# Test Definition: CRMTS

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

## Overview

### Useful For

**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

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

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Indirect Immunofluorescence Assay (IFA)

### NY State Available

Yes

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## Specimen

### Specimen Type
Serum

### Specimen Required
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### 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 | Refrigerated (preferred) | 28 days | |
| | Ambient | 72 hours | |
| | 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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<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 specimen is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with the specimen and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Specimens that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated. 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;4[5]:e385. Published 2017 Jul 18. 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
2 days

### Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

## 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 |