

## Overview

### Useful For

Evaluating children with autoimmune central nervous system disorders using spinal fluid specimens

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
PCCI	Peds Autoimmune CNS Interp, CSF	No	Yes
AMPCC	AMPA-R Ab CBA, CSF	No	Yes
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	No	Yes
CS2CC	CASPR2-IgG CBA, CSF	No	Yes
DPPCC	DPPX Ab CBA, CSF	No	Yes
GABCC	GABA-B-R Ab CBA, CSF	No	Yes
GD65C	GAD65 Ab Assay, CSF	Yes	Yes
GFAIC	GFAP IFA, CSF	No	Yes
LG1CC	LGI1-IgG CBA, CSF	No	Yes
GL1IC	mGluR1 Ab IFA, CSF	No	Yes
NCDIC	Neurochondrin IFA, CSF	No	Yes
NMDCC	NMDA-R Ab CBA, CSF	No	Yes
NMOFC	NMO/AQP4 FACS, CSF	Yes	Yes
PCTRC	Purkinje Cell Cytoplasmic Ab Type Tr	No	Yes

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AMPIC	AMPA-R Ab IF Titer Assay, CSF	No	No
AN1BC	ANNA-1 Immunoblot, CSF	No	No
AN2BC	ANNA-2 Immunoblot, CSF	No	No
DPPTC	DPPX Ab IFA Titer, CSF	No	No
GABIC	GABA-B-R Ab IF Titer Assay, CSF	No	No
GFACC	GFAP CBA, CSF	No	No
GFATC	GFAP IFA Titer, CSF	No	No
GL1CC	mGluR1 Ab CBA, CSF	No	No
GL1TC	mGluR1 Ab IFA Titer, CSF	No	No
NMDIC	NMDA-R Ab IF Titer Assay,	No	No

	CSF		
NMOTC	NMO/AQP4 FACS Titer, CSF	No	No
PCTBC	PCA-Tr Immunoblot, CSF	No	No
AN1TC	ANNA-1 Titer, CSF	No	No
NCDCC	Neurochondrin CBA, CSF	No	No
NCDTC	Neurochondrin IFA Titer, CSF	No	No
PCTTC	PCA-Tr Titer, CSF	No	No

**Testing Algorithm**

If the indirect immunofluorescence assay (IFA) pattern suggests antineuronal nuclear antibodies (ANNA)-1, then the ANNA-1 immunoblot, ANNA-1 IFA titer and ANNA-2 immunoblot will be performed at an additional charge.

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

If the N-methyl-D-aspartate receptor (NMDA-R) antibody cell-binding assay (CBA) result is positive, then the NMDA-R IFA titer will be performed at an additional charge.

If the gamma-aminobutyric acid B receptor (GABA-B-R) antibody CBA result is positive, then the GABA-B-R IFA titer will be performed at an additional charge.

If the dipeptidyl-peptidase-like protein-6 (DPPX) antibody CBA result is positive, then the DPPX IFA titer will be performed at an additional charge.

If the IFA pattern suggests metabotropic glutamate receptor 1 (mGluR1) antibody, then the mGluR1 antibody CBA and mGluR1 IFA titer will be performed at an additional charge.

If the IFA pattern suggests glial fibrillary acidic protein (GFAP) antibody, then the GFAP antibody CBA and GFAP IFA titer will be performed at an additional charge.

If the neuromyelitis optica/aquaporin-4-IgG (NMO/AQP4-IgG) fluorescence-activated cell sorting (FACS) screen assay requires further investigation, then the NMO/AQP4-IgG FACS titration assay will be performed at an additional charge.

If the IFA pattern suggests neurochondrin antibody, then the neurochondrin antibody CBA and neurochondrin IFA titer will be performed at an additional charge.

If alpha-amino-3-hydroxy-5 methyl-4-isoxazolepropionic acid (AMPA)-receptor antibody CBA result is positive, then AMPA-receptor antibody IFA titer assay will be performed at an additional charge.

For more information, see the following:

[Pediatric Autoimmune Encephalopathy/Central Nervous System Disorders Evaluation Algorithm-Spinal Fluid](#)

[Pediatric Autoimmune Central Nervous System Demyelinating Disease Diagnostic Algorithm](#)

**Special Instructions**

- [Pediatric Autoimmune Encephalopathy/CNS Disorders Evaluation Algorithm-Spinal Fluid](#)
- [Pediatric Autoimmune Central Nervous System Demyelinating Disease Diagnostic Algorithm](#)

**Method Name**

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

NMOFC, NMOTC: Flow Cytometry

AMPIC, ANN1C, AN1TC, DPPTC, GABIC, GFAIC, GFATC, GL1IC, GL1TC, NCDIC, NCDTC, NMDIC, PCTRC, PCTTC: Indirect Immunofluorescence Assay (IFA)

GD65C: Radioimmunoassay (RIA)

AN1BC, AN2BC, PCTBC: Immunoblot (IB)

PCCI: Medical Interpretation

**NY State Available**

Yes

**Specimen****Specimen Type**

CSF

**Ordering Guidance**

Multiple neurological phenotype-specific autoimmune/paraneoplastic evaluations are available. For more information as well as phenotype-specific testing options, refer to [Autoimmune Neurology Test Ordering Guide](#).

When more than one evaluation is ordered on the same order number the duplicate test will be canceled.

For a list of antibodies performed with each evaluation, see [Autoimmune Neurology Antibody Matrix](#).

**Necessary Information**

Provide the following information:

- Relevant clinical information
- Ordering healthcare professional's name, phone number, mailing address, and email address

**Specimen Required**

**Container/Tube:** Sterile vial

**Preferred:** Collection vial number 1

**Acceptable:** Any collection 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

Gross hemolysis	Reject
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	

### Clinical & Interpretive

#### Clinical Information

Autoimmune encephalitis and myelitis is increasingly recognized as a cause of central nervous system disease in children and adolescents. N-methyl-D-aspartate receptor antibody (NMDA-R) encephalitis and myelin oligodendrocyte glycoprotein (MOG) autoimmunity are most common, although other entities, including aquaporin-4 autoimmunity, contactin-associated protein-like 2 (CASPR2) autoimmunity, autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy, and paraneoplastic encephalomyopathies, may also occur in children.

#### Reference Values

Test ID	Reporting name	Methodology	Reference value
PCCI	Peds Autoimmune CNS Interp, CSF	Medical interpretation	Interpretive report
AMPCC	AMPA-R Ab CBA, CSF	CBA	Negative
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative
CS2CC	CASPR2-IgG CBA, CSF	CBA	Negative
DPPCC	DPPX Ab CBA, CSF	CBA	Negative

GABCC	GABA-B-R Ab CBA, CSF	CBA	Negative
GD65C	GAD65 Ab Assay, CSF	RIA	< or =0.02 nmol/L Reference values apply to all ages.
GFAIC	GFAP IFA, CSF	IFA	Negative
GL1IC	mGluR1 Ab IFA, CSF	IFA	Negative
LG1CC	LGI1-IgG CBA, CSF	CBA	Negative
NCDIC	Neurochondrin IFA, CSF	IFA	Negative
NMDCC	NMDA-R Ab CBA, CSF	CBA	Negative
NMOFC	NMO/AQP4 FACS, CSF	FACS	Negative
PCTRC	Purkinje Cell Cytoplasmic Ab Type Tr	IFA	Negative

**Reflex Information:**

Test ID	Reporting name	Methodology	Reference value
AMPIC	AMPA-R Ab IF Titer Assay, CSF	IFA	<1:2
AN1BC	ANNA-1 Immunoblot, CSF	IB	Negative
AN1TC	ANNA-1 Titer, CSF	IFA	<1:2
AN2BC	ANNA-2 Immunoblot, CSF	IB	Negative
DPPTC	DPPX Ab IFA Titer, CSF	IFA	<1:2
GABIC	GABA-B-R Ab IF Titer Assay, CSF	IFA	<1:2
GFACC	GFAP CBA, CSF	CBA	Negative
GFATC	GFAP IFA Titer, CSF	IFA	<1:2
GL1CC	mGluR1 Ab CBA, CSF	CBA	Negative
GL1TC	mGluR1 Ab IFA Titer, CSF	IFA	<1:2
NCDCC	Neurochondrin CBA, CSF	CBA	Negative
NCDTC	Neurochondrin IFA Titer, CSF	IFA	<1:2
NMDIC	NMDA-R Ab IF Titer Assay, CSF	IFA	<1:2
NMOTC	NMO/AQP4 FACS Titer, CSF	FACS	<1:2
PCTTC	PCA-Tr Titer, CSF	IFA	<1:2
PCTBC	PCA-Tr Immunoblot, CSF	IB	Negative

\*Methodology abbreviations:

Immunofluorescence assay (IFA)

Cell-binding assay (CBA)

Fluorescence activated cell sorting assay (FACS)

Radioimmunoassay (RIA)

Immunoblot (IB)

\*Neuron-restricted patterns of IgG staining that do not fulfill criteria for ANNA-1 or PCA-Tr may be reported as "unclassified antineuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

**Interpretation**

This profile is consistent with an autoimmune central nervous system disorder.

### Cautions

Negative results do not exclude a diagnosis of an autoimmune central nervous system disorder.

### Clinical Reference

1. Dubey D, Pittock SJ, Krecke KN, et al. Clinical, radiologic, and prognostic features of myelitis associated with myelin oligodendrocyte glycoprotein autoantibody. *JAMA Neurol.* 2019;76(3):301-309 doi:10.1001/jamaneurol.2018.4053
2. McKeon A, Lennon VA, Lotze T, et al. CNS aquaporin-4 autoimmunity in children. *Neurology.* 2008;71(2):93-100
3. Dubey D, Hinson SR, Jolliffe EA, et al. Autoimmune GFAP astrocytopathy: Prospective evaluation of 90 patients in 1 year. *J Neuroimmunol.* 2018;321:157-163
4. Philipps G, Alisanski SB, Pranzatelli M, et al. Purkinje cell cytoplasmic antibody type 1 (anti-Yo) autoimmunity in a child with Down syndrome. *JAMA Neurol.* 2014;71(3):347-349
5. Lopez-Chiriboga AS, Klein C, Zekeridou A, et al. LGI1 and CASPR2 neurological autoimmunity in children. *Ann Neurol.* 2018;84(3):473-480
6. Lopez-Chiriboga AS, Majed M, Fryer J, et al. Association of MOG-IgG serostatus with relapse after acute disseminated encephalomyelitis and proposed diagnostic criteria for MOG-IgG-associated disorders. *JAMA Neurol.* 2018;75(11):1355-1363
7. Clardy SL, Lennon VA, Dalmau J. Childhood onset of stiff-man syndrome. *JAMA Neurol.* 2013;70(12):1531-1536
8. Banwell B, Tenembaum S, Lennon VA, et al. Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. *Neurology.* 2008;70(5):344-352

### Performance

#### Method Description

##### Cell-Binding Assay:

Patient sample is applied to a composite slide containing transfected and nontransfected EU90 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; FA\_112d-1\_A\_UK\_C13, 02/25/2019)

##### Fluorescence-Activated Cell Sorting Assay:

Human embryonic kidney cells (HEK 293) are transfected transiently with a plasmid (pIRES2-*Aequorea coerulescens* green fluorescent protein [AcGFP]) encoding both green fluorescent protein (AcGFP) and AQP4-M1. After 36 hours, a mixed population of cells (transfected expressing AQP4 or MOG on the surface and AcGFP in the cytoplasm and nontransfected lacking AQP4 or MOG and AcGFP) are lifted and resuspended in live cell-binding buffer. Cells are incubated with patient sample and an AlexaFluor 647-labeled secondary antibody is added. Two populations are gated on the basis of AcGFP expression: positive (high AQP4 or MOG expression) and negative (low or no AQP4 or MOG expression). Positivity is based on the ratio (positive >2.0) of the average median fluorescence intensity (MFI) of each cell population (MFI GFP positive:MFI GFP negative).(Unpublished Mayo method)

##### Indirect Immunofluorescence Assay:

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)

**Radioimmunoassay:**

(125)I-labeled recombinant human antigens or labeled receptors are incubated with patient sample. After incubation, anti-human IgG is added to form an immunoprecipitate. The amount of (125)I-labeled antigen in the immunoprecipitate is measured using a gamma-counter. The amount of gamma emission in the precipitate is proportional to the amount of antigen-specific IgG in the sample. Results are reported as units of precipitated antigen (nmol) per liter of patient sample.(Griesmann GE, Kryzer TJ, Lennon VA. Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In: Rose NR, Hamilton RG, et al, eds. *Manual of Clinical and Laboratory Immunology*. 6th ed ASM Press; 2002:1005-1012; Walikonis JE, Lennon VA. Radioimmunoassay for glutamic acid decarboxylase [GAD65] autoantibodies as a diagnostic aid for stiff-man syndrome and a correlate of susceptibility to type 1 diabetes mellitus. *Mayo Clin Proc*. 1983;58(12):1161-1166; Jones AL, Flanagan EP, Pittock SJ, et al. Responses to and Outcomes of Treatment of Autoimmune Cerebellar Ataxia in Adults. *JAMA Neurol* 2015;72(11):1304-1312. doi:10.1001/jamaneurol.2015.2378)

**Immunoblot:**

All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient sample (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 antihuman IgG antibodies (alkaline phosphatase-labeled) for 30 minutes. The strips are again washed to remove unbound antihuman IgG antibodies and nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolyl phosphate (NBT/BCIP) 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: GABA receptor autoimmunity: A multicenter experience. *Neurol Neuroimmunol Neuroinflamm*. 2019;6[3]:e552 doi:10.1212/NXI.0000000000000552)

**PDF Report**

No

**Day(s) Performed**

Profile tests: Monday through Sunday; Reflex tests: Varies

**Report Available**

8 to 12 days

**Specimen Retention Time**

28 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**

86255 x 11

86341

86053

86256 AMPIC (if appropriate)

84182 AN1BC (if appropriate)

86256 AN1TC (if appropriate)

84182 AN2BC (if appropriate)

86256 DPPTC (if appropriate)

86256 GABIC (if appropriate)

86255 GFACC (if appropriate)

86256 GFATC (if appropriate)

86255 GL1CC (if appropriate)

86256 GL1TC (if appropriate)

86255 NCDCC (if appropriate)

86256 NCDTC (if appropriate)

86256 NMDIC (if appropriate)

86053 NMOTC (if appropriate)

84182 PCTBC (if appropriate)

86256 PCTTC (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
PCDEC	Peds Autoimm Enceph CNS, CSF	101416-6

Result ID	Test Result Name	Result LOINC® Value
3852	ANNA-1, CSF	44768-0

21631	PCA-Tr, CSF	90845-9
21702	GAD65 Ab Assay, CSF	94359-7
61513	NMDA-R Ab CBA, CSF	93502-3
61514	AMPA-R Ab CBA, CSF	93491-9
61515	GABA-B-R Ab CBA, CSF	93426-5
38325	NMO/AQP4-IgG FACS, CSF	46718-3
64280	LGI1-IgG CBA, CSF	94288-8
64282	CASPR2-IgG CBA, CSF	94286-2
64927	mGluR1 Ab IFA, CSF	94361-3
64934	DPPX Ab CBA, CSF	94283-9
605156	GFAP IFA, CSF	94360-5
605132	Peds Autoimmune CNS Interp, CSF	69048-7
618906	IFA Notes	48767-8
615866	Neurochondrin IFA, CSF	101451-3