Novel Biomarker Detects Early Rheumatoid Arthritis Better than Conventional Methods Alone, According to Journal of Rheumatology Study

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Testing for the protein 14-3-3eta may improve the diagnosis of RA, including in early stages when treatment is most likely to improve outcomes

MADISON, N.J., Aug. 27, 2014 /PRNewswire/ -- A novel biomarker for rheumatoid arthritis (RA) has significant potential to help physicians better identify early-stage disease, when treatment can often arrest further disease progression and disability, according to a new study in The Journal of Rheumatology.

Researchers from Quest Diagnostics (NYSE: DGX) and other institutions found that elevated blood-serum levels of the 14-3-3eta protein outperformed conventional antibody-serum testing, including rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA, also known as antibodies to cyclic citrullinated peptides or CCP), for the identification of RA.

In the study, 64% of patients with early RA were positive for 14-3-3eta, compared to 59% and 57% for either ACPA or RF, respectively. When results of all three markers were assessed, 78% of patients with early-stage RA (3.4 months) and 96% of patients with established RA (11.5 years) were identified. This compares to 72% of patients with early-stage RA and 88% of patients with established RA identified by just RF and/or ACPA. Physicians often consider results of separate RF and ACPA test results to aid the diagnosis of RA.

The study also found that 14-3-3eta was more sensitive at detecting patients whose early blood test results by RF and ACPA were negative. In these "seronegative" patients, 14-3-3eta positively identified 21% of patients with early RA and 67% with established RA. Seronegativity in both early and established RA is a major limitation of RF and ACPA, as it can delay initiation of treatment.

"While previous research established that 14-3-3eta is found in higher levels in patients with RA than healthy patients, our study demonstrates the clinical usefulness of 14-3-3eta for improved diagnostic capacity of testing for early RA. Combined testing of 14-3-3eta with established markers will help provide physicians with more definitive diagnostic information and help facilitate early treatment with disease modifying anti-rheumatic drugs," said Walter Maksymowych, M.D., medical research professor, Medicine and Rheumatologist, the University of Alberta, Canada and the study's principal investigator.

The study, "Serum 14-3-3eta is a Novel Marker that Complements Current Serological Measurements to Enhance Detection of Patients with Rheumatoid Arthritis," is available at: http://jrheum.org/content/early/2014/08/21/jrheum.131446.full.pdf+html

RA is an autoimmune disorder affecting an estimated 1.3 million American adults. In cases of RA, the immune system attacks the body's own tissues, especially the membranes that line the joints. As a result, fluid builds up in the joints, causing pain and systemic inflammation, leading to joint destruction if untreated.

An early diagnosis of RA has been a challenge for clinicians because symptoms are often subtle and can be similar to those of other autoimmune disorders. Diagnosis and initiation of treatment of RA within 12 weeks of symptom onset – referred to by the study authors as the "window of opportunity for therapy intervention" – can help prevent joint damage and improve long-term function and patient prognosis. Yet many patients are not diagnosed during this time frame.

For the analysis, researchers analyzed the serum 14-3-3eta levels of 99 de-identified early RA patients from the Toronto Early Arthritis Cohort (TEACH; Mount Sinai, Canada), the Intensified-Combination Therapy with Rheumatoid Arthritis cohort (COBRA; VU University Medical Center, Netherlands) and the Reade prospective early RA cohort (Reade, Netherlands) and 135 de-identified established RA patients from the Rheumatoid Arthritis Pharmacovigilance Program of Outcomes Research Team (RAPPORT) cohort from the University of Alberta, Canada, and from Bioreclamation Inc. in the United States. The levels were compared to the levels of 14-3-3eta in 385 de-identified patients in control groups, included individuals presumed healthy, patients with osteoarthritis, and patients diagnosed with other autoimmune diseases.

Additional key findings from the study:

- The association of 14-3-3eta with identification of early RA may reflect a more severe phenotype of disease. The study found that 14-3-3eta positive patients had significantly worse disease based on clinical measures when compared to 14-3-3eta negative patients.

- 14-3-3eta serum levels were higher in individuals with early and established RA, compared to healthy individuals and those in all control groups, suggesting the biomarker may help discriminate patients with RA from those with certain other autoimmune diseases as well as healthy patients.
- The differential diagnosis between osteoarthritis and early RA is often difficult for primary practitioners. Serum 14-3-3eta levels were significantly higher in patients with early RA than in patients with osteoarthritis, suggesting 14-3-3eta results may help primary care physicians identify patients for referral to a rheumatologist.
- 14-3-3eta serum levels were significantly higher in patients with erosive psoriatic arthritis (PsA) compared to nonerosive PsA, an autoimmune disease.

"Our finding that the 14-3-3eta protein is elevated in RA and to a lesser extent in erosive PsA, but not in other inflammatory diseases, offers clinical utility for physicians because test results can help lead to a differentiated diagnosis," said Stanley J. Naides, M.D., F.A.C.P., F.A.C.R., medical director, Immunology R&D, Quest Diagnostics and one of the study's authors. "Additionally, the correlation between 14-3-3eta positivity and disease onset and severity may assist clinicians in personalizing the best course of treatment for the patient."

Quest Diagnostics exclusively offers 14-3-3eta testing as part of its lab-developed Rheumatoid Arthritis Diagnostic Panel IdentRA™ through a 14-3-3eta-biomarker licensing agreement with Augurex Life Sciences. Quest Diagnostics offers a broad menu of immunology diagnostic information services for assessing immune function and autoimmunity.

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