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## Immuno Genomic Profile Results

This profile identifies genetic single nucleotide polymorphisms associated with increased risk of developing defects in immune competence and surveillance. Immune system polymorphisms have been associated with increased risk of asthma, atopy, osteopenia, arthritis, heart disease, auto-immunity and infectious diseases.

### Chronic Inflammation

**IL-1 $\beta$ :** Interleukin 1-beta, produced mainly by blood monocytes, mediates the panoply of host inflammatory reactions collectively known as acute phase response. Polymorphisms in IL-1 $\beta$  may predispose individuals to chronic inflammatory conditions by upregulating COX2 activity and prostaglandin production. Other effects include hypochlorhydria, predisposition to H. pylori infection and gastric cancer.

### TH-1 Cytokine (Viral Infection & Cancer)

**TNF- $\alpha$ :** Tumor necrosis factor-alpha is a pro-inflammatory cytokine that can contribute to arthritis, asthma and osteoporosis. Polymorphisms of TNF- $\alpha$  inappropriately activate inflammatory response and increase TNF- $\alpha$  production.

### TH-2 Cytokines (Allergy, Asthma & Atopy)

**IL-4:** Polymorphisms in Interleukin-4 lead to increased IL-4 production and to decreased barrier function in lung epithelial cells causing a hyper-responsiveness to antigen stimulus, leading to increased risk and severity of bronchial asthma.

**IL-6:** Interleukin-6 contributes to inflammatory response and also affects adipose tissue metabolism, lipoprotein lipase activity, and hepatic triglyceride secretion. This particular SNP has been associated with elevations in serum triglycerides in response to carbohydrate intake and decreased levels of HDL cholesterol.

**IL-10:** Interleukin-10 has an inhibitory effect on TH-1 cytokine production. Polymorphisms in IL-10 may affect the risk of frequent viral infections, cancer and auto-immune diseases such as rheumatoid arthritis or lupus (SLE).

**IL-13:** Interleukin-13 acts to promote IgE synthesis and IgE-based mucosal inflammation typical of atopy and bronchial asthma. These SNPs are associated with increased IL-13 production and activity.

## Immune Markers

### Chronic Inflammation

IL-1 $\beta$



### TH-1 Cytokine

TNF- $\alpha$



### TH-2 Cytokines

IL-4



IL-6



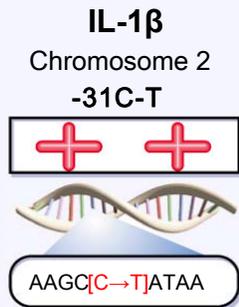
IL-10



IL-13



## Chronic Inflammation

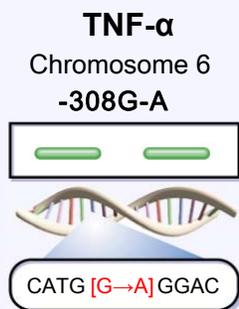


**HEALTH IMPLICATIONS:** Interleukin-1 $\beta$ , produced mainly by blood monocytes, is an inflammatory cytokine that can inhibit acid secretion in the stomach and stimulate bone resorption. This polymorphism increases IL-1 $\beta$  production, leading to increased inflammation. Increased IL-1 $\beta$  has also been shown to suppress hydrochloric acid secretion in the stomach, as well as increase susceptibility to *Helicobacter pylori* infection, gastritis and gastric cancer in *H. pylori*-infected individuals, and liver cancer in individuals with hepatitis C. This genotype may provide some protection against breast and lung cancer and GERD.

**MINIMIZING RISKS:** If *H. pylori* infection is present, eradication and mucosal repair are essential. Once repaired, regular betaine hydrochloride with meals may be warranted to prevent re-infection. Risk of atrophic gastritis and infection may be diminished by reduced alcohol consumption, avoiding smoking, and regularly ingesting fruit. Be careful with all NSAIDs, which reduce gastric blood flow and increase IL-1 $\beta$ . Production of IL-1 $\beta$  is suppressed by agents such as fish oils, L-glutamine, milk thistle (silymarin), curcumin, boswellia, ginkgo biloba, and resveratrol.

**FURTHER EVALUATION:** *H. pylori* stool antigen should be checked to determine if there is an active infection, especially if gastric ulcer symptoms are present. A bone resorption profile is recommended, especially in post-menopausal women.

## TH-1 Cytokine (Viral Infection & Cancer)

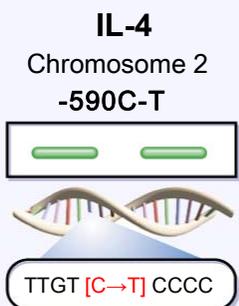


**HEALTH IMPLICATIONS:** Tumor necrosis factor, alpha (TNF- $\alpha$ ) is a pro-inflammatory cytokine secreted from activated macrophages, which plays an important role in host defense against infection. Excessive TNF- $\alpha$  release can result in inflammatory reactions and oxidative stress. A homozygous negative (- -) genotype is associated with decreased production of TNF- $\alpha$ , consequently decreased inflammatory tendency and oxidative stress. Risk is reduced for autoimmune disease, osteoporosis, and insulin resistance, but may also be associated with an increased risk of some cancers because of TNF- $\alpha$ 's anti-neoplastic properties.

**MINIMIZING RISKS:** Risk of inflammatory disorders is minimal. A diet and lifestyle associated with minimizing cancer risks is still prudent, including a diet rich in vegetables, fruits, and fiber, and properly balanced in essential fatty acids. Avoid smoking and minimize exposure to environmental pollution and toxins.

**FURTHER EVALUATION:** None indicated for this polymorphism.

## TH-2 Cytokine (Allergy, Asthma, & Atopy)

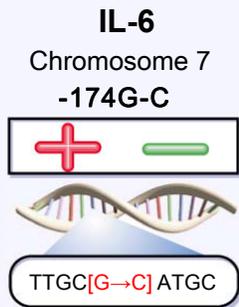


**HEALTH IMPLICATIONS:** Interleukin-4 is secreted by antigen presenting cells (e.g., macrophages and dendritic cells) and stimulates the differentiation of TH-2 cells and the increased production of IgE. Homozygous negative individuals for the IL-4 polymorphism have lower circulating levels of IgE and are at reduced risk for developing eczema, atopy, or asthma.

**MINIMIZING RISKS:** None recommended for this polymorphism.

**FURTHER EVALUATION:** If allergic symptoms are present, food and inhalant antibody assessment is warranted. If food antibodies are present, an intestinal permeability assessment may be of clinical value.

## TH-2 Cytokine (Allergy, Asthma & Atopy)



**HEALTH IMPLICATIONS:** Excess interleukin-6 inhibits lipoprotein lipase and stimulates hepatic triglyceride secretion. This polymorphism of IL-6 is associated with elevated plasma triglycerides, decreased HDL cholesterol, and increased fasting serum glucose. Thus the risk of developing heart disease and adult-onset diabetes is increased substantially with this polymorphism.

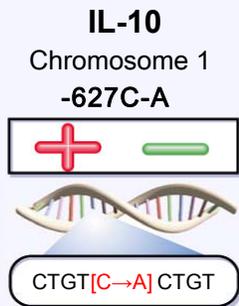
**MINIMIZING RISKS:** Since carbohydrates are the primary macronutrient stimulus for triglyceride synthesis, a lower carbohydrate diet with the elimination of simple carbohydrates is indicated. However, since excess IL-6 also impairs lipoprotein lipase activity, a low-fat diet is also indicated. Optimally a low-calorie, higher protein, lower carbohydrate, low-fat diet may be optimal. Fish oil supplementation has also been shown to decrease triglyceride levels.

Chronic stress increases concentrations of IL-6 in all individuals, thus, stress reduction and regulation may prove beneficial. Adequate sleep and regular aerobic exercise reduce stress response. Supplements that improve adrenal function and balance include vitamins C and B5, glycyrrhiza (licorice), and adaptogens like the various ginsengs, cordyceps, bacopa and ashwaganda (withania).

Both melatonin and beta-sitosterols from pine trees have been shown to decrease IL-6 production dramatically, reducing inflammatory tendency and improving cell mediated immunity.

**FURTHER EVALUATION:** A comprehensive cardiovascular assessment is indicated to estimate functional risk and to monitor therapeutic effectiveness. A metabolic dysglycemia assessment, including fasting glucose and insulin, can evaluate the risk of developing adult-onset diabetes. Individuals with a family history of heart disease should consider a Cardio Genomic profile for thorough assessment of predictive genomic risk.

## TH-2 Cytokine (Allergy, Asthma & Atopy)



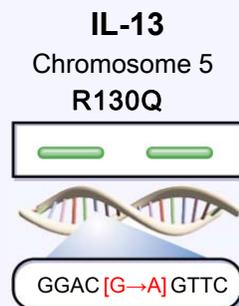
**HEALTH IMPLICATIONS:** Interleukin-10 is a predominately anti-inflammatory cytokine. IL-10 inhibits the synthesis of other, pro-inflammatory interleukins and acts synergistically with glucocorticoids to reduce inflammation. This polymorphism is associated with reduced secretion of IL-10 and therefore with greater tendency toward chronic inflammation including atherosclerosis, rheumatoid arthritis, inflammatory bowel disease, psoriasis, etc.

**MINIMIZING RISKS:** Therapies that reduce pro-inflammatory stimuli and that inhibit the acute-phase response may be beneficial. Specifically, regular consumption of cold water fish or supplementation with fish oils may reduce tendency to inflammation. Specific anti-inflammatories like boswellia, curcumin, quercetin, hesperedin, ginger, etc. may reduce inflammation, especially during acute inflammatory reactions.

Since IL-10 works synergistically with glucocorticoids, optimizing adrenal function may be helpful. Glycyrrhiza (licorice) has a well-documented glucocorticoid effect, with few of the side-effects associated with steroid use. Vitamins C and B5, as well as ashwaganda (withania) and the ginsengs may optimize adrenal responsiveness.

**FURTHER EVALUATION:** Since IL-10 is a TH-2 cytokine and plays an important role in humoral immunity, evaluation of food and inhalant antibody levels may be useful in identifying antigenic triggers of the inflammatory cascade.

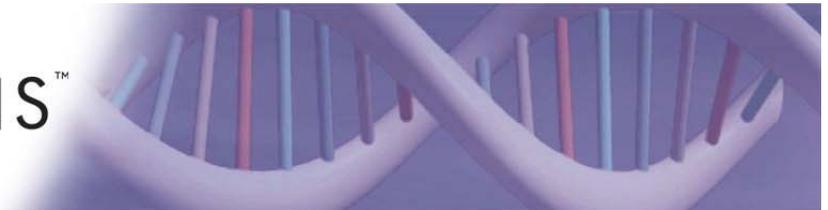
## TH-2 Cytokine (Allergy, Asthma & Atopy)



**HEALTH IMPLICATIONS:** Interleukin-13 stimulates inflammation in the airways and is required for the progression of hyper-responsiveness of airways to antigens leading to symptomatic asthma. The homozygous negative wild-type has normal serum IL-13 concentrations and has no increased risk for developing atopy and asthma. Polymorphisms in IL-4 are also known to play a role in developing asthma and atopy. These are measured elsewhere in this profile.

**MINIMIZING RISKS:** None indicated for this polymorphism.

**FURTHER EVALUATION:** None indicated for this polymorphism.



## *Optimizing your Genomic Potential*

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in the patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. The patient may have additional risk that is not measured by this test. Negative findings do not imply that the patient is risk-free.

DNA sequencing is used to detect polymorphisms in the patient's DNA sample. The sensitivity and specificity of this assay is < 100%.



## *Optimizing your Genomic Potential*

### **What is Inflammation?**

Inflammation is the primary means by which the body repairs cells and tissues that have been damaged. Inflammation also is the primary defense mechanism of our immune system fighting against a hostile environment that includes allergens, viruses, bacteria, yeast, etc. Cytokines are a class of polypeptide chemical compounds within the body that regulate both types of inflammation response. Interleukins are a specific subset of cytokines produced by white blood cells. Specific cytokines and interleukins can be either pro-inflammatory or anti-inflammatory. While a certain level of cytokines is always present in the blood, increased cytokine production can result from external stimulus (e.g., pollen or physical injury) but cytokine levels may also vary based on genetic polymorphisms. Increased production of a pro-inflammatory cytokine or decreased production of an anti-inflammatory cytokine can both result in chronic inflammatory conditions.

### **Your Body's Immune System**

The body's immune system may be broadly divided into two major functional categories: cell-mediated immunity (a.k.a. TH-1 immunity) that protects against viral infections and cancer; and humoral immunity (a.k.a. TH-2 immunity) that controls allergic response and antibody formation. These two branches of the immune system are mildly antagonistic: if one is up-regulated, the other is often down-regulated and vice-versa.

### **Immune-related Illnesses**

Imbalanced cell-mediated immunity can lead to frequent infections and to increased risk of developing certain cancers. Imbalanced humoral immunity can contribute to the development of allergy, asthma, atopy, eczema, inflammatory bowel disease, autoimmune disease, osteoporosis, and even atherosclerosis and heart disease. It is important for our long-term health to maintain balance in our immune response. We need adequate inflammation to ensure environmental defense and tissue repair, but without excess inflammation that can cause substantial cellular damage and numerous disease states.



## *Optimizing your Genomic Potential*

### Personalized Recommendations for Minimizing Risk

#### *Diet*



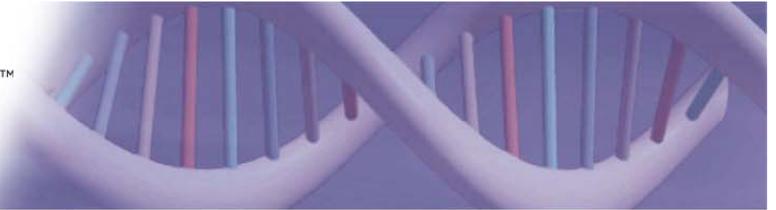
This section offers **dietary supplementation** considerations based on your unique genetic makeup. These are provided for educational purposes only and are not intended to diagnose or to treat any specific condition. Please consult with your healthcare practitioner for specific interpretation and therapeutic options.

-  Eat a diet rich in colorful fruits and vegetables as these are not only high in mineral content but also the primary source of dietary anti-oxidants, essential for minimizing inflammation.
-  A diet that is lower in total calories, lower in carbohydrates and higher in protein may be best suited for your genetic constitution.
-  Increased consumption of cold water fish and/or the consumption of fish oils should be considered in reducing the overall tendency toward inflammation.

#### *Lifestyle / Environment*



This section offers **lifestyle/environment** considerations based on your unique genetic makeup. These are provided for educational purposes only and are not intended to diagnose or to treat any specific condition. Please consult with your healthcare practitioner for specific interpretation and therapeutic options.



## Optimizing your Genomic Potential

### Nutritional Supplementation



This section offers **nutritional supplementation** considerations based on your unique genetic makeup. These are provided for educational purposes only and are not intended to diagnose or to treat any specific condition. Please consult with your healthcare practitioner for specific interpretation and therapeutic options.

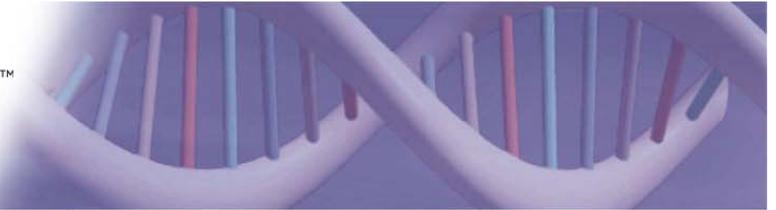
-  Betaine hydrochloride and deglycyrrhizinized licorice (DGL) should be considered to improve stomach HCl and mucous production. HCl should only be administered after gastric ulcers are ruled out. Long-term therapy may be needed.
-  Fish oils and milk thistle have been shown to suppress interleukin production directly, which in part accounts for their anti-inflammatory actions in the body.
-  If signs and symptoms of chronic inflammation are present, consider the use of botanical anti-inflammatories like boswellia (frankincense), glycyrrhiza (licorice), ginger, hesperedin and curcumin (tumeric).
-  Beta-sitosterols and beta-sitosterol glycosides extracted from pine trees have been shown to reduce IL-6 production.
-  Botanical support of adrenal function and stress reduction should be considered. Herbs to consider include ashwaganda, bacopa, cordycaps, licorice and American, Korean or Siberian ginseng.
-  Licorice, because of its glucocorticoid-like activity may be well suited for your genotype to minimize inflammatory tendencies.

### Pharmaceutical Considerations



This section offers **pharmaceutical considerations** based on your unique genetic makeup. These are provided for educational purposes only and are not intended to diagnose or to treat any specific condition. Please consult with your healthcare practitioner for specific interpretation and therapeutic options.

-  If signs and symptoms of acute or uncontrolled inflammation are present, consider the short-term use of corticosteroids like cortisol or prednisone.



## *Optimizing your Genomic Potential*

### *Genomic/Functional Laboratory Testing*



This section offers **genomic/functional laboratory testing** considerations based on your unique genetic makeup. These are provided for educational purposes only and are not intended to diagnose or to treat any specific condition. Please consult with your healthcare practitioner for specific interpretation and therapeutic options.

-  This individual has polymorphisms that increase his or her risk of developing heart disease. A full CardioGenomic profile may reveal more personalized therapeutics as a preventative strategy.
-  This individual may have polymorphisms that increase his or her risk of increased bone resorption and of developing osteopenia and osteoporosis. A full OsteoGenomic profile may reveal more personalized therapeutics as a preventative strategy.
-  IL-1B polymorphisms are associated with H. pylori infection and gastric ulcers; screening for serum H. pylori antibodies is recommended, especially if signs and symptoms of ulcers are present.
-  A bone resorption profile to assess the rate at which bone is being lost is indicated. This test may be run sequentially to assess effectiveness of your therapeutic protocol. A baseline bone density scan may also be indicated.
-  Markers present on your profile suggest the potential for chronic inflammation that may increase risk of developing heart disease. A comprehensive cardiovascular assessment should be considered to evaluate functional risk.
-  A metabolic dysglycemia profile including fasting and 2-hour insulin and glucose should be considered, especially if the waist-to-hip ratio is increased to >1.0 for men or >0.8 for women.
-  An adrenal stress profile may be warranted to assess your functional capacity for stress adaptation and response.