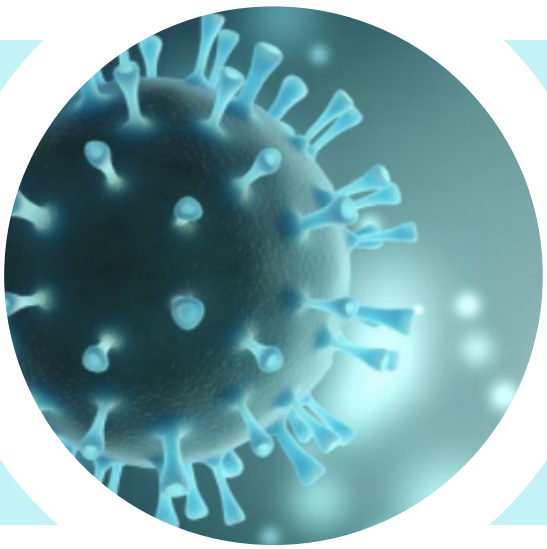
NUTRITION GENOME

12 WEEK PRACTITIONER TRAINING



WEEK 12, TOPIC 1:
GENETIC SUSCEPTIBILITIES TO AUTOIMMUNE DISORDERS

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Autoimmunity is believed to develop when genetically predisposed individuals encounter environmental agents that trigger the disease. The number of validated genes is growing rapidly in the field of autoimmune disorders, and the most recent research is showing that the environment can contribute to autoimmunity by modifying gene expression through epigenetic mechanisms.

⁎Studies (⁎Refer to online article for study link) in identical twins have shown that the genetic susceptibility, however, is insufficient and that the environmental epigenetic effect appears to be playing a stronger role in autoimmune disease. It is the epigenetic component that researchers haven't been able to fully elucidate.

Many autoimmune diseases occur more frequently in women, and researchers have pointed towards the hormonal connection which alters Th1-mediated immune responses and altered T cell homing. When combined with chronic stress and toxicity, the Th1 immune system can become dysfunctional. It can become more complicated case by case with Th1 and Th2 balancing, but we will be focusing on understanding how the Nutrition Genome Report can help determine genetic susceptibilities and epigenetic triggers for each individual.

Genes, Heavy Metal Detoxification and Autoimmune Disorders

The genes associated with mercury levels and toxicity include MTHFR 1298, GSTM1, GSTP1. Mercury-sensitive individuals are more likely to have allergies, asthma, and autoimmune-like symptoms, especially rheumatoid-like ones. The ingestion of mercury is oftentimes associated with increased levels of yeasts, bacteria, and molds which are thought to function in a protective manner to absorb excess mercury from the body.

Aggressively eliminating Candida albicans and other pathogens by antibiotics with a significant body burden of toxic metals may cause the sudden release of large amounts of toxic metals. **Mercury overload has been associated with a number of autoimmune conditions including Hashimoto's disease, multiple sclerosis, rheumatoid arthritis, and lupus.**

Mercury affects insulin, estrogen, testosterone, and adrenaline levels. Insulin has three sulfur-binding sites which can be bound by mercury causing the interference with normal biological function and a dysregulation of blood glucose levels.

One ⁎Studies (⁎Refer to online article for study link) provided robust evidence that brain-reactive antibodies are increased in mothers of an Autism Spectrum Disorder (ASD) child and may be associated with autoimmunity. The analysis of ASD mothers with brain-reactive antibodies also revealed an increased prevalence of autoimmune diseases, especially rheumatoid arthritis and lupus.

HLA Genes and Autoimmune Disorders?

Much of the current literature has focused on the HLA genes for autoimmune disorders. However, the HLA genes have also been associated with gluten sensitivity, peanut allergies, and mold sensitivity. The problem is that the results are inconsistent. When the Nutrition Genome Report looked at the HLA genes for gluten sensitivity and peanut allergies, it was inaccurate for the majority of patients despite what the research literature said. This is why we say that genes need to pass the research test and the clinical test.

The reason that these were inaccurate markers is that epigenetic factors are much more relevant. Unlike true celiac disease, gluten sensitivity stems from epigenetic changes to the microbiome and the digestive system that creates a sensitivity. We have seen this and peanut allergies skyrocket. Theories for this increase include changes in the microbiome, the obsession with antibacterial products and a sterile environment, low vitamin D levels, and a poorly diversified diet early in life. Cruciferous vegetables and omega-3 fatty acids in particular have been shown to suppress food allergies in mice studies.

It doesn't appear that autoimmune disorders and mold sensitivities are coming from one set of genes, but a combination of genetic pathways that involve hormones, deficiency, toxicity, and inflammation. Second, it appears that many autoimmune disorders have a similar etiology, yet the subtle differences in individual biochemistry manifest as unique autoimmune disorders.

Hashimoto's Disease

In many cases, hypothyroidism is caused by Hashimoto's Disease. Hypothyroidism occurs 10 times more in women than in men. The list is long for what affects the thyroid. In terms of heavy metals, autopsy studies in 1975 revealed that the thyroid and pituitary retain and accumulate more inorganic mercury than the kidneys. Mercury blocks thyroid hormone production by occupying iodine-binding sites and inhibiting or altering hormone action leading to the impairment of body temperature control, hypothyroidism, thyroid inflammation and depression. Fluoride and bromide will also block iodine uptake.

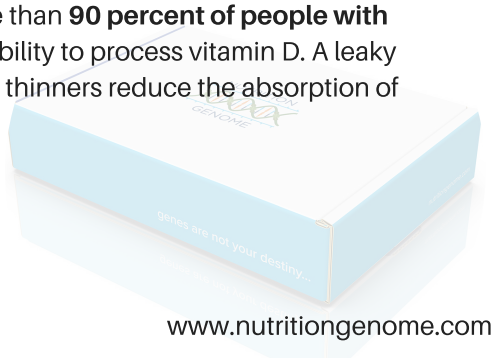
Thyroid peroxidase antibodies (TPO Ab) is an enzyme in the thyroid responsible for thyroid hormone production. A test for TPO is the most important because Hashimoto's most commonly occurs when the immune system attacks TPO. Thyroglobulin antibodies (TGB) is produced in the thyroid and is used by the gland to produce thyroid hormones. New moms are at a greater risk for Hashimoto's and some women flip from hyperthyroidism to hypothyroidism after pregnancy, which can look puzzling on blood work. People with Hashimoto's are also at increased risk of developing other autoimmune disorders.

Here are the potential triggers of Hashimoto's Disease:

- Estrogen fluctuations after pregnancy
- Gluten intolerance
- Insulin resistance
- Polycystic Ovary Syndrome
- Vitamin D deficiency
- Epstein Barre
- Lyme Disease
- Mold infections
- Poor digestion
- Environmental toxins
- Heavy metal toxicity

Genetic Connections to Hashimoto's Disease

VDR and CYP2R1: Studies in Japanese, Chinese and Croatian patients found that more than **90 percent of people with autoimmune thyroid disease** have a genetic polymorphisms in VDR that affect their ability to process vitamin D. A leaky gut, high stress, obesity, inflammation and certain medications like antacids and blood thinners reduce the absorption of vitamin D absorption further.



The VDR receptor requires magnesium, calcium, vitamin A, vitamin K2, boron and zinc to function properly. Assessing these nutrients both through genetic SNP requirements, diet, supplementation and medication-induced depletions help determine receptor requirements.

FADS1 and FADS2: Variants in these genes can help show you a higher need for EPA and DHA, which support T-regulatory cells. There have been a number of clinical trials assessing the benefits of fish oil in several inflammatory and autoimmune diseases in humans, including rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, lupus, multiple sclerosis and migraines.

Multiple Sclerosis (MS)

Research claims that HLA gene factors account for 20–60% of the MS genetic risk. However, there is a discordance rate of 70% among identical twins that shows environmental factors in disease pathogenesis. Studies of individuals with similar genetic backgrounds but living in different parts of the world have revealed significant differences in disease prevalence, especially from sunlight exposure. The Epstein–Barr virus (EBV) infection has also been implicated in the inflammatory response in MS. Increased levels of the proinflammatory cytokines IL1, IL4, IL6 and TNFα, and decreased levels of anti-inflammatory cytokines IL10 and IL4 have been reported to correlate with disease progression.

GAD1 Genes

MS affects three times as many women as men, showing a hormone connection. Both estrogen and testosterone have been shown to be neuroprotective. Both hormones have been shown to reduce glutamate-induced neuronal cell death.

T cells of MS patients respond abnormally to glutamate. Glutamate by itself activates resting normal human T cell and induces/elevates key T cell functions. T cells can even produce and release glutamate and affect other cells and themselves via their own glutamate. In MS, there are excess glutamate levels, and multiple abnormalities in glutamate degrading enzymes, glutamate transporters, glutamate receptors and glutamate signaling. Glutamate released from autoreactive T cells induces excitotoxic cell death of neurons. The evidence accumulated shows that abnormal glutamate levels and signaling in the nervous system, direct activation of T cells by glutamate, and glutamate release by T cells, can all contribute to MS. Review all of the genes associated with glutamate in Week 6.

Histamines and MS

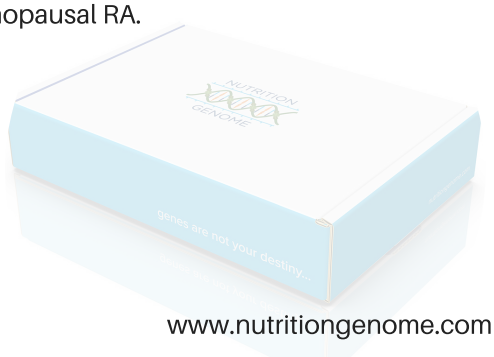
Cerebrospinal fluid histamine levels in MS patient samples have been *found (*Refer to online article for study link) to be significantly higher, making the histamine genes also points of interest.

CYP2R1, VDR, GAD1, BDNF (found *lower (*Refer to online article for study link) - in MS patients), PEMT (choline is neuroprotective), APB1 and HNMT should be reviewed for MS.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting approximately 3% of the population worldwide and characterized by chronic inflammation and destruction of the synovial joints leading to progressive joint damage and disability. Familial and twin studies suggest a greater than 50% genetic contribution to RA. The familial risk due to the HLA genes has been estimated to be less than 30%, suggesting that non-HLA genes may play a significant role in RA susceptibility.

Sex hormones appear to play an important role as modulators of autoimmune disease onset/perpetuation. The peak incidence in females rheumatoid arthritis coincides with menopause when the ovarian production of sex hormones drops markedly. Animal studies have revealed distinct beneficial effects of estrogens on arthritis, and a positive effect of bioidentical hormone replacement therapy has been reported in women with postmenopausal RA.



GAD1 and BDNF Genes

Glutamate signaling is very relevant for rheumatoid arthritis. **Glutamate concentrations in synovial fluid have been reported to increase more than 50-fold in patients with RA compared to controls**. The common treatment for RA is the drug sulfasalazine, which targets glutamate signaling. Researchers have stated that "modulation of glutamate signaling may alleviate RA symptoms."

CYP2R1 and VDR Gene

Vitamin D plays an important immunomodulatory role and appears to appreciably reduce RA symptoms. **A Swiss trial found that 86% of 272 RA patients had deficient or insufficient levels of vitamin D.**

The vitamin D receptor is located on the surface of immune cells. Because immune cells play an important role in promoting inflammation in RA, it seems logical that vitamin D would also have a role in RA mediated inflammation. Vitamin D does more than just arrest damaging immune cells, it also strengthens protective immune cells. T-reg cells are specialized components of the immune system that help keep immunity balanced. If too few T-reg cells are present, the immune system becomes overactive as in autoimmune diseases like RA. Vitamin D increases the number of protective T-reg cells, restoring equilibrium to an overactive immune system.

NBPF3 and TNF-α Gene

The prevalence of vitamin B6 deficiency is elevated in people with RA. This deficiency has been associated with more severe symptoms. A study found that treatment with 100mg daily of vitamin B6 reduced blood levels of TNF-α and other pro-inflammatory cytokines in people with RA. A folate deficiency is particularly common in people RA being treated with methotrexate, as this drug depletes folate.

Curcumin (turmeric) is one of the recommendations for lowering TNF-α in the Nutrition Genome Report. One study found curcumin alone powerfully suppressed CRP (a marker of inflammation in the blood) by 52% from baseline, while diclofenac sodium alone only decreased CRP by 1.5%. The investigators of this trial remarked that "Taken together, our present results provide a clear proof-of-principle for the superiority of curcumin, and the lack of any synergistic or additive efficacy, when used in conjunction with diclofenac strongly favors the safe and effective application of curcumin alone in clinical settings for the management of rheumatoid arthritis and other pro-inflammatory diseases including cancer in the future."

Summary

When reviewing the Nutrition Genome Report for patients with autoimmune disorders, it is useful to review the genetic susceptibilities to discover the most relevant pathways to understand the manifestation of the disorder, but perhaps more importantly, analyze the epigenetic triggers and how are they affecting those genes.