MAYO CLINIC LABORATORIES

Test Definition: RNAP

RNA Polymerase III Ab, IgG, S

Overview

Useful For

Evaluating patients suspected of having systemic sclerosis as part of systemic sclerosis criteria antibody tests

Providing diagnostic and prognostic information in patients with systemic sclerosis

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.5 mL

Submission Container/Tube: Plastic vial

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK
Heat-treated	Reject

Specimen Minimum Volume

0.4 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Systemic sclerosis (SSc) is a multisystem autoimmune connective tissue disease characterized by vascular dysfunction, fibrotic changes in the skin and internal organs as well as an autoimmune response manifested by production of diverse antibodies.(1,2) While the clinical manifestations and severity of SSc are highly variable, two main subsets are widely recognized. These include the limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc) subtypes of which the diffuse form has the worse prognosis and survival rates.(2) Immunologically, SSc is characterized by the presence of several disease-specific and mutually exclusive autoantibodies considered helpful in the diagnosis, stratification, and prognosis of disease.(1-3) Of the described autoantibodies, the 2013 American College of Rheumatology/European League against Rheumatism classification criteria for SSc recommends testing for centromere, topoisomerase I (topo I or Scl 70), and RNA polymerase III autoantibodies.(3) Antibodies to Scl 70 and RNA polymerase III are generally associated with dcSSc while those to centromere typically correlate with the lcSSc form of disease.(1-3)

The human nuclei consist of three RNA polymerases, RNA polymerase I, II and III.(4) Of these, antibodies targeting RNA polymerases I and III are always present together and are most common in patients with SSc. The RPC155 immunodominant epitope has been identified in autoantibodies associated with anti-RNA polymerase I/III in patients with SSc and is widely used in solid-phase immunoassays for the detection and quantification of anti-RNA polymerase III antibodies in clinical laboratories.(5)

The prevalence of anti-RNA polymerase III antibodies in patients with SSc is variable with a pooled prevalence of 11% and ranges from 0 to 41% in different studies.(4) This variability may be due to environmental and genetic factors as well as lack of harmonization of immunoassays for the detection of antibodies.(4,6) Positivity for anti-RNA polymerase III antibody is generally mutually exclusive of other SSc-specific antibodies such as centromere and Scl 70.(1-3) In addition, SSc patients who test positive for anti-RNA polymerase III antibody have increased risk for the diffuse cutaneous involvement, hypertensive kidney disease, and poor prognosis.(1,2)

Reference Values

<20.0 U (negative)

20.0-39.9 U (weak positive)

40.0-80.0 U (moderate positive)

>80.0 U (strong positive)

Interpretation

A positive result for RNA polymerase III antibody may support a diagnosis of systemic sclerosis (SSc) in the appropriate clinical context (see Cautions). Anti-RNA polymerase III autoantibody in patients with SSc is associated with the diffuse cutaneous form of disease and an increased risk of sclerodermal renal crisis.

A negative result indicates no detectable IgG antibodies to RNA polymerase III and does not rule out a diagnosis. The RNA polymerase III IgG ELISA tests only for the RP155 dominant epitope, other epitopes in the antigenic complex are absent and cannot be detected.(6) The overall pooled prevalence of anti-RNAP polymerase III antibody is reported to be 11%, 95% confidence interval: 8 to 14, range of 0 to 41% in published studies.(4)

Cautions

A positive result indicates detectable anti-RNA polymerase III above assay cutoff and does not unequivocally establish a diagnosis of systemic sclerosis.(6,7)

Enzyme immunoassay to detect anti-RNA polymerase III antibody uses an immunodominant epitope as antigen. Negative result does not also rule out the presence of antibodies targeting other epitopes in the RNA polymerase I/III antigens.

The level of RNA polymerase III autoantibodies does not indicate the severity of disease in patients with systemic sclerosis (SSc). However, patients with high positive anti-RNA polymerase III antibody titers are more likely to have SSc compared to those with low antibodies.(7)

Anti-RNA polymerase III antibodies may occur prior to clinical onset of SSc.(7)

The presence of immune complexes or other immunoglobulin aggregates in the patient specimen may cause an increased level of nonspecific binding and produce false-positive results with this assay.

Clinical Reference

1. Stochmal A, Czuwara J, Trojanowska M, Rudnicka L: Antinuclear antibodies in systemic sclerosis: An update. Clin Rev Allergy Immunol. 2020 Feb;58(1):40-51

2. Nihtyanova SI, Sari A, Harvey JC, et al: Using autoantibodies and cutaneous subset to develop outcome-based disease classification in systemic sclerosis. Arthritis Rheumatol. 2020 Mar;72(3):465-76

3. van den Hoogen F, Khanna D, Fransen J, et al: 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheum. 2013 Nov;49:399–412

4.Sobanski V, Dauchet L, Lefevre G, et al: Prevalence of anti-RNA polymerase III antibodies in systemic sclerosis: New data from a French cohort and a systematic review and meta-analysis. Arthritis Rheumatol. 2014 Feb;66(2):407-417

5. Kuwana M, Kimura K, Kawakami Y: Identification of an immunodominant epitope on RNA polymerase III recognized by systemic sclerosis sera: application to enzyme-linked immunosorbent assay. Arthritis Rheum. 2002 Oct;46(10):2742-2747

6. Damoiseaux J, Potjewijd J, Smeets RL, Bonroy C: Autoantibodies in the disease criteria for systemic sclerosis: The need for specification for optimal application. J Transl Autoimmun. 2022 Jan 4;5:100141

7. Burbelo PD, Gordon SM, Waldman M, et al: Autoantibodies are present before the clinical diagnosis of systemic sclerosis. PLoS One. 2019 Mar 26;14(3);e0214202

Performance

Method Description

The immunodominant fragment of RNA polymerase III antigen is derived from recombinant DNA technology. Purified RNA polymerase III antigen is adsorbed to the wells of a polystyrene microtiter plate under conditions that preserve the antigen in its antigenic state. Prediluted controls and diluted patient sera are added to separate wells. Unbound sample is washed away, and an enzyme-labeled antihuman IgG conjugate is added to each well. After incubation and washing away of unbound enzyme-labeled antihuman IgG, the bound conjugate is measured by adding a chromogenic substrate. The intensity of the absorbance produced is measured with an automated microwell plate reader. Results are calculated by comparison to a single-point calibrator.(Package insert: QUANTA Lite RNA Pol III. INOVA Diagnostics; 02/2019)

PDF Report

No

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees & Codes

Test Definition: RNAP

RNA Polymerase III Ab, IgG, S

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

83516

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
RNAP	RNA Polymerase III Ab, IgG, S	79182-2

Result ID	Reporting Name	LOINC®
RNAP	RNA Polymerase III Ab, IgG, S	79182-2