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

ESTROGEN GENOMICS

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

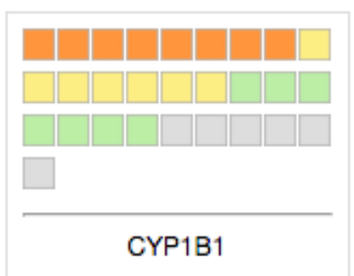
When it comes to a particular disease or syndrome, most SNPs have rather small ORs. This does not mean that they are unworthy of attention, but rather that the findings must be interpreted as part of an integrated whole, including: other SNP results that also support the conclusion; lifestyle factors;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

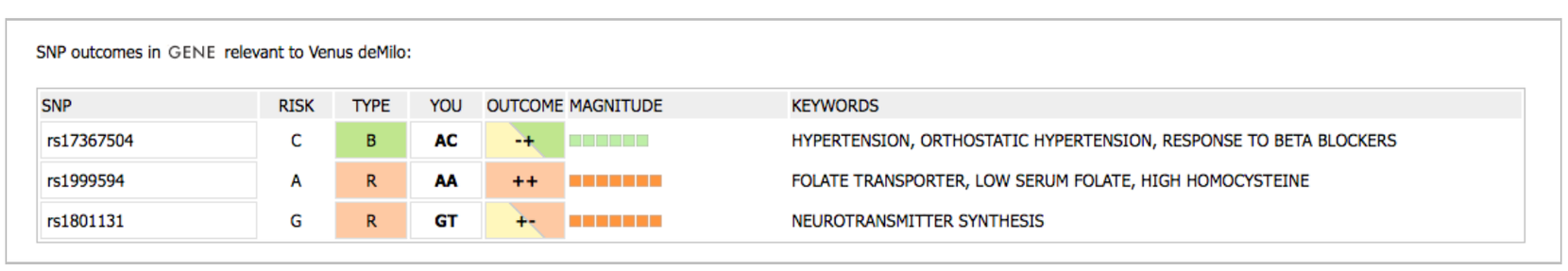
The data provided by Opus23 Explorer is for informational purposes only and is not designed or intended to suggest the treatment or diagnosis of any disease or condition. Opus23 Explorer and Datapunk Bioinformatics, LLC, take no responsibility for any harm arising from incorrect data being uploaded to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

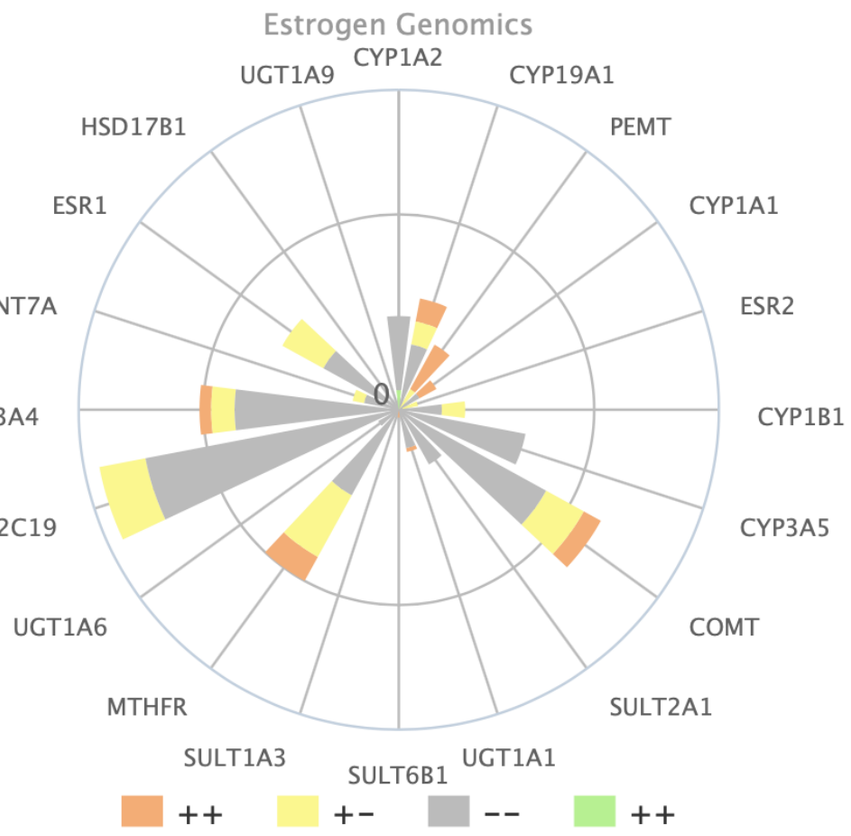
For example, a simple macro to determine if you should get out of bed might be:

- 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.



ESTROGEN GENOMICS

Estrogen Genomics

The liver is a site for biosynthesis of estrogens but it is also the main site for further biotransformation of them. Once the estrogens are synthesized by aromatase in peripheral tissues including the liver, they will be released to the circulation. Estrone is in equilibrium with estradiol and 17-b-hydroxysteroid dehydrogenase (17bHSD) in this respect. The estrogens are taken up by the liver where they will be biotransformed further in to different metabolites. The major oxidative routes of estrone and estradiol are 2- and 4-hydroxylation by cytochrome P450 (CYP) 2B1, 1A and 3A. Other minor oxidative pathways are also identified (not shown in the pathway). The 2- and 4-hydroxy derivatives (and other metabolites) will be further converted to 2- and 4-methoxy metabolites by catechol-O-methyltransferase (COMT). While the hydroxylated metabolites appear to result in DNA damage and contribute to the tumorogenic effect of estrogen, the methoxy-derivatives appear to exhibit beneficial cardiovascular effects. Estrone and estradiol and their metabolites undergo sulfation by sulfotransferases (SULTs) and glucuronidation by glucoronyltransferases (UGTs). Estrone and estradiol sulfates could be deconjugated by sulfatases (STs). Once synthesized by the aromatase enzyme from androgens, they bind to estrogen receptors (ER1 and ER2), recruit appropriate coactivators or corepressors leading to dimerization, conformational change and binding to estrogen response elements (EREs) upstream of estrogen responsive genes. This leads to increased expression of genes responsible for cell proliferation in breast tissue.

CYP1A2

cytochrome P450, family 1, subfamily A, polypeptide 2

This gene encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are important detoxification enzymes which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. Inducers bind to repressors of an enzyme and prevent it from being inhibited. The protein encoded by this gene is found in the endoplasmic reticulum and its expression is induced by some polycyclic aromatic hydrocarbons (PAHs), some of which are found in cigarette smoke. CYP1A2 helps metabolize many drugs, including antidepressants, NSAIDS (naproxen), blood pressure medications (propranolol), melatonin, caffeine and estradiol. It is inhibited by the herb St. John's Wort, tumeric, cumin and grapefruit juice. Production of the CYP1A2 enzyme also appears to be induced by various dietary constituents, including tobacco, broccoli, cabbage, cauliflower, brussels sprouts, echinacea, chargrilled meat, cauliflower and proton pump inhibitor ulcer medications.

CYP450 family member plays a much greater role in the regulation of oxidative stress due to its redox effects. When upregulated it is a major contributor of ROS and major consumer of reducing agent NADPH, important in glutathione recycling.

CYP1A2 is inhibited by saffron but only in males.

SNP outcomes in CYP1A2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs28399424	T	R	**CC**	--		DECREASED ACTIVITY, CAFFEINE, COFFEE
rs2069526	G	R	**TT**	--		DECREASED ACTIVITY, CAFFEINE, COFFEE
rs762551	A	B	**AA**	++		A A IS FAST METABOLIZER IN SMOKERS AND HABITUAL COFFEE DRINKERS
rs12720461	T	R	**CC**	--		CAFFEINE, COFFEE, DECREASED CYP1A2 ACTIVITY

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).
- *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.
- To *Catalyze* is to cause or accelerate (a reaction) by acting as a catalyst.
- *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.

CYP19A1

cytochrome P450, family 19, subfamily A, polypeptide 1

CYP19A1 (also known as 'aromatase') catalyzes the last steps of in the synthesis of estrogen. Polymorphisms in this gene can result in either increased or decreased aromatase activity. Aromatase activates many reactions involved in the production of steroids. In particular, aromatase is responsible for the aromatization of androgens (testosterone, DHEA, DHT) into estrogens. The aromatase enzyme can be found in many tissues including gonads, brain, adipose tissue, placenta, blood vessels, skin, and bone, as well as in tissue of endometriosis, uterine fibroids, breast cancer, and endometrial cancer. It is an important factor in sexual development.

CYP450 family member plays a much greater role in the regulation of oxidative stress due to its redox effects. When upregulated it is a major contributor of ROS and major consumer of reducing agent NADPH, important in glutathione recycling. CYP450 family also play a major role in cell danger signaling and cell turnover as it interacts electrically with the apoptosis mechanisms controlled by mitochondria.

SNP outcomes in CYP19A1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs10046	A	R	**AA**	**++**		ENDOMETRIOSIS, HARM AVOIDANCE PERSONALITY TRAIT, PSA LEVELS, BREAST CANCER, HYPERTENSION IN MALES, RECURRENT MISCARRIAGE, SPERM CONCENTRATION
rs4775936	C	R	**TT**	**--**		REDUCED PROSTATE CANCER SURVIVAL, ENDOMETRIAL CANCER, LOWER BMD
rs2470152	A	R	**AG**	**+-**		HIGHER ESTROGEN LEVELS AND BMD IN MEN, PROSTATE CANCER SURVIVAL, HETEROZYGOUS INHIBITS AROMATASE AND CAUSES HYPERANDROGENISM IN PCOS, FRACTURE RISK
rs10459592	T	R	**GG**	**--**		PROSTATE CANCER, LOWER RISK OF HEPATOCELLULAR CARCINOMA, REDUCED AROMATASE ACTIVITY

New concepts:

- *Apoptosis* is the process of programmed cell death that may occur in multicellular organisms. In contrast to traumatic cell death from cellular injury, apoptosis is a highly regulated and controlled process that confers advantages during an organism's lifecycle.
- *Mitochondria* are a cell constitutent (organelle) found in large numbers in most cells, in which the biochemical processes of respiration and energy production occur.
- An *androgen* is any natural or synthetic compound, usually a steroid hormone, that stimulates or controls the development and maintenance of male characteristics.

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

New concepts:

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

CYP1A1

cytochrome P450, family 1, subfamily A, polypeptide 1

Phase I Detoxification reactions transform a toxin into a chemical form that can be metabolized by the phase II detoxification enzymes. CYP1A1 is involved in phase I xenobiotic and drug metabolism (one substrate of it is theophylline). It is inhibited by fluoroquinolones andmacrolides and induced by aromatic hydrocarbons. CYP1A1 is involved in the metabolic activation of aromatic hydrocarbons (polycyclic aromatic hydrocarbons, PAH), for example, benzo(a)pyrene (BP), by transforming it to an epoxide. MSG, arsenic, cadmium and chromium can make this enzyme more active.

CYP40 family members compete for activity and process hormones and xenobiotics variably in patients. CYP450 family member plays a much greater role in the regulation of oxidative stress due to its redox effects. When upregulated it is a major contributor of ROS and major consumer of reducing agent NADPH, important in glutathione recycling. They also plays a major role in cell danger signaling and cell turnover as it interacts electrically with the apoptosis mechanisms controlled by mitochondria.

SNP outcomes in CYP1A1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs2606345	A	R	**AA**	++		BILIARY STONES DEPRESSION
rs1799814	T	R	**GG**	--		LUNG CANCER, NON-SMALL CELL

New concepts:

- A *xenobiotic* is a chemical compound foreign to the body. Xenobiotics include drugs, and environmental compounds such as pollutants that are not produced by the body. In the environment, xenobiotics include synthetic pesticides, herbicides, and industrial pollutants that would not be found in nature.

ESR2

estrogen receptor 2 (ER beta)

This gene encodes an estrogen receptor. Estrogen and its receptors are essential for sexual development and reproductive function, but also play a role in other tissues such as bone. Estrogen receptors are also involved in pathological processes including breast cancer, endometrial cancer, and osteoporosis. ESRs interact with COMT via methylation reactions.

- ESR function may be helped by the inclusion of sulforaphanes (a sulfur containing detoxifying compound) in the diet. Sulforaphane has been identified in broccoli sprouts, which, of the cruciferous vegetables, have the highest concentration. It is also found in Brussels sprouts, cabbage, cauliflower, bok choy, kale, collards, Chinese broccoli, broccoli raab, kohlrabi, mustard, turnip, radish, arugula, and watercress.

SNP outcomes in ESR2 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1256030	A	R	**AG**	**+-**		BONE MINERAL DENSITY OVARIAN CANCER

New concepts:

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

CYP1B1

cytochrome P450, family 1, subfamily B, polypeptide 1

CYP1B1 belongs to the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. The enzyme encoded by CYP1B1 detoxifies and metabolizes procarcinogens such as polycyclic aromatic hydrocarbons and 17beta-estradiol.

CYP450 family members compete for activity, and process hormones and xenobiotics variably in patients. CYP450 family members play a much greater role in the regulation of oxidative stress due to their effects on reduction/oxidation. When upregulated, CYP1B1 is a major contributor of reactive oxygen species and a major consumer of the reducing agent NADPH, important in glutathione recycling. CYP1B1 and other CYP450 enzymes also play a major role in cell danger signaling and cell turnover, as they interact electrically with the apoptosis mechanisms controlled by mitochondria. Increased activity of this enzyme as a result of genetic variants in the CYP1B1 gene in combination with environmental factors may lead to an increased risk of breast or ovarian cancer, and affects the metabolism of certain chemotherapy agents.

SNP outcomes in CYP1B1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1056836	C	R	**CG**	**+-**		UPREGULATED CYP1B1 ACTIVITY, OXIDATIVE STRESS, RISK OF OVARIAN CANCER IN SMOKERS, RISK OF BREAST CANCER IN MENOPAUSAL HORMONE USERS, CHEMOTHERAPY METABOLISM
rs9282671	T	R	**AA**	**--**		GLAUCOMA
rs1800440	C	R	**TT**	**--**		PANCREATIC CANCER, BREAST CANCER, PROSTATE CANCER, COLORECTAL CANCER, DNA ADDUCTS

New concepts:

- A *monooxygenase* is any of a group of enzymes that catalyze both the addition of a single oxygen atom from molecular oxygen into a substrate

CYP3A5

cytochrome P450, family 3, subfamily A, polypeptide 5

This gene encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are phase I detoxification enzymes which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. CYP3A5 metabolizes drugs as well as the steroid hormones testosterone and progesterone. CYP3A5 expression is induced by glucocorticoids and some pharmacological agents. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. The human CYP3A subfamily, CYP3A4, CYP3A5, CYP3A7 and CYP3A43, is one of the most versatile of the biotransformation systems that facilitate the elimination of drugs (37% of the 200 most frequently prescribed drugs in the U.S. are eliminated via these mechanisms).

SNP outcomes in CYP3A5 relevant to Venus deMilo:

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

COMT

catechol-O-methyltransferase

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

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

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

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

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

SNP outcomes in COMT relevant to Venus deMilo:

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

New concepts:

- A *mutation* is an alteration of genetic material such that a new variation is produced.
- A *polymorphism* is a difference in DNA sequence among individuals.
- An *allele* is one of two or more alternative forms of a gene at the same site in a chromosome, which determine alternative characters in inheritance.

SULT2A1

sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA)-preferring, member 1

This gene encodes a member of the sulfotranserase (SULT) family. SULTs aid in the metabolism of drugs and endogenous compounds by converting thsese substances into more soluble conjugates that can be easily excreted. The protein encoded by SULT2A1 may have a role in the inherited adrenal androgen excess in women with polycystic ovary syndrome.

SULT2A1 assists detoxification of compounds such as thyroid and adrenal hormones, serotonin, retinol, ascorbate and vitamin D by converting these substances into more easily excreted water soluble sulfate conjugates. In contrast to other phase II enxymes, SULT2A1 can convert a number of procarcinogens (such as heterocyclic amines from cooked meats) into highly reactive intermediates which may act as chemical carcinogens and mutagens.

SNP outcomes in SULT2A1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs4149452	T	R	**CC**	**--**		
rs4149449	T	R	**CC**	**--**		

New concepts:

- *Amines* are organic compounds contain a basic nitrogen atom. Important amines include amino acids, histamine, dopamine and serotonin.

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 *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.
- *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.

CYP2C19

cytochrome P450, family 2, subfamily C, polypeptide 19

The CYP2C19 gene is a member of the cytochrome P450 gene family. Enzymes produced from cytochrome P450 genes are involved in the formation and breakdown (metabolism) of various molecules and chemicals within cells. The CYP2C19 gene provides instructions for making an enzyme that is found primarily in liver cells in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport.

The CYP2C19 enzyme plays a role in the processing or metabolizing of at least 10 percent of commonly prescribed drugs, including a drug called clopidogrel (also known as Plavix). Clopidogrel is an antiplatelet drug, which means that it prevents blood cell fragments called platelets from sticking together (aggregating) and forming blood clots. The CYP2C19 enzyme converts clopidogrel to its active form, which is necessary for the drug to function in the body. The active drug then stops (inhibits) a receptor protein known as P2RY12 that is found on the surface of platelets. During clot formation, the P2RY12 receptor protein helps platelets cluster together to form a clot in order to seal off damaged blood vessels and prevent blood loss.

CYP2C19 also acts on drugs that treat pain associated with ulcers, such as omeprazole, antiseizure drugs such as mephenytoin, the antimalarial proguanil, and the anxiolytic diazepam. Genetic polymorphisms exist for CYP2C19 expression, with approximately 3–5% of Caucasian and 15–20% of Asian populations being poor metabolizers with no CYP2C19 function. This may reduce the efficacy of clopidogrel (Plavix). In patients with an abnormal CYP2C19 variant certain benzodiazepines should be avoided, such as diazepam (Valium), lorazepam (Ativan), oxazepam (Serax), and temazepam (Restoril).

The CYP2C19 'poor-metabolism' phenotype was initially discovered by studies on impaired mephenytoin metabolism and the major molecular defect responsible for the trait is the CYP2C19*2 (c.681G > A; rs4244285) loss-of-function allele.

Multiple variations (polymorphisms) in the CYP2C19 gene have been associated with clopidogrel resistance, a condition in which the drug clopidogrel is less effective than normal in people who are treated with it. The polymorphisms that are associated with clopidogrel resistance decrease the enzyme's ability to convert the drug to its active form.

The normal version of the gene, written as CYP2C19*1, provides instructions for producing a normally functioning CYP2C19 enzyme. If a person has two copies of the CYP2C19*1 version of the gene in each cell, they are able to convert clopidogrel normally. The two most common CYP2C19 gene polymorphisms associated with clopidogrel resistance (known as CYP2C19*2and CYP2C19*3) result in the production of a nonfunctional CYP2C19 enzyme that is unable to activate clopidogrel.

Individuals with clopidogrel resistance can be classified into two groups: intermediate metabolizers or poor metabolizers. People who have one copy of the CYP2C19*1 version of the gene and one copy of either the CYP2C19*2 or CYP2C19*3 version of the gene have a reduced ability to convert clopidogrel to its active form and are classified as intermediate metabolizers. People who have the CYP2C19*2 or CYP2C19*3 versions of the gene for both copies of the gene can convert very little or none of the drug and are classified as poor metabolizers. Because conversion of clopidogrel to its active form is impaired in people with clopidogrel resistance, the drug is unable to inhibit P2RY12 receptor function. Without active clopidogrel to interfere, the P2RY12 receptor continues to promote platelet aggregation and blood clot formation, which can lead to heart attacks, strokes, and thromboses in individuals with a history of these conditions.

It is important to note that not all individuals with CYP2C19 gene mutations have clopidogrel resistance. These individuals who are at increased risk for developing clopidogrel resistance may or may not have a bad reaction when treated with the drug. In addition to changes in specific genes, many other factors, including gender, age, weight, diet, and other medications, play a role in how the body reacts to clopidogrel.

Polymorphisms in the CYP2C19 gene that are associated with clopidogrel resistance (described above) can also affect the processing of other drugs. Because the CYP2C19 enzyme is involved in the metabolism of many drugs, changes to the enzyme can have wide-ranging effects. Other drugs that are affected by CYP2C19 gene polymorphisms include proton pump inhibitors, used to treat stomach ulcers and other conditions; antidepressants, used to treat psychiatric disorders; anticonvulsants, used to treat seizure disorders; hypnotics and sedatives, used as sleep aids; antimalarial drugs, used to prevent malarial infections; and antiretroviral drugs, used to prevent viruses from replicating.

Most often, changes in the CYP2C19 gene lead to impaired metabolism of these drugs, which reduces their effectiveness. One change in the CYP2C19 gene (known as CYP2C19*17) increases the enzyme's ability to metabolize drugs. Individuals with two copies of the CYP2C19*17 polymorphism are typically classified as ultra-rapid metabolizers.

SNP outcomes in CYP2C19 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs12248560	T	R	**CC**	--		ULTRARAPID METABOLIZER
i6009445	G	R	**AA**	--		POOR METABOLIZER OMEPRAZOLE MEPHENYTOIN LOSS OF FUNCTION
rs4986893	A	R	**GG**	--		LOSS OF FUNCTION. POOR DRUG METABOLIZER: OMEPRAZOLE MEPHENYTOIN PROGUANIL CLOPIDOGREL
i6009456	T	R	**CC**	--		ULTRARAPID METABOLIZER
rs28399504	G	R	**AA**	--		POOR METABOLIZER OMEPRAZOLE MEPHENYTOIN LOSS OF FUNCTION
rs41291556	C	R	**TT**	--		REDUCED FUNCTION POOR OR INTERMEDIATE METABOLIZER
rs4244285	A	R	**AG**	+-		NON-FUNCTIONING ALLELE NON-METABOLIZER ENDOMETRIOSIS
rs72552267	A	R	**GG**	--		POOR METABOLIZER, LOSS OF FUNCTION
rs4986894	C	R	**CT**	+-		LOSS OF FUNCTION POOR METABOLIZER

New concepts:

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

CYP3A4

cytochrome P450, family 3, subfamily A, polypeptide 4

CYP3A4 is an important enzyme in the body, mainly found in the liver and in the intestine. Its purpose is to oxidize small foreign organic molecules (xenobiotics), such as toxins or drugs, so that they can be removed from the body. While many drugs are deactivated by CYP3A4, there are also some drugs which are *activated* by the enzyme. Some substances, such as grapefruit juice and some drugs, interfere with the action of CYP3A4. These substances will therefore either amplify or weaken the action of those drugs that are modified by CYP3A4. This enzyme is involved in the metabolism of approximately half the drugs in use today, including acetaminophen, codeine, cyclosporin A, diazepam and erythromycin. The enzyme also metabolizes some steroids and carcinogens. In 1998, various researchers showed that grapefruit juice, and grapefruit in general, is a potent inhibitor of CYP3A4, which can affect the metabolism of a variety of drugs, increasing their bioavailability. In addition to grapefruit, other fruits have similar effects. Noni (M. citrifolia), for example, is a dietary supplement typically consumed as a juice and also inhibits CYP3A4; pomegranate juice has this effect as well.

CYP40 family members compete for activity and process hormones and xenobiotics variably in patients. CYP450 family member plays a much greater role in the regulation of oxidative stress due to its redox effects. When upregulated it is a major contributor of ROS and major consumer of reducing agent NADPH, important in glutathione recycling. They also plays a major role in cell danger signaling and cell turnover as it interacts electrically with the apoptosis mechanisms controlled by mitochondria.

SNP outcomes in CYP3A4 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs28371759	G	R	**AA**	**--**		INCREASED ACTIVITY
rs4986910	G	R	**AA**	**--**		
rs55785340	G	R	**AA**	**--**		
rs3091339	C	R	**TT**	**--**		
rs2740574	C	R	**TT**	**--**		INCREASED ACTIVITY
rs55901263	C	R	**GG**	**--**		
rs2246709	G	R	**AA**	**--**		
rs4646437	A	R	**AG**	**+-**		DRUG METABOLISM

ESR1

estrogen receptor 1

This gene encodes an estrogen receptor. Estrogen and its receptors are essential for sexual development and reproductive function, but also play a role in other tissues such as bone. Estrogen receptors are also involved in pathological processes including breast cancer, endometrial cancer, and osteoporosis. ESRs interact with COMT via methylation reactions.

- ESR function may be helped by the inclusion of sulforaphanes (a sulfur containing detoxifying compound) in the diet. Sulforaphane has been identified in broccoli sprouts, which, of the cruciferous vegetables, have the highest concentration. It is also found in Brussels sprouts, cabbage, cauliflower, bok choy, kale, collards, Chinese broccoli, broccoli raab, kohlrabi, mustard, turnip, radish, arugula, and watercress.
- Transcription factors, vitamin D and A support repression of cell proliferation.
- Upregulating COMT aids in the clearance of carcinogenic estrogen metabolites.

SNP outcomes in ESR1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs9340799	G	R	**AA**	--		ENDOMETRIOSIS, ENDOMETRIAL CANCER, COGNITIVE IMPAIRMENT, AGE
rs2144025	T	R	**TC**	+-		HYPOMANIA, SCHIZOPHRENIA
rs2228480	A	R	**GG**	--		PELVIC ORGAN PROLAPSE, SPERM CONCENTRATION
rs2077647	C	R	**TT**	--		PROSTATE CANCER, RESPONSE TO ISOFLAVONES, BREAST CANCER, COLON CANCER, HEPATITIS B VIRUS-RELATED LIVER CIRRHOSIS, RISK OF ALZHEIMERS DISEASE IN DOWN SYNDROME, ARTERIAL STIFFNESS, ANOGENITAL DISTANCE
rs3020314	T	R	**CT**	-+		BREAST CANCER
rs2234693	C	R	**TT**	--		BREAST CANCER CORONARY HEART DISEASE MIGRAINE BILIARY STONES, HEPATITIS B VIRUS-RELATED LIVER CIRRHOSIS

New concepts:

- *Transcription* is the synthesis of an RNA copy from a sequence of DNA (a gene); the first step in gene expression
- A *metabolite* is a product of metabolism; a substance essential to the metabolism of a particular organism or to a particular metabolic process.

SULT1A1

sulfotransferase family, cytosolic, 1A, phenol-preferring, member 1

Sulfotransferase enzymes (SULTs) enable the addition of sulfate to many hormones, neurotransmitters, phenolic drugs, and toxic environmental compounds. SULT1A1 is an important phase II detoxificiation enzyme. They have protein-protein interactions with DIO1 and 2 enzymes. In contrast to other Phase II enzymes, SULT1A1 can convert a number of procarcinogens (such as heterocyclic amines from cooked meats) into highly reactive intermediates which may act as chemical carcinogens and mutagens. SULT1A1 helps the safe elimination of acetominophen. Sulfotransferases are inhibited by quercetin, red wine, black and green tea, caffeine and carmoisine in red food coloring.

SNP outcomes in SULT1A1 relevant to Venus deMilo:

SNP	RISK	TYPE	YOU	OUTCOME	MAGNITUDE	KEYWORDS
rs1042157	A	R	**AG**	+-		LIVER

ESTROGEN GENOMICS

MULTI-SNP MACROS

Lower risk for endometriosis, normal risk for endometrial cancer, more cognitive impairment with age

Genes	ESR1
Repute:	BENEFIT
Magnitude:	2
Frequency:	64%

INTERPRETATION: The rs9340799 SNP on the ESR1 Estrogen Receptor gene has been associated with womens' endometrial conditions and poor memory in old age. Your genetics relating to this SNP mean that you have a lower risk of endometritis (inflammation of the lining of the womb), normal risk of endometrial cancer, and more memory problems with age.

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

Your results: rs9340799 (**AA**)

Estrogen Genomics macro algorithms returning as false:

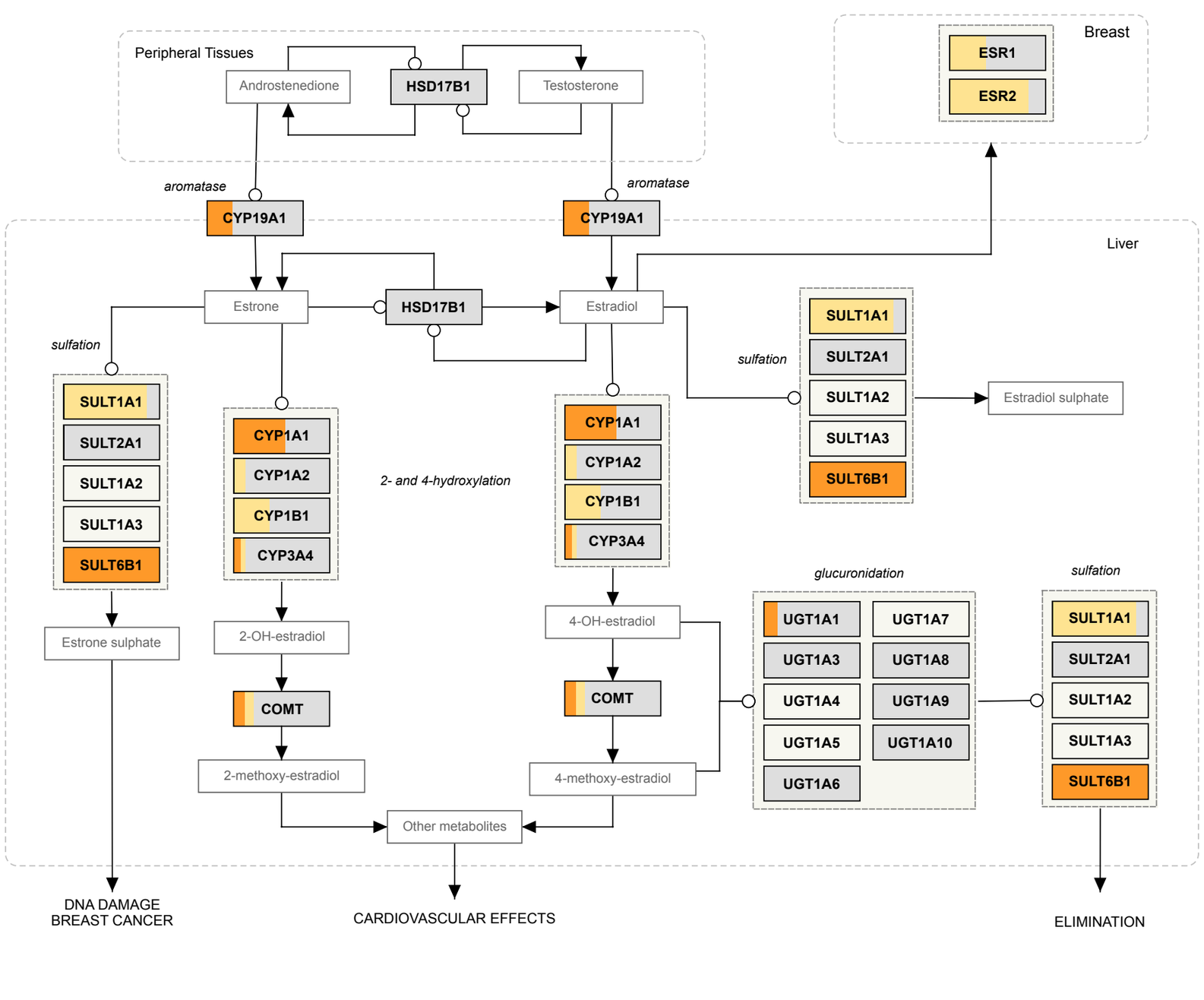
- Decreased risk of hypertensive disorder complicating pregnancy
- Evidence of earlier onset of menarche/ breast development

ESTROGEN GENOMICS

NETWORK MAPS

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

Estrogen Metabolism in the Liver



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.	Omega 3 Fatty Acids	
2.	Omega 6 Fatty Acids	
3.	Cigarette smoke	
4.	Multivitamin	
5.	Folate-rich diet	
6.	Quercetin	
7.	Resveratrol	
8.	Caloric restriction	
9.	Curcumin	
10.	Estrogen	
11.	Phosphatidylserine	
12.	Phosphatidylcholine	
13.	Silymarin	
14.	Choline	
15.	Cannabidiol	
16.	Sulforaphane	
17.	Kava kava (Piper methysticum)	
18.	Rhodiola rosea	
19.	Myricetin	
20.	Epigallocatechin gallate (EGCG)	
21.	Alpha-Linolenic acid ALA	
22.	unmetabolized folic acid	
23.	5-methyltetrahydrofolate	
24.	Tetrahydrofolate	
25.	Binge drinking	

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