

Discovery to Recovery

CLINICAL AND RESEARCH HIGHLIGHTS AT HSS | FALL 2013

HOSPITAL
FOR
SPECIAL
SURGERY



150
YEARS

The Tow Foundation Awards \$5.6 Million for New HSS Genomics Center

Hospital for Special Surgery has received a \$5.6 million grant from The Tow Foundation to establish the HSS Genomics Center to advance genetic research and ultimately lead to better therapies for patients with rheumatoid arthritis (RA) and lupus.

Genomics is the study of an organism's complete set of genetic material including gene sequence, structure and function, regulation of gene expression, and gene-environment interactions. DNA codes for genes that are translated to create proteins, which can be associated with specific diseases. Over the last two decades, HSS scientists and others have discovered that certain proteins, including tumor necrosis factor and interleukin 6, are associated with rheumatoid arthritis or lupus. These discoveries have revolutionized treatment for patients with autoimmune disease, leading to the development of effective new medications that have greatly improved their quality of life.

The HSS Genomics Center will use genomic approaches to further understand the regulation and function of the genes associated with these proteins, as well as identify new genes associated with lupus and rheumatoid arthritis. The goal is to develop more effective treatments with fewer side effects.

HSS scientists have long been leaders in lupus and RA research, where laboratory scientists work closely with rheumatologists and

their patients to ensure that research findings are translated into improved treatments and care. "At HSS, all laboratory research is conducted with the goal of improving outcomes for patients. This is the mission of the new HSS Genomics Center as well," says Steven R. Goldring, MD, HSS chief scientific officer and Richard L. Menschel Research Chair.

HSS is home to more than 30 rheumatologists who care for an estimated 2,600 patients with rheumatoid arthritis and 300 patients with lupus, and many of its scientists are internationally recognized experts in their respective fields. Because of the large volume of patients treated at the Hospital, HSS scientists have access to patient registries and repositories that store DNA linked with clinical information, which has led to key discoveries.

The Genomics Center will focus on several aspects of research, including an analysis of how the environment controls gene expression and thus impacts disease, called epigenetics. "In recent years, researchers have identified DNA sequences, previously thought to be junk DNA, that regulate the

expression of genes and are affected by the environment, for example hormones or smoking. It turns out that a lot of susceptibility to diseases falls within these regulatory regions," says Lionel B. Ivashkiv, MD, the Genomics Center's director and David H. Koch Chair for Arthritis and Tissue Degeneration Research. "We are very excited

we think that would also have a very big impact on improving patients' lives."

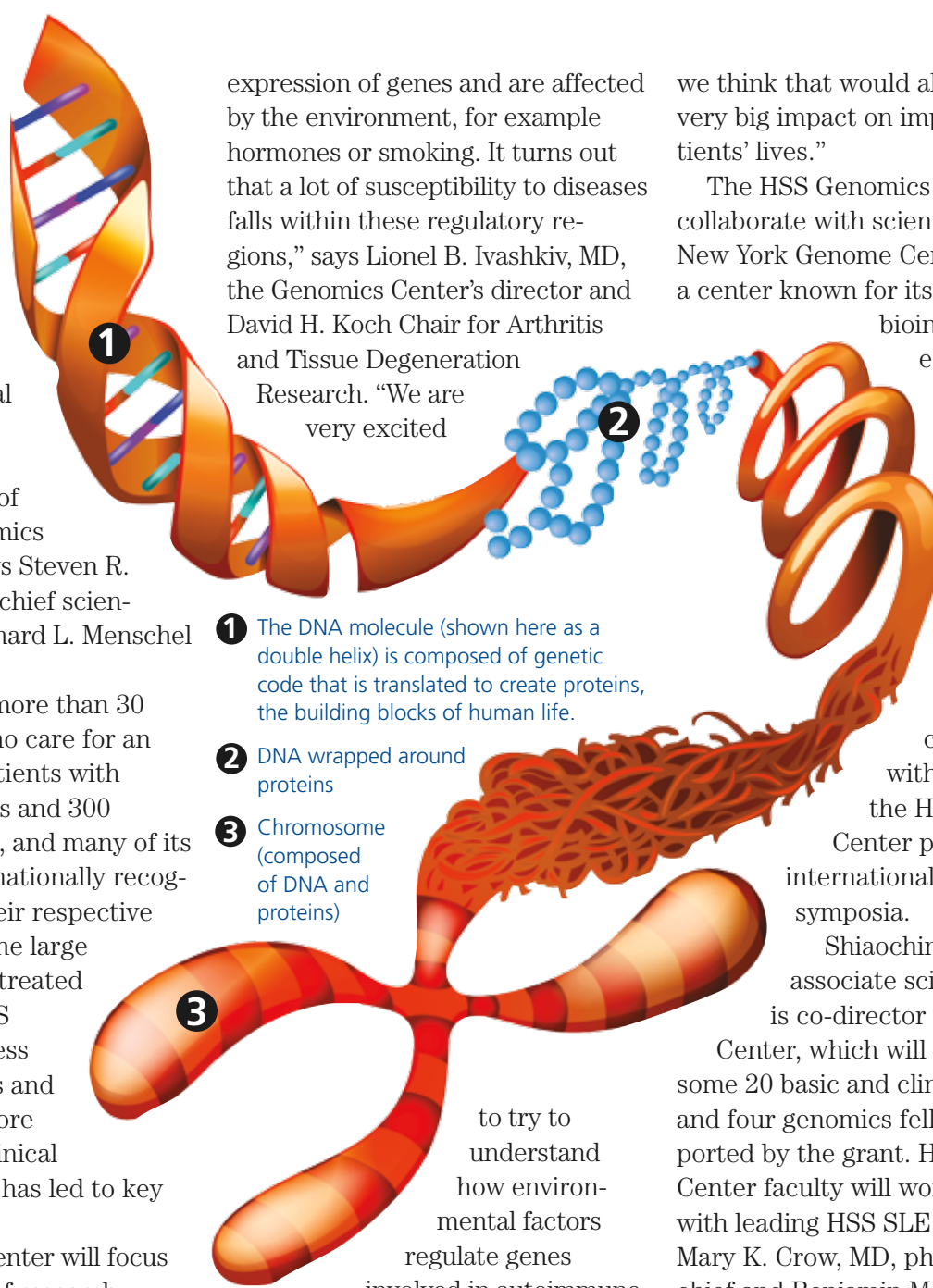
The HSS Genomics Center will collaborate with scientists at the New York Genome Center (NYGC), a center known for its technical, bioinformatic, and educational

resources that houses genome sequencing machines. HSS is an associate founding member of the NYGC. In collaboration with the NYGC, the HSS Genomics Center plans to host international research symposia.

Shiaoching Gong, PhD, associate scientist at HSS, is co-director of the new

Center, which will also include some 20 basic and clinical scientists and four genomics fellows supported by the grant. HSS Genomics Center faculty will work closely with leading HSS SLE investigators Mary K. Crow, MD, physician-in-chief and Benjamin M. Rosen Chair in Immunology and Inflammation Research; Jane E. Salmon, MD, senior scientist and Collette Kean Research Chair; Alessandra Pernis, MD, senior scientist and Peter Jay Sharp Chair in Lupus Research; and Inez Rogatsky, PhD, Steel Fellow in Musculoskeletal Research.

"We are honored that The Tow Foundation has provided a generous grant to support our continued leadership in exploring the mysteries of autoimmune disease," says Louis A. Shapiro, president and CEO of Hospital for Special Surgery. "Thanks to The Tow Foundation's gift, our scientists and physicians will offer hope to our patients with these challenging diseases." ●



- 1 The DNA molecule (shown here as a double helix) is composed of genetic code that is translated to create proteins, the building blocks of human life.
- 2 DNA wrapped around proteins
- 3 Chromosome (composed of DNA and proteins)

to try to understand how environmental factors regulate genes involved in autoimmune disease. This knowledge would represent a new way to drive therapy."

A future focus of the new center will be whole genome sequencing. "We would like to look at the genomes of individuals and try to understand how the variation in genes among different people, which occurs normally, influences an individual's disease susceptibility and response to treatment. This part of the research will look at the genetic makeup of an individual and potentially make predictions about disease prognosis and, equally important, try to find which treatments might work the best for them. This is called personalized medicine," says Dr. Ivashkiv. "That is a very complex undertaking, but

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Moving Forward, Positioned for Strength

Hospital for Special Surgery is celebrating its 150th anniversary this year, an exciting milestone. Founded at the height of the Civil War in 1863, HSS has achieved continuous success by maintaining its culture of excellence, innovation, and caring in a rapidly changing world. As we complete this anniversary year, our vision is held steadfastly on the future.

In July, we were once again ranked #1 in orthopedics, and #4 in rheumatology by *U.S. News & World Report*. For 23 consecutive years and counting, HSS has been among the top-ranked hospitals in these specialty areas. Orthopedics and rheumatology have advanced tremendously since our Hospital was founded, and continue to modernize at a fast pace. New knowledge of how diseases work has led to new treatments that allow people around the world to live longer, healthier, and more active lives. Many of these advances originated at HSS, where physicians and scientists conduct today's cutting-edge research in orthopedics and rheumatology.

This issue of *Discovery to Recovery* highlights HSS's world-renowned specialists in adult and pediatric orthopedics and rheumatology whose research continues to improve patient outcomes. You will read about our physicians' role in developing the modern total shoulder replacement, the fastest growing joint replacement procedure today. You will read about a



generous grant from The Tow Foundation to create the HSS Genomics Center, where HSS scientists will continue their investigation into the hows and whys of autoimmune disease to find better treatment options for patients.

HSS began as a hospital for children with severe disabilities, so it is appropriate that this anniversary coincides with the completion of a multiyear effort to offer children and their families a comprehensive, state-of-the-art "hospital within a hospital" with the opening of the Alfred and Norma Lerner Children's Pavilion. The HSS pediatric team collaborates to help children achieve their milestones and enjoy their childhoods, providing outstanding care and conducting research to improve outcomes and continuing to ensure safety. In this issue, we feature our diverse pediatric research studies and clinical options.

The commitment of every member of the HSS family to raise the bar in patient care through research, innovation, and compassion is stronger than ever, resulting in external recognition and, most importantly, positive feedback from patients. HSS is well-positioned to continue to lead in clinical care, research, and education in our specialty areas.

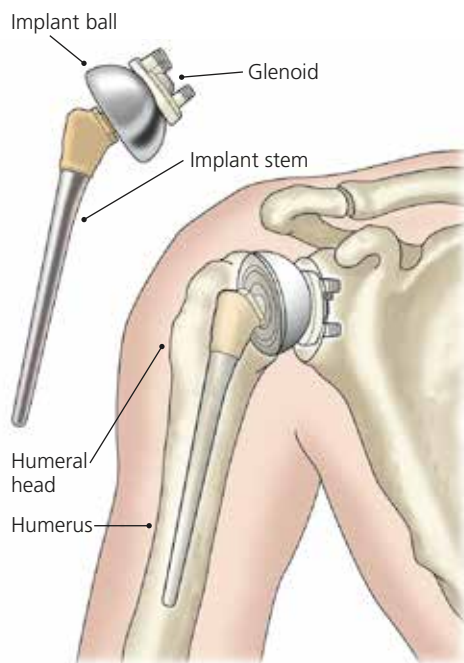
Louis A. Shapiro
President and CEO

Thomas P. Sculco, MD
Surgeon-in-Chief

Steven R. Goldring, MD
Chief Scientific Officer

Designing the Modern Total Shoulder

HSS Sports Medicine and Shoulder Service surgeons Edward Craig, MD, MPH, David Dines, MD, and Surgeon-in-Chief Emeritus Russell Warren, MD, have collaborated for nearly thirty years to invent new implant designs that have transformed the field of shoulder replacement. Through a shared commitment to innovation and improving results for their patients, they have helped



shoulder replacement become the fastest growing joint replacement procedure today. Currently, some 73,000 shoulder replacements are performed each year in the United States, and that number is growing by more than ten percent annually. HSS is one of the highest volume centers in the country for these procedures. "The success of our designs is the reason these numbers have risen. The results have been excellent," says Dr. Dines.

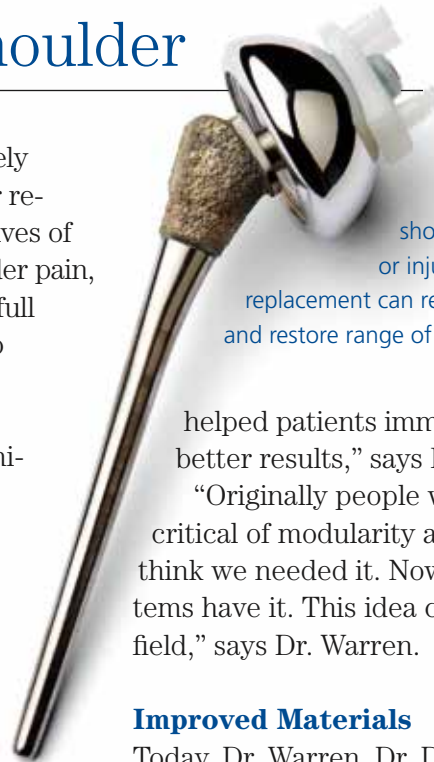
Shoulder replacement surgery can be highly successful in reducing extreme shoulder pain and improving range of motion for people with

advanced arthritis or a severely displaced fracture. "Shoulder replacement has changed the lives of patients with extreme shoulder pain, often giving them back their full range of motion and ability to function without pain," says Dr. Craig.

Shoulder implants are similar to hip implants – with a ball and stem to replace the damaged humeral head, or ball. Shoulder implants are attached to the socket in the shoulder blade known as the "glenoid." Initially, both hip and shoulder implants were single pieces of metal containing both a ball and a stem. In the early 1980s, hip implant design evolved into a modular design – the balls and stems were now separate pieces manufactured in a variety of sizes, so that surgeons could select combinations to give each patient a perfect fit, closely mimicking the patient's healthy joint.

Achieving A Perfect Fit

HSS surgeons realized that shoulder implants would benefit from a modular design as well. They teamed up with a company called Biomet to design a modular shoulder implant, which entered the market in 1988 and offered many sizes and combinations of stems and balls. The modular implant became the basis of all shoulder implant systems used today. Better fit led to improved short-term and long-term results for patients, who experienced reduced pain, improved range of motion, and less implant loosening over time. "Now we could fit the implant for the patient instead of fitting the patient for the implant. It was patient-specific. This



For patients with severe shoulder arthritis or injury, shoulder replacement can relieve pain and restore range of motion.

helped patients immediately get better results," says Dr. Dines.

"Originally people were very critical of modularity and didn't think we needed it. Now all systems have it. This idea changed the field," says Dr. Warren.

Improved Materials

Today, Dr. Warren, Dr. Dines and Dr. Craig still collaborate to invent new and improved systems. In designing an implant, materials are as important as shape and size. From the beginning, the HSS design used titanium for its ability to stimulate bone in-growth. Bone in-growth leads to a tight fit and minimizes implant loosening down the road. "With our design we usually don't need to use cement in patients with osteoarthritis – we put the implant in with a 'press fit.' So the loosening of the prosthesis with this system is extremely uncommon," says Dr. Warren.

While HSS surgeons achieve good outcomes in total shoulder replacement, the leading long-term complication has always been glenoid socket loosening. To address this problem, in the early 2000s, the HSS surgeons and their Biomet collaborators invented a "hybrid glenoid" made of Regenerex® Porous Titanium Construct, a porous surface that stimulates bone growth. This innovation has improved long-term fixation of the implant, reducing implant loosening over time.

While the team is still studying long-term outcomes of the hybrid glenoid, early results are positive for bone in-growth and implant fixation. "We're going to keep following patients over the long term, but we predict that this model will last much longer than earlier models. That's what we do – continuous follow-up to make sure loosening doesn't occur," says Dr. Craig.

Continuous Improvement

Dr. Warren, Dr. Dines, and Dr. Craig remain committed to advancing total shoulder replacement surgery. For instance, they worked with Biomet to design a "Reverse Shoulder Prosthesis," making it possible for patients with badly damaged rotator cuffs to undergo shoulder replacements by reversing their anatomy with the insertion of the plastic socket onto the stem and inside the humeral bone, and the metal ball on the socket side of the glenoid.

While the initial concept for the Reverse Shoulder originated in Europe, the HSS surgeons were instrumental in bringing an improved version of this procedure to patients in the United States. The newest model allows for a conversion from a total shoulder replacement to a reverse system without removing the stem, significantly simplifying surgery when a revision is necessary and improving results.

In the future, they hope to achieve even better fixation and better materials that will further enhance the patient experience. "Everyone at HSS is constantly looking at results so we can make changes and improvements. This process forces you to be a better doctor," says Dr. Dines. ●

New Technologies Make Surgery More Accurate, Less Invasive for Kids

Recent advances in technology and surgical techniques have dramatically improved pediatric surgery, which has become more accurate, more predictable, and often less invasive. At HSS, surgeons conduct more than 3,100 surgeries for children and adolescents each year. We interviewed Roger Widmann, MD, chief of Pediatric Orthopedic Surgery at HSS, about recent advances that have transformed the field.

Guided Growth

Guided growth procedures allow surgeons to achieve major changes in limb alignment through minimally invasive surgery for children with limb length discrepancy, bow legs, knock knees, and even some spine curvatures. In these procedures, surgeons insert small plates and screws that guide growth plates to grow in the desired alignment, essentially tricking growth plates to grow straighter. HSS pediatric orthopedic surgeon Daniel Green, MD, helped invent a guided device that is used around the country to correct bow legs in children.

In the recent past, surgeons needed to cut the bone in a major surgical procedure called an osteotomy, in which large plates and screws were used to correct and maintain alignment. Today, pediatric surgeons routinely correct alignment with less than a one-inch



Roger Widmann, MD, uses advanced technology to ensure that broken bones and limb abnormalities are fixed with precision.

incision, resulting in a much faster and less painful recovery.

“We want kids to get back to their normal lives as soon as possible. Kids are back to full activity within weeks of a guided growth procedure, whereas recovery from an open osteotomy usually takes months,” says Dr. Widmann.

Growing Rods

Guided growth procedures have also transformed care for children with spinal curvatures. Surgeons now insert internal lengthening devices – a “growing rod” in the spine or a VEPTR in the ribs – that allow a child’s spine to continue to grow as it is straightened. Every six months, the surgeon lengthens the rod in a minimally invasive outpatient visit to match the child’s growth.

Fifteen to twenty years ago, children’s spines were surgically straightened before they were fully grown, which led to pulmonary complications. Today, children are

generally managed with guided growth tools until they are fully grown, at which time spinal fusion surgery may or may not be necessary.

In development are internal magnetically controlled lengthening devices that may soon allow surgeons to lengthen the rods without any surgery whatsoever. The surgeon will insert an electromagnetic device in a patient’s back, and the rod will lengthen with a press of a button. “There is good evidence to support this technology, both basic science and clinical evidence, so this is something that’s just around the corner,” says Dr. Widmann.

“Then another procedure will become noninvasive.”

Computer-Guided Surgery

A new technology called “computer-guided surgical correction” has dramatically improved the precision of limb deformity surgery over the past ten years. Surgeons now precisely program the desired

correction into a computer following surgery, and then gradually achieve that correction using external fixators that are adjusted during follow-up outpatient visits.

“This technology allows us to correct all aspects of complex deformities – including length, angulation, and rotation – simultaneously, whereas ten years ago we would have corrected each one of those things separately and sequentially and with less accuracy,” says Dr. Widmann. “We are now very confident that we can achieve correction in all three planes.”

Low-Dose Imaging for Safety

At HSS, the entire pediatric team is focused on patient safety, and exposing children to as little radiation as possible is a high priority. Pediatric imaging experts increasingly use MRI and ultrasound to minimize children’s exposure to X-rays. For situations in which X-rays are necessary, HSS is one of the first centers to acquire an EOS® system – a low dose X-ray imaging system for spine and limbs – which gives a 3-D image with only ten percent of the radiation of a standard X-ray machine.

Taking Care of Children

“While the surgical principles remain the same, there are very few procedures that from a technical standpoint we do the same way as we did ten to 15 years ago,” says Dr. Widmann. “In many cases, children can get back to their lives faster following surgery, since new techniques have shortened the recovery time and improved expected outcomes.” ●

Pediatric Orthopedics at HSS Then and Now

Q&A with Leon Root, MD, chief emeritus of Pediatric Orthopedics (1972-1997), about the evolution he’s seen in pediatric orthopedics in his 46 years at HSS.



Leon Root, MD

What was pediatric orthopedic care at HSS like when you started practicing?

When I came to HSS, everyone did pediatric orthopedics. You had different teams of attending physicians who rotated on the adult and children’s services. In 1972, when Dr. Philip Wilson, Jr., became surgeon-in-chief, he decided that pediatric orthopedics should be a specific service.

What was the patient experience like when you joined HSS?

In the 1960s and 1970s, a child’s hospital stay would last for weeks, not days. We even had a public school in the Hospital. A child with scoliosis would stay in casts for six months or longer. In those days the parents weren’t

allowed to stay at night. Today we encourage a parent to stay overnight with the child. In many cases, after surgery, the child will go home that night or, at the most, stay three or four days. The sooner the child gets out of the hospital, the sooner they recover.

What improvements have you seen in pediatric orthopedics?

It’s always interesting that things change and they don’t change. In orthopedics, you’re dealing with the human body – muscles, bones, joints – and that stays the same. We deal with them differently, and get better at treating patients.

A major improvement we’ve seen is a decrease in bone infection. Now we have antibiotics to treat the individual bacteria causing infection. Our ability to diagnose infection is much better, too. MRI helps us diagnose infection early and shows how far the infection extends so we can treat it much more effectively.

What new injuries or conditions are you seeing?

Years ago at least half the children in the Hospital had polio. In this modern age, we

are seeing more sports injuries. Children are getting involved at a younger age in intense sport activities. They’re tearing ligaments that need to be repaired in a different way than those of adults because children are growing, so you must be careful not to injure their growth plates.

What role does rehabilitation play in pediatric orthopedics?

We talk about rehabilitation – bringing a child or adult back to normal function. We also have children who have never walked, such as with cerebral palsy. We have to “habilitate” because they don’t know how. Our goal is to teach these children how to walk, how to use their hands.

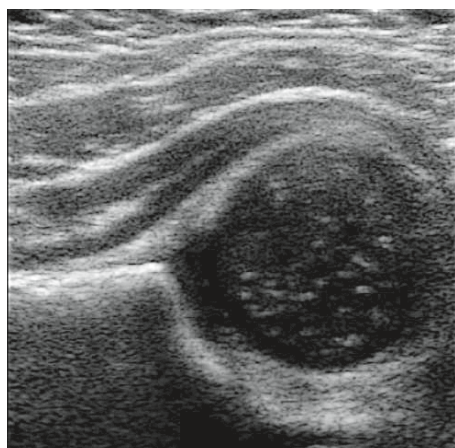
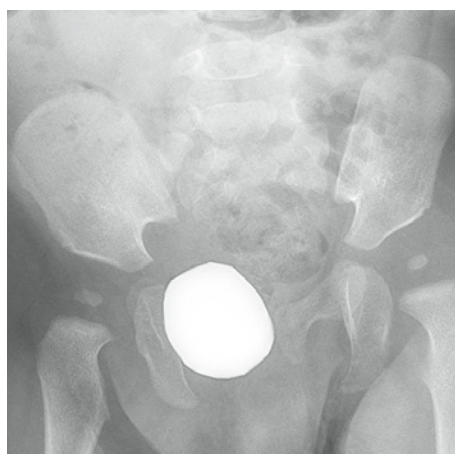
What’s next for pediatric orthopedics?

We want to prevent problems before they start, such as with folic acid that prevents spina bifida. We’re trying to eliminate disease if we can. ●

To read more of our interview with Dr. Root, visit the HSS blog at www.hss.edu/onthemove and watch him on video on our HSS YouTube channel at www.youtube.com/hspecialcharsurgery.

THE P

HAPPENINGS AROUND THE HOSPITAL



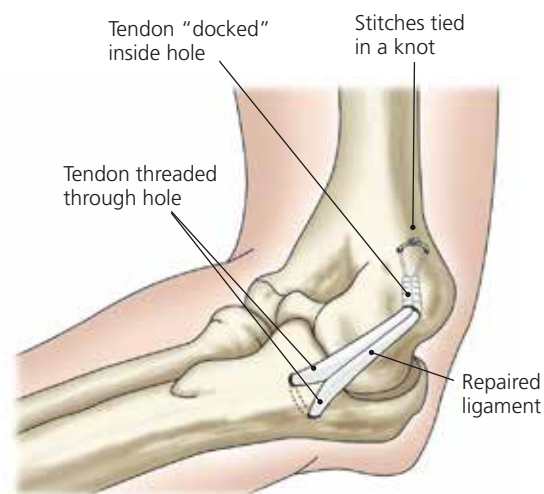
An X-ray (top) and sonogram (bottom) of a six-month-old baby's hip on the same day both show that the head of the femur (ball) is concentrically located in the hip socket as it should be, but both images depict a slightly shallow hip socket indicating mild hip dysplasia, which will be monitored.

< Safer Imaging for Babies with Hip Dysplasia

Ultrasound images prove to be an effective alternative to X-rays for diagnosing dislocated hips in infants who were previously treated for developmental dysplasia of the hips (DDH), according to a study by HSS pediatric orthopedic surgeons. The current standard practice is to reim-age these infants with an anterior-posterior pelvis X-ray after six months of their initial treatment. This type of X-ray is safe and exposes children to low levels of ionizing radiation, but ultrasound is even safer, with no radiation. "We anticipate that this is something that our colleagues around the world will adopt as well to reduce the amount of radiation an infant is exposed to," says Shevaun Doyle, MD, an HSS pediatric orthopedic surgeon and study author.

Getting Young Athletes Back > in the Game

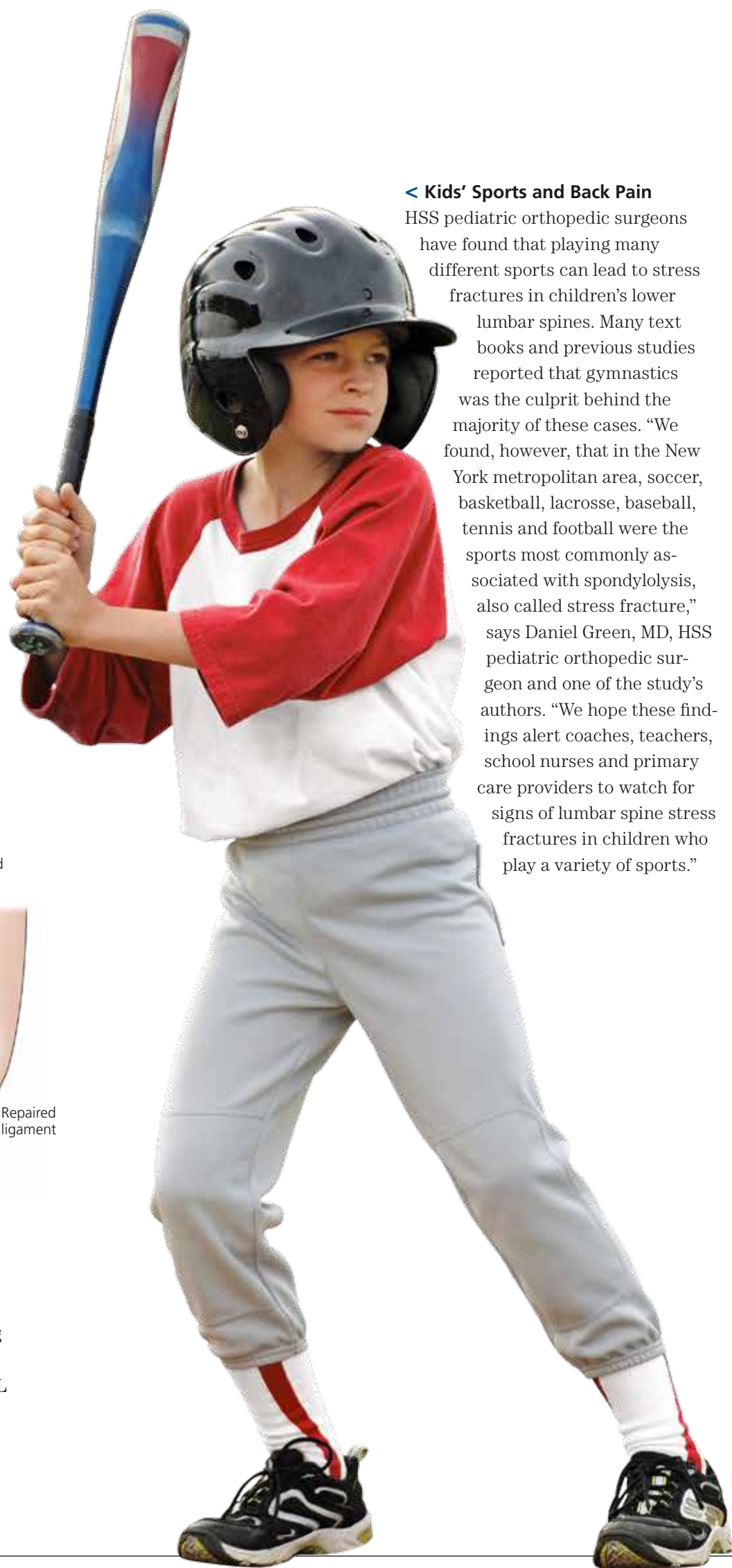
HSS doctors have found that a less traumatic surgical procedure can get young athletes back in the game and playing at the same or higher level of competition after tearing an elbow ligament. "Research has demonstrated that modifying the ulnar collateral ligament (UCL) reconstructive surgery, also called Tommy John surgery, with the docking technique improves surgical outcomes in younger athletes," says David W. Altchek, MD, co-chief of the Sports Medicine and Shoulder Service at HSS and senior author of the study.



By using the docking technique, surgeons are able to replace the torn ligament with a tendon from the patient's forearm or hamstring and graft it to the elbow by gently splitting the muscles instead of detaching them, as is the norm in traditional UCL reconstructive surgery.

< Kids' Sports and Back Pain

HSS pediatric orthopedic surgeons have found that playing many different sports can lead to stress fractures in children's lower lumbar spines. Many text books and previous studies reported that gymnastics was the culprit behind the majority of these cases. "We found, however, that in the New York metropolitan area, soccer, basketball, lacrosse, baseball, tennis and football were the sports most commonly associated with spondylolysis, also called stress fracture," says Daniel Green, MD, HSS pediatric orthopedic surgeon and one of the study's authors. "We hope these findings alert coaches, teachers, school nurses and primary care providers to watch for signs of lumbar spine stress fractures in children who play a variety of sports."



NEWS



< Celebrating 150 Years of Excellence

HSS was founded in 1863 as a 28-bed hospital for children with severe disabilities.

In May, HSS celebrated its 150th anniversary with the release of Director of Alumni Affairs David B. Levine, MD's book, *Anatomy of a Hospital: Hospital for Special Surgery 1863-2013*, which is now available for purchase at the HSS online store (www.hss.edu/store).

As a special gift, all Hospital staff received a DVD copy of a commemorative documentary that brought the Hospital's dynamic 150-year history to life. The lobby and second floor of the main building are now decorated with fascinating displays featuring several highlights of the Hospital's past and visions for the future.



Meeting the Challenge ^

On June 12, 2013, more than 400 HSS colleagues walked together from the main Hospital campus to Central Park to participate in the J.P. Morgan Corporate Challenge, a 3.5-mile race in support of camaraderie, healthy living, and the Central Park Conservancy. Members of the HSS family ran or walked to the finish line in original shirts designed for the occasion. "We work hard every day to help our patients lead active lives. This event was a wonderful opportunity for the HSS family to practice the healthy behavior we recommend to our patients while having fun together in beautiful Central Park," says Susan Cardamone, MBA, associate director, Department of Anesthesiology, and HSS team captain for the event.

Reaching New Heights v

Children in treatment at HSS for cerebral palsy conquered the Rockies as they hit the slopes in Colorado with physical therapists from the CA Technologies Rehabilitation Center. In February, a group of four teenagers and a nine-year-old traded in their wheelchairs and walkers for sit skis and outriggers that enabled them to go down the mountain and, for

many, experience speed for the first time. Seventeen-year-old Daniel Cruz exclaimed, "I never thought I would ski!" as he swooshed past Magdalena Oledzka, PT, MBA, PCS, and Maureen Suhr, PT, DPT, PCS, of the HSS pediatric rehabilitation team. Along with four days of intense exercise, the patients enjoyed pushing each other to surpass goals and create new ones.



Q&A With HSS Leaders in Rheumatology

We spoke with three world-renowned HSS rheumatologists whose research has led to major treatment advances for patients with autoimmune disease: Physician-in-Chief Mary K. Crow, MD, Benjamin M. Rosen Chair in Immunology and Inflammation Research; Jane E. Salmon, MD, Collette Kean Research Chair and director of the HSS Systemic Lupus Erythematosus and Antiphospholipid Syndrome Center of Excellence; and Associate Chief Scientific Officer Lionel B. Ivashkiv, MD, David H. Koch Chair for Arthritis and Tissue Degeneration Research. To date they have practiced at HSS for a combined 85 years. They discussed their experiences in a rapidly evolving medical specialty and their vision for the future.

What drew you to rheumatology?

Dr. Crow: As a medical student and medical resident I found that patients with systemic autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis (RA) were by far the most challenging and complex. Having a background in immunology research prior to starting medical school, rheumatology seemed like an ideal field that would combine the intellectual stimulation of unraveling diseases based in altered immune function with the rewards of helping people with very significant and often debilitating diseases.



Mary K. Crow, MD

Dr. Ivashkiv: At the time, people asked me why I wanted to go into a field with so little understanding of how the diseases worked, and with such imperfect treatments. I saw that as an opportunity to learn more about these diseases and find some answers.

Dr. Salmon: As a student and resident, I took care of young women with lupus. Women are much more likely to get this disease than men, and I was compelled to find better ways to help them.

What have been the most exciting advances in rheumatology in the past 30 years?

Dr. Salmon: The most important advance is biologic therapy. Biologics are bioengineered molecules that target specific immune

mediators and cells involved in an autoimmune disease. We've identified specific targets, specific inflammatory molecules that we can inhibit with biologics, to prevent joint destruction, skin rash, and kidney inflammation.



Jane E. Salmon, MD

Because of biologic therapies, patients with rheumatoid arthritis rarely need joint replacements, they can work, they're not tired. The ability of these drugs to change the natural history of RA has been extraordinary.

Dr. Crow: And what was exciting as a rheumatologist is that rheumatology led the medical community in the introduction of these biological and targeted therapies in the 1990s. RA was one of the first diseases in which they were successful. Rheumatologists' success with biologics gave other disciplines confidence to use them to treat many other diseases.

Dr. Ivashkiv: Biologics really did change the field and practice. There is now another advance – the introduction of JAK-inhibitors – which just came onto the market this year. We think that these new medications will be just as effective as the biologics, and they can be taken by mouth, which will make it much easier. Patients receive biologics through infusion therapy or injection. JAK-inhibitors work in part by blocking signaling by the protein interleukin 6 and probably other cytokines that we have been studying for years at HSS.

We started investigating JAK-STAT in my HSS lab in 1992 as soon as it was discovered, and we were the first to link JAK-STAT signaling with RA. It was very gratifying as the science moved from the laboratory to pre-clinical studies and now patients are using it and everyone thinks it really works. In the first 20 years of my career I've been privileged to be part of the progression of an innovation from the laboratory bench to the patient's bedside.

What future advances are in the works?

Dr. Crow: We're on the cusp of making great strides in the area of genomics and figuring out how environmental factors, such as smoking, interact with an individual's genes to make some people more likely to get sick. Improved understanding of the cell alterations that contribute to lupus have led to new concepts for drug development that are now being tested and should yield more effective therapies in the next five to ten years.

New Advances in Pediatric Rheumatology Research

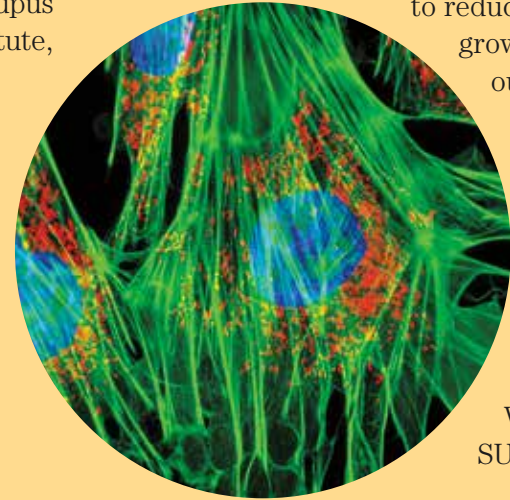
Theresa Lu, MD, PhD, associate scientist in the Autoimmunity and Inflammation Program at HSS, is one of only about 200 pediatric rheumatologists in the United States and one of only a handful who conduct research in the laboratory. With support from the NIH and the Lupus Research Institute, Dr. Lu and her team recently made significant progress, moving closer to potential new therapies for children as well as adults with lupus.

Dr. Lu's research has long focused on lymph node blood vessels that provide nutrients for autoimmune cells, called T cells, that live in lymph nodes. Another type of cell, called a fibroblast, is situated around and near blood vessels. Fibroblasts can dampen the immune activity of T cells.

Recently, Dr. Lu showed that in a model of lupus, a disease in which immune cells become activated in response to their own body, abnormally activated T cells are sequestered in a compartment away from the fibroblasts to which they are usually near. Treatment with a drug called SU5416 disrupted the sequestration and normalized the physical association of T cells with the fibroblasts. Bringing the T cells and fibroblasts back

together correlated with dampening of T cell activation and reduced autoantibody generation. The drug seems to have interrupted the abnormal autoimmune response that occurs in lupus.

"We originally used SU5416 to reduce blood vessel growth and starve out the activated immune cells, but the SU5416 had only a temporary effect on the blood vessels. We think the SU5416 had a desirable effect by breaking open the



Fibroblasts work with T cells to regulate the immune system.

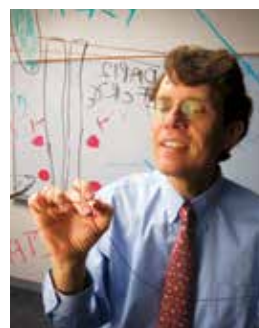
compartments that sequestered the abnormal T cells, allowing the T cells to come into contact with a more immune-dampening environment," says Dr. Lu. "We are very excited about the idea of a treatment strategy that dampens immune cell activity by altering the microenvironment."

Further research will determine if SU5416 or drugs in the same class are good treatments for lupus patients and whether better medications can be developed to achieve the same benefits with fewer side effects.

"I always want my laboratory research to be relevant to patient care," says Dr. Lu. "In the end that's always the goal – to develop better therapies for patients." ●

Dr. Salmon: We will ultimately be able to determine exactly which therapy will work best for which patient by understanding each individual's genes and genetic regulators.

Dr. Ivashkiv: This is one of the goals of the new HSS Genomics Center (see cover). We hope to identify new targets and also personalize therapy to find the best way to treat a specific person. Right now, rheumatologists still try one thing and see if it



Lionel B. Ivashkiv, MD

works, and then try the next thing if the patient doesn't respond well. We'd like to be able to select the best drug right from the get-go, and genomics will allow us to do this.

What is special about being a rheumatologist at HSS?

Dr. Salmon: Research here is always rooted in patient care, and patients are our partners in research – they are active participants. It is rewarding to see patients with lupus feel good, live normal lives, enjoy their families the way they couldn't when I was in medical school.

Dr. Crow: Rheumatology at HSS is all about collaboration. Scientists and physicians work together to help patients, and patients inspire us to push towards new advances. ●

Planned Giving: A Gift for the Future

Maria Coppersmith lived with polyarteritis nodosa, a rare autoimmune disease that caused peripheral neuropathy – a loss of power and feeling in her extremities. After visiting a series of rheumatologists and internists at other hospitals who were unfamiliar with treatment options for her condition, Mrs. Coppersmith and her husband, Morris, came to Hospital for Special Surgery in 2002 to see Michael Lockshin, MD.

The Coppersmiths discovered that HSS and Dr. Lockshin offered a different, personalized experience for patients with autoimmune diseases. Dr. Lockshin listened to Maria and took a comprehensive approach, strategically addressing the complexity of her case.

“Dr. Lockshin is one of only a few physicians who are familiar with

Maria’s condition,” Morris once said. “Under his care, she found both comfort and relief.” Dr. Lockshin’s experience treating patients with polyarteritis nodosa eventually helped relieve Maria’s debilitating symptoms, allowing her to once again enjoy life in the Bronx with Morris.

Dr. Lockshin partnered with Maria for many years as they worked together towards her recovery. “Getting people to understand realistic expectations is an important part of the rheumatologist and patient relationship,” says Dr. Lockshin. “It’s an ongoing relationship – it involves short-term and long-term planning.” Over time, Maria went into full remission. Dr. Lockshin continued to monitor her for recurrences throughout her life.

In appreciation for the exceptional care both Maria and Morris received at HSS, the Coppersmiths



Michael Lockshin, MD, with a patient's child.

named HSS in their will, becoming members of the Hospital’s legacy society, the Wilson Society, in 2004. As Morris said, “My wife and I want to leave our estate to organizations that have made an impact on our lives, such as HSS.”

After Morris passed away in 2010, HSS received the couple’s bequest; Maria predeceased Morris by only one year. “They were both special to each other, which was fun

to see, and quite good to see,” remembers Dr. Lockshin. “This gift will benefit other patients with rare autoimmune diseases.”

By making HSS part of their legacy, the Coppersmiths continue to provide vital support for Dr. Lockshin and the Rheumatology Division. HSS experts rely on the generosity of individual donors, like the Coppersmiths, to treat patients with complex conditions every day and to enable the research that leads to medical advances. ●

To find out more about planned giving at HSS and the benefits of being a Wilson Society member, or to learn more about the research being conducted to help patients with rheumatologic conditions, please call 212.774.7527 or visit us online at hss.edu/legacy.

ACL Research Advances Treatment

Anterior cruciate ligament (ACL) injuries are common in adult and child athletes. The ACL is an important soft tissue structure in the knee that connects the femur to the tibia. ACL tears are usually treated through reconstructive surgery, in which the torn ligament is replaced with a tissue graft to mimic the natural ACL. Some 175,000 ACL reconstructions are done each year in the U.S., and the number is increasing. At HSS, our surgeons perform close to 1,500 ACL repairs per year, nearly tripling in the past ten years.

At HSS, specialists take an interdisciplinary approach to treating patients with ACL injury, with physiatrists, surgeons, and imaging and rehabilitation professionals collaborating to find the best treatment option for each patient. Because patients with ACL injury are more likely to develop early-onset osteoarthritis, HSS physicians and scientists are investigating ACL repair with the goal of improving short-term and long-term outcomes for patients. A few of their studies are highlighted below.

The Youngest Athletes

While the standard adult method of ACL reconstruction is performed successfully on older teenagers, there are a variety of options available to treat young children with ACL tears. One option developed at HSS by pediatric orthopedic surgeon Daniel W. Green, MD, and orthopedic surgeon Frank A. Cordasco, MD, is called the All-Inside, All-Epiphyseal Reconstruction (AE). A recent study published in *The American Journal of Sports Medicine* found that the AE allows young athletes to return safely to sport.

Performing ACL reconstruction on children is difficult, because the typical adult-type reconstruction can cause damage to open growth plates, potentially causing uneven limb lengths or deformities. Therefore, in years past, surgeons postponed ACL surgery until children stopped growing, or used surgical techniques that were not anatomically accurate. “Non-operative treatment means telling a nine-year-old not to play sports for the rest of his or her childhood. That is a poor option for most children and their families,” says Dr. Green.

The AE technique is similar to adult ACL surgery but uses new technology and interoperative X-rays to place the new ACL graft anatomically in the knee, without the graft crossing the adjacent growth plates. It is performed arthroscopically and results in a near anatomic ACL reconstruction with a very high rate of return to play. It is one of several techniques performed successfully at HSS to repair ACL tears in children.

The investigators compared knee stress and stability between the two surgical techniques, finding that the AE allowed knees to withhold stresses better at a running angle. “This is important because most field and court sports involve knee function close to this position. Also, the AE does not require an open incision, reducing the risk of soft tissue trauma,” says Dr. Cordasco.

Elite Women Basketball Players

Investigators from the Women’s Sports Medicine Center at HSS recently analyzed health records of 506 players who entered the Women’s National Basketball Association (WNBA) combine in

2000-2008 to learn which injuries and surgeries were most common among elite women basketball players. In a study published this year in *The American Journal of Sports Medicine* they found that the most common surgery was ACL reconstruction, at fourteen percent. They also learned that a history of this surgery did not affect the players’ round drafted or career length, indicating that ACL reconstruction can be highly successful at getting athletes back to elite sports.

“Not enough research exists about women’s sports injuries and response to treatment. Outcomes data are important when treating athletes with ACL injury, which is increasingly common in female athletes” says Jo A. Hannafin, MD, PhD, director of Orthopedic Research at HSS, co-director of the Center and a study author. “It is gratifying that the data show what we suspected: that ACL reconstruction does not keep women from playing basketball,” says Lisa R. Callahan, MD, co-director of the Center and a study author.

Nonsurgical Options

At HSS, an interdisciplinary team evaluates each patient with an ACL tear to determine if surgery is necessary. A new study published by HSS surgeons in *Knee Surgery, Sports Traumatology, Arthroscopy* found that roughly a quarter of recreational skiers who tear their ACL

while hitting the slopes can be successfully treated without surgery.

“Some patients who injure their ACL while skiing can get away without surgery. In such cases, their ligament heals by itself, they will have stable knees, and they will be able to do whatever they want, including skiing,” says Robert Marx, MD, an orthopedic surgeon who led the study.



WNBA player Essence Carson chose HSS for her ACL reconstruction surgery in early 2013. For more on Essence Carson, watch her video on HSS Back in the Game at www.hss.edu/backinthegame.

The study found that at six to twelve weeks post ACL tear, results from the physical examination of the knee can identify skiers who will recover without surgery. “ACL injuries resulting from recreational skiing can be less traumatic than ACL tears seen in sports that involve pivoting and contact, such as soccer or football,” says Dr. Marx. ●

Josh Baxter, PhD, and **Jonathan Deland, MD,** received an American Orthopaedic Foot & Ankle Society grant to study “A Biomechanical Comparison of a Novel Spring Ligament Reconstruction Technique with Previously Reported Techniques.”

Carl Blobel, MD, PhD, Virginia F. and William R. Salomon Chair in Musculoskeletal Research, received a Bayer Hemophilia Award to support his research; was an invited speaker at the Ernest Just Symposium at the Medical University of South Carolina, held in Charleston, South Carolina; and was chair of a session at the Gordon Conference on Matrix Metalloproteinases in Il Ciocco, Italy. Dr. Blobel and **Jane Salmon, MD,** received a new research award from the Alliance for Lupus Research (ALR) and Pfizer’s Centers for Therapeutic Innovation (CTI) to study “iRhom2 - A New Target for Treatment of SLE.”

Adele Boskey, PhD, Starr Chair in Mineralized Tissue Research, was honored at HSS by a symposium on bone disease research entitled “Studies of How Bones Mineralize and the Clinical Impact of These Studies.” Dr. Boskey was also an invited speaker at the Osteogenesis Imperfecta Basic Science meeting held in Illinois.

Tony Chen, PhD, received a new two-year KL2 Scholar Award from the Weill Cornell Medical College Clinical and Translational Science Center to study “Dynamic Load Bearing Characteristics of Implants for Osteochondral Defects.”

Mary Crow, MD, Benjamin M. Rosen Chair in Immunology and Inflammation Research, was one of four invited speakers at the 21st Annual Faculty of Medicine Symposium held at the University of Calgary, Canada; and was invited to present the Kroc Lecture at the University of Texas Southwestern Medical School. Dr. Crow received a new research award from the Alliance for Lupus Research (ALR) and Pfizer’s Centers for Therapeutic Innovation (CTI) to study “Identification and

Validation of Biomarkers Associated with Lupus Flare.”

David Dines, MD, was the keynote academic participant in The Paris International Shoulder Meeting; participated in the International Congress of Shoulder and Elbow Surgery in Nagoya, Japan; and performed three live shoulder surgeries at the Annecy Live Surgery Meeting in Annecy, France.

Mark Drakos, MD, Jeremy LaMothe, MD, and **Josh Baxter, PhD,** received an American Orthopaedic Foot & Ankle Society Grant to study “Syndesmotic Disruption: Changes in Tibiofibular Motion and Ankle Contact Stresses.”

Christopher Dy, MD, MSPH, received a new one-year award from the American Foundation for Surgery of the Hand to study “The Impact of Coronal Alignment on Distal Radius Fracture.”

Doruk Erkan, MD, was an invited speaker at the 7th International Advances in Rheumatology Meeting held in Santiago, Chile.

Peter D. Fabricant, MD, MPH; Alex Robles, BS; Timothy Downey-Zayas, BS; Huang T. Do, MS; Robert G. Marx, MD, MSc; Roger F. Widmann, MD; Daniel W. Green, MD, MS, won the AOSSM Excellence in Research Award for “Development and Validation of a Pediatric Sports Activity Rating Scale.”

Mary Goldring, PhD, Ira W. DeCamp Fellow in Musculoskeletal Genetics, served as chair of the Program Committee for the ORS Annual Meeting held in San Antonio, Texas.

Steven Goldring, MD, Richard L. Menschel Research Chair, was an invited speaker at the Advances in Targeted Therapies Meeting in Nice, France, and participated in the NIH Roundtable on the Role of Inflammation in Osteoarthritis.

Jo Hannafin, MD, PhD, was honored by Castle Connolly as Physician of the Year for Clinical Excellence; and was an invited speaker at the International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) Congress held in Toronto, Canada.

Howard Hillstrom, PhD, co-authored a poster presentation on “Association of Radiographic Knee Osteoarthritis and Pain with Gait Asymmetry: The Multicenter Osteoarthritis Study,” which won the Best Knee Poster at the 2013 ORS Annual Meeting and was selected to be displayed at the AAOS Annual Meeting.

Xiaoyu Hu, MD, PhD, received a new three-year grant from the Lupus Research Institute to study “Hes1 as a Novel Regulator of the Type 1 Interferon Pathway in SLE.”

George Kalliolias, MD, PhD, received an Arthritis National Research Foundation grant to study “TNF Alpha Modifies FLS Chromatin Landscape to Induce Disease State.”

Patrick O’Leary, MD, received the College of Medicine & Health Alumnus Achievement Award from the University College Cork in Ireland.

Hollis Potter, MD, Coleman Chair in MRI Research, presented the annual Kilcoyne Lecture: “MRI of Articular Cartilage, MRI of Arthroplasty,” at the Colorado Radiological Society meeting.

Sarah Pownder, DVM, received a new one-year Planning Award from the Weill Cornell Medical College Clinical & Translational Science Center to study “Improved Magnetic Resonance Imaging of Large Fracture Repair Using an Equine Model.”

Edward Purdue, PhD, and **Steven Goldring, MD,** received a new four-year research grant from the NIH/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) in collaboration with the University of Nebraska Medical Center to study “Early Detection and Intervention of Orthopedic Implant Loosening Using Polymer Theranostics.”

Jane Salmon, MD, Collette Kean Research Chair, received a new three-year grant from the Lupus Research Institute to study “Activation of iRhom2/ADAM17/HB-EGF/EGFR Pathway in Immune Complex Nephritis.”

Louis A. Shapiro has been named chair elect of the Greater New York Hospital Association for the 2013-2014 term.

Mark Stasiak, ME, received a new two-year TL1 Training Award from the Weill Cornell Medical College Clinical & Translational Science Center to study “Validation of a Device to Evaluate Rehabilitation Protocol Effect on ACL Repair.”

Peter Torzilli, PhD, served on an NIH/NIAMS Scientific Review Group for Small Grant Programs for New Investigators and participated in the Bioengineering Division of American Society of Mechanical Engineers’ (ASME) Strategic Planning Retreat in Washington, DC. Dr. Torzilli presented two invited lectures at the 4th Annual Mechanobiology Symposium held at the University of Auckland, New Zealand – “Micro-to-Nano Mechanobiology Mechanisms in Osteoarthritis” and “Osteoarthritis and Tumor Metastasis – Is There a Difference?”

Scott Wolfe, MD, was an invited guest Professor at the Turkish Society for Orthopaedics and Traumatology in Istanbul, Turkey.

Timothy Wright, PhD, F.M. Kirby Chair in Orthopaedic Biomechanics, was an invited “Classics in Orthopaedics” speaker at the 31st Annual Meeting of the Mid-America Orthopaedic Association held at Amelia Island, Florida. ●

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Noteworthy

Making History

Jo A. Hannafin, MD, PhD, director of Orthopedic Research and orthopedic director of the Women’s Sports Medicine Center at HSS, has been named the first female president of the American Orthopaedic Society for Sports Medicine (AOSSM). With 3,042 members, the Society is an international organization of orthopedic surgeons and other allied health professionals dedicated to advancing sports medicine education, research, communication and fellowship.

Dr. Hannafin is currently head team physician for the Women’s National Basketball Association New York Liberty. A lifelong rower and a physician for the U.S. National Rowing team, she also served as an Olympic physician for rowing and



Jo Hannafin, MD, PhD

other sports in 1984. A renowned clinician-scientist, Dr. Hannafin has published more than 85 peer-reviewed articles, 20

book chapters, and the book, *Say Goodbye to Knee Pain*.

“I became the 21st female member of the organization in 1997. Today, just over five percent of the members are women, and it’s an honor to be the first woman chosen for the leadership position,” says Dr. Hannafin.

“HSS takes pride in the achievements of Dr. Hannafin, and we are delighted to congratulate her on her new position,” says Louis A. Shapiro, president and CEO of Hospital for Special Surgery. ●

Legacy of Learning

When surgeon, researcher, and educator Dick Laskin, MD, chief of the HSS

Arthroplasty Service and friend and mentor to many, passed away on March 1, 2008, he left a legacy of caring, innovation, and learning that endures through an endowed chair in his name and the *HSS Journal*, which he founded in 2005 as its first editor-in-chief. This multidisciplinary, peer-reviewed musculoskeletal journal continues to highlight new research from around the world and HSS. Charles Cornell, MD, serves as the Journal’s editor-in-chief and is the first holder of the Richard S. Laskin MD Chair in Musculoskeletal Education, which supports the Hospital’s continued efforts to improve patient care through research and education. ●

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