Functional Immunology Review

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Dr. Aristo Vojdani has published nearly 200 articles in scientific magazines and peer-reviewed journals. He is also the holder of 17 US patents in lab technology, and is considered the Father of Functional Immunology.

Welcome to our first issue! This new Cyrex publication is focused on topics related to the latest advancements in functional immunology. This will include reviews of scientific articles, the latest developments in laboratory testing, case studies, as well as Cyrex-related news and advancements.

The chief editor of this publication is Aristo Vojdani, PhD, a leading immunologist, a pioneer in laboratory technology, Chief Scientific Advisor of Cyrex Laboratories LLC, and the inventor of IgG testing for food sensitivities. His latest book, "Food-Associated Autoimmunities: When Food Breaks Your Immune System," is a powerful industry-forming guide providing unique insights into the world of lab testing and functional immunology. Dr. Vojdani's forward thinking, and pioneering spirit, along with his unmatched scientific expertise, has fueled innovations for 40 years, which have helped form the world of functional immunology as we know it today. In 2019, Dr. Vojdani received the Life Time Achievement Award from Dr. Jeffrey Bland at the Personalized Lifestyle Medicine Institute (PLMI) Conference in recognition of his contributions to the field of functional and personalized medicine.

In this issue, we will be discussing how the worlds of conventional and functional medicine are coming together in the area of cognitive decline.

New Perspectives on Alzheimer's Disease from the 2019 Alzheimer's Association International Conference

The following is a review by Aristo Vojdani, PhD., of the recently-held 2019 Alzheimer's Association International Conference in Los Angeles. In this review Dr. Vojdani will be highlighting several key correlations between the presentations in this international conference, and his own recently published research and immunological perspectives:

The annual Alzheimer's Association International Conference (AAIC), hosted in Los Angeles, July 14-18, 2019, brought together the world's foremost researchers in the field of dementia-related disorders. More than 1,000 presentations were given with nearly 6,000 participants in attendance.

"While there is no proven cure or treatment for Alzheimer's, a large body of research now strongly suggests that healthy habits promote good brain health and reduce your risk of cognitive decline," said Maria C. Carrillo, PhD., Alzheimer's Association chief science officer. "The research reported today at AAIC gives us attainable, actionable recommendations that can help us all live a healthier life."

Speakers at the AAIC - Los Angeles 2019

Experts from prestigious US research centers presented their latest findings. Among these eminent presenters were:

- National Institutes of Health
- Columbia University Medical Center
- Harvard Medical School/Massachusetts General Hospital
- Johns Hopkins University School of Medicine
- University of California
- Stanford University
- University of Texas
- Weill Cornell Medicine
- Yale School of Medicine

Since Alzheimer's disease (AD) is a pandemic, researchers from around the globe joined their US colleagues on stage at the AAIC. Countries represented included Australia, Belgium, France, Germany, Ireland, Japan, Netherlands, South Korea, Spain, Sweden, and the United Kingdom.

The greatest take-away message for me was that this very conventional group has turned its sights in the direction of functional medicine. Highlights of the conference pointed to research showing that a healthy lifestyle may offset environmental and genetic risk factors for Alzheimer's disease.

The main conclusion of the event seemed to be that a healthy lifestyle is key for combating cognitive decline even in the presence of genetic markers and environmental triggers.

There were five major categories of presentations that caught my attention.

1. Lifestyle modification
2. Neuroimaging
3. Blood-based biomarkers
4. Environmental factors (infections, medications)
5. Microbiota

Multiple presenters elaborated on these key areas with original study data. Although neuroimaging has been discussed from the beginning of dementia research, the session on blood-based biomarkers including autoantibodies saw an expansion beyond tau and amyloid-beta; pathogen research found new culprits; the influential microbiome was finally recognized; and lifestyle modification based on environmental factors played a starring role for the first time.

Lifestyle Modification

Everyone agrees that a healthy lifestyle decreases the risks for acquiring a variety of disorders. As AD is a multifactorial disorder, meaning no two AD patients have the same symptoms or disease pathophysiology, identifying the appropriate lifestyle modifications for each individual is fundamental. Having a blood-based assay to assess key individual risk factors would be a useful clinical tool in developing customized lifestyle programs. These lifestyle modifications include, but are not limited to, a healthy diet that supports the immune system, a regimen of helpful prebiotics and probiotics, avoidance of toxic chemicals which can be found in a surprising number of places and commonly used products, the nurturing of the microbiome, and the treatment of infections brought about by pathogens involved in AD.

Now for the first time, key environmental risk factors can be identified, and personalized lifestyle programs can be developed accordingly.

Blood-Based Biomarkers

Most of the presentations in this category focused on the measurement of levels of amyloid beta ($A\beta_{40}$, $A\beta_{42}$), neurofilaments, tau, and α-synuclein in cerebrospinal fluid (CSF) as well as in blood. But, considering that the half-life of these brain proteins in the blood is about five hours, direct measurements of the levels of these proteins in serum would be subject to fluctuations. On the other hand, a serum-based test for antibodies against these and many more other proteins would not only be stable for 30 days or more, but would be measuring factors that have a direct role in the induction of neurotoxicity in AD. Finally, Cyrex's Alzheimer's LINX™, for the first time, provides an insight into the role of antibodies produced by the immune system against these proteins. Alzheimer's LINX can indicate damaging mechanisms at play, and can also aid in the implementation of preventive strategies.

In 2018, I wrote three research articles based on more than a year-long study dealing with different aspects of amyloid-beta peptide aggregation and its role in the pathogenesis of Alzheimer's disease.

- Vojdani A, Vojdani E, Saidara E, Kharrazian D. **Reaction of amyloid-ß peptide antibody with different infectious agents involved in Alzheimer's disease**. J Alzheimer Dis, 2018; 63:847-860.

- Vojdani A and Vojdani E. **Amyloid-beta 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A-beta-P-42**. International J Alzheimer Dis, 2018; 2018: article ID 1672568.

- Vojdani A and Vojdani E. I**mmunoreactivity of anti-AßP-42 specific antibody with toxic chemicals and food antigens**. J Alzheimers Dis Parkinsonism, 2018; 8:441.

The novelty of my research was recognized by the Journal of Alzheimer's Disease through an invitation to become an associate editor for the years 2018-2019, after accepting my work for publication. I was honored to take on this task.

From the research published in the above publications, I was able to identify strong serum immunoglobulin G (IgG) biomarkers for AD. The brain protein antibodies that should be included in assessing risks for AD are tau, amyloid-beta peptide, rabaptin-5, presenilin, neurofilaments, and alpha-synuclein. In addition to these brain proteins, biomarkers should also include growth factors such as beta nerve growth factor, brain derived neurotrophic factor (BDNF), neurotrophins and somatotropin, in order to assess how well a patient is able to recover from brain tissue degeneration. As with many disorders, the gut plays a key role, so measuring antibodies against the enteric nerve, vasoactive intestinal peptide and transglutaminases provides valuable insight to assess the gut-brain connection. However, the most critical tissues to assess are those composing and supporting the blood-brain barrier (BBB). If the blood-brain barrier is functioning and intact, there is less risk for AD.

If the BBB is compromised and/or brain proteins are spilling into the bloodstream, the risk for AD increases exponentially.

Key Environmental Factors

1. Pathogens

Different pathogens, from oral or gut invaders to stealth organisms, may play a role in the onset of AD. Some of the pathogens discussed at the AAIC 2019 included herpes simplex virus-1, Chlamydia pneumoniae, Borellia burgdorferi, gut bacteria such as Enterococcus faecalis, Escherichia coli, Salmonella typhosa, Campylobacter jejuni, and their toxins. How exactly do these pathogens ignite or exacerbate the development of AD? By the infiltration of cross-reactive antibodies and inflammatory molecules through the broken blood-brain barriers, and their cross-ractivity with amyloid-beta peptide. These reactions and more can lead to amyloid plaques and/or neurofibrillary tangles. I **recently identified the pathogens and their related antigens that cross-react with amyloid-beta**. Testing for these pathogens or their by-products may be critical in the war on AD. My research has further identified oral bacteria as important risk factors in AD, particularly as they can bypass the blood-brain barrier. **The IgG made against these antigens was shown to cross-react with amyloid-beta peptide. In the presence of BBB breakdown, these interactions can contribute to plaque formation in the brain. However, knowledge of these pathogens and the role they play in AD is moot without the ability to measure their effect using reliable blood-based biomarkers.**

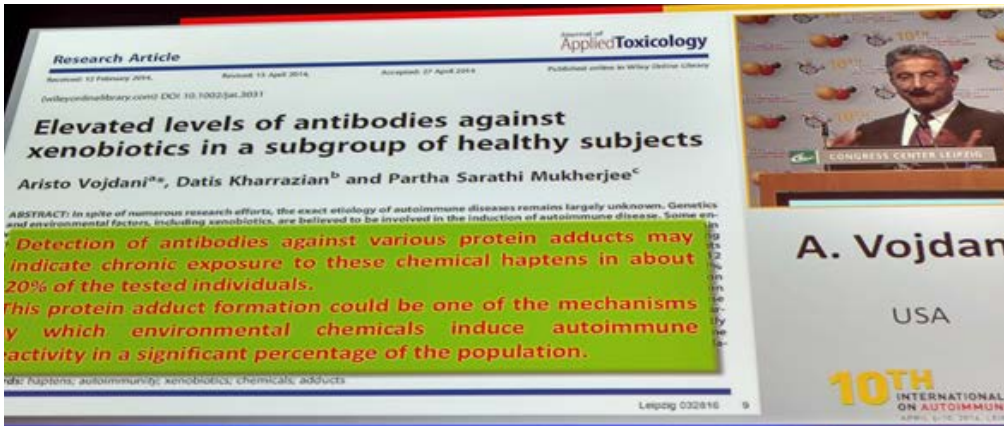
2. Chemicals

The role of aluminum and mercury in AD has been elucidated and well documented. In my study, I found that multiple aluminums, dinitrophenyl,

ethyl- and methyl-mercury and phthalates can contribute to AD. In the simplest terms, when these chemicals enter the body, they can bind to human tissue proteins. **When the chemical binds to the tissue protein, it can misfold the protein into a structure that is similar to amyloid-beta.** Because the new structure looks so similar to amyloid-beta, the antibodies made against the chemical bound to the human tissue can actually target the amyloid-beta peptide. This immune reactivity can lead to amyloid plaque formation. The Cyrex Alzheimer's LINX™ test exclusively measures antibodies in blood against these environmental toxins bound to human tissue proteins. Cyrex Array 11 - Multiple Chemical Immune Reactivity Screen™ offers blood testing for an expanded range of environmental chemical toxins bound to human tissues. The technology to test antibodies to these toxin-tissue complexes looks for immune reactivity to these toxins rather than merely their levels in blood or urine. Detection of high levels of chemicals in blood or urine is not an indication of the body burden of chemicals. This is why both Alzheimer's LINX™ and Array 11 measure antibodies to chemicals bound to human tissue proteins, which are an indication of the body burden of chemicals and its possible association with autoimmunities. Both of these panels are the result of years of research and development, and are available exclusively through Cyrex Labs.

3. Foods

As most scientific conferences focus on infections as a factor involved in AD, food as a trigger has been overlooked by the AAIC. This was also the case at the **International Congress on Autoimmunity** which meets every two years. But in 2016, speakers from Cyrex gave presentations for the first time on the correlation between food-specific antibodies, chemicals, and autoimmunity. In 2018, this prestigious international congress further embraced autoimmunity and neurodegenerative disorders as being triggered by food and other environmental triggers, with additional presentations by the Cyrex team.



Furthermore, I have been given the privilege of chairing an important session on the topic of diet and autoimmunity in next year's 12th International Congress on Autoimmunity May 20-24, 2020 in Athens, Greece.

To fully benefit from the Alzheimer's LINX™ test, it is recommended to repeat this test at least once a year in order to obtain an updated picture of the progression of key risk factors and the long-term effects of any intervention or lifestyle modifications.

The interaction between the immune system and food antigens with its potential to induce autoimmunity has now become so important that in July, 2019 an article was published in the Journal of Translational Autoimmunity by Gershteyn and Ferreira that gave a name to this new field of study: **Immunodietica**. Thus, the presence and participation of Cyrex in the international arena, its many and constant presentations and espousal of this important topic, and the recent release of the book, "Food-Associated Autoimmunities: When Food Breaks Your Immune System," by myself, continues to build on the leading role that Cyrex has assumed in this vital new scientific field.

Furthermore, my own study on the potential cross-reactivity between food protein IgG and amyloid-beta peptide revealed that the most reactive food antigens were raw and cooked egg yolk, lentil lectin, pea lectin, canned (cooked) tuna, hazelnut vicilin, cashew vicilin, scallops, squid, milk caseins, alpha-gliadin, gliadin toxic peptide and non-gluten wheat proteins. Because of their major cross-reactivity with amyloid-beta, these foods were incorporated into Alzheimer's LINX™.

Cyrex's Alzheimer's LINX™ - Alzheimer's Associated Immune Reactivity, is the culmination of my years of research and development. According to Dr. Carrillo, there is a "great need for simple, reliable, inexpensive, non-invasive and easily available diagnostic tools for Alzheimer's. Families facing Alzheimer's now and in the future would benefit greatly from simple and widely accessible diagnostic tools that enable accurate diagnosis earlier in the disease process, allowing for important care and planning."

By using Alzheimer's LINX™, personalized lifestyle modifications can be implemented to fit the needs of the individual patient. Lifestyle modification could then be employed as early as possible, even before the onset of symptoms. **For those with risk factors for AD, one can never be tested too soon, or start adopting a personalized healthy lifestyle too early.**

I am looking forward to presenting new perspectives, research and scientific discoveries in this special publication. Please feel free to connect at 877-772-9739, option 1, or at newsletterfeedback@cyrexlabs.com with your feedback/questions, and how we can best help you in your clinical practice.

Warm regards,

Aristo Vojdani, PhD.

For further reading about Alzheimer's LINX™ and/or to create an account, visit JoinCyrex.com