

Health Bits and Pieces (HFN 35:4) Written By Dan Kenner

Choosing your Poison

The cancer treatment industry has been heavily promoting “precision oncology,” using genetic testing to attempt to select drugs that will target the patient’s specific mutations in tumor tissue. The goal is long-term remission and increased survival time. The hope for this new approach to oncology is built on a very small pool of apparent responders. In a search of 489 articles, 32 exceptional responders were identified. Many patients have undergone genetic sequencing in the past decade. One commercial provider of tumor profiling, Foundation Medicine, has sequenced at least 18,000 patients. The “Molecular Analysis for Therapy Choice” at the U.S. National Cancer Institute (the NCI-MATCH) trial enrolled 795 patients with relapsed solid tumors or lymphoma, but as of May 2016 it was only able to successfully pair 2% of patients with a targeted therapy. It is estimated that only 1.5% of patients receiving genetically customized therapy could benefit. It is also not clear from the data if the positive responses resulted from the treatment or if they reflect the patient’s underlying biology.

Johnson D, Dahlman K, Knol J, et al., “Enabling a genetically informed approach to cancer medicine: A retrospective evaluation of the impact of comprehensive tumor profiling using a targeted next-generation sequencing panel,” Oncologist 19:616– 622 (2014) Crossref, Medline; Prasad V, “Perspective: The precision-oncology illusion,” Nature 537, S63 (08 September 2016); doi:10.1038/537S63a.

Acetyl L-Carnitine and Depression

A review published in *Psychosomatic Medicine* stated that the amino acid acetyl L-Carnitine, one of the most researched brain nutrients, can significantly reduce symptoms of depression. The structure of acetyl L-Carnitine is similar to the neurotransmitter acetylcholine, such that it can stimulate acetylcholine receptors in the brain. In nine randomized controlled trials (RCTs), 231 individuals were treated with acetyl L-Carnitine, 216 with a placebo, and 20 with no intervention. The results showed that acetyl L-Carnitine significantly reduced symptoms of depression. In three other RCTs, acetyl-L-Carnitine was compared with antidepressant drugs, with 162 participants in each group. Acetyl L-Carnitine was found to be as effective as antidepressants in decreasing depression symptoms. With no negative side effects, the amino acid would be an obvious better choice.

Veronese N, Stubbs B, et al., “Acetyl-L-carnitine Supplementation and the Treatment for Depressive Symptoms: A Systemic Review and Meta-analysis,” Psychosomatic Medicine, 25 October 2017, doi: 10.1097/PSY.0000000000000537. [Epub ahead of print]

Leaky Gut and Glutamine

In a European study, researchers found that supplementation with glutamine prior to exercise improves intestinal permeability in runners. “Leaky gut” is a disorder of selective permeability of the intestinal barrier. The intestinal barrier is only one-cell-layer thick and excessive permeability can result in large molecules (macromolecules) and bacteria entering the blood or lymph. The body then often reacts with an inflammatory response that can affect many types of tissues. Leaky gut is a significant issue for athletes because of the sometimes-excessive stress they put on their bodies. Gastrointestinal discomfort is a common complaint among

endurance athletes who participate in marathons and triathlons as well as athletes who engage in heavy exercise such as powerlifting.

Pugh J, Sage S, et al., "Glutamine supplementation reduces markers of intestinal permeability during running in the heat in a dose-dependent manner," European Journal of Applied Physiology, 2017; 117(12):2569-2577. doi: 10.1007/s00421-017-3744-4. Epub 2017 Oct 20.

Resveratrol and Diabetes

Resveratrol is a grape polyphenol with powerful antioxidant and anti-inflammatory properties. Its cardiovascular, anti-carcinogenic, and anti-aging benefits have been widely publicized. A systematic review of 9 randomized controlled trials showed that resveratrol, at a dosage of at least 100 mg/day, significantly reduced fasting glucose levels in individuals with Type-II diabetes. It also reduced blood pressure, fasting insulin levels, and HOMA-IR, which is a method for assessing pancreatic β -cell function and insulin resistance. This study used the same dosage of 100 mg, which has been shown to reduce fasting glucose level, as used in a previous study published earlier this year in the *International Heart Journal* (where researchers demonstrated resveratrol's benefits in improving arterial stiffness and reducing oxidative damage in patients with Type-II diabetes) and as reported in the previous edition of Health Bits & Pieces (Fall 2017; Vol. 35, No.3; p. 23).

Resveratrol can benefit diabetics by means of several mechanisms. It facilitates vasodilatation by binding and activating estrogen receptors to increase nitric-oxide availability. It also decreases oxidative stress in vascular endothelial cells, such as those in the arterial lining. Oxidative stress is elevated in chronic diseases like diabetes and obesity. These results support the ability of resveratrol supplementation to improve symptoms and slow progression in patients with Type-II diabetes.

Zhu X, Wu C, et al., "Effects of resveratrol on glucose control and insulin sensitivity in subjects with type 2 diabetes: systematic review and meta-analysis," Nutrition & Metabolism, 2017 Sept 22;14:60.

Autism and Supplements

Autism spectrum disorder (ASD) is associated with various genetic, neurologic, metabolic, and immunologic factors. Pharmaceutical and behavioral therapies are often used but their success is limited. Since there is no effective conventional treatment, dietary interventions and nutritional supplements are often used with these patients. In a review published in the *European Journal of Nutrition*, researchers evaluated the safety and effectiveness of five dietary supplements in children with autism. The review examined 18 studies evaluating vitamin B-6, magnesium, methylcobalamin (a type of Vitamin B-12), Vitamin D, omega-3 fatty acids, and folic acid. Previous research has shown that Vitamin B-6 and magnesium are involved in the synthesis of three brain neurotransmitters: serotonin, dopamine, and norepinephrine. Vitamin B-12 deficiency has been associated with neurotransmitter imbalances because it is necessary for the synthesis of myelin, the membrane that envelops nerve fibers.

According to the results of the review, Vitamin B-12, Vitamin D, and essential fatty acids were recommended to address a deficiency, but Vitamin B-6 and magnesium were not. Further research is needed to determine any beneficial effect on ASD. One of the studies on Vitamin D suggested that taking it could significantly improve the core symptoms of ASD. Folic acid was

found to be effective and also improve the symptoms of ASD. Autism Spectrum Disorder has been associated with abnormalities of folic-acid metabolism. Studies have also shown a deficiency of cerebral folate in autism. Folate must be obtained in the diet or from supplementation since the body cannot synthesize it. In one study, researchers observed significant improvements in verbal communication and other ASD symptoms after 12 weeks of supplementation with folic acid.

Li YJ, Li YM, Xiang D, "Supplement intervention associated with nutritional deficiencies in autism spectrum disorders: a systemic review," European Journal of Nutrition, 2017; September 7. doi: 10.1007/s00394-017-1528-6.

Vitamin D or Flu Vaccine?

A meta-analysis of 25 high-quality studies undertaken and published in the *British Medical Journal* found that Vitamin-D supplementation is a safe and effective way to minimize risk of acute respiratory infections. The studies reviewed comprised data from almost 11,000 participants. All of the studies were randomized, double-blind, placebo-controlled studies that had been approved by a research ethics committee. According to the meta-analysis, one person out of every 33 taking Vitamin-D supplements would be spared infection, which is more effective than flu vaccination, which supposedly needs to be used in 40 people in order to prevent one case.

The study found that people who took daily or weekly Vitamin-D supplements were less likely to report acute respiratory infections, and that people with significant Vitamin-D deficiencies (blood levels below 10 [ng/mL]) taking a Vitamin-D supplement cut their risk of respiratory infection in half.

Other studies have illuminated risk vs. benefit of influenza vaccination. One study showed that people who received the seasonal flu vaccine in 2008 had twice the risk of getting the H1N1 "swine flu" compared to those who didn't receive a flu shot. Another study showed that children who receive influenza vaccinations have a three times higher risk of hospitalization from influenza.

Research also shows that taking statin drugs may undermine your immune system's ability to respond to the flu vaccine. Because of the low rate of efficacy of the flu vaccine, the effect of taking a statin could offset any possible benefit from a vaccine.

Martineau A, Jolliffe D, Hooper R, et al., "Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data," British Medical Journal, 2017; 356 :i6583 <http://www.bmj.com/content/356/bmj.i6583>; Skowronski D, De Serres G, Crowcroft N, et al., "Association between the 2008–09 seasonal influenza vaccine and pandemic H1N1 illness during spring–summer 2009: four observational studies from Canada," PLoS Medicine, 2010; Apr 6;7(4); American Thoracic Society, "Children Who Get Flu Vaccine Have Three Times Risk Of Hospitalization For Flu, Study Suggests," ScienceDaily, 20 May 2009, www.sciencedaily.com/releases/2009/05/090519172045.htm; Black S, Nicolay U, Del Giudice G, Rappuoli R, "Influence of Statins on Influenza Vaccine Response in Elderly Individuals," Journal of Infectious Diseases, 2016; Apr 15;213(8):1224-8. doi: 10.1093/infdis/jiv456. Epub 2015 Oct 28.