GenomicInsight™
POWERED BY OPUS23 EXPLORER™

Client Report

Full Name

Diagnostic Solutions Lab
www.diagnosticsolutionslab.com

Welcome to GenomicInsight

GenomicInsight® combines today's most advanced DNA testing with the powerful Opus23 Explorer® interface to produce the perfect combination of DNA testing, science, and current research. Opus23 Explorer® scans over 20 peer-reviewed, evidence-based scientific databases and cross-references their information with the results of your GenomicInsight® raw data. This report summarizes important findings from your genomic data that have been curated by your clinical team into a layperson-friendly format. Before we begin, let's introduce a few basic concepts to set the stage and advance your understanding a bit.

REPORT FOCUS

GASTROINTESTINAL

Diagnostic Solutions laboratory

OPUS23 EXPLORER

Welcome to Opus23 Explorer

Opus23 Explorer® is a very sophisticated computer program that looks for very simple things in your GenomicInsight® data: variations in the code of DNA (the A, T, C, and G of the genetic alphabet) that can exist between people. Not all of our DNA varies from person to person, but about 9% of it can. The variations are called 'snips' (SNPs) which stands for single nucleotide polymorphism.

Although SNPs are the 'letters' of individuality, genes are in fact the words and vocabulary. After all, it is the genes that have to do the work, coding for the construction for a myriad of enzymes and proteins. Because gene function is central to any sort of biochemical prediction, Opus23 Explorer® groups all the SNP outcomes with their parent gene, and presents its results as a reflection of the effectiveness of that gene. Although SNPs are pretty much unchangeable, our genes can be influenced (for better or worse) by lifestyle, diet, emotions and nutritional supplementation.

The DNA in our bodies is a double-stranded molecule, meaning that for every location that we might find a SNP there exists two letters, one for each strand. Taken together, these two letters comprise the **genotype** for that location. Over the years, much research has been done to examine whether a particular SNP variation (or mutation) can be shown to result in an effect on our health. For example, let's look at two different people, John and Jane. At location 12345678 on chromosome #1 most people, as does John, have the 'AA' genotype. It has been noticed that 15% of the population have one 'G' (genotype 'AG') while 5% of the population have genotype 'GG'. Separate studies show that people with at least one 'G' genotype have an increased risk of eczema. Jane's genotype at this location is 'GA' so she may have this susceptibility. As you might have noticed, genotypes come in two types: two identical letters ('GG', 'AA') known as *homozygous* and one of each letter ('GA' or 'AG') known as *heterozygous*.

Because the presence of a 'G' at this SNP location is associated with a condition, for this SNP 'G' is known as the *risk nucleotide* or *risk allele*. Most of the time, having the risk allele negatively impacts the function of its parent gene, but sometimes the mutations can convey a benefit or advantage.

Something like 99.6% of the human genome is identical in all people. This is true of everyone, regardless of race or heritage. However, it is at the SNP location that variation does take place. SNPs only make up a tiny portion of the genome (0.4%) but because the genome is so enormous, this equals over 12 million locations. It's the differences at these SNP locations that make each of us unique. If your genotype at SNP rs17822931 is TT, then you probably have dry earwax. If you have any other genotype at this SNP, then you have wet earwax.

By the way, you're **CC** for the rs17822931 SNP.

This owner's manual was produced by your clinician who, using the Opus23 Explorer® software, has curated what, in the great sea of data that Opus23 Explorer® provides, they believe is most important to your health care. It would be untrue (and unkind) to pretend that all of the material in this report will be easy to understand. Although the editors of Opus23 Explorer® try to provide explanations in layperson terminology when and where possible, things can get quite technical. Don't panic! Make note of your questions and remember to discuss them with your clinician at the next opportunity. Remember, this report is for your informational use only; the real magic of Opus23 Explorer® happens, like in the *Wizard of Oz*, 'behind the curtain,' where it provides a truly amazing depth of information and analysis to your clinician and where it can be used on an ongoing basis to identify, prevent and treat a wide variety of health problems.

Genetics can be complicated to the layperson. Sometimes a word is used to describe a gene function that you might not recognize. If *Opus23 Explorer* thinks that you might need some help with a technical term, 'Mr. Smart Owl' will try to explain it to you.

Now, a few caveats

Depending on how your health professional has decided to structure this report, you might find the information that follows to be intimidating or even potentially disturbing. For example, nobody enjoys hearing that they may have an increased risk for a disease or health complication. While Opus23 Explorer cannot guarantee that all of its findings will be of a positive nature, it's important to understand what this information can and cannot do. Let's discuss a few facts that you should keep in mind.

Advances in genetic technology have made the process of discovering new SNPs very easy. However the process of linking a SNP to particular trait or illness requires epidemiologic studies that are far more expensive and labor intensive. Thus there is a large gap between the SNPs we know and what in fact we know about them. Opus 23 Pro is constantly updated with new information and your health care provider can very easily update your data to include any new information as it arrives. Opus23 Pro strives to provide the most accurate possible data interpretation. As part of this mission, we constantly monitor and refine our data analysis algorithms. When an improvement is identified, the new algorithm becomes available immediately on creation. In that event, a corrected report will be available to your health care provider. Such re-analysis of patient data may lead to reclassification of your results.

Opus23 Explorer can only supply correlations and relationships

Opus23 Explorer can only compare your genetic data with published data linking your results to the outcomes in the research. It can't diagnose disease. Nor should it. However, it can point the way to areas of possible further clinical interest, and perhaps guide both you and your health care professional in the process of developing a more evidence-based approach to prevention. The etiology (cause) of many diseases is multifactorial; that is, disease can occur as a result of various factors, including both inherited and acquired genetic variants, diet, lifestyle choices and age.

Opus23 Explorer results are as good as the starting data

The interpretations given by Opus23 Explorer are the result of evaluated inherited genetic variants in data uploaded to our server, and interpretations are only as accurate as the data received from the genomic test. It is possible that inaccuracies in the genomic test results could lead to false interpretations. It is also possible that variants in genes and genetic regions not tested in the DNA sequencing test may contribute to an individual’s risk for disease. Therefore, a negative result in a gene where no pathogenic variants are detected does not eliminate the individual’s disease risk.

Genetic findings can only report the starting point

Your genome is similar to the blueprint for a house that is yet to be built. If the builder follows the architect's instructions exactly, the house will match the blueprint perfectly. However, all throughout the construction process alterations will most certainly be made: For example, if the new owners are running short on funds, perhaps the original plans for an expensive slate roof may have to be altered to a less expensive, though still-functional, asphalt version. It's the same with genomics, although variations in your gene data may reflect an increased or decreased risk of a health issue, many of these risks may have been altered by environmental factors (such as your pre-existing lifestyle and health habits) acting epigenetically to control the expression of these genes. If you've carefully watched your diet over time and kept your weight at a healthy level, a finding that you are at risk for obesity might do nothing more than encourage you to continue what you are already doing.

Genetic findings can only reflect probabilities

Very few gene mutations result in a direct, absolutely certain, health consequence. Most of the time, they instead reflect a change to your odds of developing a particular health condition. This is defined as the 'risk' for a certain event. This is usually expressed as an 'odds ratio' (OR). Understanding the meaning of an OR for a particular risk is a key to minimizing stress when encountering dire results. For example, being told you are 110% more likely to get struck by lightning (OR=1.1) is much less distressing when you realize that:

- This is a very small difference from normal
- Very few people get struck by lightning regardless

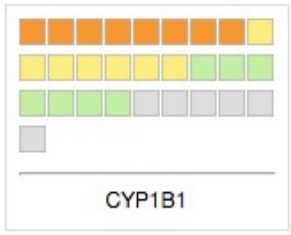
When it comes to a particular disease or syndrome, most SNPs have rather small ORs. This does not mean that they are unworthy of attention, but rather that the findings must be interpreted as part of an integrated whole, including: other SNP results that also support the conclusion; lifestyle factors; family history, and environmental exposures. Further, a positive test result does not guarantee an occurrence of disease since the SNP variants in most genes are not 100% penetrant (even genes with several risk SNPs will very likely function to some degree). Rather, pathogenic variants may predispose a person to a higher or lower risk of disease. The results of genomic testing must be interpreted in the context of your clinical history. Genetic counseling is recommended for the individual and for other at-risk family members.

And now, the usual indemnification statement:

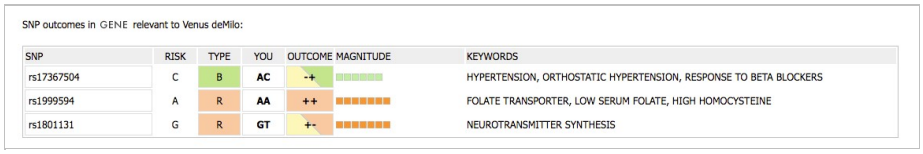
The data provided by Opus23 Explorer is for informational purposes only and is not designed or intended to suggest the treatment or diagnosis of any disease or condition. Opus23 Explorer and Datapunk Bioinformatics, LLC, take no responsibility for any harm arising from incorrect data being uploaded to our server or incorrect data interpretation, errors, or omissions by the software. By agreeing to access this Opus 23 Pro report you hereby agree to indemify Opus23 Explorer and Datapunk Bioinformatics, LLC from any consequences resulting fro the use or misuse of this information. The statements made on this page have not been evaluated by the FDA (U.S. Food & Drug Administration). This material is presented for informational and education purposes only and is not intended to diagnose, cure or prevent any disease.

Understanding the report

Each gene is depicted as a grid showing the result of its SNPs:



- The sum of the significant SNPs in the gene that indicate a higher (homozygous) risk are the orange squares
- The sum of the significant SNPs in the gene that indicate a lower (heterozygous) risk are the yellow squares
- The sum of the significant SNPs that are working just fine (no problem polymorphisms) risk are the gray squares
- You might even find that for some genes you may have a polymorphism that conveys some benefit. These are the green squares



SNP outcomes in GENE relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs17367504	C	B	AC	-+		HYPERTENSION, ORTHOSTATIC HYPERTENSION, RESPONSE TO BETA BLOCKERS
rs1999594	A	R	AA	++		FOLATE TRANSPORTER, LOW SERUM FOLATE, HIGH HOMOCYSTEINE
rs1801131	G	R	GT	+-		NEUROTRANSMITTER SYNTHESIS

Multi SNP macros

Macros (algorithms) are perhaps the most significant and flexible aspect of your Opus 23 data. They are usually the easiest result for the non-medical person to understand, because their conclusions are usually simplified statements in everyday language.

Many correlations between SNPs and various traits exist as 'haplotypes,' clusters of SNPs, often on different genes, that must be evaluated as 'true' or 'false' based on their total outcome values. Some algorithms may identify risks for certain problems, while others identify special strengths or benefits you might possess. It's helpful to think of an Opus 23 algorithm as a tiny flowchart, that depending on which way the result branches, generates a 'true or false' result.

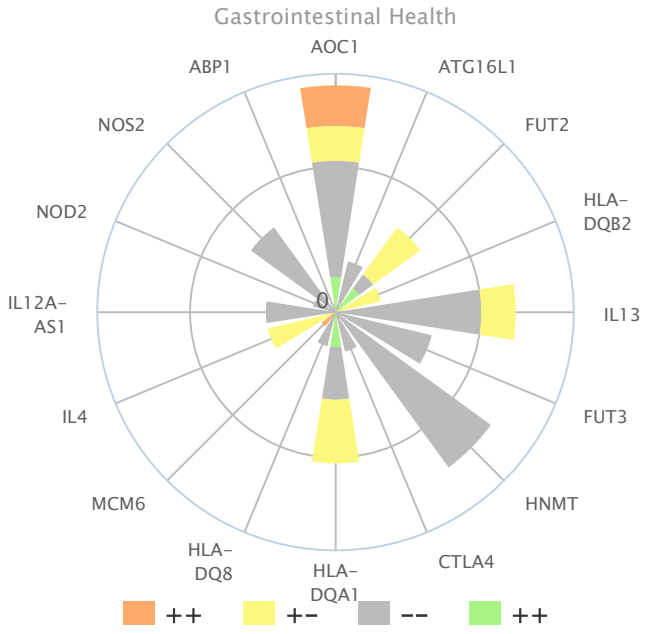
For example, a simple macro to determine if you should get out of bed might be:

- If you hear the alarm clock, open your eyes.
- If it's dark outside, go back to bed.
- If it's light outside, check the time.
- If it's earlier than 7AM, go back to bed.
- If it's later than 7AM, get up, check calendar
- If it's Saturday, go back to bed.

As can be seen, there are a lot of ways you can go back to bed with this algorithm! And this is also true as well for the Opus 23 Pro algorithms: In order for an algorithm to be true, it must fufill all of several conditions. *If even one condition fails, the whole algorithm will be false.*

Each macro algorithm is displayed in its own box, and contain information about the genes and SNPs used in its creation. The title of the algorithm is generally its conclusion. Typically, your report contains only true algoriths, although your clinical team may choose to include false algorithms as well, especially if it would be helpful to make you aware of something you're likely to not be prone to. Thus:

- An algorithm that returns a **true** will have a 'check' icon in the bottom left-hand box. The conclusions of these algorithms **pertain** to you based on your genomic data results.
- An algorithm that returns a **false** will have a 'cross' icon in the bottom left-hand box. The conclusions of these algorithms **do not pertain** to you based on your genomic data, other than perhaps the added knowledge that this is one less thing in life to worry about.



Gastrointestinal Health

Digestive diseases vary from common problems such as acid reflux to rare inherited liver conditions. Common areas that are linked to genetics involve inflammatory reactions such as seen with individuals who are sensitive to gluten (celiac); allergic reactions to foods through histamine imbalance, or foods that contain immunoreactive molecules known as lectins. Certain individuals may also be prone to GI problems due to genetic polymorphisms that influence bacterial imbalance in the gut (microbiome dysbiosis). Other GI issues may result from insufficient autophagy (Autophagy (the natural, regulated mechanism by which the cell removes unnecessary or dysfunctional components and allows the orderly degradation and recycling of cellular components.)

ABP1

amiloride binding protein 1 (amine oxidase (copper-containing))

The protein encoded by this gene is a bifunctional, cytosolic protein that functions as an essential enzyme in the TCA cycle and interacts with mRNA to control the levels of iron inside cells. When cellular iron levels are high, this protein binds to a 4Fe-4S cluster and functions as an aconitase. Aconitases are iron-sulfur proteins that function to catalyze the conversion of citrate to isocitrate. When cellular iron levels are low, the protein binds to iron-responsive elements (IREs), which are stem-loop structures found in the 5' UTR of ferritin mRNA, and in the 3' UTR of transferrin receptor mRNA. When the protein binds to IRE, it results in repression of translation of ferritin mRNA, and inhibition of degradation of the otherwise rapidly degraded transferrin receptor mRNA. The encoded protein has been

identified as a moonlighting protein based on its ability to perform mechanistically distinct functions. Alternative splicing results in multiple transcript variants [provided by RefSeq, Jan 2014]

SNP outcomes in gene ABP1 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- The *gene* is the fundamental physical and functional unit of heredity. A gene is an ordered sequence of nucleotides located in a particular position on a particular chromosome that encodes a specific product (i.e., a protein).
- A *receptor* is a molecule in a cell membrane, that responds specifically to a particular neurotransmitter, hormone, antigen, or other substance.
- *Translation* is the process in which the genetic code carried by mRNA directs the synthesis of proteins from amino acids.
- To *Catalyze* is to cause or accelerate (a reaction) by acting as a catalyst.
- *Ribonucleic acid (RNA)* is a chemical found in the nucleus and cytoplasm of cells; it plays an important role in protein synthesis and other chemical activities of the cell.
- *Proteins* are large molecules composed of one or more chains of amino acids. Proteins are required for the structure, function, and regulation of the bodys cells, tissues, and organs, and each protein has unique functions. Examples are hormones, enzymes, and antibodies.

AOC1

amine oxidase, copper containing 1

The AOC1 gene provides instructions for making the amine oxidase, copper containing 1 enzyme known as diamine oxidase, histaminase, misnamed 'DAO'. This is different to the DAO gene (D-amino-acid oxidase). It is found largely in the intestines and kidney, and breaks down histamine and other related compounds such as putrescine and spermine, substances involved in allergic response and the immune system. Lower AOC1 enzyme activity may be associated with inflammatory bowel disease such as Crohn's disease and

ulcerative colitis, as well as a form of asthma that is more easily triggered with normal levels of allergy-stimulating IgE antibodies.

SNP outcomes in gene AOC1 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2071517 *(*102G>A)*	G	B	**GG**	**++**		PROTECTIVE AGAINST HISTAMINE INTOLERANCE
rs10156191 *(47C>T Thr16Met)*	T	R	**TC**	**+-**		HISTAMINE INTOLERANCE NSAID HYPERSENSITIVITY
rs2052129 *(-691G>T)*	T	R	**TT**	**++**		HISTAMINE INTOLERANCE

ATG16L1

ATG16 autophagy related 16-like 1 (S. cerevisiae)

The ATG16L1 gene provides instructions for making a protein called autophagy related 16-like 1. This protein is part of a larger family of proteins that are required for a process called autophagy. Cells use this process to recycle worn-out cell parts and break down certain proteins when they are no longer needed. Autophagy also plays an important role in controlled cell death (apoptosis). Additionally, autophagy is involved in the body's inflammatory response and helps the immune system destroy some types of harmful bacteria and viruses.

The ATG16L1 gene belongs to a family of genes called WDR (WD repeat domain containing).

At least one variation in the ATG16L1 gene is associated with an increased risk of Crohn disease, particularly a form of the disorder that affects the lower part of the small intestine (the ileum). This increased risk has been found primarily in white populations. The identified ATG16L1variation changes a single protein building block (amino acid) in a critical region of the autophagy related 16-like 1 protein. Specifically, it replaces the amino acid threonine with the amino acid alanine at protein position 300 (written as Thr300Ala or T300A).

The effects of variations in the ATG16L1 gene on Crohn disease risk are unclear. Changes in this gene may affect the autophagy process, allowing worn-out cell parts and harmful bacteria to persist when they would otherwise be destroyed. These cell components and bacteria may trigger an inappropriate immune system response, leading to chronic inflammation in the intestinal walls and the digestive problems characteristic of Crohn disease.

SNP outcomes in gene ATG16L1 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- *Apoptosis* is the process of programmed cell death that may occur in multicellular organisms. In contrast to traumatic cell death from cellular injury, apoptosis is a highly regulated and controlled process that confers advantages during an organism's lifecycle.
- *Autophagy* (from the Greek "to eat self") is the natural, regulated process by which the cell removes unnecessary or dysfunctional cellular components, such as worn-out or mis-folded proteins and other cellular debris.
- *Amino acid* are small molecules that are the components of proteins. There are 20 different kinds of amino acids in living things. Proteins are composed of different combinations of amino acids assembled in chain-like molecules.

CTLA4

cytotoxic T-lymphocyte-associated protein 4

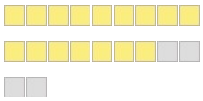
The TGFBR1 gene provides instructions for making a protein called cytotoxic T-lymphocyte-associated protein 4. It is a member of the family of immunoglobulin genes, and the protein inhibits the activity of T cells, a type of white blood cells. Mutations in this gene have been associated with insulin-dependent diabetes mellitus (type I), Graves disease (an autoimmune disorder associated with overactivity of the thyroid gland and hyperthyroidism), Hashimoto thyroiditis (an autoimmune hypothyroid disease), celiac disease (autoimmune gluten sensitivity), systemic lupus erythematosus (autiommune destruction of multiple organs), thyroid-associated orbitopathy (an immune disorder affecting the eye), autoimmune Addison's disease, rheumatoid arthritis and other autoimmune diseases, and breast cancer.

SNP outcomes in gene CTLA4 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

FUT2

fucosyltransferase 2 (secretor status included)



The FUT2 gene provides instructions for making the galactoside 2-L-fucosyltransferase (fucosyltransferase 2) enzyme. This protein is found in the stack of the Golgi apparatus, where proteins made in the cell are folded and glycosylated, having sugars added. The FUT2 enzyme is found in the digestive and respiratory tracts, and is involved in creating a part of the H antigen, which is the blood group antigen for blood type O and the base for building the blood type A and B antigens. Variations in the FUT2 gene inherited from both parents determine 'secretor' status, the ability to 'secrete' the ABO blood type antigens into the body fluids (sweat, saliva, digestive mucous, etc.). A functional fucosyltransferase 2 enzyme typically results in the Lewis blood group Lea- Leb+ (secretor). There are many health issues linked to non-secretor status (Lewis blood group Lea+ Leb-), including increased susceptibility to chronic diseases, imbalance of gut bacteria and less functional intestinal membrane, but also immunity from norovirus infection. Lewis double negative (Lewis blood group Lea- Leb-) is a rare phenotype in Western populations, but more common in Asian populations. Some diseases can prevent the Lewis blood group antigens from appearing when the genetics suggest that they should be present.

SNP outcomes in gene FUT2 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs602662 *(772G>A Gly258Ser)*	G	R	**AG**	**-+**		B12 ABSORPTION, SERUM B6, B12 LEVELS, HIGER HOMOCYSTEINE, HELICOBACTER PYLORI, G IS LIKELY SECRETOR
rs601338 *(G428A, W143X)*	A	R	**AG**	**+-**		SECRETOR STATUS, NOROVIRUS RESISTANCE
rs492602 *(204A>G A68A)*	G	B	**AG**	**-+**		B12, LINKED WITH NON-SECRETOR

New concepts:

- *Phenotype* is the observable or detectable characteristics of an individual organism--the detectable expression of a genotype.

FUT3

fucosyltransferase 3 (galactoside 3(4)-L-fucosyltransferase, Lewis blood group)

The FUT3 gene provides instructions for making the fucosyltransferase 3 enzyme, which is a type of glycolipid, a molecule of fat with a carbohydrate attached. Their role is to serve as markers for recognition of the cell by the immune system. Fucosyltransferase 3 is part of the fucosyltransferase family, which has functions in the formation of the embryo, differentiation of body tissues, metastasis of cancer cells, inflammation, and adhesion of bacteria. The fucosyltransferase 3 enzyme helps to make the Lewis blood group antigen, which is related to secretion of ABO blood group antigens. People with the Lewis negative blood group are more prone to some diseases such as heart disease, high cholesterol and diabetes. The Lewis negative blood group phenotype is found in approximately 10% of European Caucasians, and is more common in people of African descent. There are 4 known mutations in the FUT3 gene that lead to the Lewis negative phenotype.

SNP outcomes in gene FUT3 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- A *mutation* is an alteration of genetic material such that a new variation is produced.

HLA-DQ8

Human leukocyte antigen serotype DQ8

In Europe, DQ8 is associated with Type 1 diabetes and coeliac disease. The highest risk factor for type 1 diabetes is the HLA DQ8/DQ2.5 phenotype.

HLA-DQ8 (DQ8) is a human leukocyte antigen serotype within the HLA-DQ (DQ) serotype group. DQ8 is a split antigen of the DQ3 broad antigen. DQ8 is determined by the antibody recognition of β8and this generally detects the gene product of DQB1*0302. DQ8 is commonly linked to autoimmune disease in the human population. DQ8 is the second most predominant isoform linked to coeliac disease and the DQ most linked to Type 1 Diabetes. DQ8 increases the risk for rheumatoid arthritis and is linked to the primary risk locus for RA, HLA-DR4. DR4 also plays an important role in Type 1 Diabetes. While the DQ8.1 haplotype is associated with disease, there is no known association with the DQB1*0305, DQ8.4

or DQ8.5 haplotypes (see infobox) with autoimmune disease; however, this may be the result of lack of study in populations that carry these and the very low frequency.

SNP outcomes in gene HLA-DQ8 relevant to Full Name:

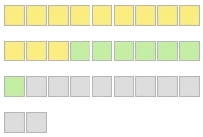
SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- A *locus* is the position on a chromosome of a gene or other chromosome marker; also, the DNA at that position.

HLA-DQA1

major histocompatibility complex, class II, DQ alpha 1



The HLA-DQA1 gene provides instructions for making a protein that plays a critical role in the immune system. The HLA-DQA1 gene is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria. HLA-DQA1 also belongs to a family of genes called immunoglobulin superfamily, C1-set domain containing.

The HLA complex is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. The HLA-DQA1 gene belongs to a group of MHC genes called MHC class II. MHC class II genes provide instructions for making proteins that are present on the surface of certain immune system cells. These proteins attach to protein fragments (peptides) outside the cell. MHC class II proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it triggers a response to attack the invading viruses or bacteria.

The protein produced from the HLA-DQA1 gene attaches (binds) to the protein produced from another MHC class II gene, HLA-DQB1. Together, they form a functional protein complex called an antigen-binding DQαβ heterodimer. This complex displays foreign peptides to the immune system to trigger the body's immune response.

Each MHC class II gene has many possible variations, allowing the immune system to react to a wide range of foreign invaders. Researchers have identified hundreds of different versions (alleles) of theHLA-DQA1 gene, each of which is given a particular number (such as HLA-DQA1*05:01).

Certain normal variations of the HLA-DQA1 gene have been associated with increased risk of autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. It is unclear how different versions of the HLA-DQA1 gene influence the risk of developing autoimmune disorders. These conditions are thought to result from a combination of multiple environmental and genetic factors. Changes in other HLA and non-HLA genes, some of which remain unknown, also likely contribute to the risk of developing these complex conditions.

At least two specific combinations of HLA gene variants (HLA haplotypes) have been found to increase the risk of developing celiac disease, a disorder in which inflammation damages the intestinal tract and other organs and tissues. One of these haplotypes, known as DQ2, is composed of the protein produced from HLA-DQA1 gene variants known as HLA-DQA1*05:01 or HLA-DQA1*05:05 bound to the protein produced from HLA-DQB1 gene variants known as HLA-DQB1*02:01 or HLA-DQB1*02:02. The other haplotype, known as DQ8, is composed of the protein produced from HLA-DQA1 gene variants known as HLA-DQA1*03:01 or HLA-DQA1*03:02 bound to the protein produced from the HLA-DQB1 gene variant known as HLA-DQB1*03:02.

The DQ2 and DQ8 haplotypes, which may occur separately or together, seem to increase the risk of an inappropriate immune response to the protein gluten, which is found in wheat, rye, and barley. This immune system malfunction results in the damage to the body's organs and tissues that occurs in celiac disease. However, the DQ2 and DQ8 haplotypes are also found in 30 percent of the general population, and only 3 percent of individuals with these haplotypes develop celiac disease.

Combinations of variations in the HLA-DQA1 gene and other HLA genes affect the risk of type 1 diabetes. Type 1 diabetes is characterized by high blood sugar levels resulting from a shortage of the hormone insulin and is caused by autoimmune damage to insulin-producing cells in the pancreas.

Type 1 diabetes risk is most increased by two HLA haplotypes involving variations of the HLA-DQA1 and HLA-DQB1 genes and another HLA gene called HLA-DRB1. One haplotype, written as DRB1*03:01-DQA1*05:01-DQB1*02, is called DR3. The other haplotype, written as DRB1*04:01/02/04/05/08-DQA1*03:01-DQB1*02, is called DR4. People at highest risk of developing type 1 diabetes have one copy of the DR3 haplotype and one copy of the DR4 haplotype in each cell. Other HLA haplotypes only mildly increase the risk of type 1 diabetes, while some haplotypes seem to protect against developing this condition. Variations in other genes and environmental factors are also thought to affect the risk of this complex disorder.

Normal variations in the HLA-DQA1 gene can affect the body's ability to recognize and react to foreign invaders (pathogens). For example, variations of this gene have been shown to increase or decrease a person's chance of getting infections such as hepatitis B and leprosy or may affect the severity of illness if infection occurs.

A particular variant of the HLA-DQA1 gene known as HLA-DQA1*02:01 increases the risk of liver damage in women with advanced breast cancer treated with a drug called lapatinib. Researchers suggest that the variant may increase immune system sensitivity to the drug, resulting in inflammation that damages the liver.

SNP outcomes in gene HLA-DQA1 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2155219 *(G > T)*	T	R	**TG**	**+-**		HAY FEVER (ALLERGIC RHINITIS), HLA-DQA1 MOLD ALLERGY IGE GRASS SENSITIZATION ALLERGY TO GRASS POLLEN EOSINOPHILIC ESOPHAGITIS
rs9272346 *(-864G>A)*	G	B	**GG**	**++**		TYPE 1 DIABETES
rs9271366 *(*15 HLA-DRB1)*	G	R	**AG**	**-+**		CROHN'S ULCERATIVE COLITIS, MULTIPLE SCLEROSIS MS

New concepts:

- An *allele* is one of two or more alternative forms of a gene at the same site in a chromosome, which determine alternative characters in inheritance.
- A *pathogen* is a bacterium, virus, or other microorganism that can cause disease.

HLA-DQB2

major histocompatibility complex, class II, DQ beta 2

HLA-DQB2 belongs to the family of HLA class II beta chain paralogs. Class II molecules are heterodimers consisting of an alpha (DQA) and a beta chain (DQB), both anchored in the membrane. They play a central role in the immune system by presenting peptides derived from extracellular proteins. Class II molecules are expressed in antigen presenting cells (APC: B lymphocytes, dendritic cells, macrophages). Polymorphisms in the alpha and beta chains specify the peptide binding specificity, and typing for these polymorphisms is routinely done for bone marrow transplantation. However this gene, HLA-DQB2, is not routinely typed, as it is not thought to have an effect on transplantation. There is conflicting evidence in the literature and public sequence databases for the protein-coding capacity of HLA-DQB2. Because there is evidence of transcription and an intact ORF, HLA-DQB2 is represented in Entrez Gene and in RefSeq as a protein-coding locus. [provided by RefSeq, Oct 2010]

SNP outcomes in gene HLA-DQB2 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2858331 *(A > G)*	G	R	**AG**	**-+**		CELIAC DISEASE RISK, IGE, TYPE 1 DIABETES

New concepts:

- *Transcription* is the first step of gene expression, in which a particular segment of DNA is copied into RNA
- A *polymorphism* is a difference in DNA sequence among individuals.
- A *paralog*is a duplicated or repetitive sequence of DNA, multiple copies of which are found in a single genome.

HNMT

histamine N-methyltransferase

HNMT provides instructions for making the histamine N-methyltransferase protein, and is also used as a neurotransmitter in the brain. Histamine is a compound released by histamine-containing cells in response to injury and in inflammatory and allergic reactions. Histamine is broken down by two major pathways: N-methylation via histamine N-methyltransferase, and oxidative deamination via diamine oxidase. The HNMT enzyme uses S-adenosyl-L-methionine (SAMe) as a cofactor. In the brain, the neurotransmitter activity of histamine is controlled only by N-methylation from the HNMT enzyme, as diamine oxidase is not found in the brain. Variations in the HNMT gene can affect the activity levels of this enzyme.

SNP outcomes in gene HNMT relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- *Methylation* is the addition of a single carbon and three hydrogen atoms (called a methyl group) to another molecule. The removal of a methyl group is called demethylation. Methylation is a key mechanism behind the regulation of gene expression.

IL12A-AS1

IL12A antisense RNA 1 (non-coding). IL12A-AS1 (IL12A Antisense RNA 1) is an RNA Gene, and is affiliated with the non-coding RNA class. SNPs on this gene are associated with celiac symptoms.

SNP outcomes in gene IL12A-AS1 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

IL13

interleukin 13

IL13 is one of a class of immune hormones known as 'cytokines'. IL13 down-regulates the activity of white blood cells known as 'macrophages', and thereby inhibits the production of pro-inflammatory cytokines and chemokines. This cytokine is found to be critical to the pathogenesis of allergen-induced asthma but operates through mechanisms independent of IgE and eosinophils. Dietary lectins have been shown to produce immunologic reactions due to their ability to stimulate IL13.

SNP outcomes in gene IL13 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs848	C	R	**AC**	-+		CROHNS

New concepts:

- *Pathogenesis* is the development of a disease and the chain of events leading to that disease.
- *Cytokines* are chemicals important in cell signaling. They are released by cells and affect the behavior of other cells. Cytokines include chemokines, interferons and interleukins. Cytokines are produced by a broad range of cells, including immune cells like macrophages, B lymphocytes and T lymphocytes.

IL4

interleukin 4

IL4 encodes a protein (cytokine) produced by activated T cells. It demonstrates a correlation with food lectin sensitivity. The interleukin 4 receptor also binds to IL13, which may contribute to many overlapping functions of this cytokine and IL13. IL4 and IL13 play important roles in allergic and inflammatory reactions. Immune reactions involving dietary lectins have been shown to induce IL4 and IL13. IL4, along with other lymphocyte-derived cytokines, is involved in the airway inflammation observed in the lungs of patients with allergic asthma. Foods highest in lectins are red kidney beans, soybeans, peanuts, tomatoes and potatoes. Refer to your blood type manual for specific lectin issues. Genetically modified foods versions of foods contain lectins.

SNP outcomes in gene IL4 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2227284 *(184-748T>G)*	G	R	**TG**	**-+**		LECTIN SENSITIVITY
rs2243250 *(-589C>T)*	T	R	**TC**	**+-**		TH1/TH2 PATHWAY, LECTIN SENSITIVITY

New concepts:

- *Interleukins* are one of a large group of proteins produced mainly by T lymphocyte cells. Interleukins participate in communication among leukocytes and are important in the inflammatory response.

MCM6

minichromosome maintenance complex component 6

The MCM6 gene provides instructions for making part of the MCM complex, a group of proteins that functions as a helicase. Helicases attach to particular regions of DNA and temporarily unwind the two spiral strands of these molecules. When a cell prepares to divide to form two cells, helicases unwind the DNA so that it can be copied. The DNA that makes up the chromosomes is duplicated (replicated) so that

each new cell will get a complete set of chromosomes. Helicases are also involved in the production of RNA, a chemical cousin of DNA.

A specific DNA sequence within the MCM6 gene called a regulatory element helps control the activity (expression) of a nearby gene called LCT. The LCT gene provides instructions for making an enzyme called lactase. This enzyme helps to digest lactose, a sugar found in milk and other dairy products. Lactose intolerance in adulthood is caused by gradually decreasing expression of the LCT gene after infancy, which occurs in most humans.

At least four variations have been identified in the regulatory element that modulates LCT gene expression. These variations change single DNA building blocks (nucleotides) in the regulatory element. Each of the variations results in sustained lactase production in the small intestine and the ability to digest lactose throughout life. People without these changes have a reduced ability to digest lactose as they get older, resulting in the signs and symptoms of lactose intolerance.

Lactose intolerance is a group of symptoms perceived after the ingestion of dairy products containing lactose, i.e. milk and fermented dairy products, characterized by excessive gas production. It causes abdominal distension, pain, borborygmi and flatulence. Excessive gas production and accumulation are strongly related to subjective symptoms. Symptoms often do not correlate to the amount of malabsorbed lactose, or to the volume or the rate of gas accumulation, but rather to altered intestinal transit and increased perception of bloating from hydrogen, carbon dioxide or methane gas production. These gases pass into the blood and are breathed out via the lungs. Expulsion of hydrogen gas can be used as an indicator of maldigested lactose. Gas production and fluid retention are the results of bacteria using the undigested lactose. This usually occurs in the small intestine in patients with dysbiosis (imbalance of gut bacteria) and small intestinal overgrowth (SIBO). For some patients complete abstinence from milk products is necessary. Correcting SIBO and dysbiosis can allow gradual reintroduction of lactose-containing products. Lactose intolerance should not be confused with milk protein allergies, which are associated with Type 1 diabetes.

SNP outcomes in gene MCM6 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

New concepts:

- A *nucleotide* is subunit of DNA or RNA consisting of a nitrogenous base (adenine, guanine, thymine, or cytosine), a phosphate molecule, and a sugar molecule. Thousands of nucleotides are linked to form a DNA or RNA molecule.

NOD2

nucleotide-binding oligomerization domain containing 2

This gene is a member of the Nod1/Apaf-1 family and encodes a protein with two caspase recruitment (CARD) domains and six leucine-rich repeats (LRRs). The protein is primarily expressed in the peripheral blood leukocytes. It plays a role in the immune response to intracellular bacterial lipopolysaccharides (LPS) by recognizing the muramyl dipeptide (MDP) derived from them and activating the NFKB protein. Mutations in this gene have been associated with Crohn disease and Blau syndrome. Alternatively spliced transcript variants encoding distinct isoforms have been found for this gene. [provided by RefSeq, Jun 2014]

SNP outcomes in gene NOD2 relevant to Full Name:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report						

NOS2

nitric oxide synthase 2, inducible

NOS2 provides instructions for making a protein that produces nitric oxide (NO) from the amino acid arginine. NO is a free radical, a molecule with a free electron that can cause damage by oxidation, but it is also essential for many functions within the body such as neurotransmitter function and helping the body deal with microbes and tumors.

This enzyme is one of three similar types of protein that synthesize NO. The NO produced by NOS2 is known as inducible NOS, or iNOS, and is produced in large quantities when needed as an oxidant in immune defense.

Other types of nitric oxide synthases, NOS1 (nNOS) and NOS3 (eNOS) are more specific to the nervous system and blood circulation.

Impaired NO production is involved in the development of several diseases such as high blood pressure, pre-eclampsia, diabetes mellitus, obesity, erectile dysfunction, and migraine.

SNP outcomes in gene NOS2 relevant to Full Name:

SNP ID	Risk Type	You	Outcome	Magnitude	Keywords
No significant SNP mutations to report					

GASTROINTESTINAL

MULTI-SNP MACROS

Lower disorder/ gluten sensitivity risk (HLA-DQA1)

Genes	HLA-DQA1
Repute:	BENEFIT
Magnitude:	2
Frequency:	N/A

INTERPRETATION: Good news! You are homozygous for a SNP genotype [rs2187668 (CC)] that is associated with a lowered risk of auto-immune disease and gluten sensitivity.

This algorithm is **true** and applies to you

Your results: rs2187668 (**CC**)

Increased risk of Crohn's disease

Genes	
Repute:	RISK
Magnitude:	4
Frequency:	15 %

INTERPRETATION: The rs12037606(A) allele is associated with a higher risk of Crohn's disease. The risk associated with AG (heterozygotes) is 1.22x, and for AA (homozygotes), 1.52x the risk of people with the GG genotype.

This algorithm is **true** and applies to you

Your results: rs12037606 (**AA**)

Gastrointestinal Health macro algorithms returning as false:

- Risk of Crohn's disease
- Moderate autoimmune disorder risk (HLA-DRA)
- Risk of autoimmune disorder/ gluten sensitivity
- Reduced risk (0.26) of Crohn's disease and ulcerative colitis
- Risk of asthma, ADHD and Parkinson's disease from high histamine
- Significant autoimmune disorder risk (HLA-DRA)
- Increased risk of non-alcoholic fatty liver disease (NAFLD)
- Risk of autoimmune disorder/ gluten sensitivity
- Reduced risk of celiac disease and other autoimmune diseases

GASTROINTESTINAL

NETWORK MAPS

Network maps allow you to visualize how certain gene pathways interact and contribute to health maintenance. These network maps allows you to visualize your genomic data directly in a number of hand-curated pathway maps. Boxes in the map generally depict genes, and the box color(s) are determined by the percentage of SNP values that are homozygous recessive for risk (orange), heterozygous for risk (yellow) and negative for risk (gray).

NATURAL PRODUCTS

This section lists the top 25 natural products that may be worthy of attention as potentially valuable therapeutic agents:

RANK	AGENT	INDICATION VALUE
1.	Calcium	
2.	Copper	
3.	Vitamin A (retinol)	
4.	6-Gingerol	
5.	Theanine	
6.	D-mannose	
7.	Drynaria fortunei (Aglaomorpha, Gu-Sui-Bu)	
8.	Isatis (Woad Root)	
9.	Nigella sativa	
10.	Calcitriol	
11.	Gynostemma pentaphyllum	
12.	Cannabidiol	
13.	Cudrania tricuspidata	
14.	Salvia miltiorrhiza (Danshen)	
15.	Chito-oligosaccharides (Chitosan)	
16.	Curcumin	
17.	Thymoquinone	
18.	Citrulline	
19.	Noni (Morinda citrifolia)	
20.	Theophylline	
21.	Ginkgo (Ginkgo biloba)	
22.	Salacia oblonga	
23.	Bifidobacterium	
24.	Probiotics	
25.	Peanut Agglutinin (PNA)	

DRUG INTERACTIONS

This section documents potential drug interactions or complications you may be genetically susceptible to.

DRUG	SNP	GENE	RISK ALLELE	YOUR GENOTYPE	SIDE EFFECT
Acitretin	rs429358	APOE	C	**TC**	Psoriasis
Acitretin	rs7412	APOE	C	**CC**	Psoriasis
Azathioprine	rs1800460	TPMT	T	**TC**	Hepatotoxicity
Caffeine	rs762551	CYP1A2	C	**AC**	Myocardial infarction
Carbamazepine	rs3909184	FLOT1	G	**GG**	Patients with the CG or GG genotype (in Asian patients) were at a higher risk of Steven-Johnson Syndrome compared to those with the CC genotype (non-carriers of HLA-b*1502)
Clozapine	rs5443	GNB3	TT	**TT**	Schizophrenia patients taking this drug more more weight than patients with at least one rs5443(c)
Leflunomide	rs762551	CYP1A2	C	**AC**	Diarrhea, vomiting, liver toxicity, headache, insomnia, rash, alopecia, hypertension, leucopenia, asthma
Mercaptopurine	rs1800460	TPMT	T	**TC**	Hepatotoxicity
Methotrexate	rs1801133	MTHFR	A	**AG**	Mucositis, hepatic toxicity, thrombocytopenia, alopecia
Almotriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Cetuximab	rs1801274	FCGR2A	A	**AA**	Increased progression free survival
Cyclophosphamide	rs2740574	CYP3A4	C	**CC**	Decreased activation of cyclophosphamide most likely contributing to worse disease free survival in adjuvant chemotherapy for node-positive breast cancer
Eletriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Frovatriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Morphine	rs1799971	OPRM1	A	**AA**	Better response to pain relief drugs
Naratriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Pravastatin	rs20455	KIF6	G	**GG**	Improved response to statin drugs
Rizatriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Rosuvastatin	rs20455	KIF6	G	**GG**	Improved response to statin drugs

Sildenafil	rs5443	GNB3	T	**TT**	Better response to drug treatment
Sildenafil	rs5443	GNB3	TT	**TT**	Better response to drug treatment. More patients experience a 'postive erectile response'
Simvastatin	rs20455	KIF6	G	**GG**	Improved response to statin drugs
Sumatriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment
Warfarin	rs1799853	CYP2C9	T	**TC**	Poor drug metabolizer, lower dose requirements
Zolmitriptan	rs5443	GNB3	T	**TT**	Better response to drug treatment