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

CARDIOMETABOLIC

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

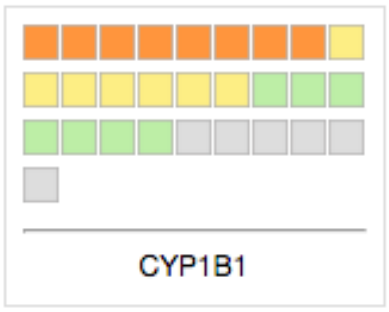
When it comes to a particular disease or syndrome, most SNPs have rather small ORs. This does not mean that they are unworthy of attention, but rather that the findings must be interpreted as part of an integrated whole, including: other SNP results that also support the conclusion; lifestyle factors;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

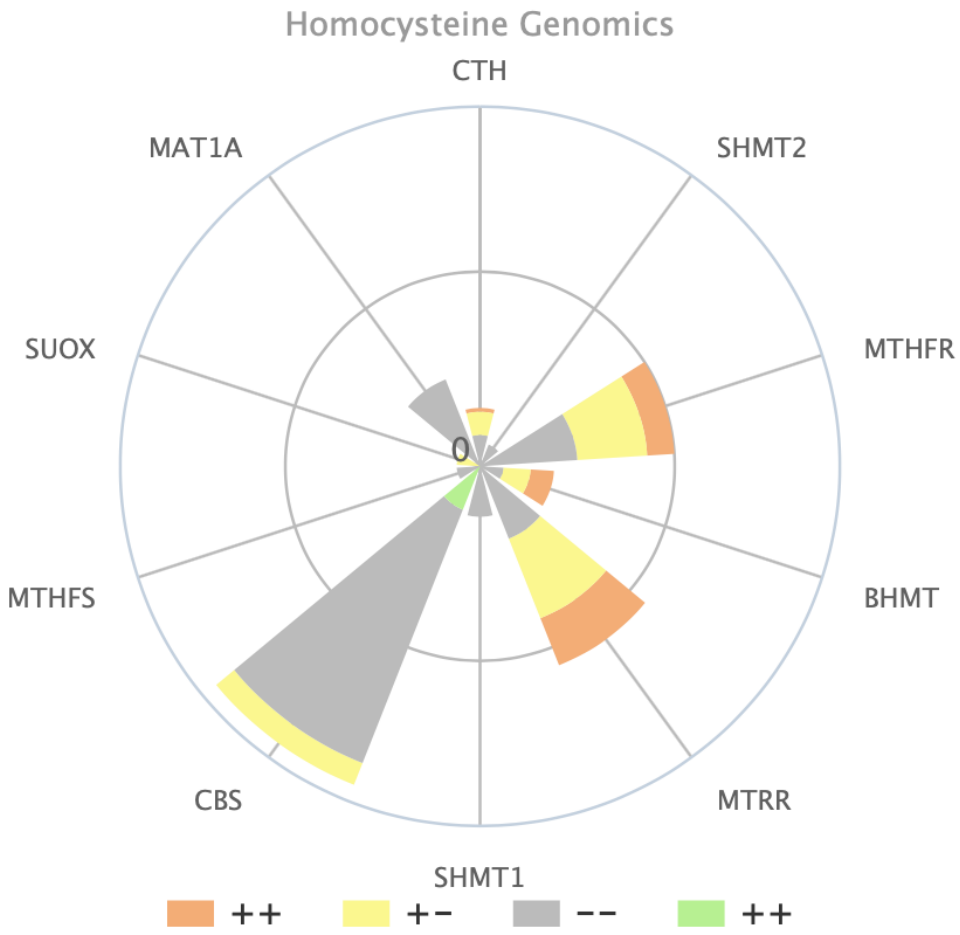
As can be seen, there are a lot of ways you can go back to bed with this algorithm! And this is also true as well for the Opus 23 Pro algorithms: In order for an algorithm to be true, it must fufill all of several conditions. *If even one condition fails, the whole algorithm will be false.*

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.

CARDIOMETABOLIC

Homocysteine Genomics



Homocysteine is a non-proteinogenic α-amino acid. It is a homologue of the amino acid cysteine, differing by an additional methylene bridge (-CH2-). It is biosynthesized from methionine by the removal of its terminal Cε methyl group. Homocysteine can be recycled into methionine or converted into cysteine with the aid of certain B-vitamins. A high level of homocysteine in the blood (hyperhomocysteinemia) makes a person more prone to endothelial cell injury, which leads to inflammation in the blood vessels, which in turn may lead to atherogenesis, which can result in ischemic injury. Hyperhomocysteinemia is therefore a possible risk factor for coronary artery disease. Coronary artery disease occurs when an atherosclerotic plaque blocks blood flow to the coronary arteries, which supply the heart with oxygenated blood.Homocysteine is not obtained from the diet. Instead, it is biosynthesized from methionine via a multi-step process. First, methionine receives an adenosine group from ATP, a reaction catalyzed by S-adenosyl-methionine synthetase, to give S-adenosyl methionine (SAM). SAM then transfers the methyl group to an acceptor molecule, (e.g., norepinephrine as an acceptor during epinephrine synthesis, DNA methyltransferase as an intermediate acceptor in the process of DNA methylation). The adenosine is then hydrolyzed to yield L-homocysteine. L-Homocysteine has two primary fates: conversion via tetrahydrofolate (THF) back into L-methionine or conversion to L-cysteine. Hyperhomocysteinemia has been correlated with the occurrence of blood clots, heart attacks and strokes, though it is unclear whether hyperhomocysteinemia is an independent risk factor for these conditions. Hyperhomoscyteinemia has also been associated with early pregnancy loss and with neural tube defects.

CTH

cystathionase (cystathionine gamma-lyase)

The CTH gene provides instructions to make an enzyme that converts one amino acid into another: cystathionine (which comes from the amino acid methionine) is converted to cysteine by cystathionine gamma-lyase. Glutathione is an antioxidant that prevents damage from free radicals, and the liver needs cysteine to make glutathione. Mutations in the CTH gene can cause cystathionine to be found in the urine (cystathioninuria), high levels of the inflammatory protein homocysteine and low levels of glutathione.

SNP outcomes in CTH relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs28941786	G	R	**CC**	**--**		CYSTATHIONINURIA
rs1021737	T	R	**TG**	**+-**		CLEFT PALATE WITH HOMOZYGOUS RISK ALLELE, HIGHER HOMOCYSTEINE, AGING

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.
- *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.

MTHFR

methylenetetrahydrofolate reductase (NAD(P)H)

Perhaps the most studied SNP-containing gene of all, Methylene tetrahydrofolate reductase (MTHFR) allows conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, needed for conversion of homocysteine (HCy) to the protein-building amino acid methionine via methylation, in the rate-limiting step of the methyl cycle. MTHFR is a highly polymorphic gene, and genetic variation influences susceptibility to occlusive vascular disease, neural tube defects, colon cancer and acute leukemia, and mutations in this gene are associated with methylenetetrahydrofolate reductase deficiency. Lower MTHFR enzyme activity results in lower levels of methylated folate, leading to elevated homocysteine (HCy). Natural variation in this gene is common in healthy people. Although some variants have been reported to influence susceptibility to occlusive vascular disease, neural tube defects, Alzheimer's disease and other forms of dementia, colon cancer, and acute leukemia, findings from small early studies have not been consistently reproduced. Two of the most investigated are C677T (rs1801133) and A1298C (rs1801131) single nucleotide polymorphisms (SNPs).

- Individuals with two copies of 677C (677CC) have the most common genotype. 677TT individuals (homozygous) have lower MTHFR activity than CC or CT (heterozygous) individuals.
- 1298AA is the "normal" homozygous, 1298AC the heterozygous, and 1298CC the homozygous for the "variant". The C mutation does not appear to affect the MTHFR protein. It does not result in thermolabile MTHFR and does not appear to affect homocysteine levels. It does, however, affect the conversion of MTHF to BH4 (tetrahydrobiopterin), an important cofactor in the production of neurotransmitters, production of nitric oxide, and detoxification of ammonia.

SNP outcomes in MTHFR relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1801133	A	R	**GG**	**--**	■■■■■■■■	HOMOCYSTEINE, AUTOIMMUNITY, CANCER MIGRAINE HEADACHE
rs17367504	G	R	**AG**	**-+**	■■■■■■	HYPERTENSION, ORTHOSTATIC HYPERTENSION, RESPONSE TO BETA BLOCKERS
rs2274976	T	R	**CC**	**--**	■■■■■	
rs2066470	T	R	**GG**	**--**	■■■■■■■	HOMOCYSTEINE, CARDIOVASCULAR RISK
rs1999594	A	R	**AA**	**++**	■■■■■■■	FOLATE TRANSPORTER, LOW SERUM FOLATE, HIGH HOMOCYSTEINE
rs1801131	G	R	**GT**	**+-**	■■■■■■■	NEUROTRANSMITTER SYNTHESIS

New concepts:

- The *genotype* is the genetic makeup of an individual. Genotype can refer to a person's entire genetic makeup or the alleles at a particular locus
- 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.
- A *mutation* is an alteration of genetic material such that a new variation is produced.
- A *homozygous* genotype has the same allele at the same locus (location) on both chromosomes. Homozygous also refers to a genotype consisting of two identical alleles of a gene for a particular trait.
- A *heterozygous* genotype consists of two different alleles of a gene for a particular trait. Individuals who are heterozygous for a trait are referred to as heterozygotes.
- The *rate limiting step* is the slowest step in a metabolic pathway or series of chemical reactions, which determines the overall rate of the other reactions in the pathway.
- A *polymorphism* is a difference in DNA sequence among individuals.
- *Methylation* is the addition of a single carbon and three hydrogen atoms (called a methyl group) to another molecule. The removal of a methyl group is called demethylation. Methylation is a key mechanism behind the regulation of gene expression.

BHMT

betaine--homocysteine S-methyltransferase

The BHMT gene (not BHMT2) provides instructions for making a protein that converts betaine (trimethylglycine) and homocysteine (a byproduct of the amino acid methionine, and toxic at high levels) to dimethylglycine and methionine, respectively. BHMT2 converts homocysteine to methionine, and the cofactor for this conversion is zinc. BHMT2 is inhibited by high levels of methionine, and does not use S-adenosylmethionine (SAMe) as a methyl donor. Defects in the BHMT gene could lead to elevated blood homocysteine levels. The product of this gene is central to the 'short cut' through the methylation cycle in helping to convert homocysteine to methionine. BHMT may therefore play a critical role in homocysteine homeostasis, or balance, when the manufacture of methionine, a folate-dependent process, is compromised by dietary or genetic influences.

The activity of the BHMT gene product can be affected by stress, by cortisol levels, and may play a role in ADD/ADHD through its affect on norepinephrine (adrenaline) levels. Phosphatidylcholine may be indicated.

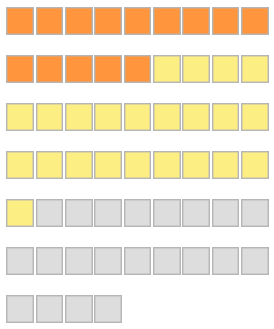
SNP outcomes in BHMT relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs6875201	G	R	**AG**	-+		LIVER, METHYLATION,
rs567754	T	R	**TT**	++		FOLATE METABOLISM, FOLATES, HOMOCYSTEINURIA
rs3733890	A	R	**GG**	--		CHOLINE, OMPHALOCELE, NEURAL TUBE DEFECTS, NSCL, NSCP, CLEFT LIP, CLEFT PALATE, NONSYNDROMIC, SHORTER TELOMERES, REDUCED RISK OF CORONARY ARTERY DISEASE

New concepts:

- *Homeostasis* is the tendency of a system, especially the physiological system of higher animals, to maintain internal stability, owing to the coordinated response of its parts to any situation or stimulus that would tend to disturb its normal condition or function.

MTRR



5-methyltetrahydrofolate-homocysteine methyltransferase reductase

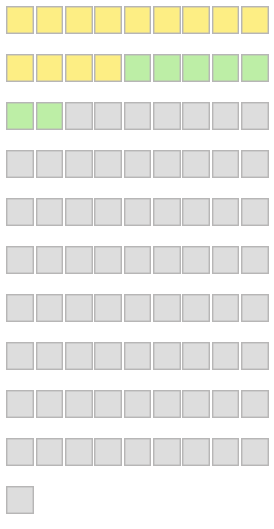
Methionine synthase reductase (MTRR) is an enzyme that is encoded by the MTRR gene. Methionine is an essential amino acid required for protein synthesis and one-carbon metabolism (methylation of the B-vitamin folate), converting homocysteine into methionine. If MTRR function is compromised due to genetic variation, toxic homocysteine levels can build up because homocysteine is not being converted into methionine. Having the MTRR 66G variant can be a part of this effect. The function of methionine synthase reductase is also inhibited by lead, arsenic, mercury and aluminum toxicity.

Medications that deplete vitamin B12 can affect MTRR function. These include: antacids and acid blockers, corticosteroids, metformin, oral contraceptives, gout medications and some cholesterol-lowering drugs.

SNP outcomes in MTRR relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs162036	G	R	**AA**	**--**		
rs7703033	A	R	**AG**	**+-**		HOMOCYSTEINE ASSOCIATION, B12 UTILIZATION
rs2303080	T	R	**TT**	**++**		CLEFT LIP AND PALATE
rs1802059	A	R	**AG**	**+-**		
rs2287780	T	R	**CC**	**--**		
rs1801394	G	R	**GG**	**++**		NEURAL TUBE DEFECT, MENINGIOMA, LOW SERUM FOLATE, REDUCED RISK PSA ELEVATION
rs1532268	T	R	**CT**	**-+**		FOLATE METABOLISM, CANCER
rs10380	T	R	**CC**	**--**		METHIONINE REGENERATION

CBS



cystathionine-beta-synthase

Cystathionine β-synthase, or the CBS enzyme that begins the transsulfuration pathway to provide sulfur groups needed for detoxification, neuroprotection by making glutathione and hydrogen sulfide, as well as for neurotransmitter and hormone modification. Sulfation can be blocked by non-steroidal anti-inflammatory drugs (e.g. aspirin), tartrazine (yellow food dye) and molybdenum deficiency.

CBS enzyme activation needs pyridoxal-5' phosphate, the active form of vitamin B6. S-adenosyl methionine regulates enzyme activity. The downstream pathway from CBS is the sulfite oxidase enzyme, made by the SUOX gene, requires molybdenum produces sulfates from toxic sulfites. SUOX can be inactivated by tungsten toxicity.

CBS may be upregulated to produce hydrogen sulfide if persists can counter the neuroprotective effects of hydrogen sulfide and deplete cofactors needed to make glutathione. Elevated homocysteine or cysteine may contribute to brain fog. Some CBS SNPs are associated with midline defects.

Issues in the methionine and folate cycle may contribute to depletion of sulfur production in the transsulfation pathway. Other subunits of transsulfation and the sulfation pathways may be involved in neurotoxicity, or neurotransmitter dysregulation.

SNP outcomes in CBS relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs234715	T	R	**GG**	**--**		AUTISM NTD RISK IN HYPOMETHYLATION
rs121964962	T	R	**CC**	**--**		PYRIDOXINE RESISTANT HOMOCYSTEINURIA
rs234709	T	R	**CT**	**-+**		METABOLISM, ARSENIC METABOLISM, LUNG CANCER
rs121964970	T	R	**CC**	**--**		MILD HOMOCYSTEINURIA B-6 REPSONSIVE
rs2298758	A	R	**GG**	**--**		DOWNREGULATION, AUTISM, CLEFT, EHLERS-DANLOS SYNDROME
rs2851391	T	R	**CC**	**--**		BLOOD, METABOLITES, HOMOCYSTEINE, OBESITY
rs121964972	A	R	**GG**	**--**		B6 UNRESPONSIVE
rs4920037	A	R	**GG**	**--**		SLOW TRANSSULFATION
rs1801181	A	B	**AA**	**++**		TRANSSULFATION NO REDUCTION OF ACTIVITY
rs234706	A	B	**AG**	**+-**		NO REDUCTION OF ACTIVITY, B-6 RESPONSIVE, RESPONSIVE TO HCY LOWERING EFFECTS OF FOLIC ACID
rs28934891	T	R	**CC**	**--**		NORMAL CBS ACTIVITY
rs6586282	T	R	**CC**	**--**		HOMOCYSTEINURIA
i5003389	A	R	**GG**	**--**		B6 UNRESPONSIVE

SUOX

sulfite oxidase

Downstream from the cystathionine beta synthase enzyme (CBS) is the sulfite oxidase enzyme, made by the SUOX gene. This requires molybdenum to produce sulfates from toxic sulfites. SUOX can be inactivated by tungsten toxicity. Sulfite sensitivity to sulfite-containing dried fruits and wines can be caused by SUOX mutations or from the bottleneck effect of up regulated transsulfation (CBS pathway) due to hyperglycemia (high blood sugar), infection and other conditions of oxidative stress.

SNP outcomes in SUOX relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs7297662	A	R	**AG**	**+-**		LEUKEMIAS IN TUNGSTEN AND ARSENIC TOXICITY

New concepts:

- *Oxidative stress* reflects an imbalance between the levels of reactive oxygen species and the body's ability to readily detoxify the reactive intermediates or to repair the resulting damage.

MAT1A

methionine adenosyltransferase I, alpha

Methionine adenosyltransferase I, alpha (MAT1A gene) provides instructions for producing the enzyme methionine adenosyltransferase. The enzyme is produced from the MAT1A gene in two forms, alpha and beta. The alpha form, called a homotetramer, is made up of four identical protein subunits. The beta form, called a homodimer, is made up of two of the same protein subunits. Both forms of the enzyme are found in the liver.

Both the alpha and beta forms of MAT1A help break down a protein building block (amino acid) called methionine. The enzyme starts the reaction that converts methionine to S-adenosylmethionine (AdoMet or SAMe). AdoMet transfers methyl groups (one carbon atom and three hydrogen atoms) to other compounds- a process called transmethylation. Transmethylation is important in many cellular processes. These include determining whether the instructions in a segment of DNA are carried out, regulating reactions involving proteins and lipids, and controlling the processing of chemicals that relay signals in the nervous system (neurotransmitters).

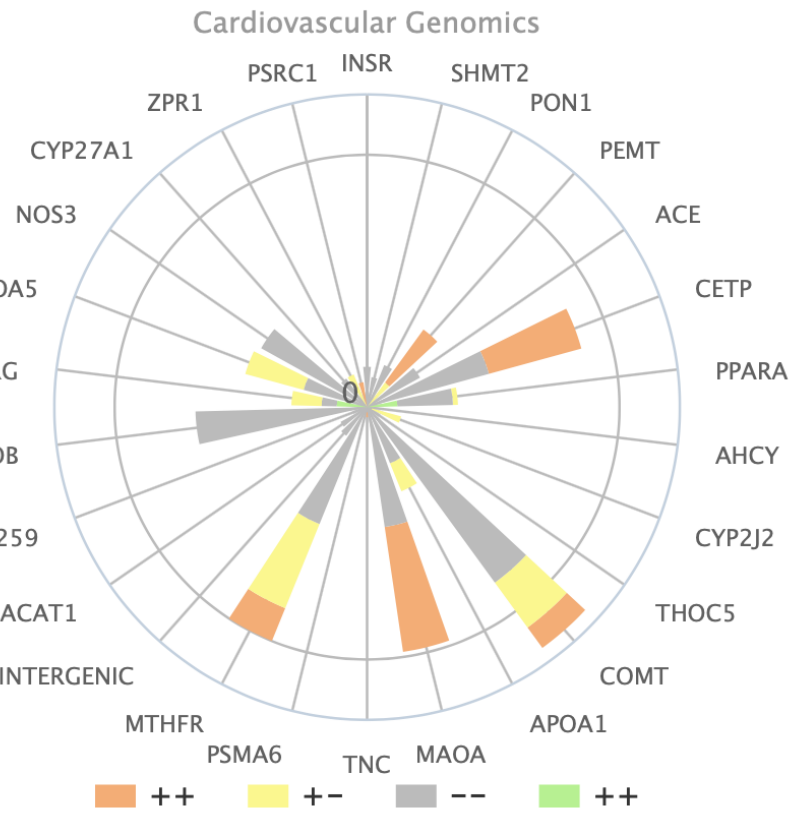
SNP outcomes in MAT1A relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs118204005	A	R	**GG**	--		HYPERMETHIONINEMIA
rs118204006	T	R	**CC**	--		HYPERMETHIONINEMIA AUTOSOMAL RECESSIVE
rs118204003	A	R	**GG**	--		HYPERMETHIONINEMIA
rs4934028	A	R	**GG**	--		CHINESE MALE GENDER ASSOCIATED LOW SAM LEVELS

New concepts:

- 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.

CARDIOMETABOLIC



Cardiovascular Genomics

Cardiovascular disease (CVD) is a class of diseases that involve the heart or blood vessels. CVD includes coronary artery diseases (CAD) such as angina and myocardial infarction (commonly known as a heart attack).Other CVDs include stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease, carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, and venous thrombosis.The underlying mechanisms vary depending on the disease. Coronary artery disease, stroke, and peripheral artery disease involve atherosclerosis. This may be caused by high blood pressure, smoking, diabetes mellitus, lack of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol consumption, among others. High blood pressure is estimated to account for approximately 13% of CVD deaths, while tobacco accounts for 9%, diabetes 6%, lack of exercise 6% and obesity 5%.[2] Rheumatic heart disease may follow untreated strep throat. It is estimated that up to 90% of CVD may be preventable by improving risk factors through: healthy eating, exercise, avoidance of tobacco smoke and limiting alcohol intake.

PEMT

phosphatidylethanolamine N-methyltransferase

Phosphatidylcholine (PC) is the most abundant phospholipid in the body, phospholipids linked to choline. The PEMT gene provides instructions to make an enzyme which converts phosphatidylethanolamine to PC by methylation in the liver. If there is limited folate metabolism (due to MTHFR, MTHFD1 SNPs or other methyl trapping risk SNPs TCN, FOLR1, MAOA) or increase need for homocysteine recycling (MTR, MTRR, BHMT-08 BHMT-02 SNPs) there is a need to consume more choline. Reduced function of this gene can increase alchohol toxicity risk (toxic aldehydes and ammonia levels)P

PC is a major constituent of cell membranes and the surface of the lung, and is commonly found in the outer part of cell membranes. It also plays a role in cell signaling and activation of other enzymes.

SNP outcomes in PEMT relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs7946	T	R	**CT**	-+		MITOCHONDRIAL CHOLINE METABOLISM, NONALCOHOLIC FATTY LIVER DISEASE, BREAST CANCER WITH LOW BETAINE INTAKE, ALZHEIMER DISEASE IN WOMEN AND APOE ε4 NON-CARRIERS
rs4244593	T	R	**TT**	++		MITOCHONDRIAL
rs12325817	C	R	**CC**	++		MITOCHONDRIAL ENDOGENOUS PHOSPHATIDYLCHOLINE SYNTHESIS

CETP

cholesteryl ester transfer protein, plasma

Cholesteryl ester transfer protein (CETP), also called plasma lipid transfer protein, assists the transport of cholesterol components and triglycerides between the lipoproteins. It collects triglycerides from very-low-density (VLDL) or low-density lipoproteins (LDL) and exchanges them for cholesterol components from high-density lipoproteins (HDL), and vice versa. Most of the time CETP trades a triglyceride for a cholesterol component or a cholesterol component for a triglyceride.

SNP outcomes in CETP relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1800775	C	R	**CC**	**++**		HDL CHOLESTEROL, LIPID LEVELS, VENOUS THROMBOEMBOLISM
rs3764261	C	R	**CC**	**++**		HDL LDL CHOLESTEROL TRIGLYCERIDES
rs2303790	G	R	**AA**	**--**		LIPID LEVELS, CARDIOVASCULAR RISK
rs5882	A	R	**AA**	**++**		AGE, AGING, DEMENTIA, HDL
rs5742907	A	R	**GG**	**--**		HDL CHOLESTEROL, HYPERALPHALIPOPROTEINEMIA, CORONARY HEART DISEASE

PPARA

peroxisome proliferator-activated receptor alpha

PPAR-alpha is a transcription factor and a major regulator of lipid metabolism in the liver. PPAR-alpha is activated under conditions of energy deprivation and is necessary for the process of ketogenesis, a key adaptive response to prolonged fasting. Activation of PPAR-alpha promotes uptake, utilization, and catabolism of fatty acids by upregulation of genes involved in fatty acid transport, fatty binding and activation, and peroxisomal and mitochondrial fatty acid β-oxidation.

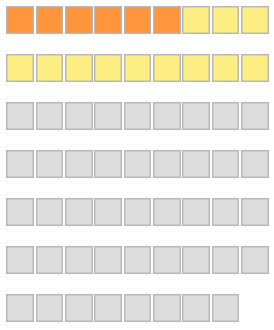
SNP outcomes in PPARA relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs135549	T	B	**CT**	**-+**		DIET INFLUENCE ON TRIGLYCERIDES AND LDL CHOLESTEROL
rs4253778	C	R	**GG**	**--**		CORONARY HEART DISEASE, DIABETES, EXERCISE, AEROBIC

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.
- *Transcription* is the first step of gene expression, in which a particular segment of DNA is copied into RNA

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:

- 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.

APOA1

apolipoprotein A-I

The APOA1 gene encodes apolipoprotein A-I, which is the major protein component of high density lipoprotein (HDL) in plasma. The protein helps move cholesterol from tissues to the liver for excretion, and it is a cofactor for lecithin cholesterolacyltransferase (LCAT), which is responsible for the formation of most forms of blood cholesterol. This gene is closely linked with other apolipoprotein genes. Defects in this gene are associated with HDL deficiencies, including Tangier disease, and with systemic non-neuropathic amyloidosis.

SNP outcomes in APOA1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1799837	T	R	**CC**	**--**		HDL DEFICIENCY
rs670	T	R	**CT**	**-+**		HDL DEFICIENCY
rs5069	A	R	**GG**	**--**		HDL DEFICIENCY

MAOA

monoamine oxidase A

Intolerance to methylfolate supplementation is due to slower breakdown of neurotransmitters including serotonin, dopamine, norepinephrine can lead to low/high levels causing mood swings, OCD, anxiety, aggression, insomnia and depression. Despite feeling depleted patients have a feeling of being overstimulated. This gene has also been associated with a variety of other psychiatric disorders, including antisocial behavior. This enzyme requires B2 (riboflavin) in sufficient levels to function normally. Because this is on the X chromosome, males will have only one allele and is why mutations have an enhanced effect. ACE deletions will also increase anxiety and lower frustration thresholds.

SNP outcomes in MAOA relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2235186	G	R	**GG**	**++**		ADHD
rs909525	T	R	**TT**	**++**		WARRIOR GENE, ANGER, AGGRESSION, SUICIDE, SUICIDALITY, METHYL TRAPPING
rs1137070	T	R	**CC**	**--**		ESTROGEN DOMINANCE AND LOW OXIDATIVE DEAMINATION OF AMINES, SUCH AS DOPAMINE, NOREPINEPHRINE, AND SEROTONIN
rs5953210	G	R	**AA**	**--**		SUBSTANCE ABUSE, GOUT
rs6323	T	R	**TT**	**++**		WILD-TYPE MAOA, CATECHOLAMINES METHYL TRAPPING ANTI-DEPRESSANT RESPONSE, MAJOR DEPRESSIVE DISORDER
rs2072743	T	R	**CC**	**--**		MAJOR DEPRESSIVE DISORDER ADHD
rs2283725	A	R	**GG**	**--**		GOUT

APOB

apolipoprotein B (including Ag(x) antigen)

The APOB gene provides instructions for making two versions of the apolipoprotein B protein, a short version called apolipoprotein B-48 and a longer version known as apolipoprotein B-100. Both of these proteins are components of lipoproteins, which are particles that carry fats and fat-like substances (such as cholesterol) in the blood.

Apolipoprotein B-48 is produced in the intestine, where it is a building block of a type of lipoprotein called a chylomicron. As food is digested after a meal, chylomicrons are formed to carry fat and cholesterol from the intestine into the bloodstream. Chylomicrons are also necessary for the absorption of certain fat-soluble vitamins such as vitamin E and vitamin A.

Apolipoprotein B-100, which is produced in the liver, is a component of several other types of lipoproteins. Specifically, this protein is a building block of very low-density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), and low-density lipoproteins (LDLs). These related molecules all transport fats and cholesterol in the bloodstream.

Low-density lipoproteins are the primary carriers of cholesterol in the blood. Apolipoprotein B-100 allows these particles to attach to specific receptors on the surface of cells, particularly in the liver. The receptors transport low-density lipoproteins into the cell, where they are broken down to release cholesterol. The cholesterol is then used by the cell, stored, or removed from the body.

More than 90 mutations in the APOB gene have been found to cause familial hypobetalipoproteinemia (FHBL), a disorder that impairs the body's ability to absorb and transport fat. Most APOB gene mutations that cause FHBL lead to the production of apolipoprotein B that is abnormally short.

The severity of the condition largely depends on the length of the abnormal apolipoprotein B. Some mutations in the APOB gene lead to the production of a protein that is shorter than apolipoprotein B-100, but longer than apolipoprotein B-48. In these cases, normal apolipoprotein B-48 is still made in the intestine. The normal-length apolipoprotein B-48 can form chylomicrons normally, but the abnormally short apolipoprotein B-100 produced in the liver is less able to produce lipoproteins. Other mutations result in a protein that is shorter than both apolipoprotein B-48 and apolipoprotein B-100. In these cases, no normal-length apolipoprotein B protein is produced. The severely shortened protein is not able to form lipoproteins in the liver or the intestine. Generally, if both versions of the protein are shorter than apolipoprotein B-48, the signs and symptoms are more severe than if some normal length apolipoprotein B-48 is produced. All of these protein changes lead to a reduction of functional apolipoprotein B. As a result, the transportation of dietary fats and cholesterol is decreased or absent. A decrease in fat transport reduces the body's ability to absorb fats and fat-soluble vitamins from the diet, leading to the signs and symptoms of FHBL.

At least five mutations in the APOB gene are known to cause a form of inherited hypercholesterolemia called familial defective apolipoprotein B-100 (FDB). This condition is characterized by very high levels of cholesterol in the blood and an increased risk of developing heart disease. Each mutation that causes this condition changes a single protein building block (amino acid) in a critical region of apolipoprotein B-100. The altered protein prevents low-density lipoproteins from effectively binding to their receptors on the surface of cells. As a result, fewer low-density lipoproteins are removed from the blood, and cholesterol levels are much higher than normal. As the excess cholesterol circulates through the bloodstream, it is deposited abnormally in tissues such as the skin, tendons, and arteries that supply blood to the heart (coronary arteries). A buildup of cholesterol in the walls of coronary arteries greatly increases a person's risk of having a heart attack.

SNP outcomes in APOB relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs12713559	A	R	**GG**	**--**		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
i4000339	A	R	**GG**	**--**		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
rs5742904	T	R	**CC**	**--**		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B, ATHEROSCLEROSIS
rs144467873	A	R	**GG**	**--**		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
rs1367117	A	R	**GG**	**--**		LDL CHOLESTEROL

New concepts:

- A *receptor* is a molecule in a cell membrane, that responds specifically to a particular neurotransmitter, hormone, antigen, or other substance.
- A *carrier* is an individual who is heterozygous for a trait that only shows up in the phenotype of those who are homozygous recessive.

APOA5

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apolipoprotein A-V

The protein coded for by APOA5 is an *apolipoprotein* that plays an important role in regulating the plasma triglyceride levels, a major risk factor for coronary artery disease. It is a component of high density lipoprotein (HDL). Mutations in this gene have been associated with hypertriglyceridemia (high triglycerides) and hyperlipoproteinemia type 5. Obesity and metabolic syndrome are both closely related to plasma triglyceride levels. Available studies show that minor APOA5 alleles could be associated with an enhanced risk of obesity or metabolic syndrome development

SNP outcomes in APOA5 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs3135506	C	R	**CG**	**+-**		TRIGLYCERIDES, HYPERTRIGLYCERIDEMIA, APOLIPOPROTEIN, INCREASED VITAMIN E LEVELS IN FEMALES ALPHA TOCOPHEROL
rs651821	C	R	**TT**	**--**		TRIGLYCERIDE LEVELS, METABOLIC SYNDROME, GUT BACTERIA LEVELS
rs10750097	A	R	**AG**	**+-**		FENOFIBRATE, STATINS, CHOLESTEROL, VITAMIN D, HDL
rs662799	G	R	**AA**	**--**		HIGH FAT DIET HIGH BMI OBESITY RISK, 2X HIGHER EARLY HEART ATTACK RISK; LESS WEIGHT GAIN ON HIGH FAT DIET FOR CAUCASIANS WITH MINOR ALLELE, INCREASED TRIGLYCERIDE, DECREASED HDL, INCREASED VITAMIN E LEVELS ALPHA TOCOPHEROL

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

New concepts:

- A *pathogen* is a bacterium, virus, or other microorganism that can cause disease.

PSRC1

proline/serine-rich coiled-coil 1

This gene encodes a target for regulation by the tumor suppressor protein p53. Thus its main role appears to be the supression of unwarranted growth. Variations appear to be associated with increased risk of coronary artery disease.

SNP outcomes in PSRC1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs599839	A	R	**AA**	**++**		

New concepts:

- A *tumor suppressor* is a gene whose function is to limit cell proliferation and loss of whose function leads to cell transformation and tumor growth.

ADIPOQ

adiponectin, C1Q and collagen domain containing

Adiponectin (AdipoQ) is a protein which in humans is encoded by the ADIPOQ gene. It is involved in regulating glucose levels as well as fatty acid breakdown. Adiponectin is a protein hormone that modulates a number of metabolic processes, including glucose regulation and fatty acid oxidation. Adiponectin is exclusively secreted from adipose tissue (and also from the placenta in pregnancy) into the bloodstream and is very abundant in plasma relative to many hormones. Levels of the hormone are inversely correlated with body fat percentage in adults. Adiponectin exerts some of its weight reduction effects via the brain. This is similar to the action of leptin, but the two hormones perform complementary actions, and can have synergistic effects.

SNP outcomes in ADIPOQ relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs17366568	A	R	**GG**	**--**		ADIPONECTIN, OBESITY, BMI
rs1501299	G	R	**GG**	**++**		BREAST CANCER

New concepts:

- *Fatty acid oxidation* is the process of fatty acids breaking down, which releases energy.

CARDIOMETABOLIC

MULTI-SNP MACROS

Risk of myocardial infarction

Genes	CDKN2B,PSRC1,MIA3,MRAS,PHACTR1,SH2B3,WDR12
Repute:	RISK
Magnitude:	3
Frequency:	N/A

INTERPRETATION: This algorithm looks for the genotypes which most strongly contribute to the risk of myocardial infarction (heart attack). The risk is higher when at least 6 out of the following 9 genotypes are true: rs10116277(TT), rs599839(AA), rs1746048(CC), rs17465637(CC), rs9818870(CC), rs12526453(CC), rs3184504(TT), rs9982601(CC),rs6725887(CC).

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

Your results:	rs10116277 (**TT**)	rs599839 (**AA**)	rs1746048 (**CC**)	rs17465637 (**AC**)	rs9818870 (**CC**)	rs12526453 (**CC**)
rs3184504 (**CC**)	rs9982601 (**CC**)	rs6725887 (**TT**)				

Celera GRS: Reduced risk of coronary artery disease.

Genes	PALLD,MYH15,KIF6,SNX19,VAMP8
Repute:	BENEFIT
Magnitude:	3
Frequency:	N/A

INTERPRETATION: You may have a reduced risk of coronary artery disease. This algorithm uses the Celera Genetic Risk Score (GRS) for coronary heart disease, based on a study in which the GRS was increased by 1 for each of the five genetic variants if the subject was homozygous (had both variants) for the risk variant, unchanged if heterozygous (one variant), and decreased by 1 if the individual did not carry the variant. Therefore, individuals carrying all 10 possible risk variants (two copies of each of the five SNPs) were assigned a GRS of 5 and those carrying no risk variants a GRS of -5. A high GRS was defined as 3 or higher. The risk homozygous genotypes are rs20455(GG), rs3900940(CC), rs7439293(AA), rs2298566(CC) and rs1010(CC)..

GRS Score -3

Although you did not have enough risk alleles to make the algorithm positive, you have variants that still independently increase your risk of CAD by 132 %.

Gene	SNP	Genotype
SNX19	rs2298566	CC

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

Your results:	rs20455 (**AA**)	rs3900940 (**TT**)	rs7439293 (**N/A**)	rs2298566 (**CC**)	rs1010 (**TT**)

Higher HDL levels

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

INTERPRETATION: The (T) allele of rs3843763 was associated with risk for lower high-density lipoprotein (HDL; the so-called 'good cholesterol') cholesterol plasma levels in studies of three independent populations, including both Caucasians and African-Americans.

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

Your results: rs3843763 (**CC**)

Increased risk of venous thromboembolism

Genes	PON1,CCR2,CETP
Repute:	RISK
Magnitude:	2
Frequency:	75%

INTERPRETATION: A small study of patients with genetic risk factors in recurring thromboembolisms (blood clots) in the veins suggested that the G variants of rs1799864 on the CCR5 gene (a receptor on white blood cells) and rs662 on PON1 (an enzyme that breaks down the toxic metabolites of some organophosphate insecticides) are associated with increased risk, while the A variant of rs1800775 on CETP (an enzyme for the transfer of cholesterol from high density lipoprotein to other lipoproteins) was associated with a reduced risk. This client's genotype suggests an increased risk of venous thromboembolism.

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

Your results: rs662 (**TT**) rs1799864 (**AG**) rs1800775 (**CC**)

Cardiometabolic macro algorithms returning as false:

- Increased risk of Atrial Fibrillation
- 300% increased risk of venous thrombosis
- Risk of salt-sensitive hypertension
- Risk of carotid artery occlusion
- Lower risk (35%) of a heart attack or cardiovascular incident

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.	Vitamin B-2 (riboflavin)	
2.	Omega 3 Fatty Acids	
3.	Omega 6 Fatty Acids	
4.	Betaine	
5.	Vitamin B-9 (folic acid)	
6.	Lithium orotate	
7.	Estrogen	
8.	Vitamin B-12 (cobalamin)	
9.	Vitamin B-6 (pyridoxine)	
10.	Binge drinking	
11.	5-methyltetrahydrofolate	
12.	Methionine	
13.	adenosyl cobalamin	
14.	Rhodiola rosea	
15.	Resveratrol	
16.	Estradiol	
17.	Quercetin	
18.	Coptis rhizome	
19.	Testosterone	
20.	Vitamin D (calciferols)	
21.	Luteolin	
22.	Berberine	
23.	Curcumin	
24.	Low-Carb Diet	
25.	Folate-rich diet	

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