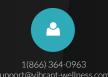


# **NEURAL ZOOMER** plus

### Neural Zoomer plus

Peptide level identification of neural sensitivity





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Final Report Date: Accession ID:		02-11-2019 13:35 1902110047	Specimen Co Specimen Re		2-10-2019 13:35 2-11-2019 07:35
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PATIENT Name: DEMO NEUR Date of Birth: 1996-0 Gender: Male Age: 22 Telephone #: 666-66 Street Address: 1021 City: SAN CARLOS State: CA Zip #: 944 Email: demo@demo.0 Fasting: FASTING	08-30 6-8888 HOWARD AVEN 070		Prac Prov Phle Stre City Stat Zip i Tele	DVIDER tice Name: Vibrant IT2 Pra vider Name: Demo Client, N botomist: et Address: 1021 HOWAR e: SAN CARLOS e: CA #: 94070 phone #: 800-842-7268 #: 222-222-2222	MD (999994)

Vibrant Wellness is pleased to present to you, 'Neural Zoomer Plus', to help you make healthy lifestyle and dietary choice in consultation with your healthcare provider. It is intended to be used as a tool to encourage a general state of health and well-being.

**The Vibrant Neural Zoomer Plus** is an array of neural antigens and genetic tests which offers very specific antibody-to-antigen recognition and potential risk to develop Neurological Autoimmune disease. The panel is designed to assess an individual's IgG, IgA and IgM sensitivity to these antigens at the peptide level. Neural Zoomer plus aims to reduce the prevalence of neurological conditions by empowering patients and physicians with a vital resource for early risk detection and an enhanced focus on personalized primary prevention.

Interpretation of Report: The test results of antibody levels to the individual proteins are calculated by comparing the average intensity of the individual protein antibody to that of a healthy reference population. Reference ranges have been established using 192 healthy individuals. The results are displayed as High Risk, Moderate or In Control. A high risk result indicates that you have an increased reactivity to the antigen with respect to the reference range. A Moderate sensitive result indicates that you have a moderate reactivity to the antigen with respect to the reference range. A Negative or In Control result indicates that you have a low reactivity to the antigen with respect to the reference range. Vibrant utilizes proprietary fluorescent analysis which is designed to assay specific total IgG (subclasses 1, 2, 3, 4), total IgA (subclasses 1, 2) and total IgM antibodies. The classification of High risk to Moderate to In Control denotes the level of antibody reactivity detected through this analysis.

The Vibrant Wellness platform provides tools for you to track and analyze your general wellness profile. Testing for Neural Zoomer + panel is performed by Vibrant America, a CLIA certified lab CLIA#:05D2078809. Vibrant Wellness provides and makes available this report and any related services pursuant to the Terms of Use Agreement (the "Terms") on its website at www.vibrant-wellness.com. By accessing, browsing, or otherwise using the report or website or any services, you acknowledge that you have read, understood, and agree to be bound by these terms. If you do not agree to accept these terms, you shall not access, browse, or use the report or website. The statements in this report have not been evaluated by the Food and Drug Administration and are only meant to be lifestyle choices for potential risk mitigation. Please consult your physician/dietitian for medication, treatment, or lifestyle management. This product is not intended to diagnose, treat, or cure any disease.

**Please Note** - It is important that you discuss any modifications to your diet, exercise and nutritional supplementation with your physician before making any changes. To schedule an appointment with Vibrant Clinical Dietitians please call: Toll-Free **866-364-0963**.

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### INTRODUCTION

Autoimmunity is a main component in nervous system diseases where a misguided immune response attacks the body's own organs and tissues. Autoimmune disorders affect 5-10% of the general population and can target virtually any structure within the central or peripheral nervous system in a highly specific way, targeting a very specific cell population (e.g., Purkinje cells of the cerebellum). Depending on the cell type that is targeted in different central nervous system (CNS) structures (e.g., the astrocyte in neuromyelitis optica), the syndromes that result may be diverse, such as those associated with optic neuritis, myelitis, and attacks of brain edema in neuromyelitis optica.<sup>1</sup>

Understanding these specific disorders requires an analysis of how the target antigen molecules affect immune cellular interactions both to generate the autoimmune reaction and to produce the immune-mediated injury of the nervous system. Autoantibodies are a novel emerging entity that is useful in providing such information in early stages of the disease with a simple blood sample. The Vibrant neurological autoimmune panel, "Neural Zoomer," includes a comprehensive spectrum of autoimmune markers responsible for a diverse range of neural autoimmune diseases that has the potential to provide the details of the specific type of autoimmune neural disease (eg: demyelination, blood brain barrier disruption, optical/peripheral neuropathy, neuromuscular disorders, brain inflammation and autoimmunity) and the degree of severity to implement the most effective treatment plan possible.



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			erate	Mode	itive	Posi									
ative	Neg		lgM	(IgG + IgA)	lgM	(IgG + IgA)									
ion Antigens	Demyelinat		Demyelination	Demyelination	Brain	Neuromuscular									
Anti-Neurofascin Anti-MAG	glycoprotein	Anti-Myelin basic protein	Antigens Anti-Tubulin Blood Brain Barrier Disruption	Antigens Anti-Myelin proteolipid protein	<b>Autoimmunity</b> <b>A</b> nti-Amyloid beta (25-35)	<b>disorders</b> <b>A</b> nti- Acetylcholine receptors									
	Anti-Microglia	Anti-Glial fibrillary acidic protein	Blood BrainAnti-s100bBarrier DisruptionAnti-GlucoseAnti-s100bregulated protein78	Blood BrainAnti-s1Barrier DisruptionAnti-GAnti-s100bregulat	Barrier Disruption Anti-s100b	Barrier Disruption Anti-s100b	Barrier DisruptionAnti-GluAnti-s100bregulate78		Brain Autoimmunity Anti-RAGE peptide						
nervous system disorder	al and Autonomic														
Anti-Recoverin Anti-CV2	Anti-Aquaporin4	Anti-Neuron specific enolase		<b>A</b> nti-GM1											
Neuropathy	Peripheral			Neuromuscular disorders Anti-Voltage gated potassium channels											
Anti-Ri Anti- Amphiphysin	Anti-Hu	Anti-GM2			gated potassium	gated potassium	gated potassium	gated potassium	gated potassium	gated potassium	gated potassium	gated potassium	gated potassium		
ular disorders	Neuromuscu		channels												
Anti-Titin	Anti-Voltage gated calcium channels	Anti-Muscle specific kinase													
oimmunity	Brain Aut														
Anti-Yo Anti-Amyloid beta (1-42) Anti-	Anti-Purkinje cell	Anti-Cerebellum													
Anti-Dopamine Hydroxytryptai	Anti-Glutamate	Anti-Tau													
Anti-Endothelin A receptor	Anti-α1 and β2 adrenergic receptors	Anti-Alpha- synuclein													
ammation	Brain Infl														
Anti-Dopamine Anti-Dopamin receptor 1 receptor 2	Anti-AMPA receptor	Anti-NMDA receptor													
Anti-Glycine Anti-Neurexin receptor	Anti-Dipeptidyl aminopeptidase like protein 6	Anti-GABA receptors													
Anti-Ma	Anti-Leucine- rich glioma- inactivated protein 1 (Anti- LGI1)	Anti-Contactin- Associated Protein-like 2 Antibodies													
ction	Infe														
Anti-EBV Anti-CMV Anti- Streptococcal A	Anti-HSV2 Anti-HHV 7	Anti-HSV1 Anti-HHV 6													

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### LIFESTYLE CONSIDERATIONS

#### Lifestyle Choices

- Treatments that rebuild and fortify a hyperpermeable intestinal barrier can aid in reversing or reducing autoimmune disease symptoms. Intestinal permeability syndrome is associated with autoimmune diseases and reversing symptoms of autoimmune diseases is accelerated with healing the lining of the gastrointestinal tract.<sup>56</sup> Vibrant's Wheat Zoomer can accurately detect the presence of intestinal permeability syndrome.
- Avoid exposure to heavy metals: Neurotoxicity of metals has been demonstrated widely. The CNS is particularly vulnerable to accumulation of these metals. The brain readily accumulates metals, which, under physiologic conditions, are incorporated into essential metalloproteins required for neuronal health and energy homeostasis. Severe consequences can arise from circumstances of excess essential metals or exposure to toxic nonessential metal.<sup>57</sup>
- Avoid exposure to mold or high mold/water-damaged environments: Mold neurotoxicity is an increasingly common occurrence that can cause memory deficits, difficulty concentrating, problems with language and reasoning, mental fatigue, depression, and anxiety.<sup>58</sup>
- Treat infections immediately: Herpes simplex virus type 2 (HSV-2) infection, for example, is responsible for significant neurological morbidity, perhaps more than any other virus. Research indicates that as many as 45 million people in the United States have been infected with HSV-2, and the estimated incidence of new infection is 1 million annually.<sup>47</sup>
- Consider following programs that may help prevent and reverse the cognitive and physiological effects of neurological disorders, including but not limited to:
  - Bredesen's ReCODE (Reversal of Cognitive Decline) protocol<sup>59</sup>, which is a comprehensive personalized program designed to improve cognition and reverse the cognitive decline of mild cognitive impairment, and early Alzheimer's disease.
  - The Wahls protocol
  - Hormone therapy<sup>60</sup>
  - Physical therapy (e.g Mulligan technique, electrical stimulation)<sup>61-63</sup>
  - Yoga<sup>64</sup>
  - Instrument-assisted soft tissue mobilization (e.g.: cupping therapy)<sup>65</sup>
  - Therapeutic taping (e.g.: Kinesiology taping)<sup>66</sup>
  - Blood flow restriction therapy<sup>67</sup>
  - Integrative dry needling<sup>68</sup>

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### LIFESTYLE CONSIDERATIONS

- Consider regular sauna bathing, as studies show high frequency of sauna use lowers the risk of dementia and Alzheimer's disease.<sup>69</sup>
- Maintain a healthy lifestyle (healthy fat-rich and vegetable-heavy diet, omega-3-fatty acids, low sugar intake, quit smoking, regular exercise)<sup>70</sup>
- Consider taking supplements: Research indicates inflammation and free radical oxidative stress play major roles in the propagation of neurodegenerative diseases. A few supplements in particular have been found to mitigate damage caused by oxidative stress and/or reduce the activity of TNF and other inflammatory cytokine pathways:
  - N-acetyl-L-cysteine (NAC) is a precursor to glutathione, the body's most important cellular antioxidant. NAC supplements have been shown to increase cellular glutathione levels.<sup>71</sup>
  - Vitamins B12, B6, and folate are metabolic cofactors important for cellular metabolism and maintenance of all tissue cell types, but particularly important to nerve cells. Deficiencies in B12 or folate can raise homocysteine levels, which have been associated with a higher risk for vascular disease and dementia.<sup>72</sup>
  - B12 absorption from the intestine tends to diminish with age. B12 deficiency can damage the nervous system leading to neuropathy, myelopathy, and dementia.<sup>73</sup>
  - Alpha Lipoic Acid (ALA) is an essential cofactor in normal cellular metabolism and cellular energy production. The use of ALA as a supplement is under investigation, and has demonstrated improvements in peripheral neuropathy, Alzheimer's disease, and insulin-resistant type II diabetes.<sup>74</sup>
  - Vitamin C and vitamin E supplements can reverse symptoms caused by vitamin C and E deficiencies.<sup>75</sup>

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### **Demyelination Antigens**

### Anti-Tubulin

Tubulin is a 55 kDa cytoplasm globular protein expressed in blood, nervous, secretory, reproductive, musculoskeletal and other internal cells. Anti-tubulin is associated with alcoholic liver disease, demyelinating disease, Grave's disease, Hashimoto's thyroiditis, infectious agent exposure PANDAS/ANDAS/OCD, rheumatoid arthritis, and recent onset type 1 diabetes.<sup>2</sup>



### Anti-Myelin basic protein

Myelin basic protein (MBP) is a protein believed to be important in the process of myelination of nerves in the nervous system. Anti-Myelin basic protein is related to the risk for multiple sclerosis, autism, PANDAS/ANDAS/OCD, and systemic lupus erythematosus (SLE).<sup>3</sup>



### Anti-Myelin oligodendrocyte glycoprotein

Myelin oligodendrocyte glycoprotein (MOG) is a glycoprotein associated with the myelination of nerves in the central nervous system (CNS). Antibodies against MOG are found in various demyelinating diseases, including multiple sclerosis, neuromyelitis optica spectrum disorders (NMOSD), idiopathic optic neuritis (ON), acute disseminated encephalomyelitis (ADEM), multiphasic disseminated encephalomyelitis (MDEM), Devic's disease, and tumefactive demyelinating disease.<sup>4</sup>



### Anti-Myelin proteolipid protein

Myelin proteolipid protein (PLP) is the major membrane protein of CNS myelin and its expression is largely limited to oligodendrocytes.<sup>5</sup> Anti-PLP is a useful marker in patients with seronegative anti-myelin basic protein, the frequent marker in active multiple sclerosis and optic neuritis.<sup>6-7</sup>



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### Anti-Neurofascin

Neurofascin (NF), a cell adhesion molecule expressed in both the CNS and the peripheral nervous system (PNS), plays important roles in developing and maintaining neural structures. Anti-neurofascin autoantibodies are found mainly in combined central and peripheral demyelination (CCPD), a rare demyelinating condition affecting both CNS and peripheral nervous system (PNS) tissues<sup>8</sup>, and also in chronic inflammatory demyelinating polyneuropathy (CIDP)<sup>9</sup> and axonal injury in patients with multiple sclerosis (MS).<sup>10</sup> Recognition of this antibody may be important in treatment management, becauseanti-neurofascin seropositive CCPD patients respond well to Intravenous Immunoglobulin or plasma exchange treatments.<sup>11</sup>



### Anti-MAG

Myelin-associated glycoprotein (MAG) is a trans-membrane protein of both the CNS and peripheral nervous system (PNS) myelin, involved in the process of myelination. Anti-MAG peripheral neuropathy is a very rare disease caused by anti-MAG antibodies that destroy MAG protein leading to disruptions of normal myelin production and healthy peripheral nerve activity.<sup>12</sup>



### **Blood Brain Barrier Disruption**

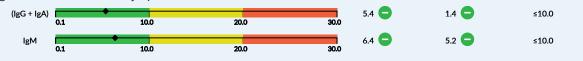
### Anti-s100b

S100B is a calcium-binding protein produced mainly by astrocytes. This protein is localized in the cytoplasm and nucleus of a wide range of cells and involved in the regulation of several cellular processes such as cell cycle progression and differentiation. Studies have shown extravasated S100B may trigger a pathologic autoimmune reaction linking systemic and CNS immune responses.<sup>13</sup>



### Anti-Glial fibrillary acidic protein

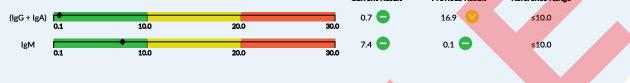
Glial fibrillary acidic protein (GFAP) is the major structural protein of the glial intermediate filament of astrocytes that forms part of the cytoskeleton of mature astrocytes and other glial cells, but is not found outside the CNS. Anti-GFAP is produced when the protein enters the bloodstream after a rupture of the blood brain barrier, thus serves as a blood based diagnostic marker of brain injury.<sup>14</sup> Current Result Previous Result Reference Range



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### Anti-Microglia

Microglia are a type of macrophage located throughout the brain and spinal cord that act as the first and main form of active immune defense in the CNS. These markers indicate a destruction of the blood brain barrier and are found to play a role in tissue destruction of Alzheimer's disease.<sup>14</sup> Current Result Reference Range



### Anti-Glucose regulated protein 78

Glucose regulated protein 78 (GRP78) is a major endoplasmic reticulum (ER) chaperone protein critical for protein quality control of the ER, as well as controlling the activation of the ER-transmembrane signaling molecules. Studies show that antibodies targeting glucose-regulated protein 78 are able to activate brain microvascular endothelial cells and induce protein extravasation in cell lines and in mice with neuromyelitis optica. Thus, these findings suggest that glucose-regulated protein 78-targeted antibodies could instigate blood brain barrier breakdown and development of hallmark anti-aquaporin-4 autoantibody pathology. Therefore, the application of these antibodies may be useful to disrupt the blood brain barrier for transit of treatments for many CNS diseases.<sup>15</sup>



### **Optical and Autonomic Nervous System Disorders**

#### Anti-Neuron specific enolase Neuron specific enclase is a protein enzyme that is encoded by the ENO2 gene. It is found in mature neurons and cells of neuronal origin. Antibodies against neuron specific enolase are found in patients with optical neuropathies. Current Result **Previous Result** Reference Range (IgG + IgA) 4.8 0.5 ≤10.0 10.0 20.0 30.0 8.3 😑 6.9 ≤10.0 IgM 10.0 30.0 20.0

### Anti-Aquaporin 4

Neuromyelitis optica is an inflammatory demyelinating disorder of the CNS. The discovery of circulating IgG antibodies against the astrocyte water channel protein aquaporin 4 (AQP4) and the evidence that AQP4-IgG is involved in the development of neuromyelitis optica revolutionized the understanding of the disease. Anti-aquaporin 4 antibodies have also been shown in patients with peripheral demyelination. In addition, human aquaporin 4 shows cross-reactivity with corn and soybean aquaporins,<sup>17</sup> hence, consider ordering Vibrant's Lectin Zoomer panel for a comprehensive assessment.



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### Anti-Recoverin

Anti-recoverin antibodies are one of the key components of antibody disorders of the CNS. They have also been shown to be associated with retinopathy, which is characterized by impaired vision and photosensitivity.



### Anti-CV2

Anti-CV2 antibodies are a group of antibodies that react with a 66-kd brain protein belonging to the family of CRMP proteins. The manifestations associated with anti-CV2 antibodies include cerebellar degeneration, uveitis, and peripheral neuropathy, and mixed axonal and demyelinating peripheral neuropathy.<sup>18</sup>



### **Peripheral Neuropathy**

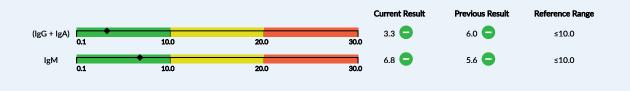
### Anti-GM1

Detection of ganglioside M1 (GM1) antibodies, usually of the IgM isotype, is associated with multi-focal motor neuropathy and lower motor neuropathy, characterized by muscle weakness and atrophy. Multi-focal motor neuropathy may occur with or without high serum titers of anti-GM1 antibodies. GM1 antibodies are detected in approximately 50 % of persons with multi-focal motor neuropathy.



### Anti-GM2

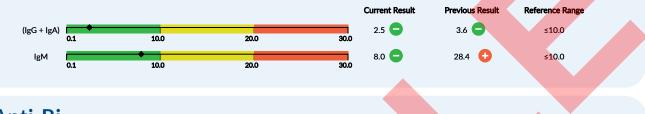
GM2 ganglioside is a potential peripheral nerve antigen for neuropathy-associated autoantibodies. Anti-GM2 IgM antibodies have been reported in some patients with dysimmune neuropathy or lower motor neuron syndrome, in whom they were often associated with a concomitant reactivity with GM1.



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### Anti-Hu

The anti-Hu antibody is the most frequent manifestation of sensory neuropathy with frequent autonomic involvement. The clinical patterns of the neuropathies is in keeping with accordance with the cellular distribution of the HuD antigen.



### Anti-Ri

Anti-Ri has been reported in serum and cerebrospinal fluid (CSF) of patients who present typically with a subacute neurological disorder involving the brainstem, cerebellum, and spinal cord. This antigen is also found in a rare disorder known as opsoclonus/myoclonus syndrome.<sup>19</sup>



### Anti-Amphiphysin

Amphiphysin is a non-intrinsic membrane protein that is concentrated in nerve terminals. The serum of patients with stiff-person syndrome often contain antibodies to this protein. Stiff-person syndrome (SPS) is a neurological disorder characterized by progressive muscle stiffness (rigidity) and repeated episodes of painful muscle spasms.



### **Neuromuscular disorders**

### Anti-Acetylcholine receptors

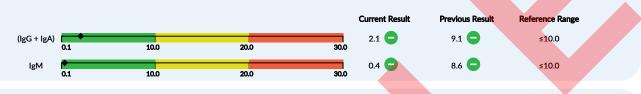
Acetylcholine receptors are responsible for binding acetylcholine, a neurotransmitter for signal transduction in CNS. They are localized in neuromuscular junctions. Antibodies against acetylcholine receptor are found in myasthenia gravis disease, which destroys the receptor function, leading to a neuromuscular transmission defect, which then causes hypofunction, fatigue, and inflammation of skeletal muscles and produces serum antibodies against muscle antigens.<sup>20</sup>



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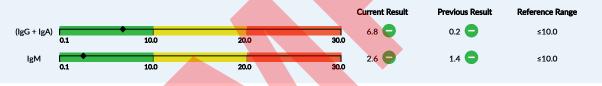
### Anti-Muscle specific kinase

Muscle-specific kinase (MuSK) is a single-pass transmembrane protein that has a critical role in signaling between motor neurons and skeletal muscle. Anti-MuSK is an important marker in patients without anti-acetylcholine receptor antibodies in myasthenia gravis disease.<sup>21</sup>



### Anti-Voltage gated calcium channels

Voltage-gated calcium channels (VGCCs) are a group of voltage-gated ion channels found in the membrane of excitable cells such as muscle, glial cells, and neurons. They are key transducers of membrane potential changes into intracellular Ca2+ transients that initiate many physiological events. In neurons, voltage-gated Ca<sup>2+</sup> channels initiate synaptic transmission. Anti-voltage-gated calcium channel autoantibodies are responsible for Lambert-Eaton myasthenic syndrome (LEMS), a rare autoimmune disorder of the neuromuscular junction.<sup>22</sup>



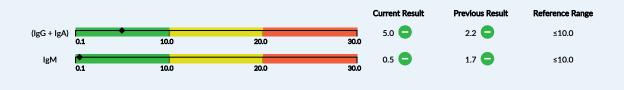
### Anti-Voltage gated potassium channels

Voltage-gated potassium channels (Kv) play a vital role in a variety of cellular processes, including the functioning of excitable cells, regulation of apoptosis, cell growth and differentiation, the release of neurotransmitters and hormones, and maintenance of cardiac activity. They are found along the axon and at the synapse of the neurons, to propagate electrical signals. In neuromyotonia, the anti-voltage-gated potassium channel autoantibodies downregulate the potassium channels expressed on the peripheral nerve terminal leading to nerve hyperexcitability.<sup>22</sup>



### Anti-Titin

Titin, also known as connectin, is a flexible filamentous protein, which is the largest protein known today. Titin is known to be important for myofibrillogenesis, sarcomere structure, and elasticity. Anti-titin antibodies are present in 70-90% of thymoma autoimmune myasthenia gravis (MG) patients, and in approximately 50% of late-onset acetylcholine-MG patients without thymoma. In general, anti-titin antibodies correlate with disease severity and may identify patients more likely to be refractory to therapy, including thymectomy.<sup>23</sup>



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### **Brain Autoimmunity**

### Anti-Cerebellum

The cerebellum is a region of the brain that plays an important role in motor control. The cerebellum does not initiate movement, but contributes to coordination, precision, and accurate timing. It receives input from sensory systems of the spinal cord and from other parts of the brain and integrates these inputs to fine-tune motor activity. Cerebellar damage produces disorders in fine movement, equilibrium, posture, and motor learning. Anti-cerebellum antibodies implicates a possible damage to the cerebellum that could lead to ataxia.<sup>24</sup> In addition, these antibodies are associated with disorders like autism and may be useful as markers for specific behavioral characteristics of autism.<sup>25</sup>



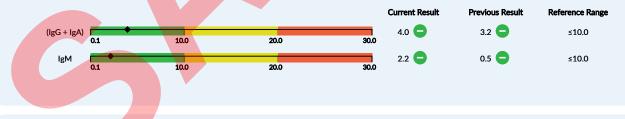
#### Anti-Purkinje cell

Purkinje cells, or Purkinje neurons, are a class of GABAergic neurons located in the cerebellum. Purkinje cells are aligned like dominos stacked one in front of the other. Their large dendritic arbors form nearly two-dimensional layers through which parallel fibers from the deeper-layers pass.



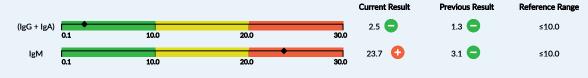
#### Anti-Yo

Anti-Yo antibodies are found in the serum of patients with neurologic paraneoplastic syndromes and reported to have activity against Purkinje cells of the cerebellum. They are found in ataxic syndrome, which is the most common variant of paraneoplastic cerebellar degeneration (PCD).<sup>26</sup>



### Anti-Amyloid beta (25-35)

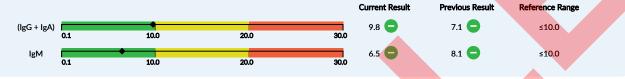
A $\beta$  is the cleavage product of the transmembrane amyloid- $\beta$  precursor protein (APP). Major species of A $\beta$  are A $\beta$ 40 and A $\beta$ 42, containing 40 and 42 amino acids, respectively. Although the pathogenesis of Alzheimer's disease (AD) is not fully understood, it is widely accepted that accumulation of A $\beta$  in the brain, especially the more amyloidogenic A $\beta$ 42, due to overproduction (familial AD) or impaired clearance (sporadic AD) initiates the pathogenic cascade, ultimately leading to neurodegeneration and dementia. The levels of autoantibodies reacting with oligomers of a short but neurotoxic fragment of A $\beta$ , A $\beta$  (25-35), were significantly higher in AD patients than in the control group who had undetectable autoantibodies to the A $\beta$  fragment.



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### Anti-Amyloid beta (1-42)

Beta-amyloid is a subunit of a larger protein called amyloid precursor protein (APP). APP extends from the inside of brain cells to the outside by passing through the fatty membrane around the cell. When APP is activated, it is cleaved to two different subunits, a chain containing 40 amino acids (the main form), and a chain containing 42 amino acids (amyloid beta 1–42). Amyloid-beta is one of the signature markers in Alzheimer's disease (AD). According to the "amyloid cascade hypothesis" that has been a cornerstone of the AD etiology for the last 20 years, the amyloid-beta deposition in the brain precipitates the formation of neurofibrillary tangles (NFTs).<sup>27</sup>



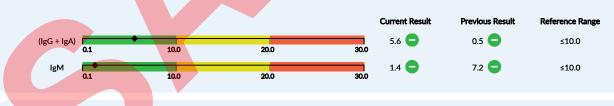
### Anti-RAGE peptide

The receptor for advanced glycosylation end products (RAGE) has been identified as the major receptor at the blood brain barrier to mediate the flux of amyloid- $\beta$  protein (A $\beta$ ) from the blood to the brain. The anti-RAGE antibodies were found in Alzheimer's disease patients. In addition, studies demonstrated that they were significantly higher in Alzheimer's disease patients with diabetes.<sup>28</sup>



#### Anti-Tau

Tau protein is found in the neurofibrillary tangles in brains of individuals who have Alzheimer's disease. Studies have shown that antibodies to the tau protein have been found in a number of AD patients when compared to healthy subjects. Other studies have also indicated that the levels of antibodies to tau are increased in patients with multiple sclerosis.



### Anti-Glutamate

Glutamate is the major excitatory neurotransmitter of the CNS and it is crucially needed for numerous key neuronal functions. These autoimmune anti-glutamate antibodies can bind neurons in a few brain regions, activate glutamate receptors, decrease glutamate receptor expression, impair glutamate-induced signaling and function, activate blood brain barrier endothelial cells, kill neurons, damage the brain, and induce behavioral/psychiatric/cognitive abnormalities and ataxia. Most of these autoantibodies are found in epilepsy, encephalitis, cerebellar ataxia, systemic lupus erythematosus (SLE) and neuropsychiatric SLE, Sjogren's syndrome, schizophrenia, mania or stroke.<sup>29</sup>



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### **Anti-Dopamine**

Dopamine is a crucial neurotransmitter in the brain and dopaminergic dysfunction is thought to underlie common human diseases, such as Parkinson's disease, Tourette's syndrome, and schizophrenia. Anti-dopamine antibody positive patients with encephalitis were found to have movement disorders characterized by parkinsonism, dystonia, and Sydenham chorea.<sup>30</sup>



#### Anti-Hydroxytryptamine

Serotonin (5-hydroxytryptamine, 5-HT) is one of the most extensively studied neurotransmitters of the CNS. These autoantibodies are found mainly in autoimmune encephalitis.<sup>31</sup>



### Anti-Alpha-synuclein

Alpha-synuclein is a presynaptic neuronal protein that is linked genetically and neuropathologically to Parkinson's disease. Anti-Alpha-synuclein autoantibodies are mainly elevated in Parkinson's disease and Alzheimer's disease.<sup>32</sup>



### Anti- $\alpha$ 1 and $\beta$ 2 adrenergic receptors

The adrenergic receptors ( $\alpha 1$  and  $\beta 2$  adrenergic receptors) are a class of G protein-coupled receptors that are targets of many catecholamine neurotransmitters like norepinephrine (noradrenaline) and epinephrine (adrenaline). The anti- $\alpha 1$  and  $\beta 2$  adrenergic receptors were found mainly in patients with different dementia forms such as unclassified, Lewy body, vascular and Alzheimer's dementia.<sup>33</sup>



### Anti-Endothelin A receptor

Endothelin peptides modulate the development of distinct neural cell types including Schwann cells, astrocytes, and neural crest cells as well as physiologic renal growth and development. The endothelin A receptor has a greater affinity for ET-1, one of the peptides of endothelin. The endothelin A receptor autoantibodies are found in vascular dementia.<sup>34</sup>



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### **Brain Inflammation**

### Anti-NMDA receptor

N-methyl-D-aspartate (NMDA) is an amino acid derivative very similar to glutamate. Because glutamate is the excitatory neurotransmitter found in most synapses of the central nervous system, pharmacologists made this analogue called NMDA to activate a sub-type of glutamate receptors. Anti-NMDA receptor encephalitis, first identified in 2007, is an autoimmune disease that occurs when antibodies turn on the brain and cause it to swell.<sup>35</sup> Anti-NMDA receptor and anti-dsDNA, a major contributor in systemic lupus disease, share a common pentapeptide sequence, thus making them candidates for cross-reactivity.<sup>36</sup> Consider ordering Vibrant's Connective Tissue Disorder panel for the most comprehensive assessment.



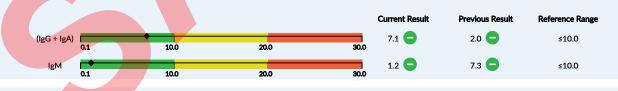
#### **Anti-AMPA receptor**

AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) is a compound that is a specific agonist for the AMPA receptor, where it mimics the effects of the neurotransmitter glutamate. In some epilepsies, antibodies to AMPA receptors leads to neuron damage. The same is true for ischemia, where oxygen deprivation leads to excitotoxicity. Conversely, Alzheimer's disease is characterized by decreased AMPA activation and synapse loss.<sup>37</sup>



### Anti-Dopamine receptor 1

Dopamine receptor 1 (DR1) expression in the central nervous system is highest in the dorsal striatum and ventral striatum. DR1 is the most abundant dopamine receptor in the central nervous system. It regulates neuronal growth and development, mediates some behavioral responses, and modulates dopamine receptor 2-mediated events. Antibodies associated with DR1 are mostly seen in brain inflammation and neuropsychiatric disorders.<sup>38</sup>



### Anti-Dopamine receptor 2

Similar to dopamine receptor 1, dopamine receptor 2 (DR2) is highly expressed in basal ganglia, for example striatum, but also in the cortex, hippocampus, and substantia nigra. Modulation of DR2 expression in the basal ganglia has been associated with schizophrenia, depression, and movement disorders. Movement and psychiatric disorders associated with DR2 antibody are biologically plausible as DR2 is intimately linked to the control of movement and behavior.<sup>30</sup>



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### **Anti-GABA receptors**

Gamma-Amino Butyric acid (GABA) is an amino acid which acts as a neurotransmitter in the CNS. It inhibits nerve transmission in the brain, calming nervous activity. Temporal lobe epilepsy (TLE), Parkinson's disease (PD) and Huntington's disease (HD) are neurodegenerative disorders that involve disruptions in gamma-amino butyric acid (GABA) signaling.<sup>39</sup>



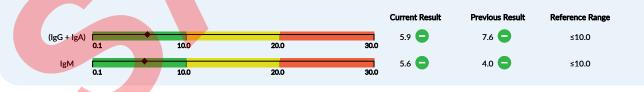
### Anti-Dipeptidyl aminopeptidase-like protein 6

Dipeptidyl aminopeptidase-like protein 6 is a protein that in humans is encoded by the DPP6 gene. This gene encodes a single-pass type II membrane protein that is a member of the S9B family in clan SC of the serine proteases. Antibodies against dipeptidyl-peptidase-like protein-6 (DPPX), an auxiliary subunit of Kv4.2 potassium channels involved in signal transduction, were identified in 7 patients with encephalitis.<sup>40</sup>



### Anti-Glycine receptor

Glycine accomplishes several functions as a transmitter in the CNS. As an inhibitory neurotransmitter, it participates in the processing of motor and sensory information that permits movement, vision, and audition. This action of glycine is mediated by the strychnine-sensitive glycine receptor, whose activation produces inhibitory post-synaptic potentials. Detection of glycine receptor antibodies may prove helpful in the diagnosis of patients with symptoms and signs that include ocular motor and other brainstem dysfunction, hyperekplexia, stiffness, rigidity, myoclonus and spasms, and their detection will support the use of immunotherapies that are likely to be clinically effective.<sup>41</sup>



### Anti-Neurexin 3

Neurexin is a presynaptic protein that helps to connect neurons at the synapse. They are located mostly on the presynaptic membrane and contain a single transmembrane domain. Neurexin- $3\alpha$  autoantibodies associate with a severe but potentially treatable encephalitis in which the antibodies cause a decrease of neurexin- $3\alpha$  and alter synapse development.<sup>42</sup>



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#### Anti-Contactin-associated protein-like 2 antibodies

CNTNAP2 (Contactin-associated protein-like 2) is a protein coding gene. This gene encodes a member of the neurexin family which functions in the vertebrate nervous system as cell adhesion molecules and receptors. Diseases associated with CNTNAP2 include Pitt-Hopkins-Like Syndrome 1 and Autism 15. Among its related pathways are neuroscience and cell adhesion molecules (CAMs).<sup>43</sup> Current Result Previous Result Reference Range



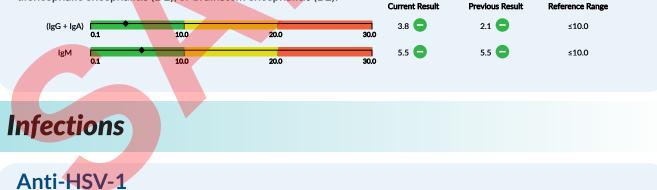
### Anti-Leucine-rich glioma-inactivated protein (Anti-LGI1)

The leucine-rich glioma inactivated-1 gene is rearranged as a result of translocations in glioblastoma cell lines. The protein contains a hydrophobic segment representing a putative transmembrane domain with the amino terminus located outside the cell. It also contains leucine-rich repeats with conserved cysteine-rich flanking sequences. This gene is predominantly expressed in neural tissues and its expression is reduced in low grade brain tumors and significantly reduced or absent in malignant gliomas. LGI1 antibody-associated encephalitis has increasingly been recognized as a primary autoimmune disorder.<sup>44</sup>



### Anti-Ma

Anti-Ma antibodies recognize Ma family proteins, which are exclusively found in neurons and testicular germ cells. Anti-Ma antibodies are found in patients with a wide range of neurological syndromes including limbic encephalitis (LE), diencephalic encephalitis (DE), or brainstem encephalitis (BE).<sup>45</sup>



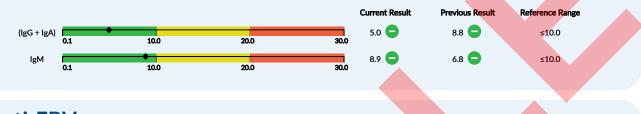
Herpes simplex virus 1 (HSV-1) is a member of the herpesvirus family, Herpesviridae, that infect humans. HSV-1 (which produces most cold sores) is ubiquitous and contagious. As a neurotropic and neuroinvasive virus, HSV-1 persists in the body by becoming latent and hiding from the immune system in the cell bodies of neurons. HSV-1 has been reported to have a pathogenesis role in Herpes simplex encephalitis (HSE) and seropositivity to HSV-1 antibodies has been correlated with increased risk of Alzheimer's disease.<sup>46</sup>



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### Anti-HSV-2

Herpes simplex virus type 2 (HSV-2)-associated neurological disease may result from primary infection or reactivation of latent HSV-2. Herpes simplex encephalitis (HSE) is a disorder commonly associated with HSV-2. HSE due to HSV-2 may occur without meningitis features. Antibodies against HSV-2 have shown positive correlation in patients with symptoms of HSE.47



### Anti-EBV

Central nervous system (CNS) complications of Epstein-Barr virus (EBV) infection occur in up to 18% of patients with infectious mononucleosis and include encephalitis, meningitis, and psychiatric abnormalities.<sup>48</sup> Antibodies against the EBV nuclear antigen complex (EBNAc) and EBNA-1 have been correlated with increased risk of multiple sclerosis (MS). The role of EBV in the pathogenesis of multiple sclerosis was attributed to molecular mimicry between EBV and central nervous system (CNS) antigen, myelin basic protein (MBP).<sup>49</sup>



### Anti-CMV

Cytomegalovirus (CMV) infections have been reported frequently to be associated with Guillain-Barre syndrome (GBS). In GBS, anti-GM2 antibodies have been detected in 22-67% of CMV-infected patients. Studies showed that anti-ganglioside antibodies that can bind to peripheral nerves and interfere with neuromuscular transmission in CMV-infected GBS patients are induced by molecular mimicry between GM2 and antigens that are induced by a CMV infection.50-51



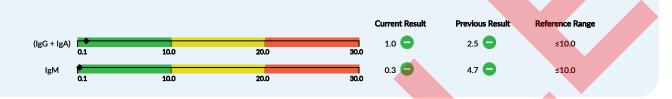
Human herpesvirus-6 (HHV-6) is frequently associated with neurologic diseases, including multiple sclerosis (MS), epilepsy, encephalitis, and febrile illness. This ubiquitous  $\beta$ -herpesvirus exists in two variants that share 95% sequence homology, HHV-6A and HHV-6B. The identical sequence homology was found between human herpesvirus-6 and myelin basic protein (MBP), one of the autoantigens implicated in MS pathology. High HHV-6 antibody titers were found in MS patients, implicating its role in MS.<sup>52</sup> Apart from MS, studies have shown increased HHV-6A in multiple brain regions in Alzheimer's disease (AD) patients implicating a potential neuropathological role in AD.<sup>46,53</sup>



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### Anti-HHV-7

HHV-7 has been less frequently associated with CNS disease than HHV-6, but found to be associated with encephalitis, meningitis, and demyelinating conditions. Similar to HHV 6A, increased levels of HHV-7 were found in multiple brain regions in Alzheimer's disease (AD) patients.<sup>46,53</sup>



### Anti-Streptococcal A

Group A beta-haemolytic streptococcal (GABHS) tonsillitis, more frequently known as streptococcal pharyngitis, is highly prevalent in children, especially in those who are between the ages of 5 and 15 years. A subset of these children may develop PANDAS characterized by pediatric obsessive-compulsive disorder (OCD) and tic disorder, and Sydenham Chorea. Anti-streptococcal A antibodies are shown to cross react with different brain proteins that could lead to neuropsychiatric symptoms.<sup>54</sup>



Key Terms/Glossary	
Acute disseminated encephalomyelitis	Acute disseminated encephalomyelitis (ADEM) is characterized by a brief but widespread attack of inflammation in the brain and spinal cord that damages myelin, the protective covering of nerve fibers.
Alzheimer's disease	Alzheimer's disease is the most common cause of dementia, a group of brain disorders that cause the loss of intellectual and social skills.
Aquaporin	Aquaporins are membrane water channels that play critical roles in controlling the water contents of cells.
Ataxia	Ataxia is typically defined as the presence of abnormal, uncoordinated movements.
Cerebellar ataxia	Cerebellar ataxia is a disorder that occurs when the cerebellum becomes inflamed or damaged. The cerebellum is the area of the brain responsible for controlling gait and muscle coordination.
Chronic inflammatory demyelinating polyneuropathy	Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms.
Demyelinating disease	A demyelinating disease is any disease of the nervous system in which the myelin sheath of neurons is damaged. This damage impairs the conduction of signals in the affected nerves.
Encephalitis	Encephalitis is an inflammation of the brain.
Epilepsy	Epilepsy is a CNS (neurological) disorder in which brain activity becomes abnormal, causing seizures or periods of unusual behavior, sensations, and sometimes loss of awareness.
Graves' disease	Graves' disease is an autoimmune disorder that causes hyperthyroidism, or overactive thyroid.

Key Terms/Glossary	
Gynecological cancers	Gynecologic cancer is an uncontrolled growth and spread of abnormal cells that originate from the reproductive organs.
Hashimoto's thyroiditis	Hashimoto's disease is an autoimmune disorder that can cause hypothyroidism, or underactive thyroid.
Huntington's disease	Huntington's disease is an inherited disease that causes the progressive breakdown (degeneration) of nerve cells in the brain.
Multi-focal motor neuropathy	Multifocal motor neuropathy (MMN) is a rare neuropathy characterized by progressive, asymmetric muscle weakness and atrophy (wasting).
Multiple sclerosis	Multiple sclerosis (MS) involves an immune-mediated process in which an abnormal response of the body's immune system is directed against the CNS.
Myasthenia gravis	Myasthenia gravis (MG) is a neuromuscular disorder that causes weakness in the skeletal muscles, which are the muscles your body uses for movement.
Myelination	Myelination is a term in anatomy that is defined as the process of forming a myelin sheath around a nerve to allow nerve impulses to move more quickly.
Neuromyelitis optica	Neuromyelitis optica (NMO), also known as Devic's disease or Devic's syndrome, is a heterogeneous condition consisting of the inflammation and demyelination of the optic nerve (optic neuritis) and the spinal cord (myelitis).
Neuromyotonia	Neuromyotonia (NMT) is a form of peripheral nerve hyperexcitability that causes spontaneous muscular activity resulting from repetitive motor unit action potentials of peripheral origin.
OCD	Obsessive-compulsive disorder (OCD) is an anxiety disorder characterized by recurrent and disturbing thoughts (called obsessions) and/or repetitive, ritualized behaviors that the person feels driven to perform (called compulsions).

Key Terms/Glossary	
Oligodendrocytes	Oligodendrocytes are the myelinating cells of the CNS.
PANDAS	PANDAS is short for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections.
Paraneoplastic opsoclonus /myoclonus syndrome	Paraneoplastic opsoclonus-myoclonus syndrome (OMS) is a rare complication of cancer characterized by chaotic, synchronous eye movements (opsoclonus), spontaneous muscle jerks (myoclonus), and ataxia.
Parkinson's disease	Parkinson's disease is a progressive nervous system disorder that affects movement.
Peripheral neuropathy	Peripheral neuropathy refers to the conditions that result when nerves that carry messages to and from the brain and spinal cord from and to the rest of the body are damaged or diseased.
Rheumatoid arthritis	Rheumatoid arthritis is an autoimmune disease that causes chronic joint inflammation.
Schizophrenia	Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves.
Sjogren's syndrome	Sjogren's (SHOW-grins) syndrome is a disorder of the immune system identified by its two most common symptoms — dry eyes and a dry mouth.
Systemic lupus erythematosus	Systemic lupus erythematosus (SLE) is a chronic disease that causes inflammation in connective tissues, such as cartilage and the lining of blood vessels, which provide strength and flexibility to structures throughout the body.
Tourette's syndrome	Tourette's syndrome (TS) is a neurological disorder characterized by repetitive, stereotyped, involuntary movements and vocalizations called tics.
Uveitis	Uveitis is a general term describing a group of inflammatory diseases that produces swelling and destroys eye tissues.

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#### Risk and Limitations

Neural Zoomer *Plus* testing has been developed and its performance characteristics determined by Vibrant America LLC and Vibrant Genomics (for ApoE testing), both CLIA certified laboratories and utilizes ISO-13485 developed technology. These assays have not been cleared or approved by the U.S. Food and Drug Administration.

The labs have effective procedures in place to protect against technical and operational problems. However, such problems may still occur. Examples include failure to obtain the result for a specific antigen due to circumstances beyond Vibrant's control. Vibrant may re-test a sample in order to obtain these results but upon re-testing the results may still not be obtained. As with all medical laboratory testing, there is a small chance that the laboratory could report incorrect results. A tested individual may wish to pursue further testing to verify any results.

Tested individuals may find their experience is not consistent with Vibrant's selected peer reviewed scientific research findings of relative improvement for study groups. The science in this area is still developing and many personal health factors affect diet and health. Since subjects in the scientific studies referenced in this report may have had personal health and other factors different from those of tested individuals, results from these studies may not be representative of the results experienced by tested individuals. Further, some recommendations may or may not be attainable, depending on the tested individual's physical ability or other personal health factors.

A limitation of this testing is that many of these scientific studies may have been performed in selected populations only. The interpretations and recommendations are done in the context of these studies, but the results may or may not be relevant to tested individuals of different or mixed ethnicities.

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