Test Definition: SCL70

Scl 70 Antibodies, IgG, Serum

Overview

Useful For

Evaluating patients with clinical features of systemic sclerosis and in the differential evaluation of individuals at-risk for connective tissue disease with Hep-2 substrate antinuclear antibody positive result, preferably using antinuclear antibodies

Testing for Scl70 antibodies is **not useful** who test negative for antinuclear antibody using Hep-2 substrate by IFA.

Testing Algorithm

For more information see Connective Tissue Disease Cascade.

Special Instructions

- Connective Tissue Disease Cascade

Method Name

Multiplex Flow Immunoassay

NY State Available

No

Specimen

Specimen Type

Serum

Specimen Required

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

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross	Reject

hemolysis	
Gross lipemia	Reject
Gross icterus	OK
Heat-Treated	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Scl 70 (DNA topoisomerase 1) is an enzyme localized in both the cytoplasm and the nucleoli of the interphase cell that is an autoantibody target in patients with systemic sclerosis (SSc).(1,2) SSc is a complex autoimmune rheumatic disease of unknown etiology, characterized by widespread vasculopathy, fibrosis of the skin and internal organs, and immunologic derangements, including the production of diverse autoantibodies.(3-5) Antibody to Scl 70 is considered specific for SSc (also referred to as scleroderma) and together with anti-centromere and anti-RNA polymerase III autoantibodies is recommended for the diagnostic classification for disease by the American College of rheumatology/European League Against Rheumatism collaborative initiative.(3) Antibody to Scl 70 is typically associated with diffuse cutaneous SSc (dcSSc), a clinical subset of SSc which is characterized by disease severity including musculoskeletal and cardiac involvement, interstitial lung disease and poor survival outcomes.(4,5) In addition, Scl 70 antibody are more commonly found in African American patients with dcSSc compared to their Caucasian counterpart.(6,7)

In general, the presence of Scl 70 antibody is associated with a positive antinuclear antibody (ANA) when tested with the HEp-2 substrate using the indirect immunofluorescence assay (IFA).(1,2) ANA positivity with HEp-2 substrate IFA referred to as Scl-70 pattern is a composite of five cellular regions: nucleus, nucleolus and cytoplasm in interphase cells; nucleolar organizing region and chromosomes in mitotic cells.(2) Antibodies to Scl 70 were traditionally tested in clinical laboratories using immunodiffusion (ID), however, with increasing demands, methods for the detection and quantification of these autoantibodies have evolved to include diverse types of solid-phase immunoassays (SPAs) such as the line immunoblot, enzyme-linked immunosorbent assay, multiplex bead immunoassay, chemiluminescence immunoassay, and fluorescence enzyme immunoassay.(6-10) These SPAs have been reported to be less specific than the ID, especially in distinguishing SSc patients from those with other rheumatic diseases, though performance characteristics of individual assays may vary.(6-8). In a recent report, it was noted that discrepancy between anti-Scl-70 antibody assays can have relevant implications for clinical care and trial enrichment strategies for SSc patients with interstitial lung disease.(9)

Data from routine clinical practice do suggest that at diagnosis, positive results for Scl 70 antibody using SPAs must be interpreted in the appropriate clinical context taking into consideration the presence of a positive ANA test using the HEp-2 substrate by IFA, and/or the level of anti-Scl 70 antibody level.(6-8, 10) Low levels of anti-Scl 70 antibodies have been reported in non-SSc patients including those with SLE.(6, 8, 10) In SLE patients, it remains to be determined if this points to a unique subset of individuals or the phenomenon is due to cross-reactivity with dsDNA antibody.(10) Based on

this observation, testing for dsDNA antibody may provide additional diagnostic clues, especially in the absence of the ID assay.(10)

For more information see Connective Tissue Disease Cascade.

Reference Values

<1.0 U (negative)
> or =1.0 U (positive)
Reference values apply to all ages.

Interpretation

A positive test result for Scl 70 antibodies may be consistent with a diagnosis of systemic sclerosis in the appropriate clinical context.

Cautions

Low positive Scl 70 antibody results should be interpreted with a high degree of suspicion. These can be seen in a number of inflammatory conditions as well as other connective tissue diseases, especially systemic lupus erythematosus.

Clinical Reference

1. Dellavance A, Gallindo C, Soares MG, et al. Redefining the Scl-70 indirect immunofluorescence pattern: autoantibodies to DNA topoisomerase I yield a specific compound immunofluorescence pattern. Rheumatology(Oxford). 2009;48(6):632-637
2. Andrade LEC, Klotz W, Herold M, et al. International consensus on antinuclear antibody patterns: definition of the ac-29 pattern associated with antibodies to DNA topoisomerase I. Clin Chem Lab Med. 2018;56(10):1783-1788
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. Ann Rheum Dis. 2013;72(11):1747-1755
4. Walker UA, Tyndall A, Czirják L,et al. Clinical risk assessment of organ manifestations in systemic sclerosis: a report from the EULAR Scleroderma Trials and Research group database. Ann Rheum Dis. 2007;66(6):754-763
5. 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;72(3):465-476
6. Nandiwada SL, Peterson LK, Mayes MD, et al. Ethnic differences in autoantibody diversity and hierarchy: More clues from a US cohort of patients with systemic sclerosis. J Rheumatol. 2016;43(10):1816-1824
7. Homer KL, Warren J, Karayev D, et al. Performance of anti-topoisomerase I antibody testing by multiple-bead, enzyme-linked immunosorbent assay and immunodiffusion in a university setting. J Clin Rheumatol. 2020;26(3):115-118
8. Lam BH, Assassi S, Charles J, et al. False positive anti-Topoisomerase I (Scl-70) antibody results in clinical practice: A case series from a scleroderma referral center. Semin Arthritis Rheum. 2022;56:152052
9. Jandali B, Salazar GA, Hudson M, et al. The Effect of anti-Scl-70 antibody determination method on its predictive significance for interstitial lung disease progression in systemic sclerosis. ACR Open Rheumatol. 2022;4(4):345-351
10. Mahler M, Silverman ED, Schulte-Pelkum J, Fritzler MJ. Anti-Scl-70 (topo-I) antibodies in SLE: Myth or reality? Autoimmun Rev. 2010 Sep;9(11):756-60.

Performance

Method Description

Recombinant Scl 70 antigen is bound to polystyrene microspheres, which are impregnated with fluorescent dyes to create a unique fluorescent signature. Scl 70 antibodies, if present in diluted serum, bind to the Scl 70 antigen on the microspheres. The microspheres are washed to remove extraneous serum proteins. Phycoerythrin -conjugated antihuman IgG antibody is then added to detect IgG anti-Scl 70 bound to the microspheres. The microspheres are washed to remove unbound conjugate, and bound conjugate is detected by laser photometry. A primary laser reveals the fluorescent signature of each microsphere to distinguish it from microspheres that are labeled with other antigens, and a secondary laser reveals the level of PE fluorescence associated with each microsphere. Results are calculated by comparing median fluorescence response for Scl 70 microspheres to a 4-point calibration curve.(Package insert: BioPlex 2200 ANA Screen. Bio-Rad Laboratories; 02/2019)

PDF Report
No

Day(s) Performed
Monday through Friday, Sunday

Report Available
1 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Jacksonville Clinical Lab

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 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
86235

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SCL70	Scl 70 Ab, IgG, S	47322-3

Test Definition: SCL70

Scl 70 Antibodies, IgG, Serum

Result ID	Test Result Name	Result LOINC® Value
SCL70	Scl 70 Ab, IgG, S	47322-3