Athena Diagnostics

NeoComplete Paraneoplastic Evaluation with Recombx

Testing that Makes a Difference.

Patient Test, 2a		Requesting Physician	Accession Number 14003778
Date of Birth 05/05/1955	Sex F	Report to Athena Diagnostics, INC.	Family Number/Kindred Number
Specimen Type Serum		Address 377 Plantation Street	Patient Number 000000000
Test Category Diagnostic (Symptomatic)		Worcester, MA 01605	Specimen Collection Date 06/18/2014
Test Requested NeoComplete Paraneoplastic Evaluation with Recombx			Submitted Patient ID
		Additional Reports to:	Report Date 06/20/2014

SUMMARY INTERPRETATION

POSITIVE

This panel of tests identified a positive result.

INTERPRETIVE RESULTS TABLE

	Test	Technical Result	Reference Range
Positive	**anti-VGCC**	**150**	**Negative <71, Borderline 71-140, Positive >140 (pmol/L)**

Comments: Only non-negative results from the panel of tests ordered are provided above. Important information regarding these results can be found in the single reports which follow this summary. No other abnormalities were detected for the other tests in this panel.

Recommendations:

Health care providers, please contact the Athena Diagnostics Client Services Department at 1-800-394-4493 if you wish to consult with a Laboratory Director regarding this test result.

Tests included in this panel: Recombx Hu Autoantibody Test, Recombx Yo Autoantibody Test, Zic4 Autoantibody Test, Recombx CV2 Autoantibody Test, Recombx MaTa Autoantibody Test, Recombx Ri Autoantibody Test, Recombx CAR (Anti-Recoverin) Autoantibody Test, VGCC Autoantibody Test (LEMS), VGKC Antibody Test, Amphiphysin Antibody Test, Ganglionic AChR Antibody Test, NMDA Receptor Antibody Test, CASPR2 Antibody Test, LGI1 Antibody Test, and GAD65 Autoantibody Test (Neurological Disorders)

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VGCC Autoantibody Test (LEMS)

POSITIVE

This test detected abnormal levels of anti-VGCC antibodies.

INTERPRETIVE RESULTS TABLE

	Test	Technical Result	Reference Range
Positive	**anti-VGCC**	**150**	**Negative <71, Borderline 71-140, Positive >140 (pmol/L)**

Comments: This test result is consistent with an autoimmune etiology for the neurological symptoms associated with paraneoplastic disorder.

Recommendations: Health care providers, please contact the Athena Diagnostics Client Services Department at 1-800-394-4493 if you wish to consult with a Laboratory Director regarding this test result.

Background information: Paraneoplastic neurological syndromes or disorders (PNS or PND) are rare immune-mediated disorders resulting from the damage to the nervous system due to remote effects of a tumor (1, 2). PND of the central nervous system may occur in association with either onconeural antibodies directed against intracellular antigens, or antibodies targeted against neuronal surface antigens (1, 3).

Clinical features of PND may include ataxia, limbic or brainstem encephalitis, sensory neuropathy, subacute cerebellar degeneration, dizziness, nystagmus, dysphagia, dysarthria, loss of muscle tone, loss of memory, vision problems, sleep disturbances, dementia, seizures, and/or sensory loss in the limbs (4). In approximately 60% of PND cases, neuropathic symptoms precede a tumor diagnosis (1). Some of the tumors related to PND include small cell lung cancer, ovarian teratoma and carcinoma, thymoma, lymphoma, breast cancer, and/or testicular cancer (2). PND may also include Lambert-Eaton myasthenic syndrome (LEMS), stiff person syndrome, encephalomyelitis, myasthenia gravis, neuromyotonia, and opsoclonus-myoclonus (4). However, these disorders can also occur in individuals without underlying cancer.

VGCC antibodies are highly associated with Lambert-Eaton myasthenic syndrome (LEMS), a neuromuscular disorder characterized by muscle weakness, sometimes accompanied by autonomic nervous system dysfunction or cerebellar ataxia (5, 6, 7). Less commonly, VGCC antibodies may be associated with paraneoplastic cerebellar degeneration (PCD). The main tumor associated with positive VGCC antibody is small-cell lung carcinoma (SCLC). SCLC is found in 50 - 60% of adult patients with LEMS. Other cancers associated with VGCC antibodies include extrapulmonary small cell carcinoma, testicular germ-cell, ovarian, or breast cancers. Since neurological symptoms often precede the detection of an occult malignancy, patient monitoring is recommended, and a search for occult cancer should be considered.

Methods:
Detection of antibodies was performed by Radioimmunoassay (RIA) methodology.

Limitations of analysis: Reagent effectiveness may affect the signal intensity of the response. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

Background References

1. Darnell, RB, et al. (2006) Semin Oncol 33: 270-98. (PMID: 16769417)
2. Titulaer, MJ, et al. (2011) Eur J Neurol 18: 19-e3. (PMID: 20880069)
3. Zuliani, L, et al. (2012) J Neurol Neurosurg Psychiatry 83: 638-45.
4. Rosenfeld, MR, et al. (2010) Oncologist 15: 603-17. (PMID: 20479279)
5. Dalmau, J, et al. (2008) Lancet Neurol 7: 327-40. (PMID: 18339348)
6. Honnorat, J, et al. (2007) Orphanet J Rare Dis 2: 22. (PMID: 17480225)
7. Graus, F, et al. (2008) Neurology 71: 930-6. (PMID: 18794496)

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Table of Genes/Tests performed in this panel

Immunology Test	Method(s) of	Results	Reference
anti-VGCC	RIA	Positive: (150)	Negative <71, Borderline 71-140, Positive >140 (pmol/L)
anti-recoverin	Western	Negative	Not applicable
anti-Hu	Western and ELISA	Negative	Not applicable
anti-Zic4	Western	Negative	Not applicable
anti-NR1	IIFT	Negative	Not applicable
anti-GAD65	ELISA	Negative	Negative <1:600, Borderline 1:600-1:1200, Positive >1:1200
anti-alpha 3AChR	RIA	Negative	Not applicable
anti-LGI1	IIFT	Negative	Not applicable
anti-VGKC	RIA	Negative: (300)	Negative <450, Borderline 450-650, Positive >650 (pmol/L)
anti-CASPR2	IIFT	Negative	Not applicable
anti-Ri	Western	Negative	Not applicable
anti-Ma1 and anti-Ma2	Western	Negative	Not applicable
anti-CV2	Western	Negative	Not applicable
anti-Yo	Western	Negative	Not applicable
anti-amphiphysin	Immunoblot	Negative	Not applicable

Panel Methods and Method Limitations

Western blot method: Detection of antibodies was performed by western blot methodology.

Limitations of western blot analysis: This method uses denaturing/reducing electrophoresis and as a result, may not detect conformational antibodies. Consequently, this methodology can only discriminate between presence and absence of non-conformational antibodies targeted against the antigen. Variable transfer rates and reagent effectiveness may affect the signal intensity of the response. Affinity of individuals' antibodies for this antigen cannot be measured using this methodology. Therefore the result provided is purely qualitative. For tests that use crude antigens cloned in *E. coli*, individuals with *E. coli* infections may exhibit false positive results. Specimen type may affect sensitivity and specificity of this assay. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

ELISA with western blot confirmation method: Detection of antibodies was performed by Enzyme Linked Immunosorbent Assay (ELISA) and confirmed by western blot methodology.

Limitations of ELISA and western blot analysis: The western blot method uses denaturing/reducing electrophoresis and as a result, may not detect conformational antibodies. Consequently, this methodology can only discriminate between presence and absence of non-conformational antibodies targeted against the antigen. Variable transfer rates and reagent effectiveness may affect the signal intensity of the response. Affinity of individuals' antibodies for this antigen cannot be measured using this methodology. Therefore western blot results provided are purely qualitative. If antigens are cloned in *E. coli*, individuals with *E. coli* infections may exhibit false positive results. Specimen type may affect sensitivity and specificity of this assay. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

Immunoblot method: Detection of antibodies was performed by Immunoblot methodology.

Limitations of immunoblot analysis: Variable transfer rates and reagent effectiveness may affect the signal intensity of the response. Affinity of individuals' antibodies for this antigen cannot be measured using this methodology. Therefore the result provided is purely qualitative. Specimen type may affect sensitivity and specificity of this assay. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

ELISA method: Detection of antibodies was performed by Enzyme Linked Immunosorbent Assay (ELISA) methodology.

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Panel Methods and Method Limitations

Limitations of ELISA analysis: Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

RIA method: Detection of antibodies was performed by Radioimmunoassay (RIA) methodology.

Limitations of RIA analysis: Reagent effectiveness may affect the signal intensity of the response. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

IIFT method: Detection of antibodies was performed by indirect immunofluorescence staining on a recombinant cell line expressing the antigen.

Limitations of IIFT analysis: Cross-interfering antibodies may be present in samples and appear as borderline or low positive results. Specimen type may affect sensitivity and specificity of this assay. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

This test was developed and its performance characteristics have been determined by Athena Diagnostics. Performance characteristics refer to the analytical performance of the test.

Laboratory oversight provided by Joseph J. Higgins, M.D., F.A.A.N., CLIA license holder, Athena Diagnostics (CLIA # 22D0069726)