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PM&R Update

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INSIDE THIS ISSUE

Sports Medicine Center Welcomes New Director of Research and Biomechanics

The Mayo Clinic Sports Medicine Center recently began a new era to enhance the research-based practice at its two Minnesota locations, the expanded Rochester facility and the recently opened downtown Minneapolis site, located across from Target Center.

Serving a wide patient demographic

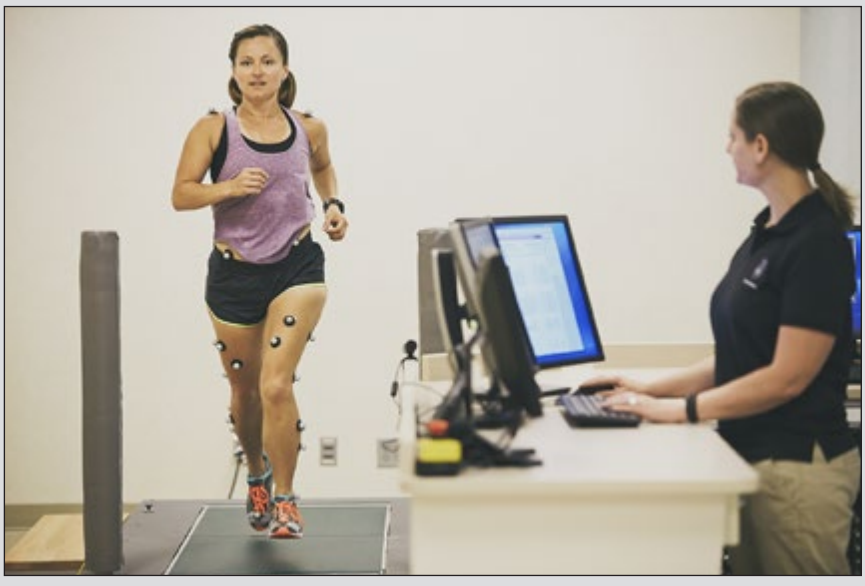
In July 2015, Timothy Hewett, Ph.D., joined the staff as director of the Biomechanics Laboratories and the Materials Structural Testing Core, and director of sports medicine research. Before coming to Mayo Clinic, Dr. Hewett was a tenured professor at Ohio State University (OSU), director of the OSU Sports Health & Performance Institute and director of research at OSU Sports Medicine in Columbus, Ohio.

Dr. Hewett's experience at OSU, a university system with 36 varsity sports teams, provided him with an exceptionally deep and broad professional expertise in performance enhancement and injury prevention. Mayo Clinic's integrated, multidisciplinary group practice model, coupled with its international reputation as an advanced medical center, greatly influenced Dr. Hewett's decision to join Mayo Clinic.

"This is a truly unique opportunity because Mayo's sports medicine practice serves high school athletes, pro athletes and older adult patients regaining mobility," explains Dr. Hewett. "From a caregiver's perspective, working with patients with diverse ages, fitness levels and athletic abilities is a tremendous opportunity to improve lives on a broad scale."

Staff members at Mayo Clinic Sports Medicine Center are excited about Dr. Hewett's arrival. "We are blessed to have the experience and expertise of one of the world's foremost sports medicine researchers now working with our team," states Edward R. Laskowski, M.D., co-director of Mayo Clinic Sports Medicine Center in Rochester, Minnesota. "Our goal of providing the world's best sports medicine care includes a practice that is based on research-proven injury protection and rehabilitation principles, and Dr. Hewett's work will further help us to achieve this mission."

"Dr. Hewett's extensive expertise spans molecular dynamics, biomechanics and physiology with an emphasis in specialized knee injury prevention programs, an area in which he is an



Timothy Hewett, Ph.D., and colleagues use a variety of tools to assess risk of ACL tear and other injuries that affect athletes. In this photo, a runner undergoes gait analysis to screen for risk factors associated with overuse injuries.


Timothy Hewett, Ph.D.

internationally recognized leader," adds Michael J. Stuart, M.D., co-director of Mayo Clinic Sports Medicine Center in Rochester, Minnesota. "His experiences and forward thinking directly influence the kind of next-generation sports medicine we offer."

Throughout the course of his career, Dr. Hewett has received many prestigious honors, including the 2015 O'Donoghue Award from the American Orthopaedic Society for Sports Medicine (AOSSM), the 2015 Hay Award from the American Society of Biomechanics (ASB), and the 2016 Orthopaedic Research and Education Foundation (OREF) Clinical Research Award from the American Academy of Orthopaedic Surgeons (AAOS) and the Orthopaedic Research Society (ORS).

A 3-prong, life span research model

Dr. Hewett's research optimizes sports performance through a three-prong model he has developed. The three prongs are:

1. Focusing on investigating and understanding mechanisms of injury
2. Identifying individuals at risk
3. Intervening to optimize injury prevention

He expects to refine this approach at Mayo Clinic Sports Medicine Center so that it can be applied across the life span for children, professional athletes and seniors.

"Given the expertise and collaborations available at Mayo Clinic, we have a unique opportunity to extend this model," explains Dr. Hewett. "Working with a broad spectrum of patients is a very, very appealing opportunity to me because, as a researcher, it enables me to investigate changes over time of human health, fitness and performance."

Currently, Dr. Hewett and colleagues are performing research to determine:

1. How adolescent girls develop the machine-motor mismatch and neuromuscular imbalances that put them at risk of anterior cruciate ligament (ACL) injury
2. What puts young active athletes at a near one-third risk of a second ACL tear after ACL reconstruction
3. If neuromuscular training targeted to specific modifiable risk factors for second ACL injuries can modify this unacceptably high risk

"We are excited to have Dr. Hewett as part of our team," states Jonathan T. Finnoff, D.O., medical director of Mayo Clinic Sports Medicine Center in Minneapolis. "His career has been highlighted by multiple breakthroughs that have impacted the way health care providers around the world approach injury prevention. We believe that his work will continue to thrive within our multidisciplinary environment of clinicians and scientists at Mayo Clinic."

Blocking the Receptor Protein PAR2 May Reduce Inflammation and Improve Recovery After Spinal Cord Trauma


Isobel A. Scarisbrick, Ph.D.

Astrogliosis and inflammation are part of the cascade of events that occurs after spinal cord injury (SCI). While certain components of this cascade worsen tissue damage and limit wound healing, other facets are essential to creating an environment favorable to repair. In a recent animal study published in *Neurobiology of Disease*, researchers at Mayo Clinic's campus in Rochester, Minnesota, examined a receptor called protease activated receptor 2 (PAR2) that appears to play a key role in promoting inflammation after SCI. Study results suggest that therapies targeting PAR2 may help limit trauma-induced astrogliosis and improve recovery of function.

Study design

Researchers induced a clinically relevant spinal cord contusion-compression injury in two groups of mice: those lacking the PAR2 gene (the PAR2 –/– group) and their wild-type littermates (the PAR2 +/+ group). Mice were randomized with respect to genotype, and investigators were blinded to genotype throughout the experiment.

Significant findings

To investigate the role of PAR2 on neurobehavioral recovery after spinal cord trauma, researchers measured and compared motor coordination and strength in the two groups the day after

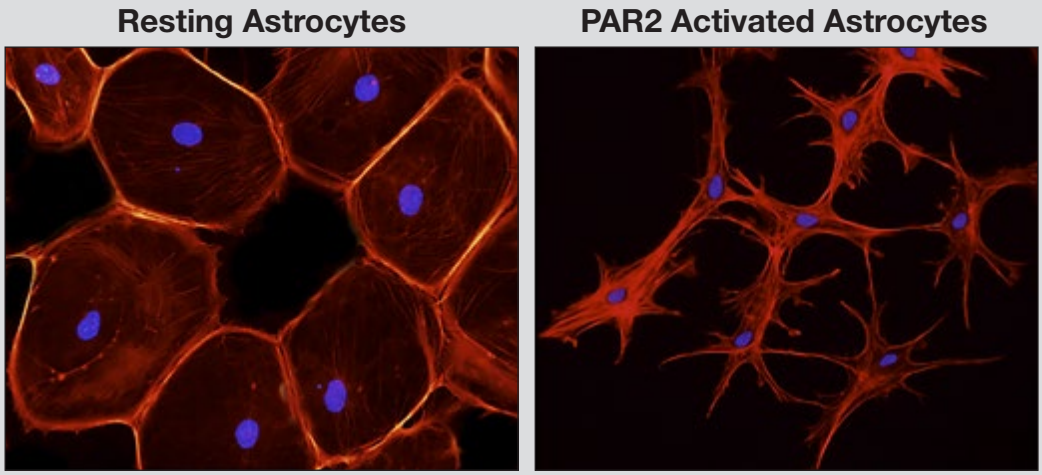


Figure. Activation of PAR2 promotes formation of a glial scar. Images show astrocytes grown in cell culture and visualized by staining of their actin cytoskeleton using rhodamine-conjugated phalloidin. Resting astrocytes have a rounded epithelioid appearance but become highly stellate with interdigitating processes upon activation of the receptor PAR2. The PAR2-mediated transformation of astrocytes to a stellate morphology with accompanying increases in IL-6 production is reminiscent of the reactive astrocyte scar that develops after spinal cord injury. Images by Maja Radulovic, Ph.D.

surgery and weekly thereafter for 30 days. Before injury, PAR2 +/+ and PAR2 –/– mice displayed identical patterns of motor activity. By one week after injury and at the one-month endpoint, however, the PAR2 –/– group showed greater improvements in motor coordination and strength than did the PAR2 +/+ group.

At one month after SCI, researchers also analyzed the injury epicenter and spinal cord segments above and below it, evaluating the tissue for signs of injury and repair. Using these tissue samples to evaluate molecular signatures of injury and repair yielded several interesting results. PAR2 –/– mice had significantly lower levels of markers for astrogliosis, including glial fibrillary acidic protein (GFAP), vimentin and neurocan, and reduced expression of proinflammatory cytokines (interleukin-6, or IL-6), tumor necrosis factor (TNF) and interleukin-1 beta (IL-1β) (Figure).

SCI in PAR2 –/– mice was also accompanied by improvements in preservation of protein kinase C gamma (PKCγ)-immunopositive corticospinal axons and reductions in expression of markers of cell death and in signal transducer and activator of transcription 3 (STAT3), a prominent proinflammatory signaling pathway. These changes reflect improvements in the lesion microenvironment that are compatible with tissue preservation and repair.

"Our study results suggest that PAR2 could serve as an extracellular switch turning on signaling pathways after SCI that limit motor recovery at least in part by promoting inflammation and astrogliosis," says Isobel A. Scarisbrick, Ph.D., the study's lead investigator and director of the Central Nervous System Injury and Neurorehabilitation Laboratory at Mayo Clinic's campus in Rochester, Minnesota. "The superior neuromotor recovery and significant reductions in astrogliosis and inflammation in PAR2 knockout mice after SCI suggest that PAR2 and its agonists could become new drug targets for recovery of function."

Dr. Scarisbrick notes that additional research is needed to define the range of cells expressing PAR2 in SCI, to determine what additional mechanisms may be involved, and to establish whether PAR2-inhibitors replicate the outcome improvements observed in animals lacking the PAR2 gene. The team of researchers is also interested in targeting this receptor in models of chronic SCI.

For more information

Radulovic M, et al. Genetic targeting of protease activated receptor 2 reduces inflammatory astrogliosis and improves recovery of function after spinal cord injury. *Neurobiology of Disease*. 2015;83:75.

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Education Opportunities

Geriatrics and Orthopedics Residencies for Physical Therapists

These yearlong post-professional clinical and didactic education training programs are designed to advance a physical therapist's preparation as a provider of patient care services.

Mayo Clinic Physical Medicine and Rehabilitation Board Review 2016

May 18-20, 2016, in Rochester, Minn.

This course is designed for candidates preparing for certification and maintenance of certification examinations in physical medicine and rehabilitation and uses a combination of online learning, didactic lecture and mock oral examinations.

14th Annual ACL Workshop

May 20-21, 2016, in Minneapolis

This course will utilize hands-on workshops and new, state-of-the-art 3-D motion analysis. Participants will learn athlete screening techniques and neuromuscular training methods that focus on proper core, knee control and landing techniques. Lectures on the latest advances in the field will include demonstrations in Mayo's new indoor turf field, rehabilitation and training floor, and 3-D Lab.

5th Annual Comprehensive Sports Medicine Update and Board Review

June 22-25, 2016, in Minneapolis

This one-of-a-kind course is designed to provide a comprehensive review of all subjects contained in the sports medicine board examination.

For more information: Visit *https://ce.Mayo.edu/physical-medicine-and-rehabilitation/pmr*, call 800-323-2688 (toll-free) or email *cme@mayo.edu*.

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