MAYO CLINIC LABORATORIES

Test Definition: 1433E

14-3-3 eta, Serum

Overview

Useful For

A potentially improved approach for the early identification of patients at-risk for or with early and established rheumatoid arthritis (RA) in combination with specific autoantibody tests

This test is intended to be used as an aid in the early diagnosis of RA and management of the disease.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

No

Specimen

Specimen Type

Serum SST

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume

Serum: 0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum SST	Refrigerated (preferred)	14 days	
	Ambient	48 hours	

	Frozen	100 days	

Clinical & Interpretive

Clinical Information

Serum 14-3-3 eta protein belongs to the 14-3-3 family of intracellular chaperone proteins (beta, gamma, epsilon, eta, sigma, theta, zeta). It is a joint-derived proinflammatory mediator that up-regulates cytokines and enzymes that perpetuate local and systemic inflammation and may contribute to joint damage.

Serum 14-3-3 eta is detectable at significantly higher levels in the serum from patients with rheumatoid arthritis (RA) when compared to healthy subjects and individuals with RA mimickers (other autoimmune conditions and viral/bacterial infections). It has also been reported as an important biomarker in diagnosing cases that are seronegative for traditional markers like rheumatoid factor (RF) and anti-citrullinated protein/peptide antibodies (ACPA).

In addition to the contribution of 14-3-3 eta in the diagnosis of RA, previous studies have reported its clinical potential of 14-3-3 eta as a predictor of poor clinical and radiographic outcomes, both at baseline and after initiation of treatment, even in Simplified Disease Activity Index (SDAI) remitters. These studies suggest that 14-3-3 eta, c-reactive protein, age, and ACPA represent independent predictors of subsequent joint damage.

Reference Values

< 0.19 ng/mL

Interpretation

Serum 14-3-3 eta was tested in a clinically characterized rheumatoid arthritis (RA) and early RA patient Mayo Clinic patient cohort, where 275 of 446 patients (82.6%) were seropositive (defined as having 3rd generation anti-CCP IgG antibody [CCP3] >20 U and/or rheumatoid factor [RF] >14 IU/mL). A 14-3-3 eta cutoff of > or =0.19 ng/mL for both early and established RA patients was used to calculate the sensitivity and specificity of 14-3-3 eta for RA (n=113) and early RA (n=95).

Serum 14-3-3 eta slightly increased sensitivity for RA (87.0%) and early RA (75.8%) when used in concert with anti-CCP3 IgG and RF, versus the use of a combination of anti-CCP3 IgG and RF alone (RA sensitivity 82.6%, and early RA sensitivity 74.7%).

The addition of 14-3-3 eta offers an increase in specificity for RA (99.1%), and early RA (99.1%), relative to observed positivity with RF and anti-CCP3 IgG antibodies without the use of 14-3-3 eta (RA specificity 94.7%, and early RA specificity 94.7%).

Serum 14-3-3 eta concentration (ng/mL)	Qualitative Interpretation
<0.19	Negative
> or =0.19-0.39	Mild positive
> or =0.40-0.79	Moderate positive
> or =0.80	Strong positive

Cautions

A test result that is inconsistent with the clinical picture and patient history should be interpreted with caution.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies or heterophile antibodies) that may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

1. Kilani RT, Maksymowych WP, Aitken A, et al. Detection of high levels of 2 specific isoforms of 14-3-3 proteins in synovial fluid from patients with joint inflammation. J Rheumatol. 2007;34(8):1650-1657
2. Maksymowych WP, Naides SJ, Bykerk V, et al. Serum 14-3-3 eta is a novel marker that complements current serological measurements to enhance detection of patients with rheumatoid arthritis. J Rheumatol. 2014;41(11):2104-2113
3. Guan SZ, Yang YQ, Bai X, et al. Serum 14-3-3 eta Could Improve the Diagnostic Rate of Rheumatoid Arthritis and Correlates to Disease Activity. Ann Clin Lab Sci. 2019;49(1):57-62
4. Subedi R, Misbah A, Najada AA, Ocon AJ. Evaluation of 14-3-3eta protein as a diagnostic biomarker in the initial assessment of inflammatory arthritis. J Rheum Dis. 2025;32(2):130-135
5. Shovman O, Gilburd B, Watad A, et al. The diagnostic value of 14-3-3 eta protein levels in patients with rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2018;32(4):610-617
6. Maksymowych WP, Boire G, van Schaardenburg D, et al. 14-3-3? Autoantibodies: Diagnostic Use in Early Rheumatoid Arthritis. J Rheumatol. 2015;42(9):1587-1594
7. Carrier N, Marotta A, de Brum-Fernandes AJ, et al. Serum levels of 14-3-3 eta protein supplement C-reactive protein and rheumatoid arthritis-associated antibodies to predict clinical and radiographic outcomes in a prospective cohort of patients with recent-onset inflammatory polyarthritis. Arthritis Res Ther. 2016;18:37
8. Hammam N, Salah S, Kholef EF, Moussa EM, Marotta A. 14-3-3 eta Protein in serum and synovial fluid correlates with radiographic damage and progression in a longitudinal evaluation of patients with established rheumatoid arthritis. Mod Rheumatol. 2020;30(4):664-670
9. Nelson HA, Martins TB, Saadalla A, Nandakumar V. Evaluation of the clinical performance of anti-mutated citrullinated vimentin antibody and 14-3-3 eta testing in rheumatoid arthritis. Clin Chem Lab Med. 2024;63:790-796

Performance

Method Description

The JOINTstat 14-3-3 eta enzyme-linked immunosorbent assay is an immunoassay that uses a microtiter plate coated with a murine monoclonal antibody specific for human 14-3-3 eta, a horseradish peroxidase (HRP)-conjugated monoclonal antibody, and a chromogenic substrate. When standards, diluted controls, and diluted patient specimens are added to the coated wells, any 14-3-3 eta present binds to the immobilized antibody. After an incubation period, the wells are washed to remove material that did not bind. An HRP-conjugated anti-14-3-3 eta antibody is then added. This conjugate binds to the captured 14-3-3 eta, forming a detectable complex. Following incubation, another wash cycle removes unbound conjugate. A chromogenic substrate is introduced, and the HRP enzyme converts the substrate into a colored product that initially appears blue. When the reaction is stopped, the color changes to yellow. The absorbance at 450 nm is measured and is proportional to the concentration of 14-3-3 eta present in the standards, controls, and patient samples.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Wednesday

Report Available
3 to 9 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
1433E	14-3-3 eta, S	75880-5

Result ID	Test Result Name	Result LOINC® Value
624066	14-3-3 eta, S	75880-5