

## Overview

### Useful For

Evaluating patients who present with a subacute neurological disorder of undetermined etiology and have risk factors for primary lung carcinoma

Reporting an end titer result from serum specimens

### Testing Algorithm

If the indirect immunofluorescence pattern suggests antineuronal nuclear antibody type 3 (ANNA-3), then this test will be performed at an additional charge.

### Method Name

Only orderable as a reflex. For more information see:

- PAVAL / Paraneoplastic, Autoantibody Evaluation, Serum
- DMS2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Serum
- ENS2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum
- EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
- MDS2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Serum
- AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum
- MAS1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Serum

Indirect Immunofluorescence Assay (IFA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Specimen Required

Only orderable as a reflex. For more information see:

- PAVAL / Paraneoplastic, Autoantibody Evaluation, Serum
- DMS2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Serum
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- EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
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- AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum

-MAS1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Serum

**Specimen Minimum Volume**

0.6 mL

**Reject Due To**

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

**Specimen Stability Information**

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

**Clinical & Interpretive****Clinical Information**

Antineuronal nuclear autoantibodies (ANNA) are recognized clinically as markers of a patient's immune response to specific cancers (paraneoplastic autoantibodies).

In 1985, an antineuronal nuclear autoantibody (now known as ANNA-1 or anti-Hu)(1) was described as a serological accompaniment of subacute sensory neuropathy related to small-cell lung carcinoma (SCLC). ANNA-1 was subsequently recognized as an IgG marker for a spectrum of encephalomyeloradiculoneuropathy (including gastrointestinal dysmotilities) related to SCLC,(2) childhood neuroblastoma, and thymoma. The second antineuronal nuclear antibody to be recognized (known as ANNA-2 or anti-Ri) is an IgG marker of neurological autoimmunity related to SCLC and breast carcinoma.(3)

ANNA-3 is an IgG marker of an immune response to SCLC in patients presenting with a subacute, usually multifocal, paraneoplastic neurologic disorder.(4) Paraneoplastic sensorimotor neuropathy, cerebellar ataxia, and limbic encephalopathy are the most common presentations. However, an ANNA-3-positive patient may present with any element of an encephalomyeloradiculoneuropathy.

Other autoantibody markers of immune responses to SCLC include amphiphysin, collapsin response-mediated protein-5 (CRMP-5) IgG, Purkinje cell antibody type 2 (PCA-2), antigliial neuronal nuclear antibody (AGNA-1), voltage-gated calcium channel (P/Q-type) and potassium channel (VGKC) antibodies and muscle acetylcholine receptor antibodies.

**Reference Values**

Only orderable as a reflex. For more information see:

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<1:240

Neuron-restricted patterns of IgG staining that do not fulfill criteria for antineuronal nuclear antibody type 3 may be reported as "unclassified anti-neuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

### **Interpretation**

A positive result confirms that a patient's subacute neurological disorder has an autoimmune basis and predicts with 90% certainty that the patient has an aerodigestive carcinoma, usually a small-cell lung carcinoma (SCLC) that is new or recurrent and confined to the chest.

Fifteen percent of patients who are eventually proven to have small-cell carcinoma have an unrelated often more obvious cancer, either coexisting or in the past.

Antineuronal nuclear antibody type 3 (ANNA-3) has not yet been encountered in healthy subjects (n=100) or patients with lung carcinoma without a neurological accompaniment (n=100) or with other cancers (n=300).

### **Cautions**

Antineuronal nuclear antibody type 3 (ANNA-3) is not detectable when it coexists with ANNA-1 or ANNA-2 unless its titer exceeds that of coexisting neuronal nuclear antibodies or is demonstrable by Western blot.

### **Clinical Reference**

1. Graus F, Cordon-Cardo C, Posner JB: Neuronal antinuclear antibody in sensory neuropathy from lung cancer. *Neurology*. 1985 Apr;35(4):538-543
2. Lucchinetti CF, Kimmel DW, Lennon VA: Paraneoplastic and oncologic profile of patients seropositive for type 1 antineuronal nuclear autoantibodies. *Neurology*. 1998 Mar;50(3):652-657
3. Vernino S, Eggenberger ER, Rogers LR, Lennon VA: Paraneoplastic neurological autoimmunity associated with ANNA-1 autoantibody and thymoma. *Neurology*. 2002 Sep 24;59(6):929-932
4. Pittock SJ, Lucchinetti CF, Lennon VA: Anti-neuronal nuclear autoantibody-type 2: paraneoplastic accompaniments. *Ann Neurol*. 2003 May;53(5):580-587
5. Chan KH, Vernino S, Lennon VA: ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. *Ann Neurol* 2001 September;50(3):301-311
6. Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. *Ann Neurol*. 2004 Nov;56(5):715-719
7. 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

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.(Honarat 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)

Western blot is performed, as needed, to confirm seropositivity.

### PDF Report

No

### Day(s) Performed

Monday through Sunday

### Report Available

5 to 8 days

### Specimen Retention Time

2 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

86256

**LOINC® Information**

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-----------------|--------------------|
| AN3TS   | ANNA-3 Titer, S | 94344-9            |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------|---------------------|
| 43433     | ANNA-3 Titer, S  | 94344-9             |