Your partner in autoimmune neurology testing

We’re here to help you find answers, accurately diagnose patients, give you access to research and discoveries, and provide the expertise and guidance you need.
Improving patient outcomes through advanced testing and consultations

A WORLD LEADER IN AUTOIMMUNE NEUROLOGY

We are recognized as leaders in the diagnosis and treatment of autoimmune neurologic disorders, one of the most rapidly evolving fields in modern neurology. These common disorders target virtually any structure within the central or peripheral nervous system.

ADVANCED PHENOTYPE-SPECIFIC EVALUATIONS

Our approach to antibody evaluations ensures a timely diagnosis and complete picture of a patient’s likelihood of autoimmune disease compared to single antibody testing.

TOP EXPERTS IN THE LAB AVAILABLE FOR CONSULTATION

Get unparalleled assistance with test selection, interpretation follow-up, treatment guidance, and unclassified antibody findings. Neurologists are available for consultation seven days a week, providing interpretive expertise and support.
Leading the way in autoantibody evaluations

A HISTORY OF INNOVATION AND DISCOVERY

Recognized as a world leader in the diagnosis and treatment of autoimmune neurologic disorders and demyelinating disease, Mayo Clinic mounts unmatched resources for uncovering novel syndromes, developing new diagnostic biomarkers and unique laboratory tests.

The Mayo Clinic Neuroimmunology Laboratory was the first to introduce comprehensive serological evaluations for the diagnosis of paraneoplastic neurologic autoimmune disorders, a group of disorders in which unusual neurologic signs and symptoms are the initial manifestations of cancer.

The laboratory continues to discover and clinically validate novel autoantibody profiles that inform neurological decision-making and guide the search for cancer.

Vanda Lennon, M.D., Ph.D., is the founder of the Mayo Clinic Neuroimmunology Laboratory. She is also the Dorothy A. Adair Professor in the Departments of Laboratory Medicine and Pathology, Neurology, and Immunology at the College of Medicine at Mayo Clinic.

A RAPIDLY EVOLVING SUBSPECIALTY

Autoimmune neurology has been advanced through discovery, research, and clinical service for decades. Recent advances validate that disorders—extending beyond MS—are more common than traditionally believed. These conditions manifest as disorders previously thought to be independent and unrelated and thus, are often treated incorrectly—with devastating consequences for patients.
Meet our team of experts

LABORATORY DIRECTORS

Andrew McKeon, M.B., B.Ch., M.D.  
John R. Mills, Ph.D.  
Sean Pittock, M.D.

CONSULTANTS

Divyanshu Dubey, M.B.B.S.  
Eoin Flanagan, M.B., B.Ch.  
Christopher Klein, M.D.  
Daniel Lachance, M.D.  
Anastasia Zekeridou, M.D.

PARTNER WITH TOP NEUROLOGISTS

Extend your network to include some of the world’s leading neurology experts. Our laboratories are directed and run by clinical neurologists who can provide the guidance you need.
Optimized screening methods

OUR AUTOIMMUNE NEUROLOGY EVALUATIONS USE THE MOST UP-TO-DATE SCREENING METHODOLOGIES AND ARE OPTIMIZED FOR EACH ANTIBODY. EVALUATIONS INCLUDE:

- An indirect immunofluorescence assay, using a tissue or cell-based test. This testing is often used to screen for paraneoplastic antibodies and antibodies related to encephalitis.

- A flow cytometry assay, used to screen for aquaporin-4 and myelin oligodendrocyte glycoprotein antibodies, which are relevant in diagnosing transverse myelitis, optic neuritis, and neuromyelitis optica.

- A radioimmunoprecipitation assay, which can detect some ion channel antibodies, including the diagnostics for Lambert-Eaton syndrome and myasthenia gravis.
Targeted evaluations to expedite diagnosis and treatment of autoimmune encephalopathy

WHAT IS AUTOIMMUNE ENCEPHALOPATHY?
Autoimmune encephalopathy extends beyond the classically recognized clinical and radiological spectrum of “limbic encephalitis.” It encompasses a diversity of neurological presentations with subacute or insidious onset, including confusional states, psychosis, delirium, memory loss, hallucinations, movement disorders, sensory or motor complaints, seizures, dyssomnias, ataxias, eye movement problems, nausea, vomiting, inappropriate antidiuresis, coma, dysautonomias, or hypoventilation.

WHEN TO CONSIDER TESTING
Consider autoimmune testing for patients presenting with new-onset encephalopathy (non-infectious or metabolic) and one or more of the following:
• Headache
• Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
• History of cancer
• Smoking history (20+ pack years) or other cancer risk factors
• Inflammatory cerebrospinal fluid
• Neuroimages suggesting inflammation (signal abnormality, limbic or extra-temporal)
• Prior treatment with immune checkpoint inhibitors
• Antibody prevalence in epilepsy and encephalopathy (APE2) score is ≥4

AUTOIMMUNE ENCEPHALOPATHY IS INCREASINGLY RECOGNIZED
Many cases of encephalopathy previously considered infectious are now recognized to have an autoimmune cause. In fact, based on a recent Mayo Clinic study, autoimmune encephalitis was found to be as common as infectious encephalitis.²

Contact a clinical specialist at 855-516-8404 or +1-855-379-3115 (International). See more at mayocliniclabs.com.
A guide to testing and evaluated antibodies

**ENC2** | Encephalopathy, Autoimmune Evaluation, Spinal Fluid
TAT: 5 days

**ENS2** | Encephalopathy, Autoimmune Evaluation, Serum
TAT: 7 days

**Clinical References**


**PLasma Membrane Specificities**

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**NUclear and CytosPlasmic Specificities**

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**Abbreviations:** 
AChR, acetylcholine receptor; AGNA, anti-glial/neuronal nuclear antibody; AMPA, α-aminoc-3-hydroxy-5-methyl-4-isoxazolepropionic acid; ANNA, antineuronal nuclear antibody; CASPR2, contactin-associated protein-like 2; CRMP-5, collapsin response-mediator protein-5; DPPX, dipeptidyl-peptidase-like protein 6; GABA, gamma-aminobutyric acid; GAD65, glutamic acid decarboxylase-65; GFAP, glial fibrillary acidic protein; LGI1, leucine-rich glioma-inactivated 1; NMDA, N-methyl D-aspartate; mGluR1, metabotropic glutamate receptor 1; PCA, Purkinje cell cytoplasmic antibody.
Epilepsy

Targeted evaluations to expedite diagnosis and treatment of autoimmune epilepsy

**WHAT IS AUTOIMMUNE EPILEPSY?**

Autoimmune epilepsy is increasingly recognized in the spectrum of neurological disorders characterized by detection of neural autoantibodies in serum or spinal fluid and responsiveness to immunotherapy. The advent of more sensitive and specific serological detection methods is increasingly revealing previously underappreciated autoimmune epilepsies. Neural autoantibodies specific for intracellular and plasma membrane antigens aid the diagnosis of autoimmune epilepsy, but no single antibody is specific for this diagnosis.

**IMPROVING PATIENT OUTCOMES THROUGH AUTOIMMUNE TESTING**

Identifying epilepsy as autoimmune-mediated is crucial because patients may benefit from immune suppression, while traditional antiepileptic therapy may not be effective.

In a Mayo Clinic study of 27 patients with suspected autoimmune epilepsy treated with immunotherapy, 81% experienced clinical improvement and 67% became seizure free.

**WHEN TO CONSIDER TESTING**

Consider autoimmune testing for patients presenting with new-onset epilepsy with incomplete seizure control, duration of less than two years, and one or more of the following:

- Subacute progression (maximal seizure frequency within three months)
- Multiple seizure types or faciobrachial dystonic seizures
- Antiepileptic drug resistance
- Psychiatric accompaniments (psychosis, hallucinations)
- Movement disorder (myoclonus, tremor, dyskinesia)
- Headache
- Cognitive impairment/encephalopathy
- Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history (20+ pack years) or other cancer risk factors
- Inflammatory cerebrospinal fluid
- Neuroimages suggesting inflammation (limbic or extra-temporal)
- Prior treatment with immune checkpoint inhibitors
- Antibody prevalence in epilepsy and encephalopathy (APE2) score is ≥4

**Autoimmune CNS**

In a Mayo Clinic study of 27 patients with suspected autoimmune epilepsy treated with immunotherapy, 81% experienced clinical improvement and 67% became seizure free.
A guide to testing and evaluated antibodies

**Epilepsy, Autoimmune Evaluation, Spinal Fluid**

TAT: 5 days

**Epilepsy, Autoimmune Evaluation, Serum**

TAT: 7 days

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**CLINICAL REFERENCES**


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**PLASMA MEMBRANE SPECIFICITIES**

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**NUCLEAR AND CYTOPLASMIC SPECIFICITIES**

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**Abbreviations:** AChR, acetylcholine receptor; AGNA, anti-glia/neuronal nuclear antibody; AMPA, α-aminomethyl-3-hydroxy-5-methyl-4-isoxazoloproptic acid; ANNA, antineuronal nuclear antibody; CASPR2, contactin-associated protein-like 2; CRMP-5, collapsin response-mediator protein-5; DPPX, dipeptidyl-peptidase-like protein 6; GABA, gamma-aminobutyric acid; GAD65, glutamic acid decarboxylase-65; GFAP, glial fibrillary acidic protein; LGI1, leucine-rich glioma-inactivated 1; NMDA, N-methyl D-aspartate; mGluR1, metabotropic glutamate receptor 1; PCA, Purkinje cell cytoplasmic antibody.
Targeted evaluations to expedite diagnosis and treatment of autoimmune dementia

WHAT IS AUTOIMMUNE DEMENTIA?
Recent case series and clinical-serological observations have shown that autoimmune encephalopathies do not always present with delirium, but sometimes present as a rapidly progressive dementia. Additionally, some cases may be paraneoplastic.

AN AUTOIMMUNE CAUSE MEANS A POTENTIALLY REVERSIBLE COURSE
If autoimmune dementia is misdiagnosed as an irreversible progressive neurodegenerative disorder, it may delay a correct diagnosis beyond the window of reversibility (6–12 months) and result in devastating consequences for the patient and family. An accurate diagnosis and early-initiated immunotherapy give patients the best possible outcome.

35% Among Mayo Clinic patients diagnosed with and treated for an autoimmune dementia, 35% were initially misdiagnosed as having a neurodegenerative disorder.

WHEN TO CONSIDER TESTING
Consider autoimmune testing for patients presenting with new-onset dementia or cognitive impairment and one or more of the following:
- Rapid onset and progression
- Fluctuating course
- Psychiatric accompaniments (psychosis, hallucinations)
- Movement disorder (myoclonus, tremor, dyskinesia)
- Headache
- Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history (20+ pack years) or other cancer risk factors
- Inflammatory cerebrospinal fluid
- Neuroimaging atypical for degenerative etiology
- Prior treatment with immune checkpoint inhibitors
- Antibody prevalence in epilepsy and encephalopathy (APE2) score is ≥4†
A guide to testing and evaluated antibodies

**DMC2** | Dementia, Autoimmune Evaluation, Spinal Fluid
TAT: 5 days

**DMS2** | Dementia, Autoimmune Evaluation, Serum
TAT: 7 days

**CLINICAL REFERENCES**


**NUCLEAR AND CYTOPLASMIC SPECIFICITIES**

**PLASMA MEMBRANE SPECIFICITIES**

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Targeted evaluations to expedite diagnosis and treatment of autoimmune movement disorders

WHAT ARE AUTOIMMUNE MOVEMENT DISORDERS?
Autoimmune movement disorders encapsulate a large and diverse group of neurologic disorders occurring either in isolation or accompanying more diffuse autoimmune encephalitic illnesses. Disorders may be ataxic, hypokinetic (parkinsonism), or hyperkinetic (myoclonus, chorea, and other dyskinetic disorders).

PERSONALIZED TREATMENT FOR EACH PATIENT
Given the variety of movement phenomena and disorders, treatment protocols should be individualized for each patient and reflect symptom severity, the type of antibody identified, and the presence or absence of cancer. In addition to oncologic therapy (when appropriate), often treatment involves immunotherapy and symptomatic therapy. Often, early-initiated immunotherapy gives patients the best possible outcomes.

53% of autoimmune cerebellar ataxia is paraneoplastic.

46% of autoimmune cerebellar ataxia patients improve with immunotherapy.

WHEN TO CONSIDER TESTING
Consider autoimmune testing for patients presenting with a new-onset movement disorder and one or more of the following:

- Fluctuating course
- Psychiatric accompaniments (psychosis, hallucinations)
- Headache
- Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history (20+ pack years) or other cancer risk factors
- Inflammatory cerebrospinal fluid
- Neuroimages suggesting inflammation (signal abnormality, limbic or extra-temporal)
- Prior treatment with immune checkpoint inhibitors

Patients with autoimmune neurologic disorders may present with multiple movement phenomena, many of which can resemble neurodegenerative disorders, such as Huntington disease. These disorders can manifest in conjunction with autoimmune encephalitic diseases, neoplasms, infections, or be completely idiopathic.

Contact a clinical specialist at 855-516-8404 or +1-855-379-3115 (International). See more at mayocliniclabs.com.
## A guide to testing and evaluated antibodies

### MDS2
- Movement Disorder Evaluation, Serum
- TAT: 7 days

### MDC2
- Movement Disorder Evaluation, Spinal Fluid
- TAT: 5 days

### PLASMA MEMBRANE SPECIFICITIES

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- ANNA, antineuronal nuclear antibody;
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- CRMP-5, collapsin response-mediator protein-5;
- DPPX, dipeptidyl-peptidase-like protein 6;
- GABA, gamma-aminobutyric acid;
- GAD65, glutamic acid decarboxylase-65;
- GFAP, glial fibrillary acidic protein;
- LG1, leucine-rich glioma-inactivated 1;
- NMDA, N-methyl D-aspartate;
- mGlur1, metabotropic glutamate receptor 1;
- PCA, Purkinje cell cytoplasmic antibody.
Targeted evaluations to expedite diagnosis and treatment of autoimmune myelopathy

WHAT IS AUTOIMMUNE MYELOPATHY?

Patients with autoimmune myelopathy present with subacute onset and rapid progression of spinal cord symptoms (weakness, gait difficulties, loss of sensation, neuropathic pain, and bowel and bladder dysfunction). Autoimmune myelopathy evaluation of serum and spinal fluid can assist in the diagnosis and aid distinction from other causes of myelopathy (multiple sclerosis, sarcoidosis, vascular disease). Early diagnosis may assist in diagnosis of occult cancer, prompt initiation of immune therapies, or both.

NOVEL BIOMARKER FOR A TREATABLE MENINGOENCEPHALOMYELITIS

A novel astrocytic autoantibody, glial fibrillary acidic protein (GFAP), has recently been described by Mayo Clinic as a biomarker of a relapsing autoimmune meningoencephalomyelitis that is responsive to immunotherapies. Seropositivity distinguishes autoimmune GFAP meningoencephalomyelitis from disorders commonly considered in the differential diagnosis.

WHEN TO CONSIDER TESTING

Consider autoimmune testing for patients presenting with spinal cord symptoms and one or more of the following:

- Rapid onset and progression
- Fluctuating course
- Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history (20+ pack years) or other cancer risk factors
- Inflammatory cerebrospinal fluid
- Neuroimaging atypical for degenerative etiology
- Prior treatment with immune checkpoint inhibitors

40%

In a Mayo Clinic study, 40% of patients with GFAP-IgG were found to have co-existing antibodies.

Contact a clinical specialist at 855-516-8404 or +1-855-379-3115 (International). See more at mayocliniclabs.com.
A guide to testing and evaluated antibodies

### Myelopathy

MAC1 | Myelopathy, Autoimmune Evaluation, Spinal Fluid  
**TAT:** 5 days

MAS1 | Myelopathy, Autoimmune Evaluation, Serum  
**TAT:** 7 days

### Clinical References


### Abbreviations:

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<th>ANTIBODY</th>
<th>SERUM</th>
<th>SPINAL FLUID</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQP4</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>MOG</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>DPPX</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>mGluR1</td>
<td>•</td>
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</tr>
<tr>
<td>P/Q and N-type calcium channel</td>
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<tr>
<td>PCA-Tr</td>
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</tbody>
</table>

### Nuclear and Cytoplasmic Specificities

<table>
<thead>
<tr>
<th>ANTIBODY</th>
<th>SERUM</th>
<th>SPINAL FLUID</th>
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<tbody>
<tr>
<td>ANNA-1 (anti-Hu)</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>ANNA-2 (anti-Ri)</td>
<td>•</td>
<td>•</td>
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<tr>
<td>ANNA-3</td>
<td>•</td>
<td>•</td>
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<tr>
<td>AGNA-1 (SOX1)</td>
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<td>•</td>
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<tr>
<td>PCA-1</td>
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<td>•</td>
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<tr>
<td>PCA-2</td>
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<tr>
<td>CRMP-5 (anti-CV2)</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Amphiphysin</td>
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<td>•</td>
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<tr>
<td>GAD65</td>
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<tr>
<td>GFAP</td>
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</table>
DIAGNOSING DEMYELINATING DISEASES

Approximately 80% of patients with NMO are seropositive for aquaporin-4 (AQP4)-IgG. In the remaining 20% of patients, myelin oligodendrocyte glycoprotein (MOG)-IgG is detected in up to a third. Detection of MOG-IgG is diagnostic of central nervous system (CNS) inflammatory demyelination, where the clinical phenotype (NMO, optic neuritis, transverse myelitis, ADEM) may be similar, but the immunopathology (astrocytopathy versus oligodendrogyopathy) and clinical outcome (worse versus better) is different.

SIMILAR CHARACTERISTICS. DIFFERENT TREATMENTS.

Although NMO and MOG-opathies can have very similar clinical and radiologic characteristics to MS, the appropriate treatments differ significantly:

- While NMO and MOG-opathies are treated by immunosuppressant therapy, MS is treated by immunomodulation therapy, which may worsen NMO.
- For patients who are AQP4 positive, optimal immunosuppressive therapy should be initiated as soon as possible (a negative result in a subject where NMO is suspected should receive follow-up in 3 to 6 months).
- For patients who are MOG positive, immunosuppressive therapy may be justified as soon as possible; follow-up in 6 to 12 months is recommended as persistence of MOG-IgG seropositivity predicts a relapsing course.1

A GUIDE TO ORDERING AQP4/MOG TESTING

<table>
<thead>
<tr>
<th>OPTIC NERVE OR SPINAL CORD INVOLVEMENT</th>
<th>SYMPTOMS OUTSIDE OPTIC NERVE OR SPINAL CORD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEFINITELY ORDER</strong></td>
<td>When either a long spinal cord lesion is present or multiple episodes of optic neuritis occur</td>
</tr>
<tr>
<td><strong>CONSIDER ORDERING</strong></td>
<td>When either a short spinal cord lesion is present or single episode of optic neuritis occur</td>
</tr>
</tbody>
</table>

Contact a clinical specialist at 855-516-8404 or +1-855-379-3115 (International). See more at mayocliniclabs.com.
A guide to testing and methodology

FACS: A SUPERIOR METHOD OF TESTING

Mayo Clinic has developed the only fluorescence activated cell sorting (FACS) live cell-binding assay that is currently available in the U.S. for antibody detection of AQP4 and MOG. FACS is recommended by international leaders in neuroimmunology for its increased sensitivity and specificity.

AQP4 by FACS

The likelihood of having a false-positive result with ELISA methodology is at least 5x greater when compared with the Mayo Clinic cell-binding assay.3

### SENSITIVITY | SPECIFICITY

| FACS LIVE CELL-BINDING ASSAY | >80% | >99% |
| ELISA | 60–65% | 99% |
| INDIRECT IMMUNOFLUORESCENCE | 50–55% | >99% |

MOG by FACS

A recent study found that live cell-based methodologies had superior PPVs to the fixed cell assays, indicating that positive results in these assays are more reliable indicators of MOG autoimmune spectrum disorders.2

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CLINICAL REFERENCES