LEADING CNS ANTIBODY TESTING SERVICES

Paraneoplastic Autoimmune Neurological Disorder Testing Services

New Tests Now Available.

athena diagnostics®

Testing that Makes a Difference.

Why Athena Diagnostics?

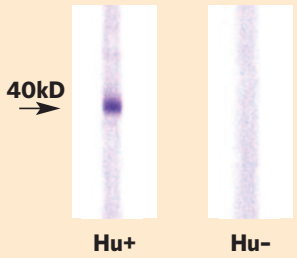
Faster, More Relevant Tests

Athena Diagnostics offers the latest in testing for CNS antibody disorders. Our newest profile, the *Paraneoplastic Neurological Syndromes, Initial Assessment (PNS-IA)* offers a result in just **three to five days**.

Recombx® Methodology

Athena's Recombx® methodology uses recombinant human antigens in conjunction with western blot to detect specific paraneoplastic antibodies. This helps eliminate non-specific reactivity, reduces the likelihood of false positives and enhances specificity by confirming the identity of proteins based on molecular weight.

For example, a band of 40kD indicates a positive result for Hu antibodies with a likely malignancy of SCLC.



Early Detection and Quick Treatment Can Make a Difference in Patient Outcomes

"Patients with disorders of the CNS associated with autoantibodies can now be diagnosed and treated."[1]

The positive identification of specific antibodies can help direct therapy to improve patient outcomes, avoid treatment that may harm the patient and/or aid in early detection and treatment of cancer.

Introducing Paraneoplastic Neurological Syndromes, Initial Assessment (PNS-IA)

Athena Diagnostics is proud to introduce the *Paraneoplastic Neurological Syndromes, Initial Assessment (PNS-IA)*. Built on six of the most well-characterized antibodies found in paraneoplastic disorders, the *Paraneoplastic Neurological Syndromes, Initial Assessment* profile is a highly-focused diagnostic tool with a three- to five-day turnaround. The PNS-IA profile tests for specific antibodies that include amphiphysin, CV2, Hu, Ma2 (MaTa), Ri and Yo, and are known to be associated with malignancy in the majority of cases.

When used in conjunction with other clinical testing, the PNS-IA profile can help physicians better understand the cause of disease.

Other CNS Autoantibodies

Immunotherapy and other treatments have been successful in patients with antibodies against *LGI1, CASPR2, VGKC, NMDA (NR1) and GAD65.* Early detection may enable better outcomes.[1]

Paraneoplastic Antibodies

In a majority of the paraneoplastic syndromes, the neurological symptoms appear before the cancer has been identified. Identification of paraneoplastic antibodies can direct the search for an underlying cancer and increase the likelihood of making an early diagnosis of the tumor.

As new discoveries are made, Athena is at the forefront with the tests needed to provide a more specific diagnosis and the best possible treatment options for your patients.

Molecular testing services for

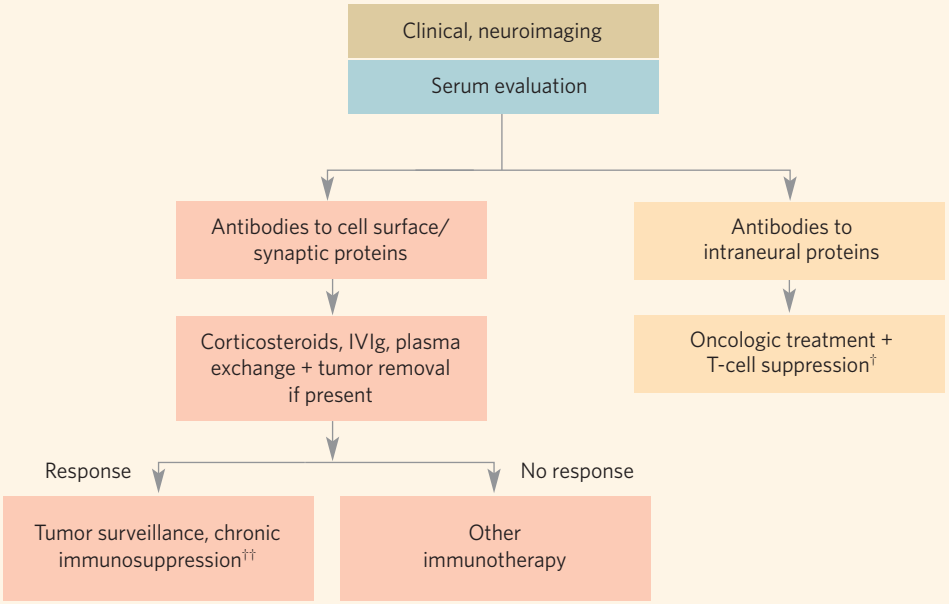
CNS Antibodies

When a patient presents with symptoms suggesting a CNS autoimmune disorder, early identification of antibodies can help direct therapy in patients likely to improve with immunotherapy treatment. Since Paraneoplastic Syndromes are degenerative autoimmune disorders due to the remote effects of cancer, identification of a specific paraneoplastic antibody can guide the search for an underlying malignancy.

Turn to Athena for:

- The most up-to-date and comprehensive antibody testing services
- Proprietary test methodologies including Recombx®

Algorithmic Approach to Diagnosis and Treatment of Encephalitis with Antibodies to Intracellular and Cell Surface Neuronal Antigens[3]



†T-cell suppression refers to strategies focused on decreasing T-cell activation (rituximab) and cytotoxic T-cell mechanisms (cyclophosphamide, tacrolimus or cyclosporine). ††Tumor surveillance and chronic immunosuppression should be considered in some disorders (AMPAR, GABA(B)-R and CASPR2) and subgroups of patients with NMDAR encephalitis with higher risk for relapse (e.g., patients without tumor) or to have an underlying tumor (older than 18 years). Reprinted with permission.

A Comprehensive Test Menu for CNS Autoimmune Disorde

Tests	Usually Non-Paraneoplastic LGI1	Paraneoplastic or Non-Paraneoplastic CASPR2	Usually Non-Paraneoplastic VGKC	Paraneoplastic or Non-Paraneoplastic[1] NMDA (NR1)	Usually Non-Paraneoplastic[1] GAD65	Paraneoplastic MaTa Recombx®	Paraneoplastic CV2/CRMP5 Recombx®	Pa An
Associated Clinical Features[1,2,4]								
Faciobrachial Dystonic Seizures	■							
Limbic Encephalitis	■	■	■	■	■	■		
Hypothalmic Encephalitis						■		
Neuromyotonia		■	■					
Morvan's Syndrome		■	■					
Peripheral Nerve Hyperexcitability		■	■					
Brainstem Encephalitis						■		
Severe Forms of Encephalitis				■				
Encephalomyelitis							■	
Stiff Person Syndrome					■			
Cancer-Associated Retinopathy								
Melanoma-Associated Retinopathy								
Lambert Eaton Myasthenic Syndrome								
Cerebellar Ataxia		■			■			
Cerebellar Degeneration							■	
Autonomic Neuropathy							■	
Sensory and/or Sensorimotor Neuropathy		■					■	
Chorea							■	
Optic Neuritis							■	
Opsoclonus-Myoclonus								
Myasthenia Gravis								
Athena Antibody Profiles						4500: Paraneoplastic Neur		
	467: NeoComplete Paraneoplastic Evaluation							
	447: NeoEncephalitis Paraneoplastic Evaluation with Recombx®							
					438: NeoCerebellar Degener			
		494: Neuromyotonia Evaluation						
							436: NeoS Paraneoplas	
Athena Tests	449	499	485	419	422	122	123	
Primarily Associated with[1,2,4]	Limbic Encephalitis; Epilepsy; SCLC (rare)	Morvan's Syndrome; Neuromyotonia; Thymoma (20-50%)	Limbic Encephalitis; Morvan's Syndrome; Neuromyotonia; Epilepsy	Ovarian Tumors	Stiff-person Syndrome; Cerebellar Ataxia; LE; Epilepsy	Testicular Cancer	SCLC, Thymoma	Br S
Treatment Notes[1,2,4] Neurologic improvement usually correlates with a decrease in serum and CSF antibody titers.[3]	Immunotherapy	Immunotherapy	Immunotherapy	Multiple treatments advantageous if started early.	Some immunotherapies might be beneficial. Early detection may enable better outcomes.	Some forms respond to immunotherapy.		
	Detection of antibodies to cell surface antigens (NMDAR, CASPR2, LGI1) carries a better prognosis. This should lead to prompt immunotherapy while screening for an underlying tumor..[5]						Classic paraneoplastic sy	

ers—Available Only from Athena Diagnostics

raneoplastic	Paraneoplastic	Paraneoplastic	Paraneoplastic	Paraneoplastic	Paraneoplastic	Paraneoplastic	Paraneoplastic	Non-Paraneoplastic	Usually Non-Paraneoplastic
mphiphysin	Hu/ANNA-1 Recombx®	Ri Recombx®	Yo/PCA1 Recombx®	Zic4 Recombx®	CAR (Anti-Recoverin) Recombx®	LEMS (VGCC)	Ganglionic AChR (gnAChR)	NMO (AQP4)	AChR/MuSK
■	■								
	■	■							
■	■								
■									
					■				
					■				
						■			
	■	■	■	■		■			
	■						■		
■	■								
								■	
		■							
									■

rological Syndromes, Initial Assessment (PNS-IA) **New!**

with Recombx®

193: Neuromyelitis Optica (NMO) Autoantibody Test

483: AChR/MuSK Reflexive Antibody Test

ation Paraneoplastic Evaluation with Recombx®

Sensory Neuropathy stic Evaluation with Recombx®

427	120	115	125	127	118	475	428	193	483
east cancer, SCLC, Stiff Person Syndrome	SCLC, Neuroblastoma, Prostate Cancer	Breast, Gyn Cancers, SCLC	Breast, Gyn Cancers	SCLC	SCLC	SCLC	SCLC, Thymoma		
	Stabilization of neurological syndrome							Steroids, immuno-suppressive agents and plasma exchange.[6]	Seropositive AChR: thymectomy, positive MuSK: IVIG[7,8]

Tumor removal accelerates improvement and decreases relapses.
yndromes do not respond to immunotherapy unless the tumor is successfully treated, and even then the response is very limited.[3]

Comprehensive Services from Athena Diagnostics

Test Menu for CNS

Test Code	Test Name	Specimen Volume	Turnaround Time
4500	Paraneoplastic Neurological Syndromes, Initial Assessment (PNS-IA) **New!**	2 mL serum	3 – 5 days
467	NeoComplete Paraneoplastic Evaluation with Recombx®	2 mL serum	21 – 28 days
447	NeoEncephalitis Paraneoplastic Evaluation with Recombx®	2 mL serum	28 days
438	NeoCerebellar Degeneration Paraneoplastic Evaluation with Recombx®	2 mL serum	28 days
494	Neuromyotonia Evaluation	2 mL serum	21 – 28 days
436	NeoSensory Neuropathy Paraneoplastic Evaluation with Recombx®	2 mL serum	7 – 14 days
449	*LGI1* Antibody Test	2 mL serum	7 – 14 days
499	*CASPR2* Antibody Test	2 mL serum	7 – 14 days
485	*VGKC* Antibody Test	2 mL serum	7 – 14 days
419	NMDA *(NR1)* Antibody Test	2 mL serum	7 – 14 days
422	*GAD65* Antibody Test	2 mL serum	7 – 14 days
122	*MaTa* Antibody Test with Recombx®	2 mL serum	3 – 5 days
123	*CV2* Antibody Test with Recombx®	2 mL serum	3 – 5 days
427	Amphiphysin Antibody Test	2 mL serum	7 – 14 days
120	*Hu* Antibody Test with Recombx®	2 mL serum	3 – 5 days
115	*Ri* Antibody Test with Recombx®	2 mL serum	3 – 5 days
125	*Yo* Antibody Test with Recombx®	2 mL serum	3 – 5 days
127	*Zic4* Antibody Test with Recombx®	2 mL serum	7 – 14 days
118	*CAR* (Anti-Recoverin) Antibody Test with Recombx®	2 mL serum	7 – 14 days
475	LEMS *(VGCC)* Antibody Test	2 mL serum	7 – 14 days
428	Ganglionic *AChR* (gnAChR) Antibody Test	2 mL serum	7 – 14 days
483	*AChR/MuSK* Reflexive Antibody Test	2 mL serum	7 – 14 days
193	Neuromyelitis Optica *(NMO)* Autoantibody Test	2 mL serum	7 – 14 days

Client Services Representatives are available from 8:30am to 6:30pm Eastern Time (U.S.). Customers in the U.S. and Canada please call toll free **800-394-4493** or visit us on our website at **AthenaDiagnostics.com.**

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Testing that Makes a Difference.

References: 1. Vincent A, Bien CG, Irani SR, Waters P. Autoantibodies associated with diseases of the CNS: new developments and future challenges. *Lancet Neurol* 2011; 10:559-72. 2. Lancaster E, Maartje GM, Huijbers BS, et al. Investigations of CASPR2, an autoantigen of encephalitis and neuromyotonia. *Ann Neurol* 2011; 69: 303-11. 3. Lancaster E, Martinez-Hernandez E, Dalmau J. Encephalitis and antibodies to synaptic and neuronal cell surface proteins. *Neurol* 2011;77:179–189. 4. Dalmau J, Rosenfield M. Paraneoplastic syndromes of the CNS. *Lancet Neurol* 2008; 7: 327-40. 5. Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol* 2011;10:63–74. 6. Okamoto T, Ogawa M, Lin Y, et al. Treatment of Neuromyelitis Optica: Current Debate. *Ther Adv Neurol Disord* 2008; 1(1): 5–12. 7. Sanders, DB, Meriggioli Matthew N, Autoimmune myasthenia gravis; emerging clinical and biological heterogeneity. *Lancet Neurology* 2009; 8:475-90. 8. Sanders, DB, et al., Clinical aspects of MuSK antibody positive seronegative MG. *Neurology* 2003; 60: (No.12) 1978-80

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