

Neuroimmunology Antibody Follow-up, Spinal Fluid

Overview

Useful For

Monitoring patients who have previously tested positive for 1 or more antibodies within the past 5 years in a Mayo Clinic Neuroimmunology Laboratory spinal fluid evaluation

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AMPCC	AMPA-R Ab CBA, CSF	No	No
AMPHC	Amphiphysin Ab, CSF	No	No
AGN1C	Anti-Glial Nuclear Ab, Type	No	No
	1		
ANN1C	Anti-Neuronal Nuclear Ab,	No	No
	Type 1		
ANN2C	Anti-Neuronal Nuclear Ab,	No	No
	Type 2		
ANN3C	Anti-Neuronal Nuclear Ab,	No	No
	Type 3		
CS2CC	CASPR2-IgG CBA, CSF	No	No
CRMWC	CRMP-5-IgG Western Blot,	No	No
	CSF		
CRMC	CRMP-5-IgG, CSF	No	No
GABCC	GABA-B-R Ab CBA, CSF	No	No
LG1CC	LGI1-IgG CBA, CSF	No	No
NMDCC	NMDA-R Ab CBA, CSF	No	No
PCTRC	Purkinje Cell Cytoplasmc	No	No
	Ab Type Tr		
PCA1C	Purkinje Cell Cytoplasmic	No	No
	Ab Type 1		
PCA2C	Purkinje Cell Cytoplasmic	No	No
	Ab Type 2		
DPPCC	DPPX Ab CBA, CSF	No	No
DPPIC	DPPX Ab IFA, CSF	No	No
GL1CC	mGluR1 Ab CBA, CSF	No	No
GL1IC	mGluR1 Ab IFA, CSF	No	No
AGNBC	AGNA-1 Immunoblot, CSF	No	No
AINCC	Alpha Internexin CBA, CSF	No	No
AMIBC	Amphiphysin Immunoblot,	No	No
	CSF		
AN1BC	ANNA-1 Immunoblot, CSF	No	No



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AN2BC	ANNA-2 Immunoblot, CSF	No	No
APBCC	AP3B2 CBA, CSF	No	No
APBIC	AP3B2 IFA, CSF	No	No
GFACC	GFAP CBA, CSF	No	No
GFAIC	GFAP IFA, CSF	No	No
GRFCC	GRAF1 CBA, CSF	No	No
GRFIC	GRAF1 IFA, CSF	No	No
IG5CC	IgLON5 CBA, CSF	No	No
IG5IC	IgLON5 IFA, CSF	No	No
ITPCC	ITPR1 CBA, CSF	No	No
ITPIC	ITPR1 IFA, CSF	No	No
NCDIC	Neurochondrin IFA, CSF	No	No
NCDCC	Neurochondrin CBA, CSF	No	No
NFHCC	NIF Heavy Chain CBA, CSF	No	No
NIFIC	NIF IFA, CSF	No	No
NFLCC	NIF Light Chain CBA, CSF	No	No
PC1BC	PCA-1 Immunoblot, CSF	No	No
PCTBC	PCA-Tr Immunoblot, CSF	No	No
SP5CC	Septin-5 CBA, CSF	No	No
SP5IC	Septin-5 IFA, CSF	No	No
SP7CC	Septin-7 CBA, CSF	No	No
SP7IC	Septin-7 IFA, CSF	No	No
PDEIC	PDE10A Ab IFA, CSF	No	No
T46CC	TRIM46 Ab CBA, CSF	No	No
T46IC	TRIM46 Ab IFA, CSF	No	No

Method Name

AMPHC, AGN1C, ANN1C, ANN2C, ANN3C, PCTRC, PCA1C, PCA2C, DPPTC, GL1IC, GFAIC, IG5IC, ITPIC, GRFIC, NIFIC, APBIC, SP5IC, SP7IC, CRMC, NCDIC, DPPIC, PDEIC, T46IC: Indirect Immunofluorescence Assay (IFA)

AMPCC, CS2CC, GABCC, LG1CC, NMDCC, DPPCC, GL1CC, GFACC, IG5CC, ITPCC, GRFCC, NFLCC, NFHCC, AINCC, APBCC, NCDCC, SP5CC, SP7CC, T46CC: Cell Binding Assay (CBA)

CRMWC: Western Blot (WB)

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

NY State Available

Yes

Specimen

Specimen Type

CSF



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Ordering Guidance

This test is only appropriate for follow-up in patients who have previously tested positive in a spinal fluid test. If patients have not previously been positive in a spinal fluid test, order one of the following:

- -DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
- -ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
- -EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
- -MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
- -MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
- -PCDEC / Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Spinal Fluid
- -SPPC / Stiff-Person Spectrum Disorders/PERM Evaluation, Spinal Fluid

This test should not be requested in patients who have recently received radioisotopes, therapeutically or diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given, and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimens received in the laboratory will be held 1 week and assayed if sufficiently decayed or canceled if radioactivity remains.

Specimen Required

Container/Tube: Sterile vial Preferred: Vial number 1 Acceptable: Any vial Specimen Volume: 4 mL

Forms

If not ordering electronically, complete, print, and send a <u>Neurology Specialty Testing Client Test Request</u> (T732) with the specimen.

Specimen Minimum Volume

2 mL

Reject Due To

Gross	Reject
hemolysis	
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

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



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Clinical & Interpretive

Clinical Information

Paraneoplastic autoimmune neurological disorders reflect a patient's humoral and cellular immune responses to cancer. The cancer may be new or recurrent, is usually limited in metastatic volume, and is often occult by standard imaging procedures. Autoantibodies specific for onconeural proteins found in the plasma membrane, cytoplasm, and nucleus of neurons or muscle are generated in this immune response and serve as serological markers of paraneoplastic autoimmunity. The most recognized cancers in this context are small-cell lung carcinoma, thymoma, ovarian (or related mullerian) carcinoma, breast carcinoma, and Hodgkin lymphoma. Pertinent childhood neoplasms recognized thus far include neuroblastoma, thymoma, Hodgkin lymphoma, and chondroblastoma. An individual patient's autoantibody profile can predict a specific neoplasm with 90% certainty but not the neurological syndrome.

Three classes of autoantibodies are recognized in the spinal fluid analysis:

- -Neuronal nuclear (antineuronal nuclear antibody-type 1 [ANNA-1], ANNA-2, ANNA-3)
- -Neuronal and muscle cytoplasmic (Purkinje cell cytoplasmic antibody, type 1 [PCA-1]; PCA-2; PCA-Tr, collapsin response-mediator protein-5 [CRMP-5], and amphiphysin)
- -Glial nuclear (antiglial nuclear antibody: AGNA)

Patients who are seropositive usually present with subacute neurological signs and symptoms. The patient may present with encephalopathy, cerebellar ataxia, myelopathy, radiculopathy, plexopathy, sensory, sensorimotor, or autonomic neuropathy, with or without coexisting evidence of a neuromuscular transmission disorder: Lambert-Eaton syndrome, myasthenia gravis, or neuromuscular hyperexcitability. Initial signs may be subtle, but a subacute multifocal and progressive syndrome usually evolves. Sensorimotor neuropathy and cerebellar ataxia are common presentations, but the clinical picture in some patients is dominated by striking gastrointestinal dysmotility, limbic encephalopathy, basal ganglionitis, or cranial neuropathy (especially loss of vision, hearing, smell, or taste). Cancer risk factors include past or family history of cancer, history of smoking, or social/environmental exposure to carcinogens. Early diagnosis and treatment of the neoplasm favor less neurological morbidity and offer the best hope for survival.

Reference Values

Test ID	Reporting Name	Methodology*	Reference Value
AGNBC	AGNA-1 Immunoblot, CSF	IB	Negative
AINCC	Alpha Internexin CBA, CSF	СВА	Negative
AMPCC	AMPA-R Ab CBA, CSF	СВА	Negative
AMPHC	Amphiphysin Ab, CSF	IFA	Negative
AMIBC	Amphiphysin Immunoblot, CSF	IB	Negative
AN1BC	ANNA-1 Immunoblot, CSF	IB	Negative
AN2BC	ANNA-2 Immunoblot, CSF	IB	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



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APBCC	AP3B2 CBA, CSF	СВА	Negative
APBIC	AP3B2 IFA, CSF	IFA	Negative
CS2CC	CASPR2-IgG CBA, CSF	CBA	Negative
CRMWC	CRMP-5-IgG Western Blot, CSF	WB	Negative
CRMC	CRMP-5-IgG, CSF	IFA	Negative
DPPCC	DPPX Ab CBA, CSF	СВА	Negative
DPPIC	DPPX Ab IFA, CSF	IFA	Negative
GABCC	GABA-B-R Ab CBA, CSF	СВА	Negative
GFACC	GFAP CBA, CSF	CBA	Negative
GFAIC	GFAP IFA, CSF	IFA	Negative
GRFCC	GRAF1 CBA, CSF	СВА	Negative
GRFIC	GRAF1 IFA, CSF	IFA	Negative
IG5CC	IgLON5 CBA, CSF	CBA	Negative
IG5IC	IgLON5 IFA, CSF	IFA	Negative
ITPCC	ITPR1 CBA, CSF	СВА	Negative
ITPIC	ITPR1 IFA, CSF	IFA	Negative
LG1CC	LGI1-IgG CBA, CSF	СВА	Negative
GL1CC	mGluR1 Ab CBA, CSF	СВА	Negative
GL1IC	mGluR1 Ab IFA, CSF	IFA	Negative
NCDCC	Neurochondrin CBA, CSF	CBA	Negative
NCDIC	Neurochondrin IFA, CSF	IFA	Negative
NFHCC	NIF Heavy Chain CBA, CSF	СВА	Negative
NIFIC	NIF IFA, CSF	IFA	Negative
NFLCC	NIF Light Chain CBA, CSF	СВА	Negative
NMDCC	NMDA-R Ab CBA, CSF	СВА	Negative
PC1BC	PCA-1 Immunoblot, CSF	IB	Negative
PCTBC	PCA-Tr Immunoblot, CSF	IB	Negative
	Purkinje Cell Cytoplasmc Ab Type		
PCTRC	Tr	IFA	Negative
	Purkinje Cell Cytoplasmic Ab Type		
PCA1C	1	IFA	Negative
	Purkinje Cell Cytoplasmic Ab Type		
PCA2C	2	IFA	Negative
SP5CC	Septin-5 CBA, CSF	CBA	Negative
SP5IC	Septin-5 IFA, CSF	IFA	Negative
SP7CC	Septin-7 CBA, CSF	СВА	Negative
SP7IC	Septin-7 IFA, CSF	IFA	Negative
	Septili-7 IFA, CSF	1	110Bative
PDEIC	PDE10A Ab IFA, CSF	IFA	Negative

^{*}Methodology abbreviations:

CBA: Cell-binding assay



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IB: Immunoblot

IFA: Immunofluorescence assay

WB: Western blot (WB)

Interpretation

Antibodies directed at onconeural proteins shared by neurons, 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 known 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 autoantibodies to be detected, each predictive of the same cancer.

Cautions

This test should only be utilized when the presence of paraneoplastic autoantibodies has been previously documented.

This test should not be requested in patients who have recently received radioisotopes, therapeutically or diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimens received in the laboratory will be held 1 week and assayed if sufficiently decayed, or canceled if radioactivity remains.

Clinical Reference

- 1. Lancaster E, Martinez-Hernandez E, Dalmau J. Encephalitis and antibodies to synaptic and neuronal cell surface proteins. Neurology. 2011;77(2):179-189. doi:10.1212/WNL.0b013e318224afde
- 2. Horta ES, Lennon VA, Lachance DH, et al. Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014;20(14):3862-3869
- 3. Gilligan M, McGuigan C, McKeon A..Paraneoplastic neurologic Disorders. Curr Neurol Neurosci Rep. 2023;23(3):67-82. doi:10.1007/s11910-023-01250-w
- 4. Graus F, Vogrig A, Muniz-Castrillo S, et al. Updated diagnostic criteria for paraneoplastic neurologic syndromes. Neurol Neuroimmunol Neuroinflamm. 2021;8(4):e1014. doi:10.1212/NXI.00000000001014

Performance

Method Description

Indirect Immunofluorescence Assay (IFA):

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)



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Cell-Binding Assay (CBA):

Patient specimen 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. (Unpublished Mayo method)

Immunoblot (IB):

All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient specimen (1:101) is added to test strips (strips containing recombinant antigen manufactured and purified using biochemical methods) in individual channels and incubated for 30 minutes. Positive samples will bind to the purified recombinant antigen, and negative samples 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-indolyl phosphate substrate is added. Alkaline phosphatase enzyme converts the soluble substrate into a colored insoluble product on the membrane to produce 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;6[3]:e552. doi:10.1212/NXI.00000000000000552)

Western Blot (WB):

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 February;49[2]:146-154; Dubey D, Jitprapaikulsan J, Bi H, et al: Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019;93[20] e1873-e1880. doi:10.1212/WNL.00000000000008472)

PDF Report

No

Day(s) Performed

Varies

Report Available

Varies

Specimen Retention Time

28 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes



Neuroimmunology Antibody Follow-up, Spinal Fluid

Fees

- Authorized users can sign in to <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact <u>Customer Service</u>.

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

84182 AGNBC (if appropriate)

86255 AINCC (if appropriate)

86255 AMPCC (if appropriate)

86255 AMPHC (if appropriate)

84182 AMIBC (if appropriate)

84182 AN1BC (if appropriate)

84182 AN2BC (if appropriate)

86255 AGN1C (if appropriate)

86255 ANN1C (if appropriate)

86255 ANN2C (if appropriate)

86255 ANN3C (if appropriate)

86255 APBCC (if appropriate)

86255 APBIC (if appropriate)

86255 CS2CC (if appropriate)

84182 CRMWC (if appropriate)

86255 CRMC (if appropriate)

86255 DPPCC (if appropriate)

86255 DPPIC (if appropriate)

86255 GABCC (if appropriate)

86255 GFACC (if appropriate)

86255 GFAIC (if appropriate)

86255 GRFCC (if appropriate)

86255 GRFIC (if appropriate)

86255 IG5CC (if appropriate)

86255 IG5IC (if appropriate)

86255 ITPCC (if appropriate)

86255 ITPIC (if appropriate)

86255 LG1CC (if appropriate)

86255 GL1CC (if appropriate)

86255 GL1IC (if appropriate)

86255 NCDCC (if appropriate)

86255 NCDIC (if appropriate)

86255 NFHCC (if appropriate)



Neuroimmunology Antibody Follow-up, Spinal Fluid

86255 NIFIC (if appropriate)

86255 NFLCC (if appropriate)

86255 NMDCC (if appropriate)

84182 PC1BC (if appropriate)

84182 PCTBC (if appropriate)

86255 PCTRC (if appropriate)

86255 PCA1C (if appropriate)

86255 PCA2C (if appropriate)

86255 PDEIC (if appropriate)

86255 SP5CC (if appropriate)

86255 SP5IC (if appropriate)

86255 SP7CC (if appropriate)

86255 SP7IC (if appropriate)

86255 T46CC (if appropriate)

86255 T46IC (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PNEFC	Neuroimmunology Ab Follow-up, CSF	80615-8

Result ID	Test Result Name	Result LOINC® Value
84299	Neuroimmunology Ab Follow-up, CSF	80615-8