MAYO CLINIC LABORATORIES

Test Definition: CRMTS

Collapsin Response-Mediator Protein-5 (CRMP-5) Neuronal IgG Titer, Serum

Overview

Useful For

Evaluation of neurological autoimmunity particularly that associated with small-cell lung carcinoma and thymoma

Reporting an end titer result from serum specimens

Testing Algorithm

If the indirect immunofluorescence pattern suggests collapsin response-mediator protein-5 (CRMP-5) neuronal IgG, then this test will be performed at an additional charge.

Method Name

Only orderable as a reflex. For more information see:
-PAVAL / Paraneoplastic, Autoantibody Evaluation, Serum
-DMS2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Serum
-ENS2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
-MDS2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Serum
-MAS1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-DYS2 / Dysautonomia, Autoimmune/Paraneoplastic Evaluation, Serum
-GID2 / Gastrointestinal Dysmotility, Autoimmune/Paraneoplastic Evaluation, Serum
-PVLE / Paraneoplastic Vision Loss Evaluation, Serum
-AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum

Indirect Immunofluorescence Assay (IFA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

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-EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum

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-MAS1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-DYS2 / Dysautonomia, Autoimmune/Paraneoplastic Evaluation, Serum
-GID2 / Gastrointestinal Dysmotility, Autoimmune/Paraneoplastic Evaluation, Serum
-PVLE / Paraneoplastic Vision Loss Evaluation, Serum
-AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum

Specimen Minimum Volume
0.6 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Ambient	72 hours	
	Refrigerated (preferred)	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information
Autoantibodies specific for neurons, glia, and muscle are important serological markers of neurological autoimmunity. Most are highly predictive of specific neoplasms that are metastatic to regional lymph nodes when diagnosed, but usually limited in spread.(1,2) The target autoantigens identified so far include cytoplasmic and nuclear proteins and plasma membrane cation channels.(3)

Collapsin response-mediator protein-5 (CRMP-5)-IgG is currently the second most common autoantibody predictive of small-cell lung carcinoma and, sometimes, occurs with thymoma.

The neurological presentation of CRMP-5-IgG seropositive patients is usually multifocal and can affect any level of the neuraxis. The presentation frequently mimics a stroke or multiple sclerosis. Syndromic manifestations encountered with lung carcinoma include subacute chorea, blindness, other cranial neuropathies (particularly loss of taste or smell), gastrointestinal dysmotility, myelopathy, and radiculoplexopathy. Fourteen percent of patients have thromboembolic phenomena. Seropositive patients who have thymoma (6%) usually present with neurological manifestations other than, or including, myasthenia gravis (eg, encephalopathy, disorders of continuous muscle fiber activity).

Reference Values

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-ENS2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
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-DYS2 / Dysautonomia, Autoimmune/Paraneoplastic Evaluation, Serum
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-PVLE / Paraneoplastic Vision Loss Evaluation, Serum
-AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum

<1:240
Note: Titers lower than 1:240 are detectable by recombinant collapsin response-mediator protein-5 (CRMP-5) Western blot analysis. CRMP-5 Western blot analysis will be done on request on stored serum (held 4 weeks). This supplemental testing is recommended in cases of chorea, vision loss, cranial neuropathy, and myelopathy. Call 1-800-533-1710 to request CRMP-5 Western blot.

Neuron-restricted patterns of IgG staining that do not fulfill criteria for CRMP-5-IgG may be reported as "unclassified antineuronal IgG." Complex patterns that include non-neuronal elements may be reported as "uninterpretable."

Interpretation

Detection of IgG autoantibody specific for the neuronal cytoplasmic antigen collapsin response-mediator protein-5 (CRMP-5) in a patient's serum or spinal fluid confirms that the patient's subacute neurological disorder has an autoimmune basis and predicts a small-cell lung carcinoma or thymoma with 75% to 80% certainty.(1)

CRMP-5-IgG titers generally fall after the neoplasm is treated, and a rising titer is indicative of tumor persistence or recurrence.

Cautions

Seronegativity does not exclude the presence of a neoplasm.

Testing for a single paraneoplastic autoantibody is not a sufficient screening test for neurological autoimmunity.

Collapsin response-mediator protein-5 (CRMP-5)-IgG is not detectable by immunofluorescence screening if the serum titer is low (<1:120) or if coexisting autoantibodies (either neuron-specific or nonorgan-specific such as antinuclear and antimitochondrial antibodies) are present, which precludes identification of CRMP-5-IgG with certainty. Interfering antibodies can usually be eliminated by absorption with liver antigens. Western blot analysis using full length recombinant human CRMP-5 protein can detect CRMP-5-IgG at 1:30 dilution.

An autoantibody independently named anti-CV2 is the same entity as CRMP-5-IgG. Its antigen in adult brain was erroneously reported to be oligodendrocyte-restricted and was misidentified in 1999 as CRMP-3.

Clinical Reference

1. Yu Z, Kryzer TJ, Griesmann GE, et al: CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related

autoimmunity. Ann Neurol. 2001 Feb;49(2):146-154
2. Cross SA, Salomao DR, Parisi JE, et al: Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. Ann Neurol. 2003 Jul;54(1):38-50
3. Galanis E, Frytak S, Rowland KM, et al: Neuronal autoantibody titers in the course of small-cell lung carcinoma and platinum associated neuropathy. Cancer Immunol Immunother. 1999 May-June;48(2-3):85-90
4. Vernino S, Tuite P, Adler CH, et al: Paraneoplastic chorea associated with CRMP-5 neuronal antibody and lung carcinoma. Ann Neurol. 2002 May;51(5):625-630
5. Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. Ann Neurol. 2004 Nov;56(5):715-719
6. Horta ES, Lennon VA, Lachance DH, et al: Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014 Jul 15;20(14):3862-3869

Performance

Method Description

The patient's sample is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with sample and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Samples that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated to an endpoint. Interference by coexisting non-neuron-specific autoantibodies can usually be eliminated by serologic absorption.(Honorat JA, Komorowski L, Josephs KA, et al: IgLON5 antibody: neurological accompaniments and outcomes in 20 patients. Neurol Neuroimmunol Neuroinflamm 2017 Jul 18;4(5):e385. doi: 10.1212/NXI.0000000000000385)

Western blot analysis with recombinant CRMP-5 (done by specific request) may be required to confirm positive results if interfering autoantibodies are present or when the titer is below 1:120. Western blot testing will also be done by specific request.

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

5 to 8 days

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

Test Definition: CRMTS

Collapsin Response-Mediator Protein-5 (CRMP-5) Neuronal IgG Titer, Serum

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

86256

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CRMTS	CRMP-5-IgG Titer, S	94815-8

Result ID	Test Result Name	Result LOINC® Value
43436	CRMP-5-IgG Titer, S	94815-8