The Mayo Clinic Center for Regenerative Medicine recently announced the launch of the Musculoskeletal Regeneration Program. Physicians and scientists in this new program are focused on the repair of diseased or injured tendons, ligaments, cartilage, muscle and bone using advanced stem cell and tissue engineering platforms. This work involves a multidisciplinary team encompassing orthopedic surgery, sports medicine, physical medicine and rehabilitation, and rheumatology with the common goal to improve the current standard of care. These emerging regenerative technologies, focusing on structural repair and functional restoration, are poised to provide innovative solutions that address unmet patient needs.

Musculoskeletal degeneration and complications from injuries are becoming more prevalent as the population lives longer and participates in rigorous athletic and recreational activities. These tissue defects may immobilize patients, as well as cause inflammation and pain.

This team represents a therapeutic pipeline from biomedical discovery to clinical application that seeks to repair, restore or rejuvenate bone, cartilage and soft tissue structures that are affected by acute injury, chronic degeneration, genetic dysfunction and cancer-related defects.

Mayo researchers will examine musculoskeletal tissue injury and repair using molecular, cellular, tissue and organ-level approaches, including molecular profiling, histology, imaging and biomechanics, to support the integration of new knowledge to improve the diagnosis and treatment of diseases and injuries of the skeleton and its associated tissues.

The Musculoskeletal Regeneration Program is based at Mayo Clinic’s campus in Rochester, Minnesota, and led by Mark W. Pagnano, M.D., chair of Orthopedic Surgery. As efforts in the Musculoskeletal Regeneration Program span the full spectrum of discovery, translation and clinical application, Andre J. van Wijnen, Ph.D., will serve as associate director, discovery; Christopher H. Evans, Ph.D., director of Mayo Clinic’s Rehabilitation Medicine Research Center, will serve as associate director, translation; and Jay Smith, M.D., vice chair of Physical Medicine and Rehabilitation, will serve as associate director, clinical application.

Listed below are a few of the current projects led by staff from Physical Medicine and Rehabilitation at Mayo Clinic.

### New Musculoskeletal Regeneration Program Represents Therapeutic Pipeline From Biomedical Discovery to Clinical Implementation

**Slowing or reversing muscle loss via myostatin inhibition**

Lead investigator: Nathan K. LeBrasseur, M.S., Ph.D., Physical Medicine and Rehabilitation, at Mayo Clinic’s campus in Rochester, Minnesota

Dr. LeBrasseur and colleagues are exploring new ways to increase muscle mass and improve strength, physical function and whole-body metabolism, and reduce frailty related to aging and chronic disease. This research focuses on the growth and differentiation factor-8 (GDF-8), also known as myostatin, which functions as a potent negative regulator of muscle growth. Mayo researchers are examining whether myostatin can serve as a mediator of sarcopenia or cachexia and as a therapeutic target. Dr. LeBrasseur’s team has just developed a novel assay to specifically and
accurately measure myostatin and related proteins in a small volume of human blood. And the team is participating in a multicenter clinical trial of a myostatin receptor antagonist in people age 70 and older with sarcopenia and reduced mobility.

**Autologous culture-expanded adipose-derived mesenchymal stromal cells for knee osteoarthritis**

*Lead investigator: Jay Smith, M.D., vice chair of Physical Medicine and Rehabilitation at Mayo Clinic, and associate director, clinical application, for the Musculoskeletal Regeneration Program*

According to Dr. Smith, this will be the first trial at Mayo Clinic to examine the safety and efficacy of culture-expanded stem cells for the treatment of knee osteoarthritis, a problem affecting millions of Americans. This trial represents a critical step in developing next-generation cellular therapies that can be delivered in the clinic. Currently, Mayo Clinic offers bone marrow concentrate (BMC) to patients with refractory arthritis who want to avoid or delay surgical intervention. BMC contains a variety of potentially beneficial cells (including stem/stromal cells) as well as bioactive factors.

**Use of gene therapy for knee osteoarthritis, phase 1 clinical trial**

*Lead investigator: Christopher H. Evans, Ph.D., director, Mayo Clinic Rehabilitation Medicine Research Center, and associate director, translation, for the Musculoskeletal Regeneration Program*

Approximately 27 million Americans have osteoarthritis, and the disease is incurable, largely untreatable and the major cause of disability among the elderly. The Mayo research team plans to use a viral vector to introduce an antiarthritic gene into the knee joints of patients with osteoarthritis. In separate studies, gene therapy is being developed to regenerate cartilage and heal bone.

**Use of platelet-rich plasma for the treatment of hip osteoarthritis**

*Lead Investigator: Jacob L. Sellon, M.D., Physical Medicine and Rehabilitation and Sports Medicine Center at Mayo Clinic’s campus in Rochester, Minnesota*

This prospective investigation will compare the effects of cortisone versus platelet-rich plasma (PRP) injections for the treatment of hip osteoarthritis. PRP, which is generated from the patient’s own blood, contains a variety of anti-inflammatory and regenerative substances and has demonstrated some promise in the treatment of knee arthritis. Mayo Clinic physiatrists have used PRP to treat tendon, ligament and joint disorders for many years to reduce pain and improve function. The effect of PRP on hip arthritis has not been well-studied. Given the high prevalence of hip arthritis and limited nonsurgical treatment options, Mayo researchers believe that this is an important topic to study.

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**Researchers Study Use of Lower Limb Exoskeletons in Patients With Spinal Cord Injuries**

Powered lower limb exoskeletons have recently gained attention as a potential rehabilitative intervention for people with spinal cord injury (SCI). Many believe that these devices have the potential to provide substantial health benefits, promote neurological and functional recovery, and provide community ambulation for individuals with SCI. However, more research is necessary to firmly identify and quantify the health benefits associated with their use.

Mayo researchers, in partnership with researchers at Vanderbilt University and the James A. Haley Veterans’ Hospital in Tampa, Florida, were recently awarded a grant from the Department of Defense to study the use of these devices in veterans with SCI who are currently wheelchair users and have limited or no ambulatory abilities using their lower limbs. The research team will test three hypotheses:

1. Regular use of an exoskeleton for walking will provide health benefits, including decreased pain and spasticity, improvement in bowel and bladder function, decreased BMI, and enhanced well-being.
2. Regular use of an exoskeleton for walking will facilitate neurological or functional recovery in individuals with incomplete injuries.
3. The level of mobility enabled by lower limb exoskeletons will be commensurate with the walking speeds, distances and surfaces required for community ambulation.

These hypotheses will be assessed in three studies, each of which represents a different specific aim and treatment setting or context. The first study will address exoskeleton use in a clinical setting. The second study will address exoskeleton walking in a clinical setting, in which the exoskeleton movement is supplemented with functional electrical stimulation of the leg and trunk muscles. The third study will address exoskeleton use in the home and community.

“These studies could yield significant findings about the potential benefits associated with lower limb exoskeleton use,” explains Kristin D. Zhao, Ph.D., director of the Assistive and Restorative
Technology Laboratory in the Rehabilitation Medicine Research Center at Mayo Clinic’s campus in Rochester, Minnesota. Dr. Zhao is serving as the Mayo Clinic study site’s principal investigator and collaborates with Michael Goldfarb, Ph.D., the study’s principal investigator who is based at Vanderbilt University. “If this device substantially mitigates the prevalence of secondary impairments outlined in our hypotheses, its use could substantially decrease the cost of health care for individuals with SCI,” says Dr. Zhao. “If we establish that exoskeleton use facilitates neurological and/or functional recovery in patients with motor-incomplete injuries, this intervention could have a substantial impact on improving rehabilitative outcomes for many individuals.”

“Outside of the clinical setting, we are hopeful that exoskeleton use will enhance the ability of people with SCI to participate in the community and possibly even facilitate their return to work, which could have significant positive economic benefits,” adds Dr. Goldfarb.

Study investigators are hopeful that a positive outcome from any of these hypotheses will have the potential to greatly improve the quality of life for individuals with SCI, and to substantially decrease the associated costs of their care.

The researchers expect to recruit 54 individuals with spinal cord injury to participate in this study, and recruitment is slated to begin in early 2016.

Mayo Researchers Receive Department of Defense Grant to Study Personal Seat Pressure Monitoring System

Despite decades of efforts to identify risk factors, improve patient education and develop interventions, sitting-acquired pressure ulcers in individuals with spinal cord injury (SCI) occur in about 35 percent of patients. In addition to their significant impact upon mortality and morbidity, pressure ulcers contribute approximately $6.3 billion a year in medical expenses in the United States. Pressure ulcers also have a profoundly negative impact on quality of life. Plenty of effective prevention strategies exist for known risk factors. However, risk factors such as cushion or equipment failure, change in weight, caregiver or lifestyle change, and unforeseen events or delays causing a shift in a person’s routine are often less predictable and preventable. When problems of this variety go undetected, an ulcer can develop.

Mayo researchers are studying in-home use of seat pressure monitoring as a means to reduce patients’ risk of pressure sores. Systems designed for use in the clinical setting use expensive components and complex data displays. In 2012, a Mayo research team that included Tamara L. Vos-Draper, O.T., ATP, an occupational therapist at Mayo Clinic’s campus in Rochester, Minnesota, set out to develop a prototype pressure-mapping system that would provide patients with in-home access to relevant information that is easily understood. Through that effort, Vos-Draper and colleagues developed and tested a prototype of a smartphone-based system that provides in-home access to pressure-mapping data. The system that the Mayo team developed consists of a thin and flexible pressure mat that wirelessly transmits data to a smartphone via a Web-based application. Using this system, patients can view their average pressure and dispersion index in real time or send the data to a seating clinic specialist at Mayo Clinic for analysis.

Vos-Draper notes that the original system had a few limitations. “We learned that we need to make the system work on multiple mobile platforms. Connection between the mobile device and mapping system on the original prototype was also not ideal, due to limitations in wireless transmission at the time. Fortunately, technology has advanced and allowed for improved connectivity options. Users have also expressed a need for features such as alerts and reminders to be included within the application.”

The Mayo Clinic research team for this phase of research includes Melissa (Missy) M. Morrow, Ph.D., Center for the Science of Health Care Delivery, principal investigator; and Vos-Draper, Katherine Carroll, Ph.D., Health Care Policy and Research, and Kenton R. Kaufman, Ph.D., Orthopedic Surgery, co-investigators. Additional research partners from the Minneapolis VA Health Care System include John Ferguson, Ph.D.; Christine Olney, R.N., Ph.D.; Andrew Hansen, Ph.D.; Gary Goldish, M.D.; and Byron Eddy, D.O.

Building upon what they learned while testing the first prototype, the team’s two primary objectives for this project focus on the collection of iterative feedback from veterans with SCI to expand development of a personal seat pressure monitoring system. Their second objective is to measure change in pressure relief behavior (movement) in wheelchair users with SCI when provided with individualized visual biofeedback that displays how much pressure they have on their buttocks.

The resulting personal seat pressure monitoring system will provide real-time visual feedback, similar to a weather map, depicting areas and amounts of pressure on a user’s seated surface (Figure). Specific and immediate feedback will
prompt positional changes to relieve pressure. “Patients will see immediate validation of reduced pressure via the live image on their mobile phone or handheld device,” says Vos-Draper.

Although the intended use for this system is outside of the clinic, Vos-Draper points out that there are important clinical applications. Communication between patient and clinician is improved when the patient has increased capability to self-monitor his or her sitting behaviors and pressure distribution when sitting.

“This information is often lacking during clinical assessments. Providers can use it to develop more individualized strategies for equipment or pressure relief techniques,” explains Vos-Draper. “In addition, early detection and early intervention can help successfully prevent a more severe and costly ulcer.”

The study will span three years. During the first year, Mayo researchers will study the system among veterans with SCI to gather evaluative feedback while the enhanced mobile application is developed. The second year will involve sending the personal seat pressure monitoring system home with six veterans with SCI for six weeks.

“Our team will gather data on usability of the system, as well as how access to the system affected the user’s pressure relief movement patterns,” says Vos-Draper. At the end of year three, Vos-Draper and colleagues are hoping to make this comprehensive seat pressure monitoring system readily available for use by all individuals with SCI for managing their skin health.

Figure. The personal seat pressure monitoring system will provide real-time visual feedback, similar to a weather map, depicting areas and amounts of pressure on a user’s seated surface.

Education Opportunities

**Mayo Clinic Rehabilitation Medicine Update at San Juan 2016**
Feb. 5-7, 2016, in San Juan, Puerto Rico
This course is designed as an update of techniques and topics pertaining to physical medicine and rehabilitation and includes osteoporosis, amputee, ultrasound injection, cancer rehabilitation, brain injury, spinal cord injury, pain, EMG, hand and more.

**Mayo Wound Symposium 2016**
Feb. 18-20, 2016, in Rochester, Minn.
Learn about the latest diagnostic and treatment strategies for comprehensive wound management via interactive workshops, hands-on demonstrations, educational sessions and case presentations.

**Neurorehabilitation Summit: Regeneration, Recovery, Reintegration 2016**
April 11-12, 2016, in Rochester, Minn.
This comprehensive course addresses the complex issues surrounding neurorehabilitation, including brain injury, brain rehabilitation, regeneration recovery and spinal cord injury.

**Mayo Clinic Physical Medicine and Rehabilitation Board Review 2016**
May 18-20, 2016, in Rochester, Minn.
This course is designed for candidates preparing for certifying and maintenance of certification examinations in physical medicine and rehabilitation and uses a combination of online learning, didactic lecture and mock oral examinations.

**5th Annual Comprehensive Sports Medicine Update and Board Review 2016**
June 22-25, 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](https://ce.Mayo.edu/physical-medicine-and-rehabilitation/pmr), call 800-323-2688 (toll-free) or email cme@mayo.edu.