



▲ Lt. Col. Steven J. Svoboda, MD, USMC

College students who enter the U.S. Military Academy at West Point anticipate a life of public service. Now, through an OREF grant, **Lt. Col. Steven J. Svoboda, MD, USMC** is providing an opportunity for these community-minded young Americans to advance our national interest in an unexpected way.

Lt. Col. Svoboda's OREF grant supports investigation of "Changes in Serum Biomarkers for Cartilage Turnover Following ACL Reconstruction and their Relationship to the Development of Osteoarthritis." West Point cadets are providing blood samples for this study, which may reveal biological indicators to identify and treat postsurgical knee-joint degeneration before

GETTING A LEG UP

OREF grant recipient hopes to help ACL patients leapfrog osteoarthritis

it detracts from quality of life and requires additional invasive and expensive surgery.

"The idea of serum biomarkers as a better strategy to monitor post-ACL reconstruction osteoarthritis isn't new," explained Lt. Col. Svoboda, an orthopaedic surgeon at Keller Army Community Hospital on the West Point campus. "But one major limitation of prior studies has been the lack of pre-injury biomarker benchmarks in postsurgical patients."

According to Lt. Col. Svoboda, West Point cadets are an ideal population to eliminate this limitation. "All cadets have blood drawn when they enter the academy, upon graduation and at two-year intervals as long as they remain in active service," he said. These samples become part of the Department of Defense Serum Repository (DODSR), a biological archive that includes all members of the armed forces, established to aid in medical surveillance, clinical diagnosis and epidemiological monitoring.

Blood samples of cadets who undergo ACL reconstruction offer a unique perspective on biomarker profiles and trends in the same individuals before and after surgery. Plus, the DODSR offers comparable data for their uninjured peers.

"We may gain important clues about normal biomarker values and who's most likely to develop osteoarthritis following ACL reconstruction," said Lt. Col. Svoboda. "Eventually, this work could suggest new intervention strategies before a total knee replacement is needed."

IMPLICATIONS FOR BOTH CIVILIAN AND MILITARY PATIENTS

The American Academy of Orthopaedic Surgeons estimates that 200,000 ACL injuries and 100,000 reconstructions take place annually. There is a growing realization—in part due to AAOS awareness efforts—that ACL injuries pose a significant risk for soldiers as well as athletes and other physically active civilians.

"Young soldiers run on rough terrain carrying heavy equipment, jump off walls and engage in other military activities that put high stress and torque on the lower limbs. Long-term macroeconomic and quality-of-life issues for ACL injury are substantial—for both young soldiers and the civilian population," explained Lt. Col. Svoboda.

ACL reconstructions are performed using a variety of grafts, and current arthroscopically assisted surgical

techniques have short- and mid-term success rates exceeding 90%. However, there is growing evidence that even highly successful reconstruction often can't completely restore long-term optimal knee biomechanics. Early functional success may not eliminate post-traumatic cartilage degeneration and eventual osteoarthritis for a significant percentage of patients.

The current gold standard for detecting post-ACL reconstruction osteoarthritis is a weight-bearing knee X-ray. But soft-tissue damage is already irreversible and has progressed to bone by the time it's visible.

Blood biomarkers could offer a cost-effective alternative to identify early signs of joint degeneration, stratify patients according to osteoarthritis risk and offer a window of intervention before function is severely affected. Early-warning biomarkers might also suggest new molecular targets for eventual new therapies that preserve or reconstitute tissue.

BIOMARKER TRENDS

Lt. Col. Svoboda made some strategic choices in designing his study and selecting biomarkers. "One challenge I faced was not being at a university with a large protein chemistry laboratory that could develop

new tests for previously unstudied biomarkers. I had to choose from the known universe of commercially available enzyme-linked radiolabeled assay (ELISA) kits.

"In fact, the analytic physiology lab I work with at West Point is administratively separate from Keller Army Community Hospital even though the two facilities are on the same campus. My OREF funding enabled me to forge a larger research team with stronger cross-institutional ties than we've fielded before. It's a new model for us."

In addition to considering commercial ELISA availability, Lt. Col. Svoboda chose four biomarkers—CPII, CS846, C1,2C and C2C—based on published literature supporting their connection to the synthesis or breakdown cycles of cartilage turnover, processes closely associated with future osteoarthritis.

The study enrolls 71 cadets who sustained an ACL injury requiring surgical reconstruction during their West Point careers and 71 uninjured controls matched for age, sex and body mass index. All participants have West Point entry and graduation blood samples archived in the DODSR.

The goal is to determine whether statistically significant trends and changes in those four biomarkers can be detected in participants

who underwent ACL reconstruction compared with uninjured participants.

Participants undergoing ACL reconstruction will also have knee X-rays taken to detect evidence of postreconstruction osteoarthritis and if present, determine whether it is tied to consistent signals in pre- and post-surgery biomarker ratios.

"Post-traumatic osteoarthritis is a very active area of research, and there will be interest in building on our OREF-funded results," noted Lt. Col. Svoboda. "Just after I learned of my OREF grant, I attended the 2008 Post-Joint Injury Osteoarthritis Conference, collaboratively sponsored by the American Orthopaedic Society for Sports Medicine and the National Institutes of Health. The conference made clear the enormous impact osteoarthritis has on quality of life and our annual health care outlays. It truly serves our national interest to find better solutions to this disabling condition." ■