Biomarker could make diagnosing knee injury easier, less costly, othopaedists say

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A recently discovered biomarker could help doctors diagnose a common type of knee injury, according to a new study.

A team of researchers led by Gaetano Scuderi, MD, clinical assistant professor of orthopaedic surgery at Stanford University School of Medicine and an orthopaedic surgeon at Stanford Hospital & Clinics, has confirmed that a particular protein complex appears in patients with painful meniscal tears. The finding, to be published Feb. 16 in *The Journal of Bone and Joint Surgery*, could be used to prevent needless surgery and to save billions of dollars in medical-imaging costs.

The menisci are two crescent-shaped pieces of cartilage in each knee joint. Contact sports, such as football, as well as sports that involve lot of pivoting, such as basketball and tennis, increase the risk of the cartilage tearing. It is also prone to tear as a result of natural degeneration, meaning older people are at increased risk. Meniscal tears are painful and usually accompanied by swelling and stiffness. Sometimes the knee joint feels as though it is locked in place.

Patients are generally advised to elevate and apply ice to the knee, as well as to take a break from physical activity that could aggravate the injury. These measures might not be enough, however, so patients can undergo a minimally invasive procedure, arthroscopic surgery, to trim away or repair the meniscus.

But identifying whether a patient's knee pain stems from a meniscal tear,

as opposed to joint arthritis or another type of leg injury, is difficult. For example, in an older patient, magnetic-resonance imaging might reveal an abnormal-looking meniscus that doctors mistake as evidence of a painful tear, even though it is just due to natural degeneration from lots of wear over the years. For such a patient, who is perhaps really suffering from joint arthritis, meniscal surgery would offer no relief.

Knee pain also can stem from other parts of the body. For example, a young athlete who complains of symptoms similar to those of a torn meniscus may undergo a costly MRI that reveals no cartilage abnormalities. In reality, an injured hip ligament could be causing the knee to hurt. "It's like someone with heart disease feeling pain in his left shoulder," Scuderi said.

In the study, Scuderi and his co-authors found that the biomarker appeared in the knee fluid of 30 patients who had suffered a painful meniscal tear. It was not present in the knees of 10 asymptomatic patients. The biomarker, a fibronectin-aggrecan complex, holds out the promise of allowing orthopaedists to quickly and accurately diagnose whether the source of a patient's discomfort is a meniscal tear, as opposed to another type of injury or abnormality, simply by taking a sample of knee fluid. It could thus obviate the need for expensive medical scans and help to prevent surgery that does not address the true cause of a patient's pain.

"The challenge is not identifying molecular markers of cartilage degeneration, dozens of which are now known," said co-author Raymond Golish, MD, PhD, who recently completed a fellowship in spine surgery at Stanford. "The difficulty is in finding markers that correlate with painful injuries, as opposed to age-related degeneration that is painless. This study is a big step in that direction."

Scuderi and his colleagues undertook the prospective study to validate

their findings from an earlier study in which they first noted the presence of the protein complex in patients with torn menisci and knee pain. (Those results were published in the July 2010 issue of *Clinical Biochemistry*.)

The researchers are now running experiments to confirm that the biomarker does not show up in other types of knee injuries, such as ACL tears unaccompanied by meniscal tears. They also are studying whether the protein complex, which is implicated in knee inflammation, could serve as a therapeutic target. "We could envision several things, such as blocking the fibronectin and aggrecan protein fragments from coming together to form a complex, or interfering with the activation of white blood cells at the site," Scuderi said.

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