromises its ability to distribute loads across the knee joint.

Asheesh Bedi, MD's research aim was to determine the contact mechanics of normal medial and lateral menisci and the changes in those mechanics following injury, repair, or partial meniscectomy. His colleagues and he used a dynamic robotic system and cadaveric knee joints to simulate normal gait and measure the location, distribution, and magnitude of contact pressure at different points during the gait cycle.

Dr. Bedi observed, "I think one of the most interesting things was how different the medial and lateral compartments behaved with regard to these injuries. For example, 90% medial tears affected peak contact pressure and contact area much less severely than 90% tears on the lateral side."

Treatments likewise produced varying results. Partial meniscectomy significantly altered mechanics on both sides, but the lateral procedure led to substantially greater changes, resulting in contact mechanics equivalent to a functional meniscectomy. Although sutures to repair torn menisci on either side failed to restore normal contact mechanics, the importance of meniscal preservation was clear.

Dr. Bedi noted, "Moving forward, we hope to build on data that demonstrate the importance of meniscus preservation. The next frontier is to improve our ability to have these meniscal repairs reliably heal."

Robert H. Brophy, MD

WASHINGTON UNIVERSITY
AT ST. LOUIS
St. Louis, Missouri

Meniscectomy and Traumatic Impact Leads to More Articular Cartilage Damage vs. Isolated Meniscectomy

Osteoarthritis of the knee causes the gradual degeneration of cartilage. Injuries to both meniscal cartilage and articular cartilage are associated with an increased risk of the onset and progression of osteoarthritis of the knee. However, few studies have investigated the combined — and presumably more deleterious — effect of injury to both meniscal and articular cartilage on subsequent degeneration of cartilage.

Robert H. Brophy, MD and colleagues used a rabbit model to assess the combined effect of meniscectomy and traumatic injury to articular cartilage on the rate of degeneration of articular cartilage in the knee.

▲ Ilkyu Han, MD

The researchers performed a medial meniscectomy on the left knee of 11 rabbits. During the surgery, they also followed an established protocol to deliver a controlled, traumatic impact to the end of the femur on six of the rabbits. The right knees served as the control group.

Microscopic analysis of the articular cartilage tissue quantified the loss of key components of the extracellular matrix — a measure of tissue stability and potential degeneration. The researchers observed that the extracellular matrix showed greater alterations in the double-injury group and that these changes occurred at a greater depth in the articular cartilage.

Dr. Brophy explained, "The result is not surprising, but we wanted to establish it in a model. Now we can go from there in terms of looking more precisely at how and why that difference occurs. Down the road, we would like to investigate potential ways to mitigate the disruption of the articular cartilage."

Ilkyu Han, MD

SEOUL NATIONAL UNIVERSITY HOSPITAL
Seoul, Korea

EMMPRIN Expression is Associated with Metastatic Phenotype in Osteosarcoma

Extracellular matrix metalloproteinase inducer (EMMPRIN) is a cell-surface protein that is overexpressed in several types of cancer. EMMPRIN is believed to induce metastasis by triggering production of matrix metalloproteinase (MMP) and vascular endothelial growth factor (VEGF) in cancer cells and other surrounding cells. MMPs are enzymes that can degrade several components of the extracellular matrix. VEGFs promote the formation of new blood vessels, which are necessary for supplying oxygen to cancerous cells.

Ilkyu Han, MD and colleagues conducted experiments to identify the expression and role of EMMPRIN in osteosarcoma metastasis. When the researchers correlated pretreatment biopsy samples from 52 osteosarcoma patients with clinical outcomes, they found high EMMPRIN expression associated with increased metastasis.

In another series of experiments with cell cultures, Dr. Han's group transfected osteosarcoma cells with a molecule that turns off EMMPRIN expression. These EMMPRIN-free cells were placed in cultures with osteoblasts. Another set of cultures had "normal" osteosarcoma cells and osteoblasts. This model, which demonstrates what happens in the absence of EMMPRIN, enabled the researchers to identify its normal role.

The researchers observed that the EMMPRIN-free cell cultures resulted in decreased MMP activity, decreased cell invasiveness, and lower VEGF production. They concluded that EMMPRIN is a mediator of osteosarcoma metastasis by regulating MMP and VEGF production.

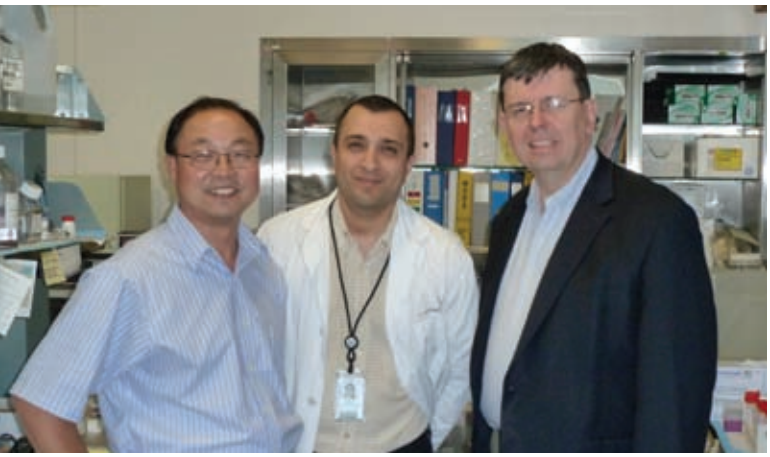
"The studies aren't going to end here," Dr. Han said. Currently his lab is working on a mouse model of EMMPRIN expression in osteosarcoma. He added, "The ultimate goal is to make EMMPRIN a therapeutic drug target."

Kivanc I. Atesok, MD

ST. MICHAEL'S HOSPITAL, UNIVERSITY OF TORONTO
Toronto, Ontario, Canada

Endothelial Progenitor Cells Promote Fracture Healing in a Segmental Bone Defect

Vascular in-growth is essential to fracture healing. Blood supply to bone can be severely damaged following the loss of a relatively large bone segment due to severe trauma, infection, or tumor removal. This may eventually cause poor bone healing and nonunion. Using a rat model of segmental bone defect in the femur, **Kivanc I. Atesok, MD** studied the effect of endothelial



▲ Dr. Atesok (center) with his supervisor, mentor, and principal investigator, **Emil H. Schemitsch, MD** (right) and co-investigator **Ru Li, MD** (left).

progenitor cells (EPCs) in promoting bone regeneration and healing.

EPCs are bone marrow-derived cells with the ability to differentiate into endothelial cells, which form the inner lining of blood vessels, and may contribute to the formation of new blood vessels.

Dr. Atesok and colleagues surgically created segmental bone defects in femurs of 14 rats and fixed the bone with a mini-plate and screws. In half of the rats, they inserted a piece of gelfoam with rat bone marrow EPCs into the fracture gap. The control group received saline gelfoam with no cells.

At 10 weeks, the researchers assessed the quality of healing in the two groups. X-ray, micro-CT, and microscopic tissue analysis revealed complete union and the development of abundant trabecular bone and cortical bone in the treatment group. The control group had no unions and new bone formation was insufficient compared to the EPC group.

Explaining the next phase in their work, Dr. Atesok said, "We now need to move to a larger animal model to understand how many cells we should use, and to identify the best matrix or scaffold to transfer the cells to the fracture environment."

Progress in this work may have implications for other treatments. Dr. Atesok stated, "I believe we may be able to use biological stimulation with EPCs to treat avascular necrosis, and to enhance healing response at tendon-bone interface and cartilage regeneration. We still need to see how this approach addresses other problems facing the orthopaedic surgeon." ■