Autoimmune Diseases: Use of Antinuclear and Specific Antibodies for Diagnosis

Autoimmune diseases are difficult to diagnose; their symptoms can be vague, vary from patient to patient, and often overlap. Moreover, there is no single diagnostic test for any one autoimmune disease. Diagnosis is most often based on a compilation of clinical information, family history, data from laboratory testing, and, in some cases, imaging tests. Laboratory tests include relatively nonspecific antinuclear antibody (ANA) testing and/or tests for individual antibodies that are more disease specific.

Antinuclear antibody is a marker of inflammation and autoimmune processes and, as such, is a general marker of autoimmune disease. Therefore, it is a good first test for suspected autoimmune disease. Several methods of ANA testing are available, including immunofluorescence assay (IFA), enzyme-linked immunosorbent assay (ELISA), and multiplex immunobead assay. The American College of Rheumatology (ACR) recommends using an IFA with HEp-2 cells, because the test is highly sensitive.[1] This sensitivity stems from the number of autoantigens (up to 150) in the HEp-2 cells. The nuclear and cytoplasmic fluorescence patterns suggest certain types of autoimmune disease.[2,3] Although these patterns are not specific for a particular disease type, the information may aid diagnosis. A positive ANA result does not necessarily indicate presence of an autoimmune disease. Healthy individuals, particularly as they age, and those with certain infectious diseases or cancer, may have positive results.[4] Therefore, ANA test results must be reviewed in the proper clinical context.

Immunoassay-based specific antibody tests are less sensitive than ANA IFA for antinuclear and anticytoplasmic autoantibody screening; however, they are often more specific for a particular autoimmune disease than is ANA IFA.[5,6] Therefore, they can be used to aid in differential diagnosis.

There is no single best way to approach laboratory testing for autoimmune disease; the approach depends on the clinical picture. Three different screening approaches are discussed here.

FIRST APPROACH: SCREEN FOR SUSPECTED AUTOIMMUNE DISEASE

The first approach begins with ANA screening alone (ANA Screen, IFA, with Reflex to Titer and Pattern, test code 249) and may be considered as part of an evaluation for possible autoimmune disease (**Figure 1**). A positive ANA result in conjunction with clinical suspicion suggests that autoimmune disease is likely. The diagnostic value of a positive ANA result depends on the condition (**Table 1**). A negative ANA result suggests the absence of many autoimmune diseases, but does not rule them out. Additional testing, for example with specific antibody tests, should be considered if clinically warranted (**Table 2**).

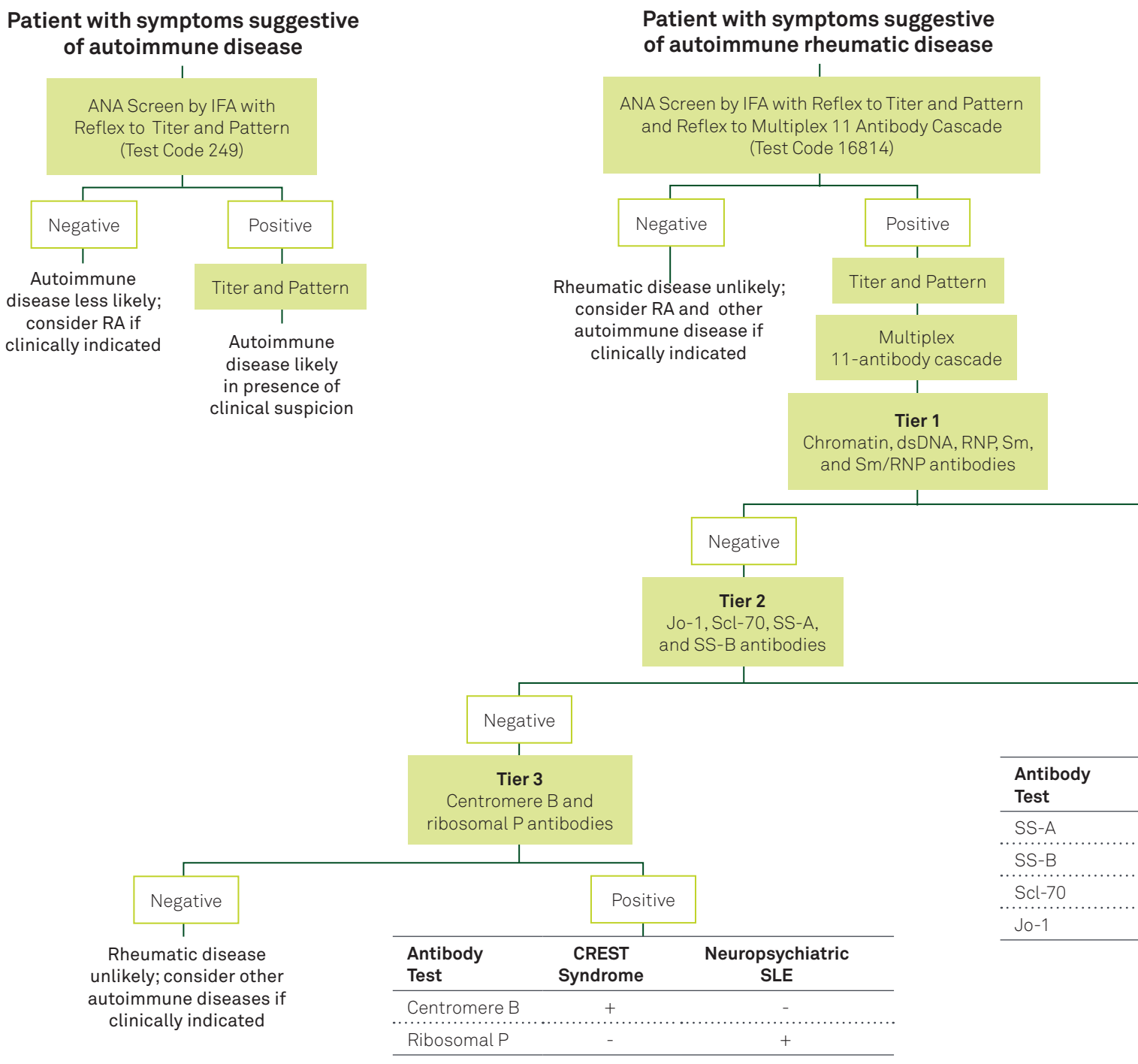
SECOND APPROACH: SCREEN FOR SUSPECTED AUTOIMMUNE RHEUMATIC DISEASE

A second screening approach begins with ANA IFA with reflex to a rheumatic disease-associated antibody panel (ANA Screen, IFA, with Reflex to Titer and Pattern and Reflex to Multiplex 11-Antibody Cascade, test code 16814) (**Figure 1**). This option is appropriate when there is clinical suspicion of a rheumatic disease. Testing for multiple autoantibodies is usually required for differential diagnosis (**Figure 1**, **Table 3**).[2,8,9] If the ANA IFA is positive, a positive result on one of the cascade tiers may suggest the presence of a certain autoimmune disease(s) (**Figure 1**, **Table 3**). If the ANA IFA is positive but the antibody cascade is negative, tests for other autoimmune diseases may be considered if clinically indicated (**Table 4**).

THIRD APPROACH: SCREEN FOR SPECIFIC AUTOIMMUNE DISEASES NOT INCLUDED IN MULTIPLEX 11-ANTIBODY PANEL (TEST CODE 16814)

A third option may be considered when the clinical picture suggests a specific autoimmune disorder not included in the rheumatic disease-associated antibody panel (test code 16814, **Figure 1**). In this case, testing can begin with an ANA IFA panel that reflexes to antibodies associated with the suspected disorder (**Table 5**). For instance, if rheumatoid arthritis is suspected, testing for rheumatoid factor and cyclic citrullinated peptide antibodies,[23] as well as 14-3-3η protein,[24] is appropriate (**Figure 1**). Positive ANA IFA and positive antibody test(s) results are consistent with the presence of the suspected disorder. If the ANA IFA is positive and the specific antibody test(s) are negative, selection of additional antibody tests will depend on the clinical picture.

Figure 1. Screening and Diagnosis of Patients With Suspected Autoimmune or Rheumatic Disease or Rheumatoid Arthritis



The acronym CREST refers to a syndrome defined by presence of calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia. CCP indicates cyclic citrullinated peptide; dsDNA, DNA; IFA, immunofluorescence assay; RA, rheumatoid arthritis; RF, rheumatoid factor; Sm/RNP, Smith/ribonucleoprotein; SS-A and -B, Sjögren syndrome A and B; Scl-70, scleroderma (topoisomerase I); and Jo-1, histidyl-tRNA synthetase.

Patient with symptoms suggestive of rheumatoid arthritis

Rheumatoid Arthritis Diagnostic IdentRA®Panel Includes RF, CCP IgG, 14-3-3η (Test Code 91472)

- Negative → RA less likely
- Positive → RA diagnosed

Positive

Antibody Test	Systemic Lupus Erythematosus	Mixed Connective Tissue Disease
dsDNA	+ (high specificity)	-
Chromatin	+ (high sensitivity)	-
Sm	+ (high specificity)	-
Sm/RNP	+	+ (high titer)
RNP	+	+ (high titer)

Positive

Sjögren Syndrome	Systemic Sclerosis	Polymyositis
+	-	-
+	-	-
-	+	-
-	-	+

This figure was developed by Quest Diagnostics based on references 5, 8, 9, 11 and 12. It is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

Table 1. Diagnostic Value of an Antinuclear Antibody Test [7,8]

Value of Positive ANA	Condition	Comments/Recommendations[a]
Critical	Drug-associated lupus	• Positive ANA part of the diagnostic criteria • ANA useful for symptomatic people who are taking a drug associated with drug-induced lupus
	Mixed connective tissue disease (MCTD)	• Positive ANA part of the diagnostic criteria • ANA recommended when clinical suspicion of MCTD • Follow-up with RNP antibody recommended to confirm diagnosis
	Autoimmune hepatitis	• Positive ANA part of diagnostic criteria • Positive ANA often seen in patients with diverse liver disease; does not exclude other hepatic diseases
Very useful	Systemic lupus erythematosus (SLE)	• ANA sensitivity 93%, specificity 57% • Best initial test when clinical suspicion of SLE is strong • SLE unlikely if ANA negative • Specific antibody tests recommended as follow-up to positive ANA
	Systemic sclerosis (SSc)	• ANA sensitivity 85%, specificity 54% • ANA recommended when clinical suspicion of SSc • If negative, consider other fibrosing illnesses (eg, eosinophilic fasciitis, linear scleroderma)
May be useful	Sjögren syndrome	• ANA sensitivity 48%, specificity 52% • Not useful for diagnosis • Can help clarify whether an underlying connective tissue disease exists when Sjögren syndrome suspected to be related to SLE
	Polymyositis/ dermatomyositis	• ANA sensitivity 61%, specificity 63% • Positive result provides only weak evidence of disease even when combined with clinical suspicion • Must consider other connective tissue diseases (SLE or overlap syndrome) regardless of ANA status

ANA, antinuclear antibody test; RNP, ribonucleoprotein.
[a] The American College of Rheumatology Ad Hoc Committee on Immunologic Testing Guidelines[7]

Table 2. Tests to Consider When Antinuclear Antibody Is Negative[a]

Test Code	Test Name
Ankylosing Spondylitis	
528	HLA-B27 Antigen
Autoimmune Thyroid Disease	
36574	T3 (Triiodothyronine) Antibody[b]
36576	T4 (Thyroxine) Antibody[b]
267	Thyroglobulin Antibodies

(Continued)

Table 2. Tests to Consider When Antinuclear Antibody Is Negative[a] *(Continued)*

Test Code	Test Name
7260	Thyroid Peroxidase and Thyroglobulin Antibodies (Panel components may be ordered separately.) Includes thyroid peroxidase (5081) and thyroglobulin (267) antibodies.
5081	Thyroid Peroxidase Antibodies
36577	TSH Antibody[b]
30551	TSI (Thyroid Stimulating Immunoglobulin)
Celiac Disease	
19955	Celiac Disease Comprehensive Panel (Panel components may be ordered separately.) Includes tissue transglutaminase antibody (IgA) (8821) with reflex(es) to endomysial antibody screen (IgA) with reflex to titer (15064); also includes serum IgA (539) with reflex to tissue transglutaminase antibody (IgG) (11070).
Gout/Pseudogout	
4563	Crystals, Synovial Fluid
905	Uric Acid
Inflammatory Bowel Disease	
70171(X)	ANCA Screen with Reflex to ANCA Titer Includes ANCA screen with reflex to C-ANCA, P-ANCA and/or atypical P-ANCA titer.
16503(X)	Inflammatory Bowel Disease Differentiation Panel (Panel components may be ordered separately.) Includes ANCA screen with reflex to P-ANCA, C-ANCA, and atypical P-ANCA titers (70171X); also includes myeloperoxidase antibody (8796), proteinase-3 antibody (34151), and *Saccharomyces cerevisiae* IgG and IgA (17609).
17609	*Saccharomyces cerevisiae* Antibodies (ASCA) (IgA, IgG)
Multiple Sclerosis	
17728(X)	Multiple Sclerosis Panel (Panel components may be ordered separately.) Includes oligoclonal bands (IgG) (674) and myelin basic protein in CSF (663).
37581(X)	Multiple Sclerosis Panel 1 (Panel components may be ordered separately.) Includes oligoclonal bands (IgG) (674) and IgG synthesis rate/index on CSF (7558X).
7085(X)	Multiple Sclerosis Panel 2[b] (Panel components may be ordered separately.) Includes oligoclonal bands (IgG) (674), IgG synthesis rate/index on CSF (7558X), and myelin basic protein In CSF (663).
Myasthenia Gravis	
10104	Myasthenia Gravis Panel[b] (Panel components may be ordered separately.) Includes acetylcholine receptor binding (206), blocking (34459), and modulating (26474) antibodies.
7550(X)	Myasthenia Gravis Panel 1[c] (Panel components may be ordered separately.) Includes acetylcholine receptor binding antibody (206) and striated muscle antibody screen with reflex to titer (266).
10211(X)	Myasthenia Gravis Panel 3[c] (Panel components may be ordered separately.) Includes acetylcholine receptor binding (206), blocking (34459), and modulating (26474) antibodies and striated muscle antibody screen with reflex to titer (266).
Myositis/Polymyositis/Dermatomyositis	
94025	Anti-PM/Scl Antibody (EIA)
TBD[d]	Idiopathic Inflammatory/Juvenile Myopathies Panel 2[b] (Some panel components may be ordered separately.) Includes EJ, Jo-1 (5810), Ku (18855), Mi-2 (17172X), OJ, P140, P155/140, PL-7, PL-12, PM/Scl (94025), SS-A (38568), SRP (16318), U1-RNP, U2-RNP, and U3-RNP antibodies.
10185	Myositis AssessR™ plus Jo-1 Antibodies (Some panel components may be ordered separately.) Includes EJ, Jo-1 (5810), Ku (18855), Mi-2 (17172X), OJ, PL-7, PL-12, and SRP (16318) antibodies.

(Continued)

Table 2. Tests to Consider When Antinuclear Antibody Is Negative[a] *(Continued)*

Test Code	Test Name
Rheumatoid Arthritis	
91472	Rheumatoid Arthritis Diagnostic IdentRA® Panel 2[b] (Panel components may be ordered separately.) Includes 14-3-3 eta protein (91455), cyclic citrullinated peptide (CCP) IgG (11173), and rheumatoid factor (4418).
19878	Rheumatoid Arthritis Diagnostic Panel 3 (Panel components may be ordered separately.) Place panel 3 ahead of panel 4 Includes cyclic citrullinated peptide (CCP) IgG (11173); rheumatoid factor IgG, IgA, and IgM (19705); SS-A (38568); and SS-B (38569) antibodies.
92812	Rheumatoid Arthritis Diagnostic IdentRA® Panel 4 (Panel components may be ordered separately.) Includes 14-3-3 eta protein (91455), cyclic citrullinated peptide (CCP) IgG (11173), rheumatoid factor antibodies (IgG, IgA, IgM) (19705), and SS-A (38568) and SS-B (38569) antibodies.
Sjögren Syndrome	
93748	Early Sjögren Syndrome Profile Includes carbonic anhydrase 6 IgG, IgM, IgA; parotid secretory protein IgG, IgM, IgA; and salivary gland protein (SP1) IgG, IgM, IgA.
7832	Sjögren Antibodies (SS-A, SS-B)
Vasculitis	
36733	ANCA Vasculitides Includes proteinase-3 and myeloperoxidase antibodies.
Viral Arthritis	
6421	Epstein-Barr Virus Antibody Panel (Panel components may be ordered separately.) Includes Epstein-Barr Virus VCA Antibody (IgM) (8426), Epstein-Barr Virus VCA Antibody (IgG) (8474), Epstein-Barr Virus Nuclear Antigen (EBNA) Antibody (IgG) (8564).
501	Hepatitis B Core Antibody, Total
499	Hepatitis B Surface Antibody, Qualitative
498	Hepatitis B Surface Antigen with Reflex to Confirmation[a]
8472	Hepatitis C Antibody with Reflex to HCV RNA, Quantitative Real-Time PCR[a]
8946	Parvovirus Antibodies (IgG, IgM)
37673	Rubella Antibodies (IgG, IgM) Diagnostic

ANCA, antineutrophil cytoplasmic antibodies; C-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies; CSF, cerebrospinal fluid; EJ, glycyl tRNA synthetase; Jo-1, histidyl-tRNA synthetase; Ku, DNA protein kinase regulatory subunit; Mi-2, helicase protein; OJ, isoleucyl tRNA synthetase; P140, nuclear matrix protein-2; P155/140, transcriptional intermediary factor 1-γ; P-ANCA, perinuclear antineutrophil cytoplasmic antibodies; PL-7, threonyl-tRNA synthetase; PL-12, alanyl-tRNA synthetase; PM/Scl, polymyositis-scleroderma; RNP, ribonucleoprotein; SRP, signal recognition particle; SS-A, SS-B, Sjögren syndrome A and B; and TBD, to be determined.

[a] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[c] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[d] Available in 2017.

Table 3. Autoantibody Prevalence (%) in Rheumatic and Related Diseases[7,10,11-22,a]

Antibody	SLE	MCTD	Sjögren Syndrome	Systemic Sclerosis	Polymyositis	CREST Syndrome[b]	Neurologic SLE
ANA	93	100	48	85	61	70	NA
Cen B	3-12	7[c]	<2	27	<2	66	
Chromatin	37-73	>80	12	14	8		
dsDNA	57-62	0-8	11-20	8	10-43		
Jo-1	<2	7[d]	<2	<2	17		
Rib P		7	<2	<2	<2		9-30
RNP	22-48	>80	12	14	8		
Scl-70	2-3	7[e]	<2	16	<2		
Sm	20-30	8	4	0	10		
Sm/RNP	30	54-94	9	4	9		
SS-A	33-52	13	>80	23	42		
SS-B	13-27	<2	>80	5	<2		

ANA, antinuclear antibody; Cen B, centromere B; dsDNA, double-stranded DNA; Jo-1, histidyl-tRNA synthetase; NA, not available; MCTD, mixed connective tissue disease; Rib P, ribosomal P; RNP, ribonucleoprotein; Scl-70, scleroderma (topoisomerase 1); SLE, systemic lupus erythematosus; Sm, Smith; Sm/RNP, Smith/ribonucleoprotein; and SS-A, SS-B, Sjögren antibodies A and B.

[a] Highlighted antibodies represent diagnostic criteria for the disease. Note that antibodies whose presence is a diagnostic criterion do not always correspond to those with the highest prevalence in that disease.

[b] CREST is a syndrome defined by presence of calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia.

[c] Typically in cases with features of polymyositis.

[d] Especially in cases with features of muscle inflammation.

[e] Especially in cases with features of systemic sclerosis.

Table 4. Tests to Consider When Antinuclear Antibody is Positive and Multiplex 11-Antibody Test is Negative[a]

Test Code	Test Name
Autoimmune Hepatitis	
15043	Actin (Smooth Muscle) Antibody (IgG)
15038	Liver Kidney Microsome (LKM-1) Antibody (IgG)
259	Mitochondrial Antibody with Reflex to Titer
Bullous Pemphigoid	
16034	Bullous Pemphigoid Antigen (BP180) Antibody
16136	Bullous Pemphigoid BP230 IgG
16033(X)	Desmoglein Antibodies (1 and 3)
Myositis/Polymyositis/Dermatomyositis	
94025	Anti-PM/Scl Antibody (EIA)
TBD[b]	Idiopathic Inflammatory/Juvenile Myopathies Panel 2[c] (Some panel components may be ordered separately.) Includes EJ, Jo-1 (5810), Ku (18855), Mi-2 (17172X), OJ, P140, P155/140, PL-7, PL-12, PM/Scl (94025), SS-A (38568), SRP (16318), U1-RNP, U2-RNP, and U3-RNP antibodies.
10185	Myositis AssessR™ plus Jo-1 Antibodies (Some panel components may be ordered separately.) Includes EJ, Jo-1 (5810), Ku (18855), Mi-2 (17172X), OJ, PL-7, PL-12, and SRP (16318) antibodies.

(Continued)

Table 4. Tests to Consider When Antinuclear Antibody is Positive and Multiplex 11-Antibody Test is Negative[a] *(Continued)*

Test Code	Test Name
Primary Biliary Cholangitis (Primary Biliary Cirrhosis)	
15043	Actin (Smooth Muscle) Antibody (IgG)
15038	Liver Kidney Microsome (LKM-1) Antibody (IgG)
259	Mitochondrial Antibody with Reflex to Titer
5081	Thyroid Peroxidase Antibodies
Rheumatoid Arthritis	
91455	14-3-3 eta Protein[c]
11173	Cyclic Citrullinated Peptide (CCP) Antibody (IgG)
91472	Rheumatoid Arthritis Diagnostic IdentRA® Panel 2[c] (Panel components may be ordered separately.) Includes 14-3-3 eta protein (91455), cyclic citrullinated peptide (CCP) IgG (11173), and rheumatoid factor (4418).
19878	Rheumatoid Arthritis Diagnostic Panel 3 (Panel components may be ordered separately.) Includes cyclic citrullinated peptide (CCP) IgG (11173); rheumatoid factor IgG, IgA, and IgM (19705); SS-A (38568); and SS-B (38569) antibodies.
92812	Rheumatoid Arthritis Diagnostic IdentRA® Panel 4 (Panel components may be ordered separately.) Includes 14-3-3 eta protein (91455), cyclic citrullinated peptide (CCP) IgG (11173), rheumatoid factor antibodies (IgG, IgA, IgM) (19705), and SS-A (38568) and SS-B (38569) antibodies.
4418	Rheumatoid Factor
19705(X)	Rheumatoid Factor (IgA, IgG, IgM)
Sjögren Syndrome	
93748	Early Sjögren Syndrome Profile Includes carbonic anhydrase 6 IgG, IgM, IgA; parotid secretory protein IgG, IgM, IgA; and salivary gland protein (SP1) IgG, IgM, IgA.
259	Mitochondrial Antibody with Reflex to Titer
4418	Rheumatoid Factor
5081	Thyroid Peroxidase Antibodies
Systemic Lupus Erythematosus	
15043	Actin (Smooth Muscle) Antibody (IgG)
37859(X)	Complement Components C3, C4, and Total (CH50)
15114	Gastric Parietal Cell Antibody, ELISA
37056(X)	Histone Antibodies
259	Mitochondrial Antibody with Reflex to Titer
37520	Reticulin IgA Screen with Reflex to Titer
4418	Rheumatoid Factor
266	Striated Muscle Antibody with Reflex to Titer
5081	Thyroid Peroxidase Antibodies

(Continued)

Table 4. Tests to Consider When Antinuclear Antibody is Positive and Multiplex 11-Antibody Test is Negative[a] *(Continued)*

Test Code	Test Name
Systemic Sclerosis	
TBD[b]	Systemic Sclerosis Nucleolar Antibodies Panel 1[c] (Some panel components may be ordered separately.) Includes Scl-70 (4942), centromere B (16088), RNA polymerase III subunit RP11, RNA polymerase III subunit RP155, PM-Scl100, PM-Scl75, U1-snRNP, U3-snRNP (fibrillarin), and Th/To antibodies.

ds, double-stranded; EJ, glycyl-tRNA synthetase; IFA, immunofluorescent assay; Jo-1, histidyl-tRNA synthetase; Ku, DNA protein kinase regulatory subunit; Mi-2, helicase protein; OJ, isoleucyl-tRNA synthetase; P140, nuclear matrix protein-2; P155/140, transcriptional intermediary factor 1-γ; PL-7, threonyl-tRNA synthetase; PL-12, alanyl-tRNA synthetase; PM/Scl, polymyositis-scleroderma; RNP, ribonucleoprotein; RP11, RNA polymerase III subunit 11; RP155, RNA polymerase subunit 155; Scl-70, scleroderma (topoisomerase I) antibody; snRNP, small nuclear ribonucleoprotein; SRP, signal recognition particle; SS-A, SS-B, Sjögren syndrome A and B; and TBD, to be determined.

[a] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

[b] Available in 2017.

[c] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

Table 5. Tests That Include Antinuclear Antibody and Markers Associated With Other Autoimmune Diseases[a]

Test Code	Test Name
Autoimmune Hepatitis	
19873	Autoimmune Hepatitis Diagnostic Panel (Panel components may be ordered separately.) Includes ANA screen (IFA) with reflex to ANA titer and pattern (249); also includes actin (smooth muscle) IgG (15043), liver kidney microsome (LKM-1) IgG (15038), and mitochondrial antibody screen with reflex to titer (259).
Connective Tissue Disease	
10547(X)	ANA Multiplex with Reflex to dsDNA Includes ANA multiplex test with reflex to dsDNA (255).
Drug-Induced Lupus	
19874(X)	ANA Screen, IFA, with Reflex to Titer and Pattern (Lupus Drug Induced Panel 1) (Panel components may be ordered separately.) Includes ANA screen (IFA) with reflex to titer and pattern (249); also includes histone antibody (37056).
Mixed Connective Tissue Disease	
19875	ANA Screen, IFA, with Reflex to Titer and Pattern/Mixed Connective Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes RNP antibody (19887).
90074	ANA Screen, IFA, with Reflex to Titer and Pattern/Mixed Connective Panel 2 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes dsDNA (255), RNP (19887), and Scl-70 (4942) antibodies.
Primary Biliary Cirrhosis	
19876	Primary Biliary Cirrhosis Diagnostic Panel (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249), SS-A (38568), SS-B (38569), mitochondrial antibody with reflex to titer (259), actin (smooth muscle) IgG (15043), thyroid peroxidase (TPO) antibody (5081), and liver kidney microsome (LKM-1) IgG (15038).
Rheumatoid Arthritis	
90071	ANA Screen, IFA, with Reflex to Titer and Pattern/Rheumatoid Arthritis Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes rheumatoid factor (4418), cyclic citrullinated peptide (CCP) IgG (11173).

(Continued)

Table 5. Tests That Include Antinuclear Antibody and Markers Associated With Other Autoimmune Diseases[a] *(Continued)*

Test Code	Test Name
92813	ANA Screen, IFA, with Reflex to Titer and Pattern/Rheumatoid Arthritis Panel 2 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes rheumatoid factor (4418), cyclic citrullinated peptide (CCP) IgG (11173), and 14-3-3 eta protein (91455).
Sjögren Syndrome	
90077	ANA Screen, IFA, with Reflex to Titer and Pattern/Sjögren's Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes rheumatoid factor (4418) and SS-A (38568) and SS-B (38569) antibodies.
19880	ANA Screen, IFA, with Reflex to Titer and Pattern/Sjögren's Panel 2 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); mitochondrial antibody screen with reflex to titer (259); rheumatoid factor (4418); and SS-A (38568), SS-B (38569), and thyroid peroxidase antibodies (5081).
Systemic Lupus Erythematosus	
19874	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Drug Induced Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes histone antibody (37056X).
90072	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes chromatin (nucleosomal) (34088), dsDNA (255), and Sm antibodies (37923).
29839	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Panel 2 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes dsDNA (255), scleroderma (Scl-70) (4942), Sm (37923), Sm/RNP (38567), SS-A (38568), and SS-B (38569) antibodies.
19881	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Panel 3 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); chromatin (nucleosomal) (34088), dsDNA (255), RNP (19887), Sm (37923), SS-A (38568), and SS-B (38569) antibodies; complement components C3c and C4c (5704); and total complement (CH50) (618).
10716	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Panel 4 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); dsDNA (255), rheumatoid factor (4418), ribosomal P (34283), Scl-70 (4942), Sm (37923), Sm/RNP (38567), SS-A (38568), SS-B (38569), and thyroid peroxidase (5081) antibodies; and complement components C3c and C4c (5704).
37491	ANA Screen, IFA, with Reflex to Titer and Pattern/Lupus Panel 5[b] (Panel components may be ordered separately.) Includes ANA screen (IFA) with reflex to titer and pattern (249); actin (IgG) (15043), gastric parietal cell (15114), rheumatoid factor (4418), ribosomal P (34283), Scl-70 (4942), Sm (37923), Sm/RNP (38567), SS-A (38568), SS-B (38569), and thyroid peroxidase (5081) antibodies; dsDNA (Crithidia) (37092), mitochondrial (259), myocardial (261), reticulin (16530), and striated muscle (266) antibody screens with reflex to titers; and complement components C3c and C4c (5704).
Systemic Sclerosis	
90073	ANA Screen, IFA with Reflex to Titer and Pattern/Systemic Sclerosis Panel 1 (Panel components may be ordered separately.) Includes ANA screen, IFA, with reflex to titer and pattern (249); also includes centromere B (16088), and Scl-70 (4942) antibodies.

ANA, antinuclear antibody; dsDNA, double-stranded DNA; IFA, immunofluorescent assay; RNP, ribonucleoprotein; Scl-70, scleroderma (topoisomerase I); Sm, Smith; and SS-A, SS-B, Sjögren syndrome A and B.

[a] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

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