GenomicInsight™
POWERED BY OPUS23 EXPLORER™

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

ENDOCRINE

Diagnostic Solutions laboratory

OPUS23 EXPLORER

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:

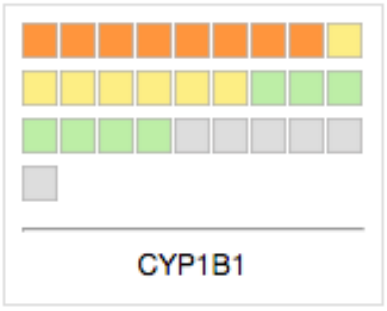
- This is a very small difference from normal
- Very few people get struck by lightning regardless

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:

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.

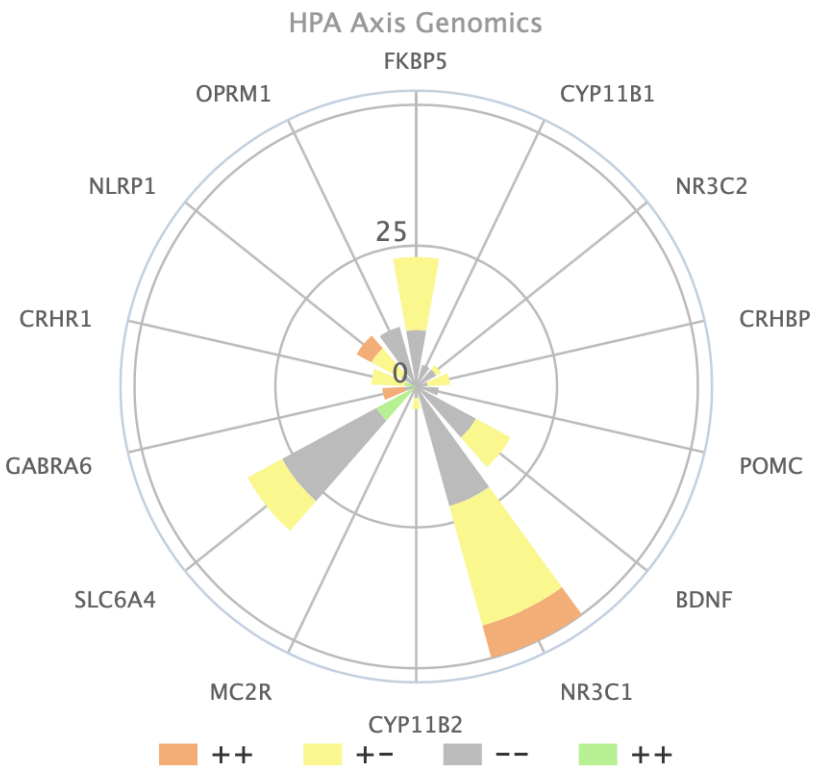
For example, a simple macro to determine if you should get out of bed might be:

- 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.



ENDOCRINE

HPA Axis Genomics

Correct regulation of cortisol levels is necessary for survival, and too little or too much cortisol exposure can result in serious harm. Therefore, both basal and stress-induced cortisol levels are maintained carefully. A healthy stress response is characterized by a quick rise in cortisol levels, followed by a rapid decline with the termination of the stressful event. When the organism is burdened by cumulative stress, however, the cortisol burden increases. This results in wear and tear on the organism from excessive exposure to the catabolic properties of glucocorticoids, stress peptides, and proinflammatory cytokines. This burden taxes the organism and can influence the development of neuropsychiatric and metabolic disorders. It therefore is essential to understand the systems that regulate cortisol production.

Three main determinants of HPA axis activity control the amount of cortisol a person is exposed to during adulthood: genetic background, early-life environment, and current life stress. In addition, studies found that post-traumatic stress disorder (PTSD) can contribute to HPA axis disturbances. Differences among individuals in cortisol responses to stress result from a complex interplay between genetic and environmental factors.

The genetic contribution to the variability in HPA axis reactivity is believed to arise from DNA variations (i.e., polymorphisms) in the genes encoding neurotransmitters involved in HPA axis regulation. Overall, heritable influences account for approximately 62 percent of the etiological variance in basal glucocorticoid levels. Recent candidate gene association studies using laboratory-based stress procedures also have implicated multiple gene variants in explaining some of the variance in cortisol responses to stress, including polymorphisms in the following genes.

FKBP5

FK506 binding protein 5

The FKBP5 gene provides instructions for making the FKBP5 protein which is involved in regulation of the immune system and directing proteins throughout the cell. In the conventional treatment of inflammatory conditions such as rheumatoid arthritis and psoriasis, this gene is often targeted by drugs which inhibit the activity of this protein. FKBP5 may influence the response to SSRI antidepressants.

SNP outcomes in FKBP5 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs9470080	T	R	**CC**	--		
rs1360780	T	R	**CC**	--		POST TRAUMATIC STRESS PTSD, REACTION TO ANTIDEPRESSANTS
rs9296158	A	R	**AG**	+-		POST TRAUMATIC STRESS DISORDER PTSD
rs3800373	A	R	**AC**	+-		HPA AXIS, DEPRESSION, STRESS RESPONSE, ANTIDEPRESSANT RESPONSE

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).
- *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.

BDNF

brain-derived neurotrophic factor

The protein encoded by this gene is a member of the nerve growth factor family. It is induced by cortical neurons, and is necessary for survival of striatal neurons in the brain. Expression of this gene is reduced in both Alzheimer's and Huntington disease patients. This gene may play a role in the regulation of stress response and in the biology of mood disorders. Multiple transcript variants encoding distinct isoforms have been described for this gene. Variation in BDNF has been associated with migraine trait and mercury detoxification.

SNP outcomes in BDNF relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs6265	T	R	**CT**	**-+**		ELEVATED CORTISOL, HEADACHE MEDICINE ANALGESIC OVERUSE OBESITY, LOW PROTEIN HIGH-CARBOHYDRATE INTAKE LOWERS TYPE II DIABETES RISK
rs2049046	A	R	**TT**	**--**		MIGRAINE TRAIT HAPLOTYPE, COGNITIVE DEFICIT IN MERCURY EXPOSURE
rs56164415	A	R	**GG**	**--**		SCHIZOPHRENIA, ASTHMA, ALZHEIMER'S

NR3C1

nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)

NR3C1 encodes the 'glucocorticoid receptor', which can activate glucocorticoid-responsive genes to activate their being 'read' (transcription) and having their instructions carried out. This receptor is typically found in the cell's cytoplasm, but upon binding, it is transported into the cell nucleus. It is involved in inflammatory responses and cellular proliferation Mutations in this gene are associated with generalized glucocorticoid resistance. Glucocorticoid s are part of the feedback mechanism in the immune system that turns immune activity (inflammation) down. They are therefore used in medicine to treat diseases caused by an overactive immune system, such as allergies, asthma and autoimmune diseases. There has been some association with variations in NR3C1 and bone mineral density, which is opposite for men and women.

SNP outcomes in NR3C1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs6189	T	R	**CC**	**--**	■■■■■	GLUCOCORTICOID RESISTANCE
rs852977	G	R	**AA**	**--**	■■■■	GENERALIZED GLUCOCORTICOID RESISTANCE, HIGH CORTISOL, CHRONIC FATIGUE SYNDROME
rs2918419	C	R	**TT**	**--**	■■■■■■	LOW BONE MINERAL DENSITY HAPLOTYPE IN WOMEN OPPOSITE IN MEN
rs6191	A	R	**AC**	**+-**	■■■■■■	LITHIUM THERAPY NON-RESPONDER HAPLOTYPE
rs6198	T	R	**TT**	**++**	■■■■■■	LITHIUM THERAPY NON-RESPONDER HAPLOTYPE
rs1866388	G	R	**AA**	**--**	■■■■	GENERALIZED GLUCOCORTICOID RESISTANCE HIGH CORTISOL CHRONIC FATIGUE SYNDROME
rs6196	G	R	**AG**	**-+**	■■■■■■	CORTICOSTEROID RESISTANCE HAPLOTYPE, LITHIUM RESPONDER HAPLOTYPE, HPA AXIS
rs33388	A	R	**AT**	**+-**	■■■■■■	LITHIUM THERAPY NON-RESPONDER HAPLOTYPE

New concepts:

- The *nucleus* is the central part of most cells that contains genetic material and is enclosed in a membrane
- A *receptor* is a molecule in a cell membrane, that responds specifically to a particular neurotransmitter, hormone, antigen, or other substance.
- *Transcription* is the first step of gene expression, in which a particular segment of DNA is copied into RNA
- *Cytoplasm* is the material or protoplasm within a living cell, excluding the nucleus.

SLC6A4

solute carrier family 6 (neurotransmitter transporter, serotonin), member 4

SLC6A4 encodes a protein that terminates the action of serotonin and recycles it in a sodium-dependent manner. This protein is a target of psychomotor stimulants, such as amphetamines and cocaine, and is a member of the sodium:neurotransmitter symporter family. A repeat length polymorphism in the promoter of this gene has been shown to affect the rate of serotonin uptake and may play a role in sudden infant death syndrome, aggressive behavior in Alzheimer disease patients, and depression-susceptibility in people experiencing emotional trauma. The activation region of the SLC6A4 gene contains a polymorphism with "short" and "long" repeats in a region: 5-HTT-linked polymorphic region (5-HTTLPR or SERTPR). The short variation has 14 repeats of a sequence while the long variation has 16 repeats. The short variation leads to less transcription for SLC6A4, and it has been found that it can partly account for anxiety-related personality traits.

SNP outcomes in SLC6A4 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs25532	G	R	--	--		MAJOR ALLELE OBSESSIVE COMPULSIVE DISORDER (OCD) HAPLOTYPE FROM HIGHER SEROTONIN TRANSPORT FUNCTION, ALCOHOL DEPENDENCE
rs216250	A	R	**GG**	--		SEROTONIN TRANSPORTER, GABA TRANSPORTER
rs1042173	C	B	**AC**	-+		SEROTONIN TRANSPORTER,, RUMINATION PERSONALITY TRAIT
rs140701	T	R	**TC**	+-		SEROTONIN TRANSPORTER, PANIC, ANXIETY, MOOD
rs4251417	T	R	**CC**	--		PLACEBO EFFECT

New concepts:

- *Amines* are organic compounds contain a basic nitrogen atom. Important amines include amino acids, histamine, dopamine and serotonin.
- In genetics, a *promoter* is a region of DNA that initiates transcription of a particular gene.
- A *polymorphism* is a difference in DNA sequence among individuals.

HSD11B1

hydroxysteroid (11-beta) dehydrogenase 1

HSD11B1 catalyzes the conversion of the stress hormone cortisol to the inactive metabolite cortisone. In addition, the encoded protein can catalyze the reverse reaction, the conversion of cortisone to cortisol. Too much cortisol can lead to central obesity, and a particular variation in this gene has been associated with obesity and insulin resistance in children.

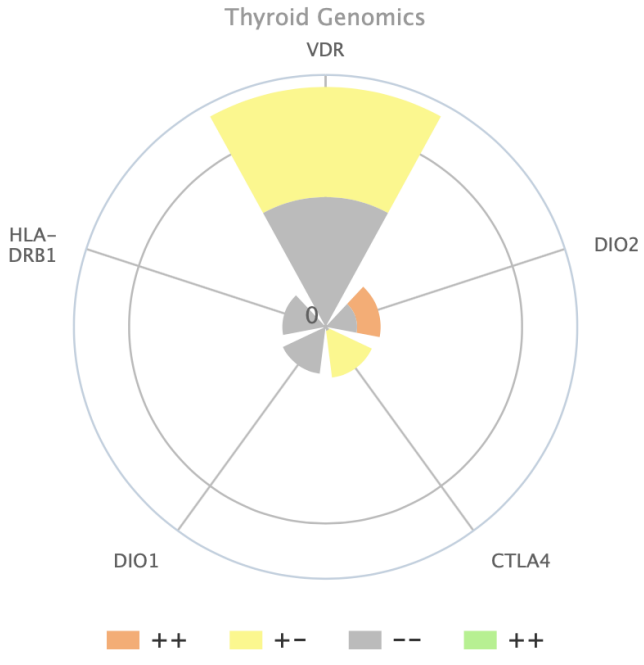
SNP outcomes in HSD11B1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs846906	T	R	**TC**	**+-**		

New concepts:

- To *Catalyze* is to cause or accelerate (a reaction) by acting as a catalyst.
- A *metabolite* is a product of metabolism; a substance essential to the metabolism of a particular organism or to a particular metabolic process.

ENDOCRINE



Thyroid Genomics

Adequate thyroid function is dependent on multiple factors, and whether or not a client has any SNPs, it is still possible that there may be thyroid problems. This becomes more likely in the presence of inflammation. DIO1 and DIO2 convert T4 to T3 by removing one iodine molecule. CTLA4 transmits an inhibitory signal to T cells, reducing the likelihood of autoimmune disease. Low vitamin D is a trigger for autoimmune thyroiditis, and the BsmI SNP of the vitamin D receptor is linked with hashimoto's thyroiditis. FOXE1 is important in thyroid growth and development. HLA-DRB1 regulates immune response to thyroid antibodies.

VDR

vitamin D (1,25- dihydroxyvitamin D3) receptor

The VDR gene provides instructions for making a protein called vitamin D receptor (VDR), which allows the body to respond appropriately to vitamin D. This vitamin can be acquired from foods in the diet or made in the body with help from sunlight. Vitamin D is involved in maintaining the proper balance of several minerals in the body, including calcium and phosphate, which are essential for the normal formation of bones and teeth. One of vitamin D's major roles is to control the absorption of calcium and phosphate from the intestines into the bloodstream. Vitamin D is also involved in several process unrelated to bone formation.

VDR attaches (binds) to the active form of vitamin D, known as calcitriol. This interaction allows VDR to partner with another protein called retinoid X receptor (RXR). The resulting complex of proteins then binds to particular regions of DNA, known as vitamin D response elements, and regulates the activity of vitamin D-responsive genes. By turning these genes on or off, VDR helps control calcium and phosphate absorption and other processes.

A VDR variant FokI is involved with Blood sugar regulation. Certain VDR mutations oppose COMT mutations in the regulation of dopamine levels. A VDR TaqI++ mutation means that a person is less sensitive to mood swings when taking methyl group supplement levels. A VDR Taq1 mutation can result in behaviors opposite to certain COMT mutations.

The vitamin D receptor plays an important role in regulating the hair cycle. Loss of VDR is associated with hair loss in experimental animals. Glucocorticoids are known to decrease expression of VDR, which is expressed in most tissues of the body and regulate intestinal transport of calcium, iron and other minerals. The VDR BsmI variant has been associated with low bone mineral density and osteoporosis.

Mutations in the VDR gene cause vitamin D-dependent rickets type 2 (VDDR2), also known as hereditary vitamin D-resistant rickets (HVDRR). This disorder of bone development is characterized by low levels of calcium (hypocalcemia) and phosphate (hypophosphatemia) in the blood, which lead to soft, weak bones (rickets) that are prone to fracture. A common feature of this condition is bowed legs.

The VDR gene mutations that cause this condition prevent the VDR protein from functioning properly. Some changes in the VDR gene lead to an abnormally short version of the VDR protein; others result in the production of an abnormal receptor that cannot bind to calcitriol, to RXR, or to DNA. Despite plenty of calcitriol in the body, the altered VDR cannot stimulate gene activity important for mineral absorption. The lack of calcium and phosphate absorption in the intestines slows deposition of these minerals into developing bone (bone mineralization), which leads to soft, weak bones and other features of VDDR2. Hypocalcemia also causes muscle weakness and seizures in some affected individuals. Most VDR gene mutations impair hair growth, leading to alopecia; however, mutations that block VDR's ability to interact with calcitriol do not cause alopecia, indicating that calcitriol is not necessary for the receptor's role in hair development.

SNP outcomes in VDR relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs3847987	A	R	**CC**	--		COPD, PULMONARY, LUNG, VITAMIN D, T1D, TYPE 1 DIABETES, DIABETES, DEFICIENCY, CHRONIC OBSTRUCTIVE PULMONARY DISEASE
rs731236	G	R	**AG**	-+		TAQ1 DOPAMINE SYNTHESIS, BREAST CANCER SUSCEPTIBILITY
rs1540339	T	R	**CC**	--		INCREASED CYP1A2 ACTIVITY
rs2238135	G	R	**CC**	--		CANCER
rs1544410	T	R	**CT**	-+		BONE DENSITY RESPONSE TO ESTROGENS AND ALENDRONATE, HASHIMOTOS THYROIDITIS, INFERTILITY
rs7139166	G	R	**CG**	-+		
rs4516035	T	R	**CT**	-+		MELANOMA
rs2107301	A	R	**GG**	--		CANCER

New concepts:

- A *mutation* is an alteration of genetic material such that a new variation is produced.
- A *methyl group* is one of the commonest structural units of organic compounds, consisting of three hydrogen atoms bonded to a carbon atom, which is linked to the remainder of the molecule.

DIO2

deiodinase, iodothyronine, type II

The DIO2 gene provides instructions for making the type II iodothyronine deiodinase enzyme. This enzyme belongs to the iodothyronine deiodinase family. It activates thyroid hormone by converting the hormone precursor thyroxine (T4) by removing a molecule of iodine to active triiodothyronine (T3). It is found in the thyroid gland, and may be responsible for the relative increase in production of T3 in the thyroid in patients with Graves disease (an autoimmune disease causing overactitity of the thyroid) and thyroid adenomas (tumors). DIO2 also shows activity in cardiac muscle. This protein contains selenocysteine. DIO2 enzyme has interactions with DIO1, sulfotransferases and glucuronidases in processing, transporting and eliminating hormones and neurotransmitters.

SNP outcomes in DIO2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs12885300	C	R	**CC**	**++**		BIPOLAR DISORDER, OSTEOARTHRITIS, INCREASED T4 LEVELS, ALTERED HPA AXIS SET POINT
rs225014	C	R	**TT**	**--**		THYROID INCREASED WELLBEING ON T3 THERAPY, LOW BRAIN T3, DIABETES T2DM, INSULIN RESISTANCE, OSTEOARTHRITIS, HETEROZYGOSITY ASSOCIATED WITH RISK OF RECURRENT DEPRESSION, MILD COGNITIVE IMPAIRMENT

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 CTLA4 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs231775	G	R	**AG**	**-+**		CELIAC, THYROID, HASHIMOTOS, GRAVES DISEASE, VITILIGO
rs231779	T	R	**TC**	**+-**		GRAVES DISEASE

FOXE1

forkhead box E1 (thyroid transcription factor 2)

This gene is a transcription factor which helps the function and growth of the thyroid. Mutations in this gene are associated with congenital hypothyroidism and cleft palate with abnormal thyroid formation of the fetus. It may also be associated with squamous cell epithelioma and a form of hereditary neuropathy.

SNP outcomes in FOXE1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs925489	T	R	**CT**	**-+**		HYPOTHYROIDISM, SERUM THYROID-STIMULATING HORMONE LEVELS
rs10984009	A	R	**GG**	**--**		
rs2997312	A	R	**AG**	**+-**		
rs1867277	A	R	**AG**	**+-**		
rs7850258	G	R	**AG**	**-+**		HYPOTHYROIDISM, CLEFT PALATE AND CLEFT LIP, THYROID CANCER

MULTI-SNP MACROS

ENDOCRINE

corticosteroid resistance/ high cortisol syndrome

Genes	NR3C1
Repute:	RISK
Magnitude:	
Frequency:	N/A

INTERPRETATION: The glucocorticoid receptor (NR3C1) binds to cortisol in the body, and regulates how fast many genes make their enzymes, as well as overall function of metabolism and the immune system. People with lowered glucocorticoid sensitivity may get low blood potassium when using diuretics. A set of mutations in the NR3C1 gene is linked with a lowered sensitivity to cortisol made by the body. You have a specific group of NR3C1 gene mutations associated with corticosteroid resistance.

The consequences of this may include

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

Your results:	rs1866388 (**AA**)	rs10482682 (**TC**)	rs6189 (**CC**)	rs2963155 (**N/A**)	rs852977 (**AA**)

Oxytocin 'social/ empathy' polymorphism

Genes	OXTR
Repute:	BENEFIT
Magnitude:	3
Frequency:	N/A

INTERPRETATION: rs53576 is a silent G to A change in the oxytocin receptor (OXTR) gene. You have the GG genotype, which appears to predispose to gaining benefits in the managment of stress form seeking social support. Understress, individuals with with one or more copies of the G version of rs53576 were more likely to seek emotional support from their friends, compared to those with two copies of the A version. Studies have demonstrated that individuals with the G allele are more empathetic, feel less lonely, employ more sensitive parenting techniques, and have lower rates of autism. GG genotype rs53576 also tend to be on average more optimistic and empathetic and handle stress well.

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

Your results: rs53576 (**GG**)

Variation in thyroid hormone levels

Genes	CHR9-LOC97793827
Repute:	RISK
Magnitude:	1
Frequency:	N/A

INTERPRETATION: The SNP rs965513 at an intergenic region near the FOXE1 (forkhead box protein E1) gene affects function necessary for the regulation of genes specific to the thyroid such as TG (thyroglobulin) and TPO (thyroperoxidase). Regulation of these genes is needed to make appropriate levels of the thyroid hormones triiodothyronine (T3) and thyroxine (T4). Thyroid stimulating hormone (TSH) is the overall regulator. In a large study of Icelanders, people with the A allele in rs965513 had lower levels of TSH and free T4, and higher levels of free T3, depending on whether they had one or two copies of the A allele.

Your results from this SNP: Reduced TSH by 5.9%, reduced FT4 by 1.2%, increased FT3 by 1.2%

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

Your results: rs965513 (**AG**)

Some indication of SHBG imbalance/ low testosterone

Genes	SHBG,FAM9B
Repute:	RISK
Magnitude:	1.2
Frequency:	N/A

INTERPRETATION: Sex hormone-binding globulin (SHBG) or sex steroid-binding globulin (SSBG) is a glycoprotein that binds to the two sex hormones: androgen and estrogen. SHBG has both enhancing and inhibiting hormonal influences. It decreases with high levels of insulin, growth hormone, insulin-like growth factor 1 (IGF-1), androgens, prolactin and transcortin. High estrogen, and thyroxine cause it to increase. Genetic variations within the SHBG gene may explain some of the inter-individual differences in SHBG concentrations and consequently, serum testosterone levels:

- rs1799941 is linked to the number of TAAAA repeats within an Alu sequence upstream of SHBG promoter and that the A version of rs1799941 is linked with the presence of six TAAAA repeats in this location which has been reported to be associated with higher SHBG concentrations.
- The rs5934505 polymorphism near FAM9B on the X chromosome was also associated with testosterone concentrations. The mean serum testosterone, late-onset hypogonadism, and calculated free testosterone but not SHBG concentrations were lower in men with T genotype than in those with C genotype.

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

Your results: rs1799941 (**AG**) rs6258 (**CC**) rs12150660 (**N/A**) rs5934505 (**T**)

Endocrine macro algorithms returning as false:

- Increased risk of high cortisol levels when under stress

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.	Acute psychological stress	
2.	Traumatic stress (PTSD)	
3.	Phosphatidylserine	
4.	Naringenin	
5.	Noni (Morinda citrifolia)	
6.	Basil	
7.	Guggulu (Commiphora mukul)	
8.	Mind-body therapies	
9.	Cayenne (Capsicum frutescens)	
10.	Emotional wellbeing	
11.	Vitamin A (retinol)	
12.	Krill oil, vitamin D3, and Lactobacillus reuteri mixture	
13.	Retinoic acid	
14.	Magnesium	
15.	Retinoic acid therapeutic levels	
16.	Lactobacillus plantarum	
17.	Vitamin B-2 (riboflavin)	
18.	Butyric Acid (Butyrate)	
19.	Vitamin D (calciferols)	
20.	Migu capsule	
21.	Strengthening Spleen prescriptions	
22.	Curcumin	
23.	Adverse early life environment or trauma (AELE)	
24.	Resveratrol	
25.	Selenocysteine	

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