DNA TESTING

FOR COMPLEX INFLAMMATION PATIENTS

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Inflammation is the body's normal defence mechanism against injury or infection. It is usually short-lived, however when it lasts too long it can become chronic. Chronic inflammation plays a crucial role in the development of conditions such as obesity, type 2 diabetes, rheumatoid arthritis, asthma, and even cancer.[1,2]

Genetic information obtained from a DNA test provides an insightful tool that can help manage and bring clarity to a patient's clinical picture. In particular, DNA testing can bring insight into three aspects of inflammation:

1. Uncovering the root cause of chronic inflammation by highlighting genetic predispositions to oxidative stress;
2. Reducing inflammation by identifying genetic weaknesses in cytokine pathways and unveiling specific anti/pro-inflammatory nutrient requirements; and
3. Contributing to understanding the body's ability to resolve inflammation by identifying genetic requirements for pro-resolving mediator lipids.

1. DNA Testing and Root Cause of Inflammation

As practitioners, it is not uncommon to deal with complex cases, where the patient presents with inflammatory traits but has not improved with conventional management. This can be frustrating both for the patient and the practitioner. DNA testing allows practitioners to focus on the predisposition to oxidative stress, a crucial aspect of inflammation. In fact, metabolically there is a tight and fundamental cross-talk between oxidative stress, DNA damage and inflammation. Genetic polymorphisms can influence the susceptibility to and how the body reacts to oxidative stress and DNA damage. Looking into key SNPs in genes linked to Glutathione, Nitric Oxide, Catalase, Superoxide dismutase and more gives the practitioner a wider understanding of the patient's genetic weaknesses and strengths that have an impact on the inflammatory response. Each of these SNPs can contribute to understanding the root cause of their condition and guide treatment recommendations.

> Under inflammatory conditions, nitric oxide is generated from nitric oxide synthases such as NOS1 and NOS2. Sustained production of nitric oxide produces oxidative stress and can cause DNA damage.

Variants in NOS1 and NOS2 have an impact on oxidative stress and therefore on inflammation pathways.[3,4] Knowing an individual's NOS1 and NOS2 genetic makeup can help understand their predisposition to oxidative stress upon inflammation and provide guidance on specific nutrients that can improve their function. Carotenoids, polyphenols, and DHA can improve NOS1 and NOS2 function.[4,5] These nutrients may be recommended to a patient with variants in these genes to help re-establish balance in their antioxidant and inflammatory pathways.

Another important player is Glutathione, which is involved in oxidative stress, detoxification and immunity. Several genetic polymorphisms in Glutathione genes including GPX1, GSTM1, and GSTP1 may predispose to low Glutathione levels, higher oxidative stress and reduced antioxidant protection.[6,7,11,12] This in turn causes too many free radicals that can damage healthy cells, leading to inflammation.

If your patient has a genetic profile with several risk variants in Glutathione-related genes, this might indicate their oxidative stress level may be causing or contributing to chronic inflammation. In this case, specific nutrients supported by the evidence that target Glutathione genes can be recommended. For example, curcumin, ginger and quercetin have the ability to induce GSTP1 expression.[13,14,15] Studies have shown that cruciferous vegetables may be beneficial for GTSM1 risk allele carriers to improve their antioxidant abilities.[6,13] Exposure to cold temperatures, vitamin C, vitamin E, and ginger can all assist GPX1 function.[7,8,9,10]

As Glycine and Cysteine are the major amino acids for Glutathione production, it's important to provide these amino acids to protect the body from oxidative damage during the immune response. A gene related to Glycine requirements is COL1A1 whose polymorphisms are associated with low type-1 collagen production, and therefore also increase Glycine requirements.[16,17] Another gene is CTH1 which converts cystathionine into cysteine and therefore has an influence on Cysteine availability. The functionality of both these genes contributes to the influence of Glutathione levels.[12] Foods rich in Cysteine such as meat, eggs, nuts and legumes are recommended for risk allele carriers of CTH1, and collagen protein from bone broth, gelatin, and meat with the skin can be recommended to increase dietary Glycine, and ultimately support Glutathione production. [19,20]

Boosting Glutathione can also be accomplished with Selenium, which supports GPX1 function.[7] Interestingly, Glutathione has been found to increase significantly with deep breathing practices like Tai Chi or yoga, as well as a combination of aerobic exercise and circuit weight training.[21,22,23]

2. DNA Testing and Reducing Inflammation

Inflammation in the body can be reduced or resolved, and these are two distinct mechanisms.

A series of immunoregulatory molecules called cytokines, together with receptors and inhibitors, control the pro- and anti-inflammatory response. Perturbations of the dynamic balance between pro- and anti-inflammatory cytokines may be due to genetic, environmental or other causes.[24] A DNA test can identify disruptions in genes affecting cytokine balance. For example, polymorphisms in the genes encoding pro-inflammatory cytokine receptor TNF-α and cytokine IL6 might contribute to a genetic predisposition to inflammation.[25,26]

Other genetic variants may influence the anti-inflammatory ability of a patient, as is the case for PEMT which catalyses the synthesis of phosphatidylcholine. Choline is a methyl-donor that plays an important role in healthy cell membranes to protect against inflammation.[27] A patient with polymorphisms in PEMT may have an increased requirement for dietary choline which is needed to help reduce inflammation.[28]

3. DNA Testing and Resolving Inflammation

Complete resolution of an inflammatory response is essential for health. **Resolution is an active process during which pro-resolution lipid mediators are generated. These mediators include molecules derived from the omega-3 essential fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[29] EPA and DHA play a crucial role in the inflammation process.** Evidence shows that changing the composition of arachidonic acid, EPA and DHA in the cells involved in inflammation appears to be especially important.[30] Therefore, having adequate levels of EPA and DHA is crucial not only for anti-inflammatory but also pro-resolving processes.

Currently, the published evidence reports several clinical studies still in progress aimed at identifying the main genes for the resolution of inflammation. What's known so far is that FADS1 and FADS2 genes are involved in fatty acid metabolism. Variants in these genes may influence the ability to convert alpha linolenic acid (ALA) to EPA, which has an impact on EPA and DHA requirements.[31] Therefore, considering a patient's genetic profile for the FADS genes can add value in understanding their inflammatory status and assist in making nutritional recommendations.

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