



**Comprehensive Connective  
Tissue Disease Assessment**

Order ID  
739813  
Provider  
Exagen  
Provider MD

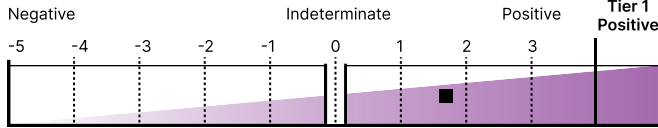
Specimen  
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10/22/2024  
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10/25/2024

Patient  
Gender  
Female  
MRN  
AB123450

Sample,  
**Susan S.**  
DOB  
01/01/1996

**AVISE Lupus Result: Positive - Index: 1.8**



**INDEX INTERPRETATION:** A Lupus Index score of 1.8 is associated with an increased likelihood of SLE. Positive results are driven by ANA (ELISA) positivity as well as classical complement activation, as indicated by the level of EC4d and/or BC4d. Results should be interpreted by a provider in conjunction with all available clinical findings.

Lupus Index Score Biomarkers	Value	Interpretation	Reference Range
Anti-dsDNA IgG (ELISA) Confirmation by Crithidia luciliae (IFA)	18.04 IU/mL	Negative N/A	<201 - Negative   201 - <302 - Equivocal   ≥302 - Positive
Anti-Smith IgG (ELFA)	<0.7 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
CB-CAP: EC4d - Erythrocyte-bound C4d (FC)	11 Net MFI	Negative	<15 - Negative   15-75 - Positive   >75 - Strong Positive
+ CB-CAP: BC4d - B-lymphocyte-bound C4d (FC)	192 Net MFI	<b>POSITIVE</b>	<61 - Negative   61-200 - Positive   >200 - Strong Positive
+ ANA IgG (ELISA)	22.93 Units	<b>POSITIVE</b>	<20 - Negative   20-<60 - Positive   ≥60 - Strong Positive
Anti-SSB/La IgG (ELFA)	0.8 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-Scl-70 IgG (ELFA)	<0.6 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-Centromere Protein B (CENP) IgG (ELFA)	0.7 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-Jo-1 IgG (ELFA)	<0.3 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-CCP IgG (ELFA)	1.2 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive

T Cell Biomarkers	Value	Interpretation	Reference Range
+ CB-CAP: TC4d (FC)	236 Net MFI	<b>POSITIVE</b>	<200 - Negative   ≥200 - Positive
+ T Cell autoantibody: TIgG (FC)	198 Net MFI	<b>POSITIVE</b>	<170 - Negative   ≥170 - Positive
+ T Cell autoantibody: TIgM (FC)	277 Net MFI	<b>POSITIVE</b>	<230 - Negative   ≥230 - Positive

ANA (Immunofluorescence)	Value	Interpretation	Reference Range
+ ANA by HEp-2 (IFA)	Titer: 1:320	<b>POSITIVE</b>	<1:80 - Negative   ≥1:80 - Positive
Nuclear Pattern: Speckled Cytoplasmic Pattern: Not Observed			

**Comments:**

- BC4d and TC4d are markers of classical complement activation. In the positive range, BC4d is present in 53% of SLE patients and in low percentages of patients with Sjogren's disease, myositis, systemic sclerosis, RA, APS, and vasculitis. In the positive range, TC4d is present in 59% of SLE patients and in low percentages of patients with Sjogren's disease, spondyloarthropathies, PsA, fibromyalgia, RA, and chronic localized pain.
- TIgG and TIgM autoantibody formation against T Cell antigens is common in SLE. In the positive range, TIgG is present in 32% of SLE patients and in low percentages of patients with Sjogren's disease, spondyloarthropathies, PsA, fibromyalgia, RA, and chronic localized pain. In the positive range, TIgM is present in 31% of SLE patients and in low percentages of patients with the previously mentioned diseases.

Signed by: Prashanti Reddy, MD

Date: 10/25/2024

Results were obtained using Flow Cytometry for complement C4d fragment bound to erythrocytes (EC4d), B-lymphocytes (BC4d), T Cells (TC4d), T Cell-bound IgG (TIgG) and T Cell-bound IgM (TIgM) autoantibodies. Results were obtained by Enzyme Linked Immunosorbent Assay (ELISA) and Indirect Immunofluorescence Assay (IFA) for determination of Antinuclear Antibodies (ANA). Results were obtained by HEp-2-ANA (by IFA) for the semi-quantitative determination of ANA. ANA by ELISA was used for the index calculation. In a study of 794 subjects comprising 304 SLE patients, 285 patients with other rheumatic diseases and 205 normal healthy controls, positivity for Tier 1 markers (anti-dsDNA by ELISA, confirmed with Crithidia by IFA, anti-Sm by Enzyme Linked Fluorescent Immunoassay (ELFA) or elevated EC4d and BC4d by Flow Cytometry yielded a sensitivity of 46% and a specificity of 97% for SLE vs. other autoimmune rheumatic diseases (ORD). Among the 164 SLE subjects negative in Tier 1, a positive index score composite of ANA (by ELISA), EC4d/BC4d and positivity for anti-CCP, SS-B/La, CENP, Jo-1 or Scl-70 (by ELFA) resulted in sensitivity of 62% for SLE and specificity of 89% for SLE vs. ORD. The overall two-tier algorithm result yielded 80% sensitivity for SLE and 86% specificity vs. ORD diseases (98% specificity for SLE vs. healthy individuals). RA33 autoantibodies are highly specific (>95%) for RA against healthy individuals. In a cohort of 161 diagnosed RA patients (60 seropositive and 101 seronegative based anti-CCP and RF), IgG, IgM, and IgA RA33 autoantibodies were collectively present in 32% of seropositive RA patients and 16% of seronegative RA patients.



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**Patients:** Positive individual biomarker results may not imply a positive disease diagnosis. Please discuss these test results with your provider in the context of all clinical information.

Rheumatoid Arthritis Biomarkers	Value	Interpretation	Reference Range
Anti-CCP IgG (ELFA)	1.2 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-RA33 IgG (ELFA)	1.5 U/mL	Negative	<8 - Negative   ≥8 - Positive
Anti-RA33 IgM (ELFA)	2.1 U/mL	Negative	<42 - Negative   ≥42 - Positive
Anti-RA33 IgA (ELFA)	0.8 U/mL	Negative	<5 - Negative   ≥5 - Positive
Rheumatoid Factor IgM (ELFA)	<0.6 IU/mL	Negative	<3.5 - Negative   3.5-5 - Equivocal   >5 - Positive
Rheumatoid Factor IgA (ELFA)	0.9 IU/mL	Negative	<14 - Negative   14-20 - Equivocal   >20 - Positive

Sjögren's Disease Biomarkers	Value	Interpretation	Reference Range
Anti-SSA/Ro52 IgG (ELFA)	0.5 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-SSA/Ro60 IgG (ELFA)	<0.4 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-SSB/La IgG (ELFA)	0.8 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive

Mixed Connective Tissue Disease Biomarkers	Value	Interpretation	Reference Range
+ Anti-U1RNP IgG (ELFA)	22.8 U/mL	<b>POSITIVE</b>	<5 - Negative   5-10 - Equivocal   >10 - Positive
Anti-RNP70 IgG (ELFA)	0.3 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive

Antiphospholipid Syndrome Biomarkers	Value	Interpretation	Reference Range
Anti-Cardiolipin IgM (ELFA)	<0.9 MPL	Negative	<10 - Negative   10-40 - Weak Positive   >40 - Positive
+ Anti-Cardiolipin IgG (ELFA)	19.3 GPL	<b>POSITIVE</b>	<10 - Negative   10-40 - Weak Positive   >40 - Positive
Anti-β2 Glycoprotein 1 IgM (ELFA)	<2.4 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
+ Anti-β2 Glycoprotein 1 IgG (ELFA)	82.6 U/mL	<b>POSITIVE</b>	<7 - Negative   7-10 - Equivocal   >10 - Positive

Systemic Sclerosis Biomarkers	Value	Interpretation	Reference Range
Anti-Sci-70 IgG (ELFA)	<0.6 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-RNA Pol III IgG (ELFA)	<0.7 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive
Anti-Centromere Protein B (CENP) IgG (ELFA)	0.7 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive



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CAP# 7201051 | NYSDOH PFI# 8369

Laboratory Director:  
**Prashanti Reddy, MD**

Provider Relations: 888.452.1522

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Myositis Biomarkers	Value	Interpretation	Reference Range
Anti-Jo-1 IgG (ELFA)	<0.3 U/mL	Negative	<7 - Negative   7-10 - Equivocal   >10 - Positive

Thyroid Biomarkers	Value	Interpretation	Reference Range
Anti-Thyroglobulin IgG (ELFA)	<12 IU/mL	Negative	<40 - Negative   40-60 - Equivocal   >60 - Positive
Anti-Thyroid Peroxidase IgG (ELFA)	<4 IU/mL	Negative	<25 - Negative   25-35 - Equivocal   >35 - Positive

**Case Remarks:**

**References**

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## 1. NEW T Cell Biomarkers for Systemic Lupus Erythematosus

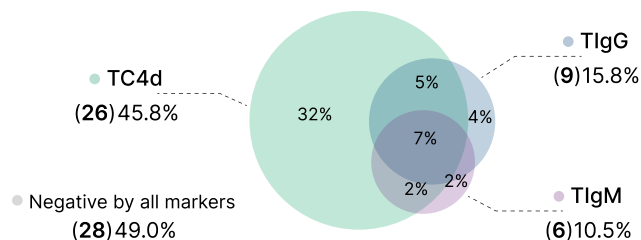
Conventional SLE biomarkers such as anti-dsDNA, anti-Smith, and complement C3/C4 have limited discriminatory power characterized by poor sensitivity in incipient cases. T Cell bound C4d (TC4d) and autoantibodies bound to T Cells (TlgG and TlgM) have superior diagnostic accuracy compared to conventional SLE biomarkers and can be informative when conventional markers are negative.

### Unique Clinical Value

Supported by scientific evidence, newly available T Cell biomarkers provide unique and unmatched diagnostic accuracy when conventional biomarkers are uninformative, facilitating earlier diagnoses and treatment decisions.

#### T Cell Lupus Biomarkers Performance Relative to Conventional SLE Biomarkers

Conventional Markers Negative/Normal (N=57)



### TC4d

TC4d is a measure of cell-bound complement on T Cells. Elevated levels of TC4d are sensitive for SLE and present in approximately 60% of SLE patients. Approximately 20% of SLE patients test TC4d positive while testing negative for all conventional SLE biomarkers. TC4d is rarely elevated in patients with other autoimmune diseases and healthy individuals.

### TlgM and TlgG

Autoantibodies (IgG and IgM) bound to T Cells are frequently present in SLE patients. Approximately 40% to 50% of SLE patients have elevated TlgM and TlgG, respectively. TlgM and TlgG are rarely elevated in patients with other autoimmune diseases and healthy individuals.

## 2. NEW Biomarkers for Rheumatoid Arthritis

Seronegative RA makes up approximately 30% of diagnosed RA and up to 50% of early RA cases. Novel RA biomarkers such as anti-RA33 and anti-CarP have narrowed the seronegative gap by providing evidence of systemic autoimmunity when conventional biomarkers are negative.

### Unique Clinical Value

Patients with inflammatory arthritis who test negative for conventional RA biomarkers face a complex differential diagnosis and potential treatment delay. The use of seronegative RA biomarkers with high specificity provides an opportunity to substantiate clinical suspicion of RA, aiding earlier diagnosis and treatment. Given the prevalence of such patients, seronegative RA biomarkers are a critically important part of a comprehensive Connective Tissue Disease evaluation.

### RA33 IgG, RA33 IgM, RA33 IgA

Autoantibodies to the RA33 antigen are highly specific (>95%) for RA against healthy individuals. Collectively, IgG, IgM, and IgA antibodies to RA33 are found in 16% of RA patients testing negative for anti-CCP and RFs.