Overview

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

Profile Information

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<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
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Reflex Tests

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Document generated July 11, 2020 at 2:00pm CDT
### Test Definition: PAC1
Paraneoplas Autoantibody Eval, CSF

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### Testing Algorithm

If indirect immunofluorescence assay (IFA) pattern suggests AGNA-1 antibody, then AGNA-1 immunoblot is performed at an additional charge.

If IFA pattern suggests ANNA-1 antibody, then ANNA-1 immunoblot is performed at an additional charge.

If IFA pattern suggests ANNA-2 antibody, then ANNA-2 immunoblot is performed at an additional charge.

If IFA pattern suggests PCA-1 antibody, then PCA-1 immunoblot is performed at an additional charge.

If IFA pattern suggests PCA-Tr antibody, then PCA-Tr immunoblot is performed at an additional charge.

If IFA patterns suggest CRMP-5-IgG, then CRMP-5-IgG Western blot is performed at an additional charge.

If IFA patterns suggest GAD65 antibody, then GAD65 antibody radioimmunoassay (RIA) is performed at an additional charge.

If IFA patterns suggest neuronal voltage-gated potassium channel-complex (VGKC) autoantibody, then VGKC-complex antibody RIA is performed at an additional charge.

If VGKC-complex antibody RIA is greater than 0.00 nmol/L, then LG1-IgG cell-binding assay (CBA) and CASPR2-IgG CBA are performed at an additional charge.

If IFA patterns suggest amphiphysin antibody, then amphiphysin immunoblot is performed at an additional charge.
If IFA pattern suggests NMDA-Receptor, then NMDA-Receptor antibody CBA and/or NMDA-Receptor titer is performed at an additional charge.

If IFA pattern suggests AMPA-Receptor, then AMPA-Receptor antibody CBA and/or AMPA-Receptor titer is performed at an additional charge.

If IFA pattern suggests GABA-B-Receptor, then GABA-B-Receptor antibody CBA and/or GABA-B-Receptor titer is performed at an additional charge.

If IFA pattern suggests DPPX, then DPPX antibody CBA and DPPX titer is performed at an additional charge.

If IFA pattern suggests mGluR1, then mGluR1 antibody CBA and mGluR1 titer is performed at an additional charge.

The following algorithms are available in Special Instructions.

- **Paraneoplastic Autoantibody CSF Evaluation Algorithm**
- **Hereditary Peripheral Neuropathy Diagnostic Algorithm**

**Special Instructions**

- [Paraneoplastic Autoantibody CSF Evaluation Algorithm](#)
- [Hereditary Peripheral Neuropathy Diagnostic Algorithm](#)

**Method Name**

AGN1C, AMPHC, AMPIC, ANN1C, ANN2C, ANN3C, CRMC, DPPIC, DPPTC, GABIC, GL1IC, GL1TC, NMDIC, PCA1C, PCA2C, PCTRC: Indirect Immunofluorescence Assay (IFA)

CRMWC: Western Blot

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

GD65C, VGKCC: Radioimmunoassay (RIA)

AMPCC, CS2CC, DPPCC, GABCC, GL1CC, LG1CC, NMDCC: Cell-Binding Assay (CBA)

**NY State Available**

Yes

**Specimen**

**Specimen Type**

CSF

**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
Test Definition: PAC1
Paraneoplas Autoantibody Eval, CSF

- Ordering provider name, phone number, mailing address, and e-mail address

**Specimen Required**

**Container/Tube:** Sterile vial

**Specimen Volume:** 4 mL

**Forms**

If not ordering electronically, complete, print, and send a [Neurology Specialty Testing Client Test Request](#) (T732) with the specimen.

**Specimen Minimum Volume**

2 mL

**Reject Due To**

<p>| | |</p>
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<tbody>
<tr>
<td>Gross hemolysis</td>
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<tr>
<td>Gross lipemia</td>
<td>Reject</td>
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<tr>
<td>Gross icterus</td>
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**Specimen Stability Information**

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<tr>
<td></td>
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**Clinical and 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 symptoms and signs 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

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<th>Methodology</th>
<th>Reference value</th>
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<td>AMPHC</td>
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<td>Indirect immunofluorescence (IFA)</td>
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<td>&lt;1:2</td>
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Reflex Information:

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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 symptoms and signs. 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**


Performance

Method Description

Indirect Immunofluorescence Assay (IFA):

The patient's sample is tested by a standardized IFA that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with sample and washing, fluorescein-conjugated goat-anti-human 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:


Immunoblot (IB):

All steps are performed at ambient temperature (18-28 degreesC) 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 EUROLinScan 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)

Radioimmunoassay (RIA):
Duplicate aliquots of patient specimen are incubated with I(125)-labeled antigen. Immune complexes, formed by adding secondary (goat) antihuman immunoglobulin, are pelleted by centrifugation and washed. Gamma emission from the washed pellet is counted, and mean counts per minute (cpm) are compared with results yielded by high positive and negative control sera. Specimen yielding cpm higher than the background cpm yielded by normal human specimen are retested to confirm positivity and titrated as necessary to obtain a value in the linear range of the assay. The antigen binding capacity (nmol per liter) is calculated from the cpm precipitated at a dilution yielding a linear range value. (Vernino S, Kryzer TJ, Lennon AV: Chapter 114: Autoimmune autonomic neuropathy and neuromuscular hyperexcitability disorders. In Manual of Clinical and Laboratory Immunology. Sixth edition. Edited by NR Rose, RG Hamilton, B Detrick. ASM Press, 2002, pp 1013-1017; Jones AL, Flanagan EP, Pittock SJ, et al: Responses to and Outcomes of Treatment of Autoimmune Cerebellar Ataxia in Adults. JAMA Neurol 2015 Nov;72[11]:1304-1312 doi: 10.1001/jamaneurol.2015.2378)

Cell-Binding Assay (CBA):

Patient serum is applied to a composite slide containing transfected and nontransfected HEK-293 cells. After incubation and washing, fluorescein-conjugated goat-antihuman IgG is applied to detect the presence of patient IgG binding. (Package insert: IIFT: Neurology Mosaics, Instructions for the indirect immunofluorescence test. EUROIMMUN, Lubeck, Germany, FA_112d-1_A_UK_C13, 02/2019)

PDF Report

No

Day(s) and Time(s) Test Performed

AGN1C, AMPHC, AMPIC, ANN1C, ANN2C, ANN3C, CRMC, PCTRC, PCA1C, PCA2C, DPPTC, DPPIC, GABIC, GL1TC, GL1IC, NMDIC:
Monday through Friday; 5 a.m., 7 a.m., 5 p.m.
Saturday, Sunday; 6 a.m.
AGNBC, AMIBC, AN1BC, AN2BC, PC1BC, PCTBC:
Monday through Friday; 6 p.m.
AMPCC, CS2CC, DPPCC, GABCC, LG1CC, NMDCC:
Monday through Friday; 10 p.m.
Sunday; 3 p.m.
CRMWC:
Monday through Thursday; 8 a.m.
GL1CC:
Monday and Thursday; 6 p.m.
GD65C:
Monday through Friday; 5 a.m., 2 p.m.
Test Definition: PAC1
Paraneoplas Autoantibody Eval, CSF

Saturday, Sunday; 7 a.m.

VGKCC:
Monday through Friday; 11 a.m., 6 p.m.
Saturday, Sunday; 6 a.m.

Analytic Time
8 days

Maximum Laboratory Time
11 days

Specimen Retention Time
28 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
86255 x 9
84182-AGNBC (if appropriate)
86255-AMPCC (if appropriate)
86256-AMPIC (if appropriate)
84182-AMIBC (if appropriate)
84182-AN1BC (if appropriate)
84182-AN2BC (if appropriate)
86255-CS2CC (if appropriate)
84182-CRMWC (if appropriate)
86255-DPPCC (if appropriate)
Test Definition: PAC1
Paraneoplas Autoantibody Eval,CSF

- 86256-DPPTC (if appropriate)
- 86255-DPPIC (if appropriate)
- 86255-GABCC (if appropriate)
- 86256-GABIC (if appropriate)
- 86341-GD65C (if appropriate)
- 86255-LG1CC (if appropriate)
- 86255-GL1CC (if appropriate)
- 86256-GL1TC (if appropriate)
- 86255-GL1IC (if appropriate)
- 86255-NMDCC (if appropriate)
- 86256-NMDIC (if appropriate)
- 84182-PC1BC (if appropriate)
- 84182-PCTBC (if appropriate)
- 83519-VGKCC (if appropriate)

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