Client Report

Venus deMilo

Opus23 Explorer

Opus23 Explorer™ is a fully functional version of the well-regarded and widely used Opus23 Pro™ genomic exploration software designed and programmed by Dr. Peter D'Adamo and distributed under license to Diagnostic Solutions Lab (DSL) by Datapunk Bioinformatics LLC for use in the interpretation of genomic raw data produced by the DSL 'Opus' genomic microarray chip.

Opus23 Explorer scans over 20 peer-reviewed, evidence-based scientific databases and cross-references their information with the results of your raw data. This report summarizes the findings from your genomic data that have been curated by your clinical team into a human-understandable format. However, before we begin, let's introduce a few genetic concepts to set the stage and advance your understanding a bit.

REPORT FOCUS

INFLAMMATION

Welcome to your owner's manual

Opus23 Explorer is a very sophisticated computer program that looks for very simple things: 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, Opus 23 Pro groups all the SNP outcomes under their parent gene, and presents its results as a reflection of their combined influence on 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 **CT** 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 much of the material in this report is 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 remeber to discuss these with your clinician next opportunity. Also, use online resources such as Google and Wikipedia as research tools.

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

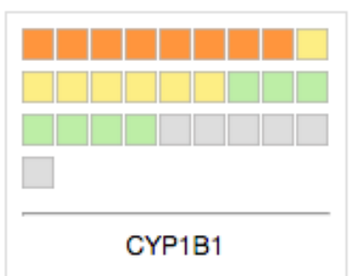
When it comes to a particular disease or syndrome, most SNPs have rather small ORs. This does not mean that they are unworthy of attention, but rather that the findings must be interpreted as part of an integrated whole, including: other SNP results that also support the conclusion; lifestyle factors; 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:

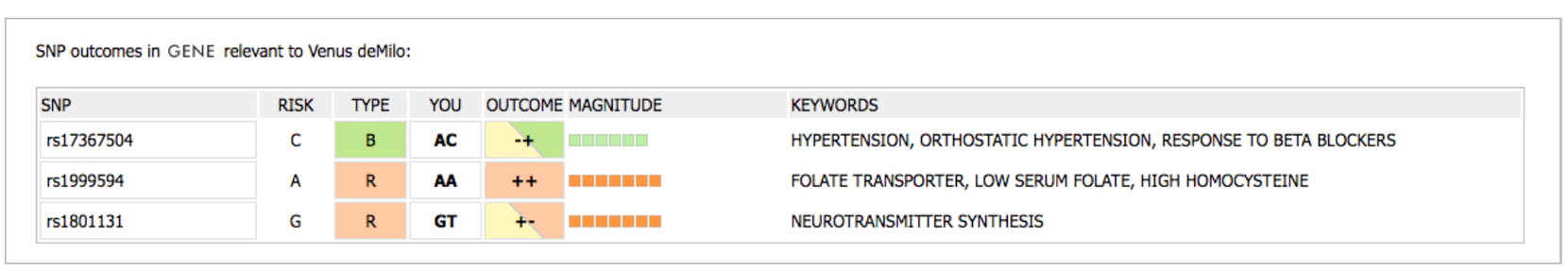
The data provided by Opus23 Explorer is for informational purposes only and is not designed or intended to suggest the treatment or diagnosis of any disease or condition. Opus23 Explorer and Datapunk Bioinformatics, LLC, take no responsibility for any harm arising from incorrect data being uploaded to 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:

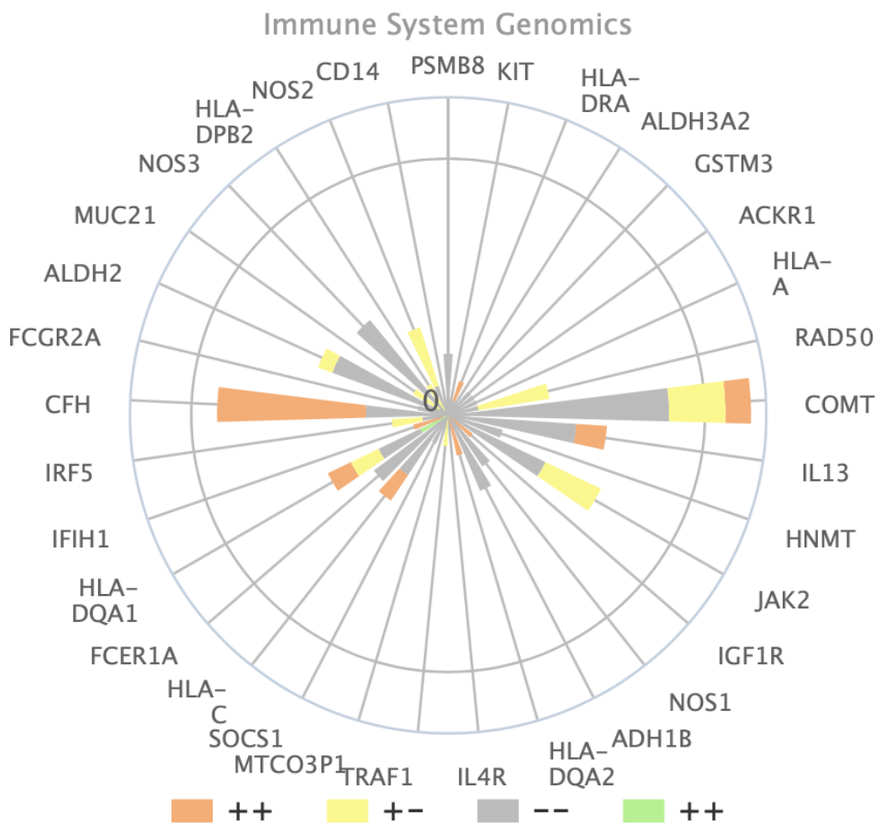
- If you hear the alarm clock, open your eyes.
- If it's dark outside, go back to bed.
- If it's light outside, check the time.
- If it's earlier than 7AM, go back to bed.
- If it's later than 7AM, get up, check calendar
- If it's Saturday, go back to bed.

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.

INFLAMMATION



Immune System Genomics

The immune system is a host defense system comprising many biological structures and processes within an organism that protects against disease. To function properly, an immune system must detect a wide variety of agents, known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue. In many species, the immune system can be classified into subsystems, such as the innate immune system versus the adaptive immune system, or humoral immunity versus cell-mediated immunity. In humans, the blood–brain barrier, blood–cerebrospinal fluid barrier, and similar fluid–brain barriers separate the peripheral immune system from the neuroimmune system, which protects the brain. Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer. Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication. In contrast, autoimmunity results from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include Hashimoto's thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and systemic lupus erythematosus.

RAD50

RAD50 homolog (S. cerevisiae)

The protein encoded by this gene is improtant for repairing breaks in the strand of DNA and various stages of the cell cycle. RAD50 is also involved in repairing telomeres, which are the caps on the end of DNA chromosomes that protect the DNA from damage over time.

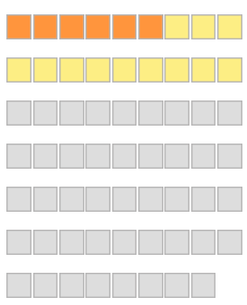
SNP outcomes in RAD50 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2040704	G	R	**AG**	**-+**		IGE, ASTHMA
rs2240032	T	R	**CC**	**--**		IGE
rs2244012	G	R	**AG**	**-+**		ASTHMA

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 *telomere* is the distal end of a chromosome arm; telomeres undergo dramatic changes during the progression of cancer. Shortening of the telomeres appear to correlate with aging.
- *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.

COMT



catechol-O-methyltransferase

Catechol-O-methyltransferase (COMT) gene helps break down the neurotransmitters dopamine and norepinephrine. A defect due to certain variants in COMT will cause higher levels of dopamine due to slower breakdown, which can contribute to anxiety and insomnia. Individuals can be more susceptible to dopamine fluctuations, and therefore mood swings. People without COMT mutations are generally more even tempered. Studies of the COMT Val158Met polymorphism have shown the variant affects cognitive tasks rated as executive function, aggression, and working memory and ratings of subjective well-being. The Val158Met variant has also been found to influence the effect of aspirin and vitamin E to lower rates of incident CVD of 40%.

COMT is implicated in ADD/ADHD and bipolar disorders. A functioning FOKI SNP in the VDR gene and/or supplementing with vitamin D enhances dopamine formation.

COMT is important in the metabolism of catechol drugs used in the treatment of hypertension, asthma, and Parkinson disease. Catechol-estrogens like 4-OH estrone, and catechol-containing flavonoids are metabolised by this enzyme, and play a role in the risk of cancer.

Persons with the G allele have an increase in risk of ADD/ADHD, Anxiety, Aggressiveness, Internet Gaming, OCD, Oppositional Defiant Disorder, Panic Disorder, and Pathological Aggression, and an increase in addiction to cannabis, cocaine, glucose (sugar cravings), Nicotine, Opioids, and Stimulants.

Persons with the A allele have an increase in addiction to alcohol, and an increase in stress intolerance / PTSD, homocysteine levels, CVD risk, testosterone requirements, anxiety, neuroticism, and postoperative pain.

SNP outcomes in COMT relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs769224	A	R	**GG**	**--**		CATECHOLAMINES DEGRADATION
rs4633	T	R	**CC**	**--**		RS4680 PAIN SENSITIVITY, PARANOID SCHIZOPHRENIA, HYPERACTIVITY, CHRONIC FATIGUE SYNDROME, ENDOMETRIAL CANCER
rs165774	A	R	**GG**	**--**		HIGH EPINEPHRINE VARIANT, BUT CATALYTICALLY ACTIVE TO DOPAMINE AND NOREPINEPHRINE DEGRADATION
rs4680	A	R	**GG**	**--**		DOPAMINE, STRESS, ESTROGEN BLOOD METABOLITES, BREAST CANCER, PAIN, MEMORY, ATTENTION, WARRIOR VS WORRIER, NICOTINE RESPONSE, PAIN SENSITIVITY, ENDOMETRIAL CANCER, REDUCED CVD RISK ON ASPIRIN AND VITAMIN E
rs6269	G	R	**GG**	**++**		HYPERACTIVITY PARKINSON'S DISEASE SCHIZOPHRENIA MAJOR DEPRESSIVE DISORDER
rs4646312	T	R	**CC**	**--**		ESTROGEN ANDROGEN METABOLIZING

New concepts:

- A *mutation* is an alteration of genetic material such that a new variation is produced.
- A *polymorphism* is a difference in DNA sequence among individuals.
- 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.

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 IL13 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1295685	A	R	**GG**	**--**		PSORIASIS, AUTOIMMUNE
rs1800925	T	R	**CC**	**--**		IGE, PSORIASIS, AUTOIMMUNE, PEDIATRIC ASTHMA
rs20541	A	R	**GG**	**--**		ELEVATED IGE LEVELS IMMUNOGLOBULIN E, HIGH IGE, PEDIATRIC ASTHMA
rs848	C	R	**CC**	**++**		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.
- A *pathogen* is a bacterium, virus, or other microorganism that can cause disease.

JAK2

Janus kinase 2

The JAK2 gene provides instructions for making a protein that promotes the growth and division (proliferation) of cells. This protein is part of a signaling pathway called the JAK/STAT pathway, which transmits chemical signals from outside the cell to the cell's nucleus. The JAK2 protein is especially important for controlling the production of blood cells from hematopoietic stem cells. These stem cells are located within the bone marrow and have the potential to develop into red blood cells, white blood cells, and platelets.

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, which are called somatic mutations, are not inherited. Somatic mutations in the JAK2 gene are associated with essential thrombocythemia, a disorder characterized by an increased number of platelets, the blood cells involved in normal blood clotting. The most common mutation (written as Val617Phe or V617F) replaces the protein building block (amino acid) valine with the amino acid phenylalanine at position 617 in the protein. This particular mutation is found in approximately half of people with essential thrombocythemia. A small number of affected individuals have a somatic mutation in another part of the JAK2 gene known as exon 12.

The V617F JAK2 gene mutation results in the production of a JAK2 protein that is constantly turned on (constitutively activated), which in essential thrombocythemia, leads to the overproduction of abnormal blood cells called megakaryocytes. Because platelets are formed from megakaryocytes, the overproduction of megakaryocytes results in an increased number of platelets. Excess platelets can cause abnormal blood clotting (thrombosis), which leads to many signs and symptoms of essential thrombocythemia.

Somatic mutations in the JAK2 gene are associated with polycythemia vera, a disorder characterized by uncontrolled blood cell production. The V617F mutation is found in approximately 96 percent of people with polycythemia vera. About 3 percent of affected individuals have a somatic mutation in the exon 12 region of the JAK2 gene.

JAK2 gene mutations result in the production of a constitutively activated JAK2 protein, which seems to improve the survival of the cell and increase production of blood cells. With so many extra cells in the bloodstream, abnormal blood clots are more likely to form. In addition, the thicker blood flows more slowly throughout the body, which prevents organs from receiving enough oxygen. Many of the signs and symptoms of polycythemia vera are related to a lack of oxygen in body tissues.

Somatic JAK2 gene mutations are also associated with primary myelofibrosis, a condition in which bone marrow is replaced by scar tissue (fibrosis). The V617F mutation is found in approximately half of individuals with primary myelofibrosis. A small number of people with this condition have mutations in the exon 12 region of the gene. These JAK2 gene mutations result in a constitutively active JAK2 protein, which leads to the overproduction of abnormal megakaryocytes. These megakaryocytes stimulate other cells to release collagen, a protein that normally provides structural support for the cells in the bone marrow but causes scar tissue formation in primary myelofibrosis. Because of the fibrosis, the bone marrow cannot produce enough normal blood cells, leading to the signs and symptoms of the condition.

Somatic JAK2 gene mutations are also associated with several related conditions. The V617F mutation is occasionally found in people with cancer of blood-forming cells (leukemia) or other bone marrow disorders. Budd-Chiari syndrome, which results from a blocked vein in the liver, can also be associated with the V617F mutation when it is caused by an underlying bone marrow disorder. It is unknown how one particular mutation can be associated with several conditions.

Another inherited (germline) mutation on the same SNP is associated with Thrombocythemia.

SNP outcomes in JAK2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2274471	G	R	**AG**	-+		MCAD, EPIGENETICS, OBESITY
rs10758669	C	R	**AA**	--		ULCERATIVE COLITIS, CROHN'S DISEASE, MYELOPROLIFERATIVE NEOPLASM
rs12340895	G	R	**CC**	--		BONE MARROW, MPNS, MPN, NEOPLASM, MYELOPROLIFERATIVE NEOPLASMS
rs10974944	G	R	**CC**	--		NEOPLASMS, MPNS, MPN, MYELOPROLIFERATIVE NEOPLASMS, BONE MARROW
rs7849191	T	R	**TC**	+-		MCAD, OBESITY
rs3780374	A	R	**GG**	--		BONE MARROW, MPN, NEOPLASMS, MPNS, MYELOPROLIFERATIVE NEOPLASMS

New concepts:

- The *nucleus* is the central part of most cells that contains genetic material and is enclosed in a membrane
- *Exons* are sections of DNA that contain the protein-coding sequences of a gene.
- *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.

IGF1R

insulin-like growth factor 1 receptor

The IGF1R gene provides instructions for making the protein that functions as the receptor for insulin-like growth factor 1 (IGF1). IGF1 is a hormone that regulates the effects of growth hormone. The receptor binds insulin-like growth factor. It is found in high levels in most cancerous cells, where it prevents the cell from dying by enhancing mechanisms for cell survival. rs2229765 in IGF1R plays a significant role in the development of a kidney disease called IgA nephropathy.

SNP outcomes in IGF1R relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2229765	A	R	**AA**	**++**		IGA NEPHROPATHY, LONGEVITY

New concepts:

- A *receptor* is a molecule in a cell membrane, that responds specifically to a particular neurotransmitter, hormone, antigen, or other substance.

ADH1B

alcohol dehydrogenase 1B (class I), beta polypeptide

The ADH1B gene provides instructions for making the beta part of three genes making alpha, beta and gamma subunits of the alcohol dehydrogenase enzyme, which can break down alcohol, vitamin A and other chemicals. The two most important variants found in the ADH1B gene increase the metabolism of alcohol and cause skin flushing when drinking, which usually prevents the individual from drinking a lot of alcohol. Variants in ADH1B are also associated with some types of cancer.

SNP outcomes in ADH1B relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
No significant SNP mutations to report						

New concepts:

- A *dehydrogenase* is an enzyme that accelerates the removal of hydrogen from metabolites and its transfer to other substances.

HLA-DQA2

major histocompatibility complex, class II, DQ alpha 2

The HLA-DQA2 gene provides instructions for making a protein that plays a critical role in the immune system. The HLA-DQA2 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.

The HLA complex is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. The HLA-DQA2 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.

A low level of HLA-DQA2 expression can be due to impaired binding of the transcription factor to the HLA-DQA2 gene promoter.

SNP outcomes in HLA-DQA2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs9275224	A	R	**AA**	**++**		IGA NEPHROPATHY

New concepts:

- In genetics, a *promoter* is a region of DNA that initiates transcription of a particular gene.
- *Transcription* is the first step of gene expression, in which a particular segment of DNA is copied into RNA

HLA-C

major histocompatibility complex, class I, C

The HLA-C gene provides instructions for making a protein that plays a critical role in the immune system. HLA-C 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 is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. Genes in this complex are categorized into three basic groups: class I, class II, and class III. In humans, the HLA-C gene and two related genes, HLA-A and HLA-B, are the main genes in MHC class I.

MHC class I genes provide instructions for making proteins that are present on the surface of almost all cells. On the cell surface, these proteins are bound to protein fragments (peptides) that have been exported from within the cell. MHC class I proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it responds by triggering the infected cell to self-destruct.

Variations in the proteins produced by HLA-C affect the way the immune system functions, and typing for HLA-C is needed for bone marrow and kidney transplants to match and avoid rejection.

SNP outcomes in HLA-C relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs4406273	A	R	**GG**	**--**		PSORIASIS
rs1265181	G	R	**GG**	**++**		PSORIASIS, AUTOIMMUNE
rs12191877	T	R	**CC**	**--**		PSORIASIS, DECREASED RISK OF RHEUMATOID ARTHRITIS

FCER1A

Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide

The FCER1A gene provides instructions for making a protein that is part of a receptor for Immunoglobulin E (IgE), an antibody made for immune defense. The immunoglobulin epsilon receptor (IgE receptor) is the trigger for response to allergies in the body. When two or more IgE receptors are brought together by IgE molecules that are bound to allergens, products that are responsible for allergy symptoms are released, such as histamine. The IgE receptor is made up of an alpha subunit, a beta subunit, and two gamma subunits. The protein encoded by the FCER1A gene is the alpha subunit.

SNP outcomes in FCER1A relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2251746	C	R	**TT**	**--**		HIGH IGE LEVELS
rs2427837	A	R	**GG**	**--**		
rs2494262	A	R	**CC**	**--**		

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 HLA-DQA1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2187668	T	R	**CC**	**--**		CELIAC, HEPATITIS, LUPUS
rs2155219	T	R	**GT**	**-+**		HAY FEVER (ALLERGIC RHINITIS), HLA-DQA1 MOLD ALLERGY IGE GRASS SENSITIZATION ALLERGY TO GRASS POLLEN EOSINOPHILIC ESOPHAGITIS
rs9272346	G	B	**GG**	**++**		TYPE 1 DIABETES
rs9271366	G	R	**GG**	**++**		CROHN'S ULCERATIVE COLITIS

IFIH1

interferon induced with helicase C domain 1

IgA deficiency association. The TGFBR1 gene provides instructions for making a protein called interferon induced with helicase C domain 1. It is a receptor for part of the immune system which acts as a sensor of viral infection and the activation of a series of antiviral responses. Mutations in TGFBR1 are related to clinically amyopathic dermatomyositis (CADM). This is a chronic inflammatory disorder that shows inflammation of the skin without muscle inflammation. It is also related to Singleton-Merten syndrome 1 (SGMRT1), an autosomal dominant disorder, occuring with one copy of the relevant inherited gene mutation. The main features are calcification of the aorta, dental anomalies, osteopenia, acro-osteolysis, and to a lesser extend glaucoma, psoriasis, muscle weakness, and loose joints. Mutations may also be related to insulin-dependent diabetes mellitus.

SNP outcomes in IFIH1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1990760	C	R	**CC**	**++**		POST VIRAL INFECTION TRIGGERED T1DM, IGA DEFICIENCY

New concepts:

- *Interferon* is a protein released by cells, usually in response to the entry of a virus, that has the property of inhibiting virus replication.

IRF5

interferon regulatory factor 5

The protein produced from the IRF5 gene, called interferon regulatory factor 5 (IRF5), acts as a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. When a virus is recognized in the cell, the IRF5 gene is turned on (activated), which leads to the production of IRF5 protein. The protein binds to specific regions of DNA that regulate the activity of genes that produce interferons and other cytokines. Cytokines are proteins that help fight infection by promoting inflammation and regulating the activity of immune system cells. In particular, interferons control the activity of genes that help block the replication of viruses, and they stimulate the activity of certain immune system cells known as natural killer cells.

Studies have associated normal variations in the IRF5 gene with an increased risk of several autoimmune disorders. Autoimmune disorders occur when the immune system malfunctions and attacks the body's tissues and organs. These disorders include systemic lupus erythematosus, Sjögren syndrome, and rheumatoid arthritis.

There is some evidence that certain variations of the IRF5 gene are associated with increased activity of the gene and elevated cytokines. However, it is unknown what role, if any, these effects play in the increased risk of autoimmune disorders. Researchers believe that a combination of genetic and environmental factors may contribute to the development of these conditions.

Several normal variations in the IRF5 gene have been associated with an increased risk of developing systemic scleroderma, which is an autoimmune disorder characterized by the buildup of scar tissue (fibrosis) in the skin and internal organs. Although the IRF5 gene is known to stimulate the immune system in response to viruses, it is unknown how the gene variations contribute to the increased risk of systemic scleroderma. Researchers believe that a combination of genetic and environmental factors may play a role in development of the condition.

SNP outcomes in IRF5 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs10488631	C	R	**TT**	**--**		AUTOIMMUNE
rs4728142	A	R	**AG**	**+-**		WEAK MACROPHAGE SWITCH LOW TH1 ACTIVITY, LUPUS, COLITIS

New concepts:

- *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.

CFH

complement factor H

The CFH gene provides instructions for making a protein known as Factor H that is secreted into the bloodstream and has an essential role in the regulation of complement activation, restricting this innate defense mechanism to microbial infections. Its principal function is to regulate the Alternative Pathway of the complement system, ensuring that the complement system is directed towards pathogens or other dangerous material and does not damage host tissue. Overactive factor H may result in reduced complement activity on pathogenic cells - increasing susceptibility to microbial infections. Underactive factor H may result in increased complement activity on healthy host cells - resulting in autoimmune diseases. It is not surprising therefore that mutations or single nucleotide polymorphisms (SNPs) in factor H often result in pathologies, and has been widely investigated in age-related macular degeneration. Variants have also been associated with schizophrenia and ischemic stroke. Moreover, the complement inhibitory activities of factor H and other complement regulators are often used by pathogens to increase virulence.

SNP outcomes in CFH relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs412852	G	R	**GG**	**++**		AGE-RELATED MACULAR DEGENERATION
rs1061170	C	R	**CC**	**++**		CFH HAPLOTYPE, REDUCED BINDING OF CRP, AGE-RELATED MACULAR DEGENERATION, VISION LOSS, LONGEVITY, CANCER, REDUCED EGFR
rs800292	A	R	**GG**	**--**		CFH HAPLOTYPE, ISCHEMIC STROKE
rs3753394	C	R	**CC**	**++**		CFH HAPLOTYPE
rs380390	C	R	**GG**	**--**		AGE-RELATED MACULAR DEGENERATION
rs3766405	C	R	**CC**	**++**		AGE-RELATED MACULAR DEGENERATION
rs1048663	G	R	**GG**	**++**		AGE-RELATED MACULAR DEGENERATION
rs6677604	A	R	**GG**	**--**		IGA DEFICIENCY, AGE-RELATED MACULAR DEGENERATION
rs1061147	A	R	**AA**	**++**		CFH HAPLOTYPE, AGE-RELATED MACULAR DEGENERATION

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.

ALDH2

aldehyde dehydrogenase 2 family (mitochondrial)

Aldehyde dehydrogenase is the second enzyme of the major metabolic pathway of alcohol metabolism. There are two major forms of aldehyde dehydrogenase, the cellular and mitochondrial forms. Most Caucasians have both major major forms while approximately 50% of Orientals have one. A remarkably higher frequency of acute alcohol intoxication among Asians than among Caucasians could be related to the absence of a the missing form in Asian populations. Variation in ALDH2 may contribute to esophageal cancer.

SNP outcomes in ALDH2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2238152	T	R	**GG**	--		HYPERTENSION, ALCOHOL INTOLERANCE
rs968529	T	R	**CC**	--		PARKINSON'S DISEASE, PESTICIDE TOXICITY
rs16941667	T	R	**CC**	--		GASTRIC CANCER
rs671	A	R	**GG**	--		ALCOHOL FLUSH IN ASIANS, ESOPHOGEAL CANCER, GASTRIC CANCER, SMOKING

New concepts:

- *Mitochondria* are a cell constitutent (organelle) found in large numbers in most cells, in which the biochemical processes of respiration and energy production occur.

NOS3

nitric oxide synthase 3 (endothelial cell)

NOS3 provides instructions for making a protein that produces nitric oxide (NO). This is a free radical, a molecule with a missing electron that can cause damage by oxidation when in excess inside the cells, but it is also essential for many functions within the body such as neurotransmitter function and helping the body deal with microbes and tumors. NOS3 is needed for normal urea cycle function and responsible for regulation of sulfate production for lipid oxidation sparing membrane-bound cholesterol sulfate vs. nitric oxide production in acute infection.

This enzyme is one of three similar types of protein that synthesize NO. The NO produced by NOS3 is known as endothelial NOS, or eNOS, and is mainly responsible for allowing the muscles of the blood vessels to relax. It is also important in cellular reproduction and in enabling the function of white blood cells and platelets.

Other types of nitric oxide synthases, NOS1 (nNOS) and NOS2 (iNOS) are more specific to the nervous system and immune defense against pathogens.

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. Aluminum, mercury, lead and glyphosate may dysrupt endothelial Nitric oxide synthase function causing cellular injury by glycation or oxidative damage in cardiovascular disorders.

SNP outcomes in NOS3 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs7830	T	R	**GG**	--		ENOS
rs1800779	G	R	**AA**	--		ENOS, HYPOXIC-ISCHEMIC ENCEPHALOPATHY, LEUKOARAIOSIS
rs1800783	A	R	**TT**	--		DECREASED ENDOTHELIAL NITRIC OXIDE SYNTHASE ACTIVITY, DIABETIC NEPHROPATHY
rs2070744	C	R	**TT**	--		ENDOTHELIAL NOS, RECURRENT MISCARRIAGE, NEURALGIA-INDUCING CAVITATIONAL OSTEONECROSIS OF THE JAWS (NICO) FOR HOMOZYGOUS TT

HLA-DPB2

major histocompatibility complex, class II, DP beta 2 (pseudogene)

HLA-DPB2 (Major Histocompatibility Complex, Class II, DP Beta 2 (Pseudogene)) is a Pseudogene. Diseases associated with HLA-DPB2 include fibrochondrogenesis 2 and otospondylomegaepiphyseal dysplasia. Among its related pathways are PI3K-Akt signaling pathway and ERK Signaling.

SNP outcomes in HLA-DPB2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1883414	A	R	**AG**	**+-**		LOSS OF PROTECTIVE IGA IMMUNITY EFFECT

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.

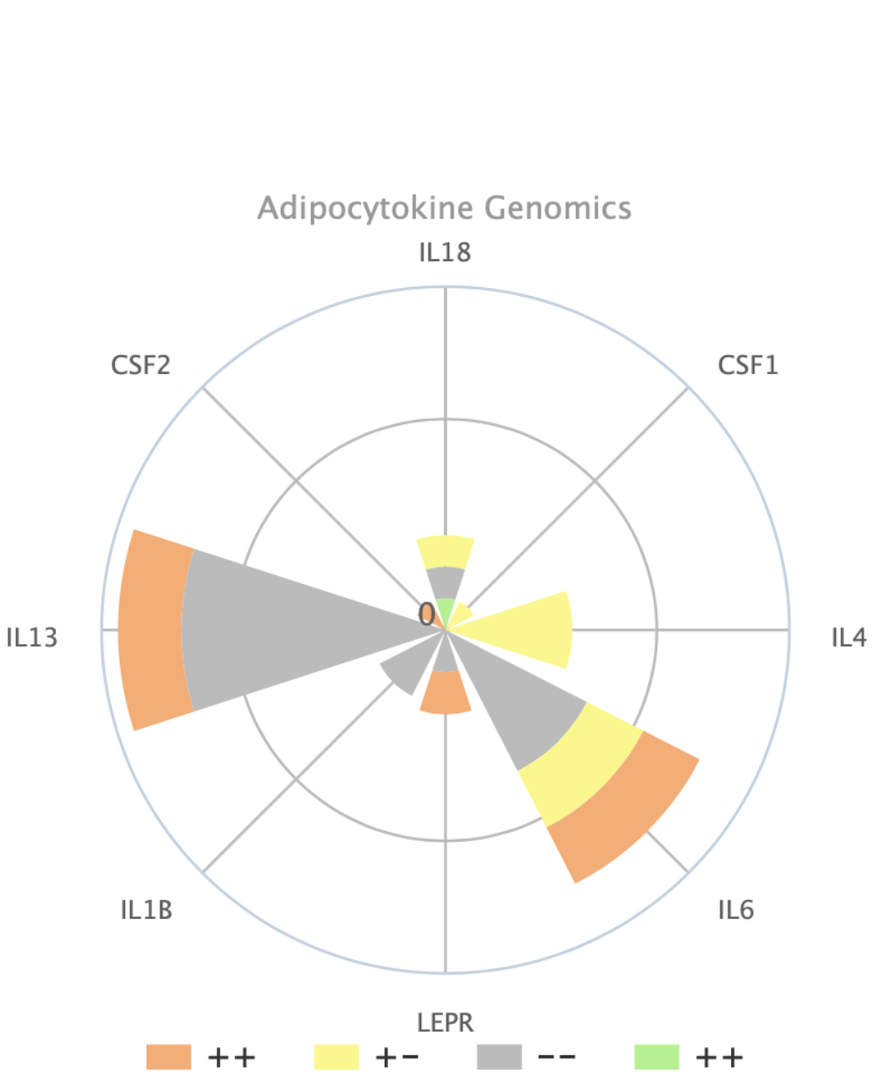
This enzyme is one of three similar types of protein that synthesize NO. The NO produced by NOS2 is known as inducible NOS, or iNOS, and is produced in large quantities when needed as an oxidant in immune defense.

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 NOS2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2248814	A	R	**AG**	**+-**		IMMUNE NOS
rs2297518	A	R	**GG**	**--**		IMMUNE NOS
rs2274894	T	R	**TG**	**+-**		IMMUNE NOS



Adipocytokine Genomics

Cytokines are a broad and loose category of small proteins (~5–20 kDa) that are important in cell signaling. They are released by cells and affect the behavior of other cells. Cytokines can also be involved in autocrine signaling. Cytokines include chemokines, interferons, interleukins, lymphokines, tumour necrosis factor but generally not hormones or growth factors (despite some terminologic overlap). Cytokines are produced by a broad range of cells, including immune cells like macrophages, B lymphocytes, T lymphocytes and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells; a given cytokine may be produced by more than one type of cell.They act through receptors, and are especially important in the immune system; cytokines modulate the balance between humoral and cell-based immune responses, and they regulate the maturation, growth, and responsiveness of particular cell populations. Some cytokines enhance or inhibit the action of other cytokines in complex ways.They are different from hormones, which are also important cell signaling molecules, in that hormones circulate in much lower concentrations and hormones tend to be made by specific kinds of cells.They are important in health and disease, specifically in host responses to infection, immune responses, inflammation, trauma, sepsis, cancer, and reproduction.

IL6

interleukin 6 (interferon, beta 2)

IL6 is a cell signalling protein activated in response to various inflammatory triggers. A mutated SNP causes a fixed response with or without inflammatory triggers. Normally IL6 is a signalling protein secreted by T cells and macrophages to stimulate immune response, e.g. during infection and after trauma, especially burns or other tissue damage leading to inflammation, either an acute and chronic inflammation response. A mutated gene will induce chronicity.

IL6 encodes a cytokine that functions in inflammation and the maturation of B lymphocyte cells. In addition, the protein encoded by IL6 has been shown to be an endogenous pyrogen capable of inducing fever in people with autoimmune diseases or infections. The protein is primarily produced at sites of acute and chronic inflammation, where it is secreted into the serum and induces a transcriptional inflammatory response through interleukin 6 receptor, alpha. The functioning of this gene is implicated in a wide variety of inflammation-associated disease states, including suspectibility to diabetes mellitus and systemic juvenile rheumatoid arthritis.

Polymorphism (-174CC) predicts greater severity of common cold symtoms.

SNP outcomes in IL6 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2069837	G	R	**AA**	**--**		INFLAMMASOME CHRONIC HBV
rs2066992	T	R	**GT**	**-+**		INFLAMMASOME CHRONIC HBV
rs1800795	C	R	**GG**	**--**		HRV & RSV SEVERITY OF SYMPTOMS, ISCHEMIC STROKE, FIBRINOGEN LEVELS, HETEROZYGOUS SHOWED LESS EXPRESSED HSP70, DIABETES, CANCER, HYPERTENSION, ALZHEIMER'S, PERIODONTITIS, SUDDEN INFANT DEATH, CELIAC DISEASE IN GIRLS
rs2069852	G	R	**GG**	**++**		INFLAMMASOME CHRONIC HBV

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.

LEPR

leptin receptor

The leptin hormone regulates adipose-tissue mass through hypothalamus effects on hunger and energy use. It acts through the leptin receptor (LEP-R), a single-transmembrane-domain receptor of the cytokine receptor family. This protein is a receptor for leptin (an adipocyte-specific hormone that regulates body weight), and is involved in the regulation of fat metabolism. Variations in the leptin receptor have been associated with obesity. Excess secretion of Leptin due to stress increases glucocorticoids and decreases a-MSH allowing the stimulation of the hunger gene.

SNP outcomes in LEPR relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2025804	G	R	**GG**	**++**		LEPTIN, OBESITY, HUNGER CRAVINGS, INCREASED SNACKING AND FOOD SEEKING BEHAVIOR
rs1137101	A	R	**GG**	**--**		HUNGER, OBESITY LEPTIN RECEPTOR POLYMORPHISM

MULTI-SNP MACROS

C-Reactive Protein Genotypes, Nutritional Status and Inflammation

Genes	CRP
Repute:	SEE TABLE
Magnitude:	4
Frequency:	N/A

INTERPRETATION: C-reactive protein is a protein produced by the CRP gene in response to inflammatory signals from interleukin 6. It activates complement, which enhances the ability of the immune system to remove pathogens. Inflammation, as indicated by CRP levels in the blood, is a risk factor for chronic diseases. Several SNPs (rs3093058, rs3093062, rs2808630) on the CRP gene are related to foods influencing genetic susceptibility to heightened systemic inflammation. This algorithm uses a combination of major and minor alleles for these three SNPS to determine your potential risk for several diet-related factors. The results of your algorithm calculations are summarized inthe following table.

Effects of cholesterol/ triglycerides	You are unlikely to experience increased inflammation as a result of high CRP if you have cholesterol and triglycerides in your diet.
Effects of weight loss	You will most likely not experience reduced inflammation as a result of lower CRP levels when you lose weight.

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

Your results: rs3093058 (**TT**) rs3093062 (**CC**) rs2808630 (**CC**)

Inflammation macro algorithms returning as false:

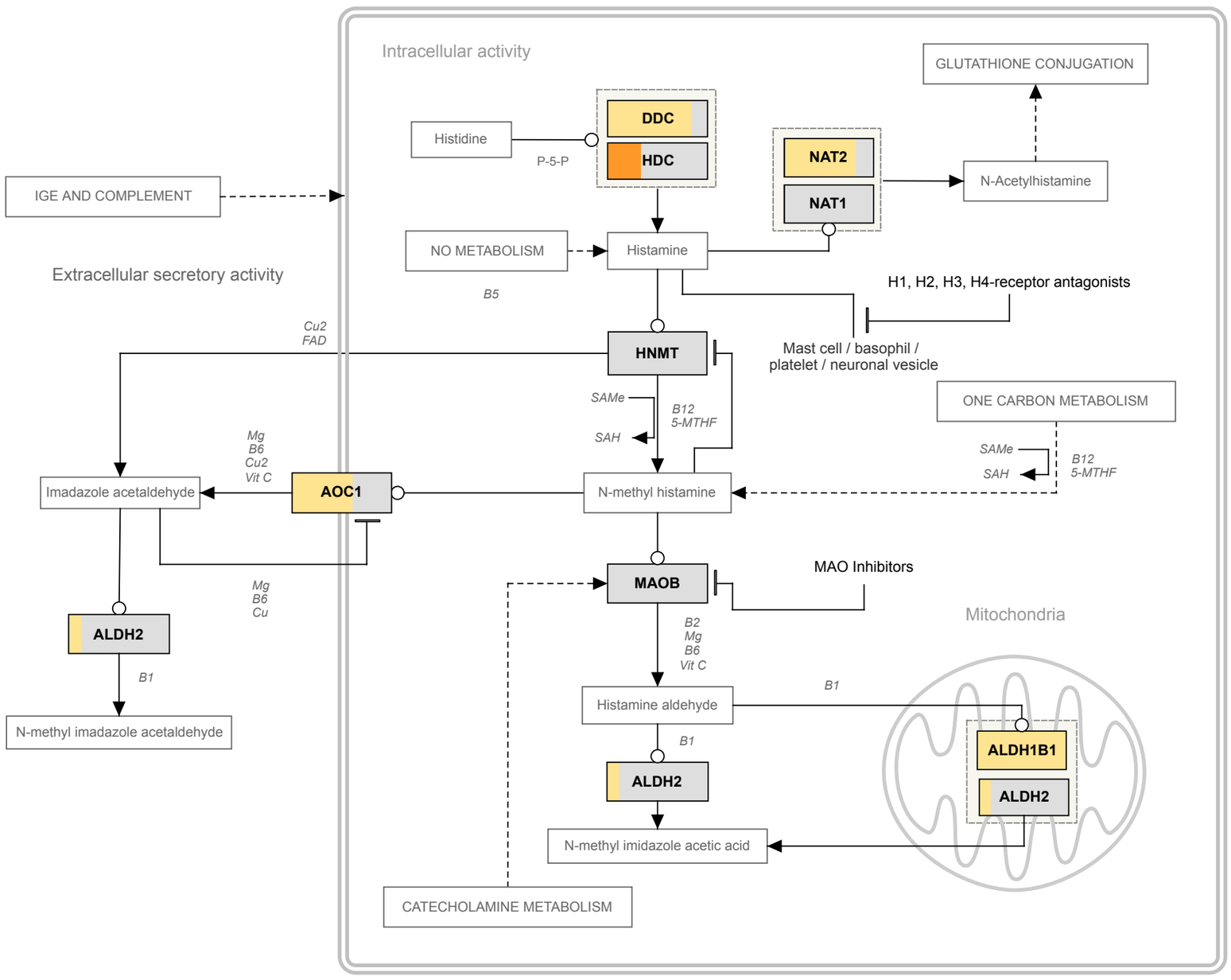
- Significant autoimmune disorder risk (HLA-DRA)
- Increased risk of chronic fatigue syndrome
- Moderate autoimmune disorder risk (HLA-DRA)
- Risk of autoimmune disorder/ gluten sensitivity
- Risk of autoimmune disorder/ gluten sensitivity
- Increased risk of several autoimmune diseases

INFLAMMATION

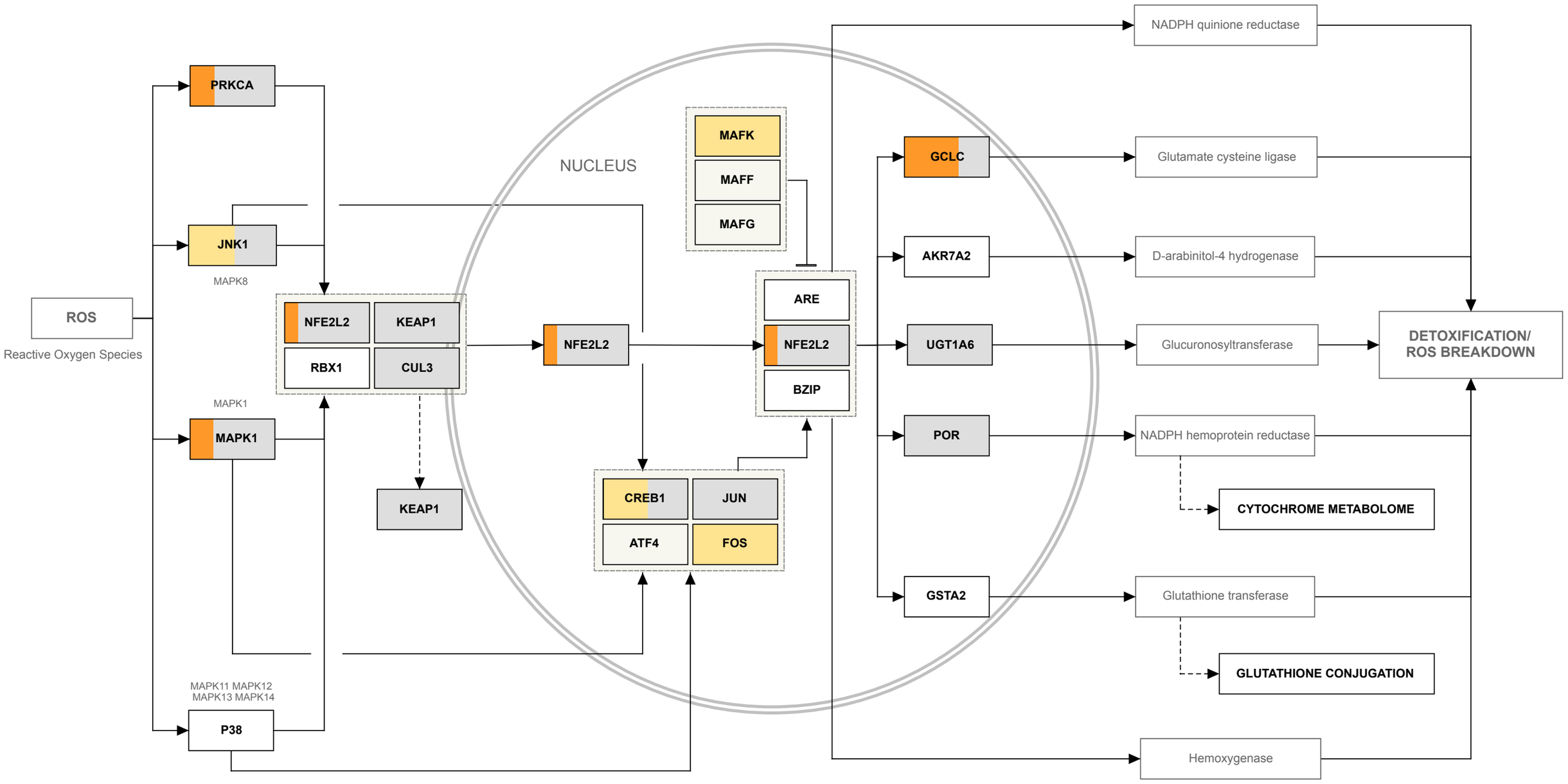
NETWORK MAPS

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).

Histamine Metabolism



Oxidative Stress-induced Gene Expression



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.	Selenium	
2.	Theanine	
3.	Salacia oblonga	
4.	Epigallocatechin gallate (EGCG)	
5.	Ginkgo (Ginkgo biloba)	
6.	Citrulline	
7.	D-mannose	
8.	Dexamethasone	
9.	Rhodiola rosea	
10.	Salvia miltiorrhiza (Danshen)	
11.	Isatis (Woad Root)	
12.	Curcumin	
13.	Ursolic acid	
14.	Bromelain	
15.	Myrcene	
16.	Bisphenol A (BPA)	
17.	Sedum sarmentosum	
18.	L-Arginine	
19.	Cigarette smoke	
20.	Genistein	
21.	Tyrosol	
22.	Kaempferol	
23.	Alcea rosea (Althaea rosea, Hollycock)	
24.	Lupeol	
25.	Fructus mume	

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	rs7412	APOE	C	**CC**	Psoriasis
Amitriptyline	rs4244285	CYP2C19	A	**AG**	Those with the AA or AG genotype are poor metabolizers of amitriptyline
Azathioprine	rs1800460	TPMT	T	**CT**	Hepatotoxicity
Azathioprine	rs1142345	TPMT	C	**CT**	Hepatotoxicity
Azathioprine	rs1142345	TPMT	C	**CT**	Patients with CC or CT genotype have decreased inactivation of thiopurines and increased risk of toxicity
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)
Cisplatin	rs1695	GSTP1	A	**AG**	Tinnitus, hearing impairment, Raynaud syndrome
Clobazam	rs4244285	CYP2C19	G	**AG**	Clobazem is metabolized into N-desmethylclobazem (NCLB) mostly by CYP3A4. NCLB is primarily metabolized by 2C19. Those with one 2C19*2 allele mutation (1*/2*) are intermediate metabolizers of NCLB. Those with two (2*/2*) mutations will metabolize NCLB poorly in comparisone to extensive metabolizers (1*/1*). Levels of NCLB can be five times higher in poor metabolizers, and two times higher in intermediate metabolizers as compared to individuals who are extensive metabolizers. The safety and efficacy of clobazem may be affected by polymorphic expression of CYP2C19*2.
Cyclosporine	rs231775	CTLA4	A	**AG**	Gingival overgrowth, periodontal disease
Fluorouracil	rs1695	GSTP1	A	**AG**	Hematological toxicity, gastrointestinal toxicity
Gefitinib	rs2231142	ABCG2	T	**GT**	Diarrhea
Gefitinib	rs2231142	ABCG2	T	**GT**	In non-small lung cancer patients, those that are heterozygous (ABCG2 421C>A) have a higher risk of diarrhea.
Irinotecan	rs4149056	SLCO1B1	C	**CT**	Diarrhea, leucopenia, neutropenia
Isoniazid	rs6413419	CYP2E1	GG	**GG**	Hepatotoxicity
Mercaptopurine	rs1800460	TPMT	T	**CT**	Hepatotoxicity
Mercaptopurine	rs1142345	TPMT	C	**CT**	Hepatotoxicity
Venlafaxine	rs5030655	CYP2D6	I	**II**	Nausea, vomiting diarrhea
Almotriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment
Citalopram	rs1954787	GRIK4	C	**CC**	Improved response to antidepressant medication
Clopidogrel	rs4244285	CYP2C19	A	**AG**	Patients are poor metabolizers of clopidogrel. More likely to experience poor cardiovascular outcomes.
Clopidogrel	rs4244285	CYP2C19	A	**AG**	Patients are poor metabolizers of clopidogrel. More likely to experience poor cardiovascular outcomes.
Codeine	rs5030655	CYP2D6	I	**II**	Poor drug metabolizer, lower dose requirements
Dextromethorphan	rs5030655	CYP2D6	II	**II**	Poor drug metabolizer, lower dose requirements
Eletriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment
Frovatriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment
Infliximab	rs1801274	FCGR3A	GG	**GG**	Better ACR20 response
Modafinil	rs4680	COMT	GG	**GG**	Those with the GG genotype respond better to drug therapy (improved vigor and well being). Those with the AA genotype do not respond well to drug therapy
Morphine	rs1799971	OPRM1	A	**AA**	Better response to pain relief drugs
Naratriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment
Rizatriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment

Rosuvastatin	rs2231142	ABCG2	T	**GT**	Greater response to drug therapy
Sildenafil	rs5443	GNB3	T	**CT**	Better response to drug treatment
Sumatriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment
Trastuzumab	rs351855	FGFR4	G	**AG**	Reduced response to herceptin
Venlafaxine	rs5030655	CYP2D6	I	**II**	Poor drug metabolizer, lower dose requirements, nausea, vomiting and diarrhea
Venlafaxine	rs5030655	CYP2D6	I	**II**	Poor drug metabolizer, lower dose requirements, nausea, vomiting and diarrhea
Zolmitriptan	rs5443	GNB3	T	**CT**	Better response to drug treatment