

CLINICAL SPECIFICATIONS

AQUAPORIN-4

Function:

Aquaporin is the predominant water channel protein in the human brain. Aquaporin-4 (AQP4) is abundantly expressed in the endfeet of astrocytes supporting the blood vessels of the blood-brain barrier (BBB) and in astrocytic processes in contact with synapses. There are four plant aquaporins that contribute to the generation of antibodies targeting human AQP4; corn, spinach, soy, and tomato. The function of AQP4 is to ensure bi-directional cerebral water balance and removal of harmful substances, and thus, a dysfunction of AQP4 has implications in neuropathological disorders, including brain edema, stroke, and head injuries.

Associated With:

Neuromyelitis optica¹
 Neuromyelitis Optica spectrum disorders²
 Multiple sclerosis³
 Longitudinally extensive transverse myelitis⁴
 Optic neuritis⁴

Known Cross-Reactions: A β ₄₂ peptide;⁵ Corn aquaporin, Soybean aquaporin, Spinach aquaporin, Tomato aquaporin;⁶ *Escherichia coli* aquaporin-Z⁷

Clinical Significance:

Aquaporin-4 (AQP4) and S100B are two major components of the blood-brain barrier (BBB). A breakdown of the BBB and the release of AQP4 and S100B proteins ignites antibody production against them. These antibodies are involved in neuromyelitis optica (NMO), and dementia, among others. AQP4 is the primary target in the autoimmune disease neuromyelitis optica. Primarily affecting the optic nerves and spinal cord, AQP4-specific autoantibodies (NMO-IgG) activate complement-mediated inflammatory demyelination and necrosis.⁸ AQP4 IgG has been shown to play a pathophysiological role in central nervous system lesions, as seen in NMO patients.⁹ A marked rise in levels of AQP4 antibodies prior to relapse was seen in patients with NMO, while during remission (>30 days from relapse) AQP4 antibody levels were detectable, but most patients had levels below the median value.¹ AQP4 antibody-positive patients showed higher frequencies of relapse of optic neuritis or transverse myelitis compared with AQP4 antibody-negative patients.¹⁰ Taking into consideration that not all NMO patients make antibodies to AQP4,^{reviewed in} ¹¹ Jarius *et al.* found the sensitivity and specificity of AQP4 IgG for NMO to be 66.7% and 98.7% respectively.¹¹ A patient making AQP4 antibodies may have a broken BBB, and since AQP4 antibodies have been shown to cross-react with amyloid beta peptide,⁵ the patient would be at greater risk for developing Alzheimer's disease or other neurological disorder.

References:

- Jarius *et al.* Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain*, 2008; 131:3072-3080.
- Tuller *et al.* Characterization of the binding pattern of human aquaporin-4 autoantibodies in patients with neuromyelitis optica spectrum disorders. *J Neuroinflammation*, 2016; 13:176.
- Vojdani *et al.* Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Dis*, 2015; 2015.
- Waters *et al.* Evaluation of aquaporin-4 antibody assays. *Clin Exp Neuroimmunol*, 2014; 5:290-303.
- Vojdani and Vojdani. Amyloid-beta 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A-beta-P-42. *Int J Alzheimers Dis*, 2018; 2018:1672568.
- Vaishnav *et al.* Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J Neuroimmunol*, 2013; 260: 92-98.
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- Wingerchuk *et al.* The spectrum of neuromyelitis optica. *Lancet Neurol*, 2007; 6:805-815.
- Hinson *et al.* Molecular outcomes of neuromyelitis optica (NMO)-IgG binding to aquaporin-4 in astrocytes. *PNAS*, 2012; 109(4):1245-1250.
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- Jarius *et al.* Testing for antibodies to human aquaporin-4 by ELISA: Sensitivity, specificity, and direct comparison with immunohistochemistry. *J Neurologic Sci*, 2012; 320:32-37.

CLINICAL SPECIFICATIONS

CORN AQUAPORIN

Function:

Aquaporin (AQP) is the predominant water channel protein that is found in both the human brain and plants. In plants, AQP acts as a transporter of water into and out of the plant as needed to sustain it. These channel proteins also facilitate the transport of boron, silicon or carbon dioxide.

Associated With:

Neuromyelitis optica¹
 Neuromyelitis Optica spectrum disorders²
 Multiple sclerosis³
 Longitudinally extensive transverse myelitis⁴
 Optic neuritis⁴

Known Cross-Reactions: Human Aquaporin⁵

Clinical Significance:

Autoreactive antibodies made against environmental antigens such as dietary proteins or pathogens constantly circulate in the blood stream. These autoreactive antibodies may cross-react with tissues in the brain and nervous system. As long as the BBB is intact, those autoreactive antibodies cannot harm the delicate brain and nervous system tissues. However, should the BBB be broken, these autoreactive antibodies can enter the brain and trigger neuroinflammation, neuroautoimmunity and neurodegeneration. The more circulating autoreactive antibodies that cross the barriers, the more damage to the brain.⁶ If a patient tests positive for the biomarkers of BBB permeability, it is essential to remove known cross-reactors (see Array 20 and Array 7 spec sheets) in order to prevent neurological damage and improve BBB healing time. Antibodies against both human and plant aquaporins have been detected in patients with neuromyelitis optica, patients with multiple sclerosis, and patients with celiac disease.^{3,5,7} Furthermore, it has been demonstrated that antibody made against A β -42 peptide reacts with aquaporins. This may indicate that detected antibodies against both A β -42 and aquaporins may play a role in the breakdown of the BBB as well as the pathophysiology of Alzheimer's disease.⁸⁻⁹

References:

1. Jarius et al. Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain*, 2008; 131:3072-3080.
2. Tuller et al. Characterization of the binding pattern of human aquaporin-4 autoantibodies in patients with neuromyelitis optica spectrum disorders. *J Neuroinflammation*, 2016; 13:176.
3. Vojdani et al. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Dis*, 2015; 2015:905208.
4. Waters et al. Evaluation of aquaporin-4 antibody assays. *Clin Exp Neuroimmunol*, 2014; 5:290-303.
5. Vaishnav et al. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J Neuroimmunol*, 2013; 260: 92-98.
6. Vojdani. Brain-reactive antibodies in traumatic brain injury. *Funct Neurol Rehabil Ergon*, 2013; 3(203):173-181.
7. Vojdani et al. Fluctuation of zonulin levels in blood versus stability of antibodies. *World J Gastroenterol*, 2017; 23(31):5669-5679.
8. Vojdani et al. Reaction of amyloid- β peptide antibody with different infectious agents involved in Alzheimer's disease. *J Alzheimers Dis*, 2018; 63(2018): 847-860.
9. Vojdani et al. Amyloid- β 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A β P-42. *Int J Alzheimers Dis*, 2018; 2018: Article ID 1672568.

CLINICAL SPECIFICATIONS

SOY AQUAPORIN

Function:

Aquaporin (AQP) is the predominant water channel protein that is found in both the human brain and plants. In plants, AQP acts as a transporter of water into and out of the plant as needed to sustain it. These channel proteins also facilitate the transport of boron, silicon or carbon dioxide.

Associated With:

Neuromyelitis optica¹
 Neuromyelitis Optica spectrum disorders²
 Multiple sclerosis³
 Longitudinally extensive transverse myelitis⁴
 Optic neuritis⁴

Known Cross-Reactions: Human Aquaporin⁵

Clinical Significance:

Autoreactive antibodies made against environmental antigens such as dietary proteins or pathogens constantly circulate in the blood stream. These autoreactive antibodies may cross-react with tissues in the brain and nervous system. As long as the BBB is intact, those autoreactive antibodies cannot harm the delicate brain and nervous system tissues. However, should the BBB be broken, these autoreactive antibodies can enter the brain and trigger neuroinflammation, neuroautoimmunity and neurodegeneration. The more circulating autoreactive antibodies that cross the barriers, the more damage to the brain.⁶ If a patient tests positive for the biomarkers of BBB permeability, it is essential to remove known cross-reactors (see Array 20 and Array 7 spec sheets) in order to prevent neurological damage and improve BBB healing time. Antibodies against both human and plant aquaporins have been detected in patients with neuromyelitis optica, patients with multiple sclerosis, and patients with celiac disease.^{3,5,7} Furthermore, it has been demonstrated that antibody made against A β -42 peptide reacts with aquaporins. This may indicate that detected antibodies against both A β -42 and aquaporins may play a role in the breakdown of the BBB as well as the pathophysiology of Alzheimer's disease.⁸⁻⁹

References:

1. Jarius et al. Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain*, 2008; 131:3072-3080.
2. Tuller et al. Characterization of the binding pattern of human aquaporin-4 autoantibodies in patients with neuromyelitis optica spectrum disorders. *J Neuroinflammation*, 2016; 13:176.
3. Vojdani et al. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Dis*, 2015; 2015:905208.
4. Waters et al. Evaluation of aquaporin-4 antibody assays. *Clin Exp Neuroimmunol*, 2014; 5:290-303.
5. Vaishnav et al. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J Neuroimmunol*, 2013; 260: 92-98.
6. Vojdani. Brain-reactive antibodies in traumatic brain injury. *Funct Neurol Rehabil Ergon*, 2013; 3(203):173-181.
7. Vojdani et al. Fluctuation of zonulin levels in blood versus stability of antibodies. *World J Gastroenterol*, 2017; 23(31):5669-5679.
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CLINICAL SPECIFICATIONS

SPINACH AQUAPORIN

Function:

Aquaporin (AQP) is the predominant water channel protein that is found in both the human brain and plants. In plants, AQP acts as a transporter of water into and out of the plant as needed to sustain it. These channel proteins also facilitate the transport of boron, silicon or carbon dioxide.

Associated With:

Neuromyelitis optica¹
 Neuromyelitis Optica spectrum disorders²
 Multiple sclerosis³
 Longitudinally extensive transverse myelitis⁴
 Optic neuritis⁴

Known Cross-Reactions: Human Aquaporin⁵

Clinical Significance:

Autoreactive antibodies made against environmental antigens such as dietary proteins or pathogens constantly circulate in the blood stream. These autoreactive antibodies may cross-react with tissues in the brain and nervous system. As long as the BBB is intact, those autoreactive antibodies cannot harm the delicate brain and nervous system tissues. However, should the BBB be broken, these autoreactive antibodies can enter the brain and trigger neuroinflammation, neuroautoimmunity and neurodegeneration. The more circulating autoreactive antibodies that cross the barriers, the more damage to the brain.⁶ If a patient tests positive for the biomarkers of BBB permeability, it is essential to remove known cross-reactors (see Array 20 and Array 7 spec sheets) in order to prevent neurological damage and improve BBB healing time. Antibodies against both human and plant aquaporins have been detected in patients with neuromyelitis optica, patients with multiple sclerosis, and patients with celiac disease.^{3,5,7} Furthermore, it has been demonstrated that antibody made against A β -42 peptide reacts with aquaporins. This may indicate that detected antibodies against both A β -42 and aquaporins may play a role in the breakdown of the BBB as well as the pathophysiology of Alzheimer's disease.⁸⁻⁹

References:

1. Jarius et al. Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain*, 2008; 131:3072-3080.
2. Tuller et al. Characterization of the binding pattern of human aquaporin-4 autoantibodies in patients with neuromyelitis optica spectrum disorders. *J Neuroinflammation*, 2016; 13:176.
3. Vojdani et al. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Dis*, 2015; 2015:905208.
4. Waters et al. Evaluation of aquaporin-4 antibody assays. *Clin Exp Neuroimmunol*, 2014; 5:290-303.
5. Vaishnav et al. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J Neuroimmunol*, 2013; 260: 92-98.
6. Vojdani. Brain-reactive antibodies in traumatic brain injury. *Funct Neurol Rehabil Ergon*, 2013; 3(203):173-181.
7. Vojdani et al. Fluctuation of zonulin levels in blood versus stability of antibodies. *World J Gastroenterol*, 2017; 23(31):5669-5679.
8. Vojdani et al. Reaction of amyloid- β peptide antibody with different infectious agents involved in Alzheimer's disease. *J Alzheimers Dis*, 2018; 63(2018): 847-860.
9. Vojdani et al. Amyloid- β 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A β P-42. *Int J Alzheimers Dis*, 2018; 2018: Article ID 1672568.

CLINICAL SPECIFICATIONS

TOMATO AQUAPORIN

Function:

Aquaporin (AQP) is the predominant water channel protein that is found in both the human brain and plants. In plants, AQP acts as a transporter of water into and out of the plant as needed to sustain it. These channel proteins also facilitate the transport of boron, silicon or carbon dioxide.

Associated With:

Neuromyelitis optica¹
 Neuromyelitis Optica spectrum disorders²
 Multiple sclerosis³
 Longitudinally extensive transverse myelitis⁴
 Optic neuritis⁴

Known Cross-Reactions: Human Aquaporin⁵

Clinical Significance:

Autoreactive antibodies made against environmental antigens such as dietary proteins or pathogens constantly circulate in the blood stream. These autoreactive antibodies may cross-react with tissues in the brain and nervous system. As long as the BBB is intact, those autoreactive antibodies cannot harm the delicate brain and nervous system tissues. However, should the BBB be broken, these autoreactive antibodies can enter the brain and trigger neuroinflammation, neuroautoimmunity and neurodegeneration. The more circulating autoreactive antibodies that cross the barriers, the more damage to the brain.⁶ If a patient tests positive for the biomarkers of BBB permeability, it is essential to remove known cross-reactors (see Array 20 and Array 7 spec sheets) in order to prevent neurological damage and improve BBB healing time. Antibodies against both human and plant aquaporins have been detected in patients with neuromyelitis optica, patients with multiple sclerosis, and patients with celiac disease.^{3,5,7} Furthermore, it has been demonstrated that antibody made against A β -42 peptide reacts with aquaporins. This may indicate that detected antibodies against both A β -42 and aquaporins may play a role in the breakdown of the BBB as well as the pathophysiology of Alzheimer's disease.⁸⁻⁹

References:

1. Jarius et al. Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain*, 2008; 131:3072-3080.
2. Tuller et al. Characterization of the binding pattern of human aquaporin-4 autoantibodies in patients with neuromyelitis optica spectrum disorders. *J Neuroinflammation*, 2016; 13:176.
3. Vojdani et al. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Dis*, 2015; 2015:905208.
4. Waters et al. Evaluation of aquaporin-4 antibody assays. *Clin Exp Neuroimmunol*, 2014; 5:290-303.
5. Vaishnav et al. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J Neuroimmunol*, 2013; 260: 92-98.
6. Vojdani. Brain-reactive antibodies in traumatic brain injury. *Funct Neurol Rehabil Ergon*, 2013; 3(203):173-181.
7. Vojdani et al. Fluctuation of zonulin levels in blood versus stability of antibodies. *World J Gastroenterol*, 2017; 23(31):5669-5679.
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