

Overview

Useful For

Aiding in the diagnosis of paraneoplastic neurological autoimmune disorders related to carcinoma of lung, breast, ovary, thymoma, or Hodgkin lymphoma using spinal fluid specimens

Profile Information

| Test Id | Reporting Name                       | Available Separately | Always Performed |
|---------|--------------------------------------|----------------------|------------------|
| PNEOI   | Paraneoplastic Interpretation, CSF   | No                   | Yes              |
| AMPHC   | Amphiphysin Ab, CSF                  | No                   | Yes              |
| AGN1C   | Anti-Glial Nuclear Ab, Type 1        | No                   | Yes              |
| ANN1C   | Anti-Neuronal Nuclear Ab, Type 1     | No                   | Yes              |
| ANN2C   | Anti-Neuronal Nuclear Ab, Type 2     | No                   | Yes              |
| ANN3C   | Anti-Neuronal Nuclear Ab, Type 3     | No                   | Yes              |
| CRMC    | CRMP-5-IgG, CSF                      | No                   | Yes              |
| PCTRC   | Purkinje Cell Cytoplasmic Ab Type Tr | No                   | Yes              |
| PCA1C   | Purkinje Cell Cytoplasmic Ab Type 1  | No                   | Yes              |
| PCA2C   | Purkinje Cell Cytoplasmic Ab Type 2  | No                   | Yes              |

Reflex Tests

| Test Id | Reporting Name               | Available Separately | Always Performed |
|---------|------------------------------|----------------------|------------------|
| AGNBC   | AGNA-1 Immunoblot, CSF       | No                   | No               |
| AMIBC   | Amphiphysin Immunoblot, CSF  | No                   | No               |
| AN1BC   | ANNA-1 Immunoblot, CSF       | No                   | No               |
| AN2BC   | ANNA-2 Immunoblot, CSF       | No                   | No               |
| CRMWC   | CRMP-5-IgG Western Blot, CSF | Yes                  | No               |
| PC1BC   | PCA-1 Immunoblot, CSF        | No                   | No               |
| PCTBC   | PCA-Tr Immunoblot, CSF       | No                   | No               |
| AGNTC   | AGNA-1 Titer, CSF            | No                   | No               |

|       |                           |    |    |
|-------|---------------------------|----|----|
| AN1TC | ANNA-1 Titer, CSF         | No | No |
| AN2TC | ANNA-2 Titer, CSF         | No | No |
| AN3TC | ANNA-3 Titer, CSF         | No | No |
| APHTC | Amphiphysin Ab Titer, CSF | No | No |
| CRMTC | CRMP-5-IgG Titer, CSF     | No | No |
| PC1TC | PCA-1 Titer, CSF          | No | No |
| PC2TC | PCA-2 Titer, CSF          | No | No |
| PCTTC | PCA-Tr Titer, CSF         | No | No |

Testing Algorithm

If the indirect immunofluorescence assay (IFA) pattern suggests AGNA-1 antibody, then AGNA-1 immunoblot (IB) and AGNA-1 IFA titer will be performed at an additional charge.

If the IFA pattern suggests antineuronal nuclear antibody type 1 (ANNA-1), then ANNA-1 IB, ANNA-1 IFA titer, and ANNA-2 IB will be performed at an additional charge.

If the IFA pattern suggests ANNA-2 antibody, then ANNA-2 IB, ANNA-2 IFA titer, and ANNA-1 IB will be performed at an additional charge.

If the IFA pattern suggests ANNA-3 antibody, then ANNA-3 titer will be performed at an additional charge.

If the IFA pattern suggests Purkinje cytoplasmic antibody type 1 (PCA-1), then PCA-1 IB, and PCA-1 IFA titer will be performed at an additional charge.

If the IFA pattern suggests PCA-2 antibody, then PCA-2 IFA titer will be performed at an additional charge.

If the IFA pattern suggests PCA-Tr antibody, then PCA-Tr immunoblot, and PCA-Tr IFA titer will be performed at an additional charge.

If client requests or the IFA patterns suggest CRMP-5-IgG, then CRMP-5-IgG IFA titer and CRMP-5-IgG western blot will be performed at an additional charge.

If the IFA patterns suggest amphiphysin antibody, then amphiphysin IB and amphiphysin IFA titer will be performed at an additional charge.

The following algorithm is available: [Paraneoplastic Evaluation Algorithm-Spinal Fluid](#).

Special Instructions

- [Paraneoplastic Evaluation Algorithm-Spinal Fluid](#)

Method Name

AGN1C, AMPHC, ANN1C, ANN2C, ANN3C, CRMC, PCA1C, PCA2C7, PCTRC, AGNTC, APHTC, AN1TC, AN2TC, AN3TC, CRMTC, PC1TC, PC2TC, PCTTC: Indirect Immunofluorescence Assay (IFA)

CRMWC: Western Blot  
AGNBC, AMIBC, AN1BC, AN2BC, PC1BC, PCTBC: Immunoblot (IB)

NY State Available  
Yes

Specimen

Specimen Type  
CSF

Ordering Guidance  
This test **no longer contains all known, clinically relevant antibodies** for patients suspected of autoimmune neurological disorders. Instead, consider a comprehensive neurological phenotype-specific autoimmune/paraneoplastic evaluation (eg, encephalopathy, movement disorders, myelopathy, axonal neuropathy). For more information as well as phenotype-specific testing options, refer to [Autoimmune Neurology Test Ordering Guide](#) or the [Neurology specialty website](#).

Additional Testing Requirements  
In patients with a history of tobacco use or other lung cancer risk, or if thymoma is suspected, PAVAL / Paraneoplastic Autoantibody Evaluation, Serum is also recommended.

Necessary Information  
Provide the following information:  
-Relevant clinical information  
-Ordering provider name, phone number, mailing address, and e-mail address

Specimen Required  
Container/Tube: Sterile vial  
Preferred: Vial number 2  
Acceptable: Any vial  
Specimen Volume: 4 mL

Specimen Minimum Volume  
2 mL

Reject Due To

|                 |        |
|-----------------|--------|
| Gross hemolysis | Reject |
| Gross lipemia   | Reject |
| Gross icterus   | Reject |

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Several antineuronal and glial autoantibodies are recognized clinically as markers of a patient's immune response to specific cancers (paraneoplastic autoantibodies). Seropositive patients present with neurologic signs and symptoms in more than 90% of cases. The cancers are most commonly small-cell lung carcinoma, ovarian (or related mullerian) carcinoma, breast carcinoma, thymoma, or Hodgkin lymphoma. The cancers may be new or recurrent, are usually limited in metastatic volume, and are often occult by standard imaging procedures. Detection of the informative marker autoantibodies allows early diagnosis and treatment of the cancer, which may lessen neurological morbidity and improve survival.

Serum is the preferred specimen for paraneoplastic autoantibodies. However, cerebrospinal fluid (CSF) results are sometimes positive when serum results are negative (especially for collapsin response-mediator protein-5-IgG [CRMP-5] and other inflammatory central nervous system autoimmunity). Additionally, CSF is more readily interpretable because it generally lacks the interfering nonorgan-specific antibodies that are common in the serum of patients with cancer. Because neurologists typically perform spinal taps in these patients, the recommendation is to submit CSF specimens with serum specimens, either for simultaneous testing or to be held for testing only if serum is negative.

CRMP-5-IgG western blot is also performed by specific request for more sensitive detection of CRMP-5-IgG. Testing should be requested in cases of subacute basal ganglionic disorders (chorea, parkinsonism), cranial neuropathies (especially loss of vision, taste, or smell), and myelopathies.

Reference Values

| Test ID | Reporting name                       | Methodology | Reference value |
|---------|--------------------------------------|-------------|-----------------|
| AMPHC   | Amphiphysin Ab, CSF                  | IFA         | Negative        |
| AGN1C   | Anti-Glial Nuclear Ab, Type 1        | IFA         | Negative        |
| ANN1C   | Anti-Neuronal Nuclear Ab, Type 1     | IFA         | Negative        |
| ANN2C   | Anti-Neuronal Nuclear Ab, Type 2     | IFA         | Negative        |
| ANN3C   | Anti-Neuronal Nuclear Ab, Type 3     | IFA         | Negative        |
| CRMC    | CRMP-5-IgG, CSF                      | IFA         | Negative        |
| PCTRC   | Purkinje Cell Cytoplasmic Ab Type Tr | IFA         | Negative        |
| PCA1C   | Purkinje Cell Cytoplasmic Ab Type 1  | IFA         | Negative        |
| PCA2C   | Purkinje Cell Cytoplasmic Ab Type 2  | IFA         | Negative        |

Reflex Information:

| Test ID | Reporting name               | Methodology | Reference value |
|---------|------------------------------|-------------|-----------------|
| AGNBC   | AGNA-1 Immunoblot, CSF       | IB          | Negative        |
| AGNTC   | AGNA-1 Titer, CSF            | IFA         | <1:2            |
| AMIBC   | Amphiphysin Immunoblot, CSF  | IB          | Negative        |
| AN1BC   | ANNA-1 Immunoblot, CSF       | IB          | Negative        |
| AN1TC   | ANNA-1 Titer, CSF            | IFA         | <1:2            |
| AN2BC   | ANNA-2 Immunoblot, CSF       | IB          | Negative        |
| AN2TC   | ANNA-2 Titer, CSF            | IFA         | <1:2            |
| AN3TC   | ANNA-3 Titer, CSF            | IFA         | <1:2            |
| APHTC   | Amphiphysin Ab Titer, CSF    | IFA         | <1:2            |
| CRMTC   | CRMP-5-IgG Titer, CSF        | IFA         | <1:2            |
| CRMWC   | CRMP-5-IgG Western Blot, CSF | WB          | Negative        |
| PC1BC   | PCA-1 Immunoblot, CSF        | IB          | Negative        |
| PC1TC   | PCA-1 Titer, CSF             | IFA         | <1:2            |
| PC2TC   | PCA-2 Titer, CSF             | IFA         | <1:2            |
| PCTBC   | PCA-Tr Immunoblot, CSF       | IB          | Negative        |
| PCTTC   | PCA-Tr Titer, CSF            | IFA         | <1:2            |

\*Methodology abbreviations:  
Immunofluorescence assay (IFA)  
Western blot (WB)  
Immunoblot (IB)

Neuron-restricted patterns of IgG staining that do not fulfill criteria for amphiphysin, ANNA-1, ANNA-2, ANNA-3, AGNA-1, PCA-1, PCA-2, PCA-Tr, or CRMP-5-IgG may be reported as "unclassified antineuronal IgG." Complex patterns that include non-neuronal elements may be reported as "uninterpretable."

**Note:** Titers lower than 1:2 are detectable by recombinant CRMP-5 Western blot analysis. CRMP-5 Western blot analysis will be done on request on stored spinal fluid (held 4 weeks). This supplemental testing is recommended in cases of chorea, vision loss, cranial neuropathy, and myelopathy. Call 800-533-1710 to request CRMP-5 Western blot.

Interpretation

Antibodies directed at onconeural proteins shared by neurons, glia, muscle, and certain cancers are valuable serological markers of a patient's immune response to cancer. They are not found in healthy subjects and are usually accompanied by subacute neurological signs and symptoms. Several autoantibodies have a syndromic association, but no autoantibody predicts a specific neurological syndrome. Conversely, a positive autoantibody profile has 80% to 90% predictive value for a specific cancer. It is not uncommon for more than one paraneoplastic autoantibody to be detected, each predictive of the same cancer.

Cautions

No significant cautionary statements

Clinical Reference

1. Lucchinetti CF, Kimmel DW, Lennon VA: Paraneoplastic and oncological profiles of patients seropositive for type 1 anti-neuronal nuclear antibody. *Neurology*. 1998 Mar;50(3):652-657
2. Graus F, Vincent A, Pozo-Rosich P, et al: Anti-glial nuclear antibody: marker of lung cancer-related paraneoplastic neurological syndromes. *J Neuroimmunol*. 2005 Aug;165(1-2):166-171
3. Pittock SJ, Lucchinetti CF, Lennon VA: Anti-neuronal nuclear autoantibody type 2: paraneoplastic accompaniments. *Ann Neurol*. 2003 May;53(5):580-587
4. Chan KH, Vernino S, Lennon VA: ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. *Ann Neurol*. 2001 Sep;50(3):301-311
5. Hetzel DJ, Stanhope CR, O'Neill BP, Lennon VA: Gynecologic cancer in patients with subacute cerebellar degeneration predicted by anti-Purkinje cell antibodies and limited in metastatic volume. *Mayo Clin Proc*. 1990 Dec;65(12):1558-1563
6. Pittock SJ, Lucchinetti CF, Parisi JE, et al: Amphiphysin autoimmunity: paraneoplastic accompaniments. *Ann Neurol*. 2005 Jul;58(1):96-107
7. McKeon A, Pittock SJ: Paraneoplastic encephalomyelopathies: pathology and mechanisms. *Acta Neuropathol*. 2011 Oct;122(4):381-400
8. 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

Indirect Immunofluorescence Assay (IFA):

The patient's sample is tested by a standardized immunofluorescence assay (IFA) 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.0000000000000385689)

Western Blot:

Neuronal antigens extracted aqueously from adult rat cerebellum, full-length recombinant human collapsin response-mediator protein-5 (CRMP-5), or full-length recombinant human amphiphysin protein is denatured, reduced, and separated by electrophoresis on 10% polyacrylamide gel. IgG is detected autoradiographically by enhanced chemiluminescence. (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; Dubey D, Jitprapaikulsan J, Bi H, et al: Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. *Neurology*. 2019 Nov 12;93(20):e1873-e1880)

Immunoblot (IB):

All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient serum (1:12.5) is added to test strips (strips containing recombinant antigen manufactured and purified using biochemical methods) in individual channels and incubated for 30 minutes. Positive specimens will bind to the purified

recombinant antigen and negative specimens will not bind. Strips are washed to remove unbound antibodies and then incubated with anti-human IgG antibodies (alkaline phosphatase-labelled) for 30 minutes. The strips are again washed to remove unbound anti-human IgG antibodies and nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolylphosphate (NBT/BCIP) substrate is added. Alkaline phosphatase enzyme converts the soluble substrate into a colored insoluble product on the membrane to produces a black band. Strips are digitized via picture capture on the EUROBlot One instrument and evaluated with the EUROLineScan software.(O'Connor K, Waters P, Komorowski L, et al: GABAA receptor autoimmunity: A multicenter experience. Neurol Neuroimmunol Neuroinflamm. 2019 Apr 4;6[3]:e552. doi: 10.1212/NXI.0000000000000552)

PDF Report  
No

Day(s) Performed  
Profile tests: Monday through Sunday; Reflex tests: Varies

Report Available  
10 to 17 days

Specimen Retention Time  
28 days

Performing Laboratory Location  
Rochester

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  
86255 x 9  
84182-AGNBC (if appropriate)  
86256-AGNTC (if appropriate)  
84182-AMIBC (if appropriate)  
84182-AN1BC (if appropriate)  
86256-AN1TC (if appropriate)  
84182-AN2BC (if appropriate)

86256-AN2TC (if appropriate)  
86256-AN3TC (if appropriate)  
86256-APHTC (if appropriate)  
86256-CRMTC (if appropriate)  
84182-CRMWC (if appropriate)  
84182-PC1BC (if appropriate)  
86256-PC1TC (if appropriate)  
86256-PC2TC (if appropriate)  
84182-PCTBC (if appropriate)  
86256-PCTTC (if appropriate)

LOINC® Information

| Test ID | Test Order Name                   | Order LOINC® Value |
|---------|-----------------------------------|--------------------|
| PAC1    | Paraneoplas Autoantibody Eval,CSF | 94818-2            |

| Result ID | Test Result Name                   | Result LOINC® Value |
|-----------|------------------------------------|---------------------|
| 89079     | AGNA-1, CSF                        | 90827-7             |
| 5906      | Amphiphysin Ab, CSF                | 90815-2             |
| 3852      | ANNA-1, CSF                        | 44768-0             |
| 7472      | ANNA-2, CSF                        | 56959-0             |
| 21633     | ANNA-3, CSF                        | 90836-8             |
| 21650     | CRMP-5-IgG, CSF                    | 63216-6             |
| 3988      | PCA-1, CSF                         | 90841-8             |
| 21632     | PCA-2, CSF                         | 90843-4             |
| 21631     | PCA-Tr, CSF                        | 90845-9             |
| 34271     | Paraneoplastic Interpretation, CSF | 57771-8             |
| 619519    | IFA Notes                          | 48767-8             |