Welcome to Opus23 Explorer

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

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

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

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

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

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

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

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

Now, a few caveats

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

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

Opus23 Explorer can only supply correlations and relationships

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

Opus23 Explorer results are as good as the starting data

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

Genetic findings can only report the starting point

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

Genetic findings can only reflect probabilities

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

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

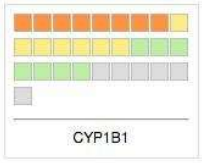
When it comes to a particular disease or syndrome, most SNPs have rather small ORs. This does not mean that they are unworthy of attention, but rather that the findings must be interpreted as part of an integrated whole, including: other SNP results that also support the conclusion; lifestyle factors;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

And now, the usual indemnification statement:

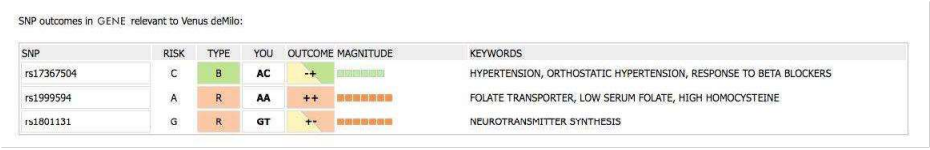
The data provided by Opus23 Explorer is for informational purposes only and is not designed or intended to suggest the treatment or diagnosis of any disease or condition. Opus23 Explorer and Datapunk Bioinformatics, LLC, take no responsibility for any harm arising from incorrect data being uploaded to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

Understanding the report

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



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



SNP outcomes in GENE relevant to Venus deMilo:

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

Depending on your data and your clinicians curation preferences, other data may show up under the description.

Selected agents: Natural products (supplements, herbs, nutriceuticals) specifically curated by your clinician and linked to the displayed gene will show here, identified by this icon

Multi SNP macros

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

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

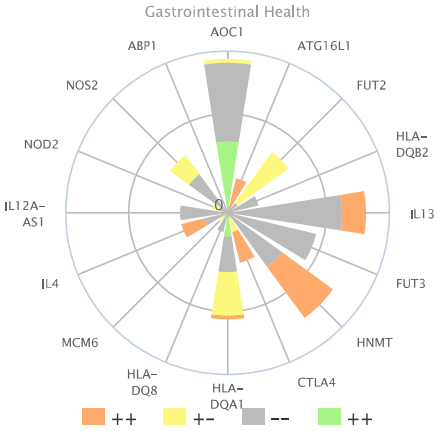
For example, a simple macro to determine if you should get out of bed might be:

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

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

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

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



Gastrointestinal Health

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

ABP1

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

The protein encoded by this gene is a bifunctional, cytosolic protein that functions as an essential enzyme in the TCA cycle and interacts with mRNA to control the levels of iron inside cells. When cellular iron levels are high, this protein binds to a 4Fe-4S cluster and functions as an aconitase. Aconitases are iron-sulfur proteins that function to catalyze the conversion of citrate to isocitrate. When cellular iron levels are low, the protein binds to iron-responsive elements (IREs), which are stem-loop structures found in the 5' UTR of ferritin mRNA, and in the 3' UTR of transferrin receptor mRNA. When the protein binds to IRE, it results in repression of translation of ferritin mRNA, and inhibition of degradation of the otherwise rapidly degraded transferrin receptor mRNA. The encoded protein has been identified as a moonlighting protein based on its ability to perform mechanistically distinct functions. Alternative splicing results in multiple transcript variants [provided by RefSeq, Jan 2014]

SNP outcomes in gene ABP1 relevant to Robert Pfoff:

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

New concepts:

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

AOC1

amine oxidase, copper containing 1

The AOC1 gene provides instructions for making the amine oxidase, copper containing 1 enzyme known as diamine oxidase, histaminase, misnamed 'DAO'. This is different to the DAO gene (D-amino-acid oxidase). It is found largely in the intestines and kidney, and breaks down histamine and other related compounds such as putrescine and spermine,

substances involved in allergic response and the immune system. Lower AOC1 enzyme activity may be associated with inflammatory bowel disease such as Crohn's disease and ulcerative colitis, as well as a form of asthma that is more easily triggered with normal levels of allergy-stimulating IgE antibodies.

SNP outcomes in gene AOC1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2071517 *(*102G>A)*	A	B	**AG**	**+-**		PROTECTIVE AGAINST HISTAMINE INTOLERANCE
i6040696 *(rs777737381 1519delG)*	D	R	**II**	**--**		
rs777737381 *(rs777737381 1519delG)*	D	R	**II**	**--**		
i6025303 *(rs371999016 599G>A Trp200null)*	A	R	**GG**	**--**		
i6056406 *(rs202107303 1240C>T Arg414null)*	T	R	**CC**	**--**		
rs2268999 *(-16-578A>T)*	T	R	**AA**	**--**		HISTAMINE INTOLERANCE
rs371999016 *(rs371999016 599G>A Trp200null)*	A	R	**GG**	**--**		
rs1049748 *(Pro574Pro)*	C	B	**CC**	**++**		DAO ACTIVITY, PROTECTIVE, IMMUNOGLOBULINS
rs10156191 *(47C>T Thr16Met)*	T	R	**CC**	**--**		HISTAMINE INTOLERANCE NSAID HYPERSENSITIVITY
rs1049742 *(Ser332Phe)*	T	R	**CC**	**--**		HISTAMINE INTOLERANCE
rs10240738	C	R	**TC**	**-+**		
rs2052129 *(-691G>T)*	T	R	**GG**	**--**		HISTAMINE INTOLERANCE
rs202107303 *(rs202107303 1240C>T Arg414null)*	T	R	**CC**	**--**		
rs2071514 *(1329G>A Ala443Ala)*	A	B	**AG**	**+-**		PROTECTIVE AGAINST HISTAMINE INTOLERANCE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *AOC1*:

- *Copper*

ATG16L1

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

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

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

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

The effects of variations in the ATG16L1 gene on Crohn disease risk are unclear. Changes in this gene may affect the autophagy process, allowing worn-out cell parts and harmful bacteria to persist when they would otherwise be

destroyed. These cell components and bacteria may trigger an inappropriate immune system response, leading to chronic inflammation in the intestinal walls and the digestive problems characteristic of Crohn disease.

SNP outcomes in gene ATG16L1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs10210302	T	R	**TT**	++		CROHN'S, CROHN'S DISEASE, ULCERATIVE COLITIS
rs2241880 *(T300A, A>G)*	G	R	**GG**	++		INFLAMMATORY BOWEL DISEASE 10, CROHNS, AUTOIMMUNE, INCREASED GUT BACTEROIDES, DYSBIOSIS, IMPAIRED AUTOPHAGY POSSIBLY LEADING INTO INFLAMMASOME ACTIVATION, OBLITERATIVE BRONCHIOLITIS, POSS COVID19ARDS, COVID19STORM, COVID REGENERON

New concepts:

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

CTLA4

cytotoxic T-lymphocyte-associated protein 4

The CTLA4, or cytotoxic T-lymphocyte-associated protein 4, is a gene that makes the CTLA4 protein, which is a member of the family of immunoglobulin genes. The protein inhibits the activity of T cells, a type of white blood cells. **Mutations in this gene have been associated with: insulin-dependent diabetes mellitus (type 1 diabetes), Graves disease, Hashimoto thyroiditis, celiac disease, thyroid issues, systemic lupus erythematosus, thyroid-associated orbitopathy, rheumatoid arthritis, Addison's disease, and some cancers including melanoma.**

CTLA-4 is also known as CD152 (cluster of differentiation 152), and is protein receptor that functions as an immune checkpoint and downregulates immune responses. CTLA4 is constitutively expressed in regulatory T cells but only upregulated in conventional T cells after activation – a phenomenon which is particularly notable in cancers. It acts as an "off" switch when bound to CD80 or CD86 on the surface of antigen-presenting cells.

Mutations in this gene have been associated autoimmune diseases including: Hashimoto's, diabetes, rheumatoid arthritis, Graves disease, thryoid problems, celiac disease, and lupus.

In general, it's much better to have more CTLA activity, except in cases of cancer in which you want a more powerful immune response.

SNP outcomes in gene CTLA4 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs231725	A	R	**AG**	+-		PRIMARY BILIARY CIRRHOSIS. ASTHMA, GRAVES DISEASE, BUT REDUCED RISK OF CHRONIC BRONCHITIS IN COPD
rs3087243 *(*1421G>A CT60 G>A +6230G>A)*	G	R	**GG**	++		TYPE 1 DIABETES T1D WITH AUTOIMMUNE THYROID DISEASE, RHEUMATOID ARTHRITIS, TRANSPLANT REJECTION, GRAVES DISEASE, CHRONIC BRONCHITIS IN COPD, TUBERCULOSIS SEVERITY, PRIMARY BILIARY CIRRHOSIS, VASCULITIS, BUT PROTECTION FROM ASTHMA
rs231779 *(110-822C>T)*	T	R	**TT**	++		GRAVES DISEASE, SCHIZOPHRENIA, BUT PROTECTION FROM CHRONIC BRONCHITIS IN COPD
rs231777 *(+923 109+814T>C)*	T	R	**CC**	--		

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CTLA4*:

- *Curcumin*

FUT2

fucosyltransferase 2 (secretor status included)

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

The "secretor" status has been associated with increased susceptibility to infection by caliciviruses (Lindesmith et al. 2003), HIV (Ali et al. 2000), and respiratory viruses (Raza et al. 1991); yet secretor subjects also display advantages compared to nonsecretors, such as lower susceptibility to urinary tract and Candida infections, and increased protection against Neisseria meningitis and Streptococcus (Haverkorn and Goslings 1969; Blackwell et al. 1990).[PMID: 18997004]

SNP outcomes in gene FUT2 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs602662 *(772G>A Gly258Ser)*	A	R	**AG**	**+-**		NONSECRETOR STATUS, HIGH LD WITH MAIN NONSECRETOR ALLELE, BUT IMPROVED B12 ABSORPTION, SERUM B6, B12 LEVELS, LOWER HOMOCYSTEINE, HELICOBACTER PYLORI, AA IS LIKELY NONSECRETOR
rs1047781 *(418A>T A385T Ile140Phe)*	T	R	**AA**	**--**		ASIAN NONSECRETOR, PARTIAL LEWIS NONSECRETOR, HIGHER VWF LEVELS, WHEAT AND CORN SENSITIVITY, POSS THROMBOSIS, COVID19METABOLIC, COVID19FUNGAL, BUT NONSECRETOR TT HAS HIGHER B12 LEVELS, NIGHTSHADES TOLERANCE, INCREASED STOMACH ACID, RESISTANCE TO NOROVIRUS AND SEVERAL OTHER VIRUSES, AND SOME PROTECTION FROM COVID19INFECTION AND COVID19ARDS ESP IN BLOOD GROUPS A AND AB
rs601338 *(G428A, W143X)*	A	R	**AG**	**+-**		NONSECRETOR STATUS, HIGHER VWF LEVELS, WHEAT AND CORN SENSITIVITY, POSS THROMBOSIS, COVID19METABOLIC, COVID19FUNGAL, BUT NONSECRETOR GG HAS HIGHER B12 LEVELS, NIGHTSHADES TOLERANCE, INCREASED STOMACH ACID, RESISTANCE TO NOROVIRUS AND SEVERAL OTHER VIRUSES, AND SOME PROTECTION FROM COVID19INFECTION, COVID19ARDS ESP IN BLOOD GROUPS A AND AB
rs492602 *(204A>G A68A)*	G	R	**AG**	**-+**		LD LINKED WITH NON-SECRETOR STATUS SNP, HIGHER VWF LEVELS, WHEAT AND CORN SENSITIVITY, POSS THROMBOSIS, COVID19METABOLIC, COVID19FUNGAL, BUT NONSECRETOR GG HAS HIGHER B12 LEVELS, NIGHTSHADES TOLERANCE, INCREASED STOMACH ACID, RESISTANCE TO NOROVIRUS AND SOME OTHER VIRUSES, AND SOME PROTECTION FROM COVID19ARDS AND POSS COVID INFECTION, ESP IN BLOOD GROUPS A AND AB

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *FUT2*:

- *Probiotics*
- *Vitamin B-12 (cobalamin)*

FUT3

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

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

SNP outcomes in gene FUT3 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs778986 *(C314T)*	A	R	**GG**	--		ONE OF FOUR LEWIS NEGATIVE SNPS
rs3894326 *(T1067A)*	T	R	**AA**	--		ONE OF FOUR LEWIS NEGATIVE SNPS
rs812936 *(202T>T, T202C)*	G	R	**AA**	--		LEWIS NEGATIVE PHENOTYPE
rs3745635 *(C>T)*	T	R	**CC**	--		LEWIS NEGATIVE PHENOTYPE, IBD, ULCERATIVE COLITIS DISTAL COLITIS, ILEOCOLONIC CROHNS AND ILEAL CROHNS DISEASE, HIGHER F8 VWF, HOMOZYGOUS TT IS LEWIS DOUBLE NEGATIVE LDN

New concepts:

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

HLA-DQ8

Human leukocyte antigen serotype DQ8

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

HLA-DQ8 (DQ8) is a human leukocyte antigen serotype within the HLA-DQ (DQ) serotype group. DQ8 is a split antigen of the DQ3 broad antigen. DQ8 is determined by the antibody recognition of β8and this generally detects the gene product of DQB1*0302. DQ8 is commonly linked to autoimmune disease in the human population. DQ8 is the second most predominant isoform linked to coeliac disease and the DQ most linked to Type 1 Diabetes. DQ8 increases the risk for rheumatoid arthritis and is linked to the primary risk locus for RA, HLA-DR4. DR4 also plays an important role in Type 1 Diabetes. While the DQ8.1 haplotype is associated with disease, there is no known association with the DQB1*0305, DQ8.4 or DQ8.5 haplotypes (see infobox) with autoimmune disease; however, this may be the result of lack of study in populations that carry these and the very low frequency.

SNP outcomes in gene HLA-DQ8 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs7454108 *(HLA DQ8 DQA1*03-DQB1*0302.)*	C	R	**TT**	--		CELIAC

New concepts:

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

HLA-DQA1

major histocompatibility complex, class II, DQ alpha 1

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

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

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

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

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

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

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

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

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

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

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

SNP outcomes in gene HLA-DQA1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs6927022 *(*1348A>G)*	A	R	**AA**	**++**		ULCERATIVE COLITIS
rs2187668 *(*03:01 82+567C>T)*	T	R	**CC**	**--**		HLA-DQ2.5, HLA-DQ2, CELIAC, GLUTEN, ZONULIN EFFECTS, HEPATITIS, LUPUS, MULTIPLE SCLEROSIS, TYPE 1 DIABETES T1D, LAMBERT-EATON MYASTHENIC SYNDROME (LEMS), SJöGREN'S SYNDROME, AUTOIMMUNE HEPATITIS, MOREEN'S ULCERATION, MULTIPLE SCLEROSIS, GRAVE'S DISEASE, HASHIMOTO'S THYROIDITIS, NON-CELIAC GLUTEN SENSITIVITY (NCGS)
rs2155219 *(G > T)*	T	R	**TG**	**+-**		HAY FEVER (ALLERGIC RHINITIS), HLA-DQA1 MOLD ALLERGY IGE GRASS SENSITIZATION ALLERGY TO GRASS POLLEN EOSINOPHILIC ESOPHAGITIS, ULCERATIVE COLITIS, INFLAMMATORY BOWEL DISEASE, IBD
rs9272346 *(-864G>A)*	G	B	**GG**	**++**		TYPE 1 DIABETES
rs9271366 *(*15 HLA-DRB1)*	G	R	**AG**	**-+**		CROHN'S ULCERATIVE COLITIS, MULTIPLE SCLEROSIS MS

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *HLA-DQA1*:

- *Salacia oblonga*

HLA-DQB2

major histocompatibility complex, class II, DQ beta 2

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

SNP outcomes in gene HLA-DQB2 relevant to Robert Pfoff:

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

New concepts:

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

HNMT

histamine N-methyltransferase

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

SNP outcomes in gene HNMT relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs17583889 *(191-12449C>A)*	A	R	**CC**	--		ANTHRACYCLINE TOXICITY
i3000469 *(rs11558538 or rs1801105, C314T Thr105Ile)*	T	R	**AA**	++		CHRONIC URTICARIA, ASTHMA, PARKINSON'S DISEASE, HISTAMINE DEGRADATION, ALLERGIC INFLAMMATION
i6036072 *(rs376127850 440A>G Deletion)*	D	R	**AA**	--		HISTAMINE METABOLISM
rs1020678	C	R	**TT**	--		
rs1050891 *(T939C or 939A>G)*	A	R	**AA**	++		CHRONIC URTICARIA, ASTHMA, PARKINSON'S DISEASE, HISTAMINE DEGRADATION, ALLERGIC INFLAMMATION
rs3100725	A	R	**GG**	--		
rs376127850 *(rs376127850 440A>G Deletion)*	D	R	**AA**	--		HISTAMINE METABOLISM

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.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *HNMT*:

- *Zinc*
- *Salacia oblonga*

IL12A-AS1

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

SNP outcomes in gene IL12A-AS1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs6441286 *(T>G)*	G	R	**TT**	--		PRIMARY BILIARY CIRRHOSIS, LUNG CANCER
rs17810546 *(3q25)*	G	R	**AA**	--		AUTOIMMUNE, CELIAC DISEASE,

IL13

interleukin 13

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

SNP outcomes in gene IL13 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs1800925 *(C1112T -1070C>T)*	T	R	**CC**	--		HIGHER IGE HIGHER IL13, PSORIASIS, AUTOIMMUNE, ASTHMA, PEDIATRIC ASTHMA, RHITINIS, LOWER FEV IN LONG-TERM SMOKERS, POSS COVID19FIBROSIS, BUT REDUCED RISK OF GRAVES DISEASE, MULTIPLE SCLEROSIS, AND POSS REDUCED RISK OF COVID STORM, COVID ARDS
rs1295685 *(+2525G>A)*	A	R	**GG**	--		ASTHMA, COPD, POSS INFECTION IN SARS-COV-2, BUT G ALLELE RISK OF PSORIASIS, POSS CYTOKINE STORM, FIBROSIS
rs20541 *(Gln144Arg, Arg130Gln, +2044G/A R130Q)*	A	R	**GG**	--		INCREASED IL13 AND IGE, ASTHMA, ATOPIC ASTHMA, ALLERGIES, PEDIATRIC ASTHMA ASIANS 2X, SYSTEMIC LUPUS ERYTHEMATOSUS, RENAL DISORDER IN SLE, AUTOIMMUNE HEPATITIS, GIANT CELL ARTERITIS, POSS COVID19FIBROSIS, BUT MAJOR ALLELE G HAS RISK OF ARDS, ALLERGIC RHINITIS, COPD, PSORIATIC ARTHRITIS, PSORIASIS, SEVERE MALARIA, POSS COVID ARDS, COVID19STORM
rs1295686 *(C>T)*	T	R	**CC**	--		INCREASED IGE, ATOPIC DERMATITIS, ASTHMA, CHILDHOOD ASTHMA, POSS COVID19FIBROSIS, BUT C ALLELE LESS IGE, POSS COVID ARDS, COVID STORM
rs848	C	R	**CC**	++		CROHNS
rs2066960	A	R	**CC**	--		SERUM IMMUNOGLOBULIN E

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *IL13*:

- *N-acetylcysteine (NAC)*
- *Vitamin D (calciferols)*
- *Copper*
- *Theanine*
- *Vitamin A (retinol)*

IL4

interleukin 4

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

SNP outcomes in gene IL4 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2227284 *(184-748T>G)*	G	R	**GG**	**++**		LECTIN SENSITIVITY
rs2243250 *(-589, -590 C>T)*	T	R	**CC**	**--**		TH1/TH2 PATHWAY, LECTIN SENSITIVITY, INCREASED IL4, ASTHMA, SEVERE ASTHMA, ASTHMA FATALITY, MUCH INCREASED IL4 IN SEVERE MALARIA, VTE IN FEMALES, POSS COVID THROMBOSIS, COVID FIBROSIS, BUT C ALLELE REDUCED IL4, ARDS, GASTRIC CANCER, ORAL CANCER OSCC, KAWASAKI DISEASE, SYSTEMIC LUPUS ERYTHEMATOSUS, ALZHEIMERS, ALLERGIC RHINITIS, CHRONIC HBV, MALARIA, CHRONIC DISSEMINATED CANDIDIASIS, POSS COVID ARDS

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *IL4*:

- *Gynostemma pentaphyllum*
- *Ginkgo (Ginkgo biloba)*
- *Theanine*
- *Vitamin A (retinol)*
- *Curcumin*
- *Low Sucrose Diet*
- *Copper*
- *Cannabidiol*

MCM6

minichromosome maintenance complex component 6

The MCM6 gene provides instructions for making part of the MCM complex, a group of proteins that functions as a helicase. Helicases attach to particular regions of DNA and temporarily unwind the two spiral strands of these molecules. When a cell prepares to divide to form two cells, helicases unwind the DNA so that it can be copied. The DNA that makes up the chromosomes is duplicated (replicated) so that each new cell will get a complete set of chromosomes. Helicases are also involved in the production of RNA, a chemical cousin of DNA.

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

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

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

SNP outcomes in gene MCM6 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs182549 *(-22018G>A)*	C	R	**TC**	**-+**		ADULT LACTOSE INTOLERANCE

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MCM6*:

- *Citral*
- *Ivermectin*

NOD2

nucleotide-binding oligomerization domain containing 2

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

SNP outcomes in gene NOD2 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs17221417	G	R	**CG**	**-+**		CROHNS DISEASE
rs2066844	T	R	**CC**	**--**		AUTOIMMUNE, IBD, IBD I, CROHN'S, BLAU SYNDROME, YAO SYNDROME, SEPSIS

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *NOD2*:

- *Omega 3 Fatty Acids*
- *Salacia oblonga*

NOS2

nitric oxide synthase 2, inducible

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

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

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

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

SNP outcomes in gene NOS2 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2248814	A	R	**GG**	**--**		IMMUNE NOS, UVEITIS
rs2297518 *(+2087, S608L G>A)*	A	R	**AG**	**+-**		PREECLAMPSIA, MIGRAINE WITH AURA, SEPSIS, SEPTIC SHOCK, ARDS, POSS COVID STORM, COVID ARDS, BUT G ALLELE POSS COVID INFECTION, COVID NOS, COVID19THROMBOSIS, CHD, CORONARY HEART DISEASE
rs2274894	T	R	**GG**	**--**		IMMUNE NOS

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *NOS2*:

- *Resveratrol*
- *Ginkgo (Ginkgo biloba)*
- *Olive Oil*
- *Sulforaphane*
- *Selenium*
- *Pterostilbene*
- *Green Tea, Kukicha, Bancha*
- *Theanine*
- *Aluminum avoidance*
- *Curcumin*
- *Co-enzyme Q10*
- *Ursolic acid*
- *Blueberries*
- *Quercetin*
- *Berberine*

GASTROINTESTINAL

MULTI-SNP MACROS

Reduced risk (0.26) of Crohn's disease and ulcerative colitis

Genes	IL23R
Repute:	BENEFIT
Magnitude:	2.7
Frequency:	9%

INTERPRETATION: The Interleukin 23 Receptor gene IL23R is related to the inflammatory bowel diseases Crohn's disease and ulcerative colitis. Having the A allele in rs11209026 (AG) gives you a lower risk of developing these conditions.

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

Your results: rs11209026 (**AG**)

Lower disorder/ gluten sensitivity risk (HLA-DQA1)

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

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

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

Your results: rs2187668 (**CC**)

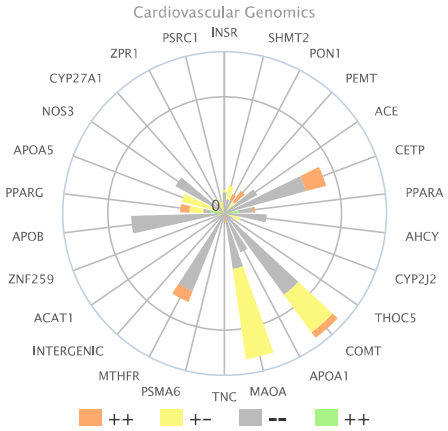
Gastrointestinal Health macro algorithms returning as false:

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

GASTROINTESTINAL

NETWORK MAPS

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



ANTI-AGING

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.

ACAT1

acetyl-CoA acetyltransferase 1

The ACAT1 gene provides instructions for making an enzyme that is found in the mitochondria, the energy-producing centers within cells. This enzyme plays an essential role in breaking down carbohydrates, proteins and fats from the diet. Specifically, it begins in the citric acid cycle to form citrate which will eventually make ATP, the energy currency of all metabolic activity. In protein catabolism, it helps process isoleucine, an amino acid that is a building block of many proteins. This enzyme is also involved in processing ketones, which are molecules that are produced when fats are broken down in the body.

Problems with ACAT gene function are significant for the following reasons:

- Cholesterol formation
- Lipid (fatty acid) balance and fluidity in the cell membranes, which impacts neurological function
- Ensuring healthy myelin nerve coating
- Contributing to energy production via the citric acid cycle and its impact on the mitochondria, which signal cellular activity and supply cellular energy
- Accumulation of oxalates, which in excess can contribute to kidney stones and cause other health problems
- Metastatic cancer

SNP outcomes in gene ACAT1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs3741049 *(579+159G>A -02)*	A	R	**GG**	--		MITOCHONDRIAL CHOLESTEROL FOAM CELL FORMATION AND ENERGY CONVERSION

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.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *ACAT1*:

- *High Fat Diet*
- *Quercetin*

ACE

angiotensin I converting enzyme (peptidyl-dipeptidase A) 1

ACE encodes an enzyme involved in catalyzing the conversion of angiotensin I into a physiologically active peptide angiotensin II. Angiotensin II is a potent vasoconstrictor and causes an increase in aldosterone levels that lead to an increase in sodium retention because the ACE enzyme controls blood pressure and fluid-electrolyte balance.

This enzyme enables sodium/potassium membrane transport for energy production and cell membrane activation. Decreased potassium can lead to fatigue and decreased energy production as cellular membrane activation, particularly for the brain and peripheral nervous system is dependent on sodium-potassium balance. Lowered frustration threshold, increased anxiety and memory loss have been studied in relationship to Angiotensin II levels. A MAO-A mutation as well as mutations in COMT, SL6A4, TH, THP, BDNF, APOE, ESR1 and CLOCK can exacerbate this effect. Many studies have associated mutations in this gene with cardiovascular pathology.

SNP outcomes in gene ACE relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs4341 *(C>G)*	G	R	**CC**	--		WEIGHT
rs4343 *(2328G>A Thr776, G2350A)*	G	R	**AA**	--		ACE INDEL, INCREASED ACE ACTIVITY, TYPE 2 DIABETES, T2D, DYSLIPIDEMIA, SODIUM POTASSIUM BALANCE, BLOOD PRESSURE REGULATION FRUSTRATION, OSTEOARTHRITIS, MIGRAINE, HYPERTENSION, ARDS, MORTALITY, PNEUMONIA, DIABETIC NEPHROPATHY, ALZHEIMERS, GALLBLADDER CANCER, POORER RESPONSE TO VIAGRA, MORE EXTREME OBESITY WITH HIGH CARB DIET, POSS COVID19ARDS, COVID19STORM, COVID19METABOLIC, IMPROVED ATHLETIC RECOVERY REDUCED MUSCLE BREAKDOWN, REDUCED CREATINE KINASE, REDUCED ODDS OF CROHNS DISEASE AND PSORIASIS, REDUCED ODDS OF BEING ENDURANCE ELITE ATHLETE, BUT HOMOZYGOUS GG INCREASED ODDS OF ELITE POWER ATHLETE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *ACE*:

- *Olive Oil*
- *Blueberries*
- *Copper*
- *Low Sucrose Diet*

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.

Elevated Adiponectin And Tnf-alpha Levels Are Markers For Gluten And Lectin Sensitivity. [https://www.ahajournals.org/doi/10.1161/circ.129.suppl_1.p354]

Endometrial cancer risk is inversely affected by adiponectin and leptin levels. There appears to be no relationship between TNFα and IL-6 and the overall risk of endometrial cancer.[PMID: 32507648]

SNP outcomes in gene ADIPOQ relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs1501299 *(276G>T)*	G	R	**TG**	**-+**		BREAST CANCER, TRIGLYCERIDES, BUT HETEROZYGOUS GT SEEMS TO HAVE HIGHER BMI, AND HOMOZYGOUS GG WHO LIKE SWEETS HAVE HIGHER BMI, AND TT ALLELE HAS LOWER A1C WHO LIKE FISH, T ALLELE BENEFITS FROM INCREASED EXERCISE
rs17366568	A	R	**GG**	**--**		ADIPONECTIN, OBESITY, BMI
rs2241766 *(45T>G)*	G	R	**TT**	**--**		BREAST CANCER, OBESITY, HIGHER TOTAL CHOLESTEROL TRIGLYCERIDES, INCREASED EXERCISE REQUIREMENTS, GG ALSO HAS HIGHER A1C AND MUCH HIGHER TRIGLYCERIDES, GG DOES NOT INCREASE HDL LEVELS WITH ALCOHOL AND SHOULD AVOID
rs16861205	A	R	**GG**	**--**		BODY WEIGHT, STROKE, ISCHEMIC STROKE, CANCER, TUMOR TISSUE,
rs17300539 *(-11391 G>>A)*	A	B	**AG**	**+-**		IMPROVED MAINTENANCE OF WEIGHT LOSS, INCREASED ADIPONECTIN LEVELS, REDUCED OBESITY, INSULIN LEVELS, WAIST CIRCUMFERENCE, BMI, HIGHER ADIPONECTIN, AND IMPROVED WEIGHT LOSS WITH HIGHER MONOUNSATURATED FAT INTAKE

New concepts:

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

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *ADIPOQ*:

- *Resveratrol*
- *Omega 3 Fatty Acids*
- *Caloric restriction*
- *Probiotics*
- *High Fat Diet*

AHCY

adenosylhomocysteinase

The AHCY gene provides instructions for producing the enzyme S-adenosylhomocysteine hydrolase which produces homocysteine for the degradation by CBS and glutatione formation. This enzyme is involved in a multistep process that breaks down the protein building block (amino acid) methionine. Specifically, S-adenosylhomocysteine hydrolase controls the step that converts the compound S-adenosylhomocysteine to the compounds adenosine and homocysteine. This reaction also plays an important role in regulating the addition of methyl groups, consisting of one carbon atom and three hydrogen atoms, to other compounds (methylation). Methylation is important in many cellular processes. These include determining whether the instructions in a particular 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 gene AHCY relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs819147 *(01)*	C	R	**TT**	**--**		HYDROLYSIS, ADOHCY HYROLYSIS, METHYLATION, AUTISM
rs819171 *(19)*	C	R	**TT**	**--**		HYDROLYSIS, ADOHCY HYDROLYSIS, METHYLATION, AUTISM
rs819134 *(02)*	G	R	**AA**	**--**		HOMOCYSTEINE

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.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *AHCY*:

- *Copper*

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 gene APOA1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs670 *(-113G>A)*	T	R	**CC**	--		HDL DEFICIENCY
rs1799837 *(-21+68G>A)*	T	R	**CC**	--		HDL DEFICIENCY
rs5069 *(-21+67C>T)*	A	R	**GG**	--		HDL DEFICIENCY

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *APOA1*:

- *Vitamin C (ascorbic acid)*

APOA5

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

Deficiency of apoC3 or apoA5 led to significant decreased or increased plasma TG levels, respectively. Recent studies indicated apoC3 and apoA5 also played roles in plasma remnant cholesterol, high density lipoprotein (HDL) and hepatic TG metabolisms. Moreover, large scale population genetic studies indicated that loss of function mutations in APOC3 and APOA5 gene conferred decreased and increased risk of coronary artery disease (CAD), respectively.

https://lipidworld.biomedcentral.com/articles/10.1186/s12944-019-1166-5

SNP outcomes in gene APOA5 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs651821 *(-3A>A)*	C	R	**TC**	**-+**		TRIGLYCERIDE LEVELS, METABOLIC SYNDROME, GUT BACTERIA LEVELS
rs10750097	A	R	**AG**	**+-**		FENOFIBRATE, STATINS, CHOLESTEROL, VITAMIN D, HDL
rs662799 *(-1131T/C)*	G	R	**AG**	**-+**		BMI, OBESITY RISK, REDUCED HDL, INCREASED TRIGLYCERIES, 2X HIGHER EARLY HEART ATTACK RISK, BUT LESS WEIGHT GAIN ON HIGH FAT DIET, LOWCARB, INCREASED VITAMIN E LEVELS, TOCOPHEROLS, HOMOZYGOUS AA WEIGHT GAIN INCREASES AS TOTAL FAT INTAKE INCREASES

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 gene APOB relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs12713559 *(R3531C, G>>>>A)*	A	R	**GG**	--		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
i4000339 *(rs144467873 10579C>T Arg3527Trp R3500W)*	A	R	**GG**	--		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
rs1042031 *(C>T)*	T	R	**CC**	--		HYPERCHOLESTEROLEMIA, FAMILIAL HYPOBETALIPOPROTEINEMIA, CARDIOVASCULAR DISEASE
rs5742904 *(Arg3527Gln, C>>>T)*	T	R	**CC**	--		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B, ATHEROSCLEROSIS
rs144467873 *(rs144467873 10579C>T Arg3527Trp R3500W)*	A	R	**GG**	--		LDL-C FAMILIAL HYPERCHOLESTEROLEMIA TYPE B
rs1367117 *(711C>T)*	A	R	**GG**	--		LDL CHOLESTEROL

New concepts:

- A *carrier* is an individual who is heterozygous for a trait that only shows up in the phenotype of those who are homozygous recessive.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *APOB*:

- *Omega 3 Fatty Acids*

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.

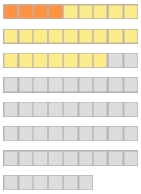
SNP outcomes in gene CETP relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs1800775 *(-656C>A)*	C	R	**AA**	--		HDL CHOLESTEROL, LIPID LEVELS, VENOUS THROMBOEMBOLISM, POSS COVID19METABOLIC
rs1532624	A	R	--	--		HDL, LDL, CHOLESTEROL
rs708272 *(TaqIB)*	A	R	**AA**	++		ALCOHOL, HDL, CORONARY DISEASE, OBESITY
rs3764261	C	R	**AA**	--		HDL LDL CHOLESTEROL TRIGLYCERIDES
rs2303790 *(Asp442Gly A>>G rare)*	G	R	**AA**	--		LIPID LEVELS, CARDIOVASCULAR RISK
rs5882	A	R	**AA**	++		AGE, AGING, DEMENTIA, HDL
rs5742907 *(1321+1, Int14G>>A rare)*	A	R	**GG**	--		HDL CHOLESTEROL, HYPERALPHALIPOPROTEINEMIA 1, CORONARY HEART DISEASE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CETP*:

- *Krill oil*
- *Fish oils*

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.

COMT upregulation as a Strategy in Endometrial (and other) Cancers: The metabolism of estrogens has been thought to play an important role in the development and pathogenesis of EC. Estrogens, 17 beta-estradiol (E2) and estron (E1) are catabolized to intermediate products, called catechol estrogens [2- or 4-hydroxyestradiol (2- or 4-OH-E2) and 2- or 4-hydroxyestrone (2- or 4-OH-E1)]. 2-OH estrogens are non-carcinogenic, however, 4-OH catechol estrogens, metabolized by CYP1B1, are potentially carcinogenic and induce DNA damage. 4-OH-E2 is then metabolized by catechol-O-methyltransferase (COMT) to 2-methoxyestradiol. COMT is a phase II enzyme, catalyzing the methylation of catechol estrogens to form 2-methoxyestradiol (2-MeO-E2) and 4-methoxyestradiol (4-MeO-E2). Taken together, these data suggest a critical role for inhibition of CYP1B1 and increase in COMT activities for reducing risk of carcinogenesis associated with estrogen catechols. High CYP1B1 and low COMT activities would lead to more DNA reactive, unconjugated catechol estrogens (4-OH forms) and lower levels of the potent anti-angiogenic 2Me-OH, increasing the risk of carcinogenesis.

SNP outcomes in gene COMT relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs737866	C	R	**TC**	**-+**		
rs769224 *(-61P199P)*	A	R	**GG**	**--**		CATECHOLAMINES DEGRADATION
rs5993882 *(-92+8113T>G)*	G	R	**TG**	**-+**		PAIN, CHRONIC FATIGUE
rs4633 *(↓ 186C>T His62= H62H)*	T	R	**CC**	**--**		LD WITH RS4680 A MET ALLELE WORRIER PHENOTYPE, REDUCED COMT, INCREASED DOPAMINE, METHYLATION ISSUES, STRESS, ANXIETY, SUICIDE, PANIC IN EUROPEANS, AGGRESSION, IMPULSIVENESS, HYPERACTIVITY, OCD IN MALES, ADHD IN MALES, PARKINSONS IN INDIANS JAPANESE AND FEMALES, LATE ONSET PARKINSONS, ESTROGEN BLOOD METABOLITES, BREAST ENDOMETRIAL PANCREATIC CANCER, REDUCED PAIN THRESHOLD, INCREASED BODILY PAIN AND SENSITIVITY, NEURAL NETWORK INFLEXIBILITY REGARDING EMOTION, VENOUS THROMBOSIS, VTE, HOMOCYSTEINE, NICOTINE RESPONSE, NICOTINE PATCH MORE EFFECTIVE, REDUCED CVD RISK ON ASPIRIN AND VITAMIN E, RECURRENT MISCARRIAGE, IMPROVED MEMORY AND EXECUTIVE FUNCTION IN EUROPEANS, BUT WARRIOR VAL G ALLELE HAS RISK OF SCHIZOPHRENIA, YOUNGER AGE AT ONSET OF PARKINSONS IN EUROPEAN MEN, OPPOSITE IN ASIANS, IMPROVED MEMORY AND EXECUTIVE FUNCTION IN HAN CHINESE, BETTER AT PROCESSING ADVERSE STIMULI, INCREASED BREAST CANCER
rs165722 *(1187C>T)*	T	R	**CC**	**--**		CANCER TREATMENT, OPIOIDS, MONOAMINE, CANCER
rs165774 *(a-COMT)*	A	R	**GG**	**--**		HIGH EPINEPHRINE VARIANT, BUT CATALYTICALLY ACTIVE TO DOPAMINE AND NOREPINEPHRINE DEGRADATION
rs4680 *(↓ 472G>A V158M)*	A	R	**GG**	**--**		A MET ALLELE WORRIER PHENOTYPE, REDUCED COMT, INCREASED DOPAMINE, METHYLATION ISSUES, STRESS, ANXIETY, SUICIDE, PANIC IN EUROPEANS, AGGRESSION, IMPULSIVENESS, HYPERACTIVITY, OCD IN MALES, ADHD IN MALES, PARKINSONS IN INDIANS JAPANESE AND FEMALES, LATE ONSET PARKINSONS, ESTROGEN BLOOD METABOLITES, BREAST ENDOMETRIAL PANCREATIC CANCER, REDUCED PAIN THRESHOLD, INCREASED BODILY PAIN AND SENSITIVITY, NEURAL NETWORK INFLEXIBILITY REGARDING EMOTION, VENOUS THROMBOSIS, VTE, HOMOCYSTEINE, NICOTINE RESPONSE, NICOTINE PATCH MORE EFFECTIVE, REDUCED CVD RISK ON ASPIRIN AND VITAMIN E, RECURRENT MISCARRIAGE, IMPROVED MEMORY AND EXECUTIVE FUNCTION IN EUROPEANS, BUT WARRIOR VAL G ALLELE HAS RISK OF SCHIZOPHRENIA, YOUNGER AGE AT ONSET OF PARKINSONS IN EUROPEAN MEN, OPPOSITE IN ASIANS, IMPROVED MEMORY AND EXECUTIVE FUNCTION IN HAN CHINESE, BETTER AT PROCESSING ADVERSE STIMULI, INCREASED BREAST CANCER, REDUCED BLOOD PRESSURE ON BP MEDICATION
rs165599 *(*522G>A)*	G	R	**GG**	**++**		ANXIETY-RELATED PERSONALITY TRAITS, ADHD, SCHIZOPHRENIA
rs6269 *(98A/G 248A/G)*	G	R	**AG**	**-+**		HYPERACTIVITY PARKINSON'S DISEASE SCHIZOPHRENIA MAJOR DEPRESSIVE DISORDER
rs737865 *(-92+701A>G TXNRD2)*	G	R	**AG**	**-+**		BUPROPION TREATMENT FOR SMOKING CESSATION, BUT A ALLELE HAS RISK OF SUICIDE IN TREATMENT RESISTANT MAJOR DEPRESSION
rs4618 *(L136L)*	G	R	**TT**	**--**		FIBROMYALGIA, CHRONIC PAIN
rs4646312 *(-91-385T>C)*	T	R	**TC**	**+-**		ESTROGEN ANDROGEN METABOLIZING
rs933271 *(-92+1987T>C)*	C	R	**TC**	**-+**		NICOTINE DEPENDANCE SCHIZOPHRENIA COCAINE PARANOIA IMPULSIVITY

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *COMT*:

- *Vitamin C (ascorbic acid)*
- *Magnesium*
- *Caloric restriction*

CYP27A1

cytochrome P450, family 27, subfamily A, polypeptide 1

CYP27A1 is a phase I detoxifying enzyme that activates many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. This enzyme is located in many different tissues where it is found within the mitochondria. It is most prominently involved in the biosynthesis of bile acids. CYP27A1 oxidizes cholesterol intermediates as part of the bile synthesis pathway. Since the conversion of cholesterol to bile acids is the major route for removing cholesterol from the body, this protein is important for overall cholesterol homeostasis.

SNP outcomes in gene CYP27A1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs4674344 *(A>T)*	T	R	**AA**	--		METABOLIC SYNDROME DUE TO LOW ADIPONECTIN/LEPTIN RATIO IN T CARRIERS
rs72551319	T	R	**AA**	--		
rs41272687	T	R	**CC**	--		
rs72551320	G	R	**AA**	--		
rs72551317	G	R	**AA**	--		

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.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CYP27A1*:

- *Gynostemma pentaphyllum*
- *Vitamin D (calciferols)*
- *Vitamin B-2 (riboflavin)*

CYP2J2

cytochrome P450, family 2, subfamily J, polypeptide 2

CYP2J2 is a phase I detoxifying enzyme and is thought to be the predominant enzyme responsible for the metabolism of arachidonic acid in the heart. Arachidonic acid is a polyunsaturated fatty acid present in the membranes of the body's cells, and is abundant in the brain, muscles, liver and skeletal muscle. In addition to being involved in cellular signaling, arachidonic acid is a key factor in bringing on inflammation, and can also act as a vasodilator.

SNP outcomes in gene CYP2J2 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs11572223	A	R	**GG**	--		
rs10889160 *(T>C)*	C	R	**TC**	-+		MYOCARDIAL INFARCTION

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CYP2J2*:

- *Vitamin D (calciferols)*

INSR

insulin receptor

After removal of the precursor signal peptide, the insulin receptor precursor is post-translationally cleaved into two chains (alpha and beta) that are covalently linked. Binding of insulin to the insulin receptor (INSR) stimulates glucose uptake. Two transcript variants encoding different isoforms have been found for this gene.

SNP outcomes in gene INSR relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs7248104	A	R	**GG**	--		
rs1051690	T	R	**CC**	--		
rs1799817 *(His1085His)*	A	R	**GG**	--		PCOS ASSOCIATION
rs4804416	G	R	**TG**	--+		INSULIN RESISTANCE, THYROID HORMONE, AUTOIMMUNE HYPOTHYROIDISM

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *INSR*:

- *Berberine*
- *Pterostilbene*

INTERGENIC

An Intergenic region is a stretch of DNA sequences located between genes. Intergenic regions are a subset of Noncoding DNA. Occasionally some intergenic DNA acts to control genes nearby, but most of it has no currently known function. Intergenic regions in humans comprise about 75% of the genome.

Historically intergenic regions have sometimes been called 'junk DNA', suggesting that they have no function. However, it has been known for a long time that these regions do contain functionally important elements such as promoters and enhancers. Also intergenic regions may contain as yet unidentified genes such as noncoding RNAs. Though little is known about them, they are thought to have regulatory functions.

SNP outcomes in gene INTERGENIC relevant to Robert Pfoff:

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

New concepts:

- In genetics, a *promoter* is a region of DNA that initiates transcription of a particular gene.

MAOA

monoamine oxidase A

Monoamine Oxidase A breaks down neurotransmitters.

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

SNP outcomes in gene MAOA relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2235186 *(1053-46A>G, 654-46A>G)*	G	R	**G**	**+-**		ADHD
rs909525 *(C42794T)*	T	R	**T**	**+-**		WARRIOR GENE, ANGER, AGGRESSION, SUICIDE, SUICIDALITY, METHYL TRAPPING
rs1137070 *(Asp337Asp Asp470=, VNTR, 1410C>T)*	T	R	**C**	**--**		ESTROGEN DOMINANCE AND LOW OXIDATIVE DEAMINATION OF AMINES, SUCH AS DOPAMINE, NOREPINEPHRINE, AND SEROTONIN, IMPULSIVITY, IMPULSIVENESS
rs5953210 *(↓ -1544G>A -2051G>A)*	G	R	**A**	**--**		SUBSTANCE ABUSE, GOUT
rs3027399 *(1052+680G>C)*	G	R	**G**	**+-**		WARRIOR, X-LINKED METHYL-TRAPPING
rs6323 *(↓ R297R, G492T, T941G, VNTR)*	T	R	**T**	**+-**		WILD-TYPE MAOA IS G, CATECHOLAMINES METHYL TRAPPING ANTI-DEPRESSANT RESPONSE, MAJOR DEPRESSIVE DISORDER
rs2072743 *(89113T>C, 1107-407T>C, 708-407T>C, VNTR)*	T	R	**C**	**--**		MAJOR DEPRESSIVE DISORDER ADHD
rs5906883 *(16535A>C)*	C	R	**C**	**+-**		ADHD
rs2283725 *(↑ 306+7301A>G)*	A	R	**G**	**--**		GOUT

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MAOA*:

- *Resveratrol*
- *Theanine*
- *Vitamin B-1 (thiamine)*
- *Curcumin*
- *Vitamin B-2 (riboflavin)*
- *Vitamin D (calciferols)*
- *Quercetin*
- *Ashwagandha (Withania somnifera)*
- *Berberine*

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 gene MTHFR relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs1801133 *(↓ C677T Ala222Val)*	A	R	GG	--		TYPE 2 DIABETES, T2D, DYSLIPIDEMIA, ASTHMA, DEPRESSION, DEPRESSION WITHOUT ANXIETY, HYPERTENSION, CANCER, RHEUMATOID ARTHRITIS, GASTRIC LUNG HEAD AND NECK RENAL CANCER, HOMOCYSTEINE, PARKINSONS, AUTOIMMUNITY, SYSTEMIC LUPUS, ERYTHEMATOSUS, MIGRAINES, HEADACHES, CLEFT LIP AND PALATE, POSS COVID19THROMBOSIS, COVID19NOS, BUT G ALLELE POSS INCREASED HCQ REQUIREMENTS, COVID19HCQ
rs13306560	T	R	CC	--		
rs17367504 *(236+160T>C A1572G)*	G	R	AA	--		HYPERTENSION, ORTHOSTATIC HYPERTENSION, RESPONSE TO BETA BLOCKERS
rs2274976 *(G1793A(R594Q))*	T	R	CC	--		
rs1999594 *(G > A)*	A	R	AA	++		FOLATE TRANSPORTER, LOW SERUM FOLATE, HIGH HOMOCYSTEINE
rs12121543	A	R	CC	--		
rs4846048	G	R	AA	--		
rs17037396	T	R	CC	--		
rs4846051 *(1305C>T T1317C Phe435Phe)*	G	R	AA	--		METHOTREXATE TOXICITY
rs13306561	G	R	AA	--		
rs1476413	T	R	CC	--		
rs1801131 *(↓ A1298C Glu429Ala)*	G	R	TT	--		LOWER NEUROTRANSMITTER SYNTHESIS, CANDIDA, LEAKY GUT, FOLATE-SENSITIVE NEURAL TUBE DEFECTS, SCHIZOPHRENIA, GASTROINTESTINAL STROMA TUMOR, RHEUMATOID ARTHRITIS, POSS COVID19THROMBOSIS, COVID19NOS, BUT T ALLELE POSS INCREASED HCQ REQUIREMENTS, COVID HCQ
rs4846049	T	R	GG	--		
rs17037390 *(475+375C>T)*	A	R	GG	--		
rs12085006 *(G>A)*	A	R	GG	--		HIGHER HOMOCYSTEINE, BREAST CANCER

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 *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.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MTHFR*:

- *Linoleic acid*
- *Vitamin B-9 (folic acid)*
- *Vitamin B-6 (pyridoxine)*
- *Vitamin B-2 (riboflavin)*
- *Omega 3 Fatty Acids*
- *Vitamin B-12 (cobalamin)*

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 gene NOS3 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs7830 *(3106+11G>T G10T)*	T	R	**GG**	--		HYPERTENSION IN FEMALES, PERIPHERAL, ARTERY DISEASE, POSS COVID19METABOLIC
rs1800779 *(↓ -949G>A)*	G	R	**AA**	--		LD WITH X0744, ENOS, HYPOXIC-ISCHEMIC ENCEPHALOPATHY, LEUKOARAIOSIS, POSS THROMBOSIS IN COVID-19, FIBROSIS, ARDS, BUT REDUCED RISK OF CYTOKINE STORM
rs1799983 *(D298E, Glu298Asp, 894G>T)*	T	R	**GG**	--		INFLAMMATION, MORTALITY, ARDS, POSS COVID THROMBOSIS, COVID19NOS, COVID RBC, COVID FIBROSIS, ENDOTHELIAL DYSFUNCTION, REDUCED NOS3 NO AND PLATELET NO FORMATION, TYPE 2 DIABETES, T2D (X3 IN OBESE), PEDIATRIC ARDS, OBESITY, POSS COVID19METABOLIC, BMI, WAIST CIRCUMFERENCE, HYPERTENSION, HTN, ERECTILE DYSFUNCTION, PRE-ECLAMPSIA, DIABETIC NEPHROPATHY, MIGRAINE, MIGRAINE WITH AURA, LOWER BLOOD OXYGEN LEVELS, DYSLIPIDEMIA, INCREASED PNEUMONIA SUSCEPTIBILITY, HAPE, PULMONARY EDEMA, INCREASED IL13 AND TH2 FROM ATTENDING DAYCARE OR HAVING OLDER SIBLINGS, BUT G ALLELE REDUCED RESPONSE TO OMEGA 3, RISK OF HAMSTRING INJURY, INCREASED MDA AND OXIDATIVE STRESS FROM AIR POLLUTION, AND CORONARY ARTERY SPASM, POSS COVID STORM
rs3918226 *(-665C>T)*	T	R	**CC**	--		REDUCED NOS3 EXPRESSION ESP IN LUNGS, CENTRAL ARTERIAL STIFFNESS, CHD-RELATED ISSUES, HYPERTENSION, HTN, PERIPHERAL ARTERY DISEASE, STROKE, REDUCED RENAL FUNCTION, GFR, AND LUNG FUNCTION, FEV, POSS COVID19ARDS, COVID19THROMBOSIS, COVID19NOS, COVID19RBC, COVID19FIBROSIS
rs2070744 *(T786C)*	C	R	**TT**	--		ENDOTHELIAL, RECURRENT MISCARRIAGE, LOWER NO LEVELS, HYPERTENSION, HTN, DIABETIC NEPHROPATHY & MICROVASCULAR COMPLICATIONS OF DIABETES, ERECTILE DYSFUNCTION, MIGRAINES, METABOLIC SYNDROME, ORAL CANCER, CORONARY ARTERY DISEASE, INCREASED EFFICACY OF STATINS IN OBESE PTS ESP. C ALLELE CARRIERS, BETTER RESPONSE TO ACE INHIBITORS, AND SILDENAFIL, POSS RISK OF COVID19METABOLIC, COVID19THROMBOSIS, COVID19NOS, COVID19ARDS, COVID19FIBROSIS, BUT T ALLELE BETTER KIDNEY TRANSPLANT OUTCOMES (OR 3.12), IMPROVED POWER ATHLETE STATUS ELITE ATHLETE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *NOS3*:

- *Resveratrol*
- *Ginkgo (Ginkgo biloba)*
- *Green Tea, Kukicha, Bancha*
- *Omega 3 Fatty Acids*
- *Vitamin C (ascorbic acid)*
- *Vitamin D (calciferols)*
- *Caloric restriction*
- *Melatonin*
- *N-acetylcysteine (NAC)*
- *Selenium*

- *Cannabidiol*

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 gene PEMT relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs7946 *(↓ V175M, +5465 G>A, 568G>A, Val190Met, Ser222Asn, Met212Val)*	T	R	**TT**	**++**		MITOCHONDRIAL CHOLINE METABOLISM, NONALCOHOLIC FATTY LIVER DISEASE, BREAST CANCER WITH LOW BETAINE INTAKE, ALZHEIMER DISEASE IN WOMEN AND APOE ε4 NON-CARRIERS
rs4646406	A	R	**AT**	**+-**		MITOCHONDRIAL

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *PEMT*:

- *Omega 3 Fatty Acids*

PON1

paraoxonase 1

The R-isoform codes for the enzyme encoded by this gene is an arylesterase that mainly hydrolyzes paroxon to produce p-nitrophenol. Paroxon is an organophosphorus anticholinesterase compound that is produced in vivo by oxidation of the insecticide parathion. Organophosphates occur in a diverse range of forms, with important examples including key biomolecules such as DNA, RNA and ATP, as well as many insecticides, herbicides, and nerve agents. Repeatedly exposed include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking, drowsiness, or insomnia. An influenza-like condition with headache, nausea, weakness, loss of appetite, and malaise has also been reported. Organophosphate pesticides degrade rapidly by hydrolysis on exposure to sunlight, air, and soil, although small amounts can be detected in food and drinking water. Organophosphates contaminate drinking water by moving through the soil to the ground water. When the pesticide degrades, it is broken down into several chemicals.(1)

In one study of leukemia in children, levels of two organophosphate metabolites were high: 3,5,6-Trichloro-2-pyridinol, a metabolite of chlorpyrifos
Diethylthiophosphate, a metabolite of numerous organophosphates such as diazinon. (2)

The Q-form more rapidly hydrolyses diazoxon and lipid-peroxides. Polymorphisms in this gene are a risk factor in coronary artery disease. The gene is found in a cluster of three related paraoxonase genes at 7q21.3. (3)

Human PON1 is a glycoprotein composed of 354 amino acids and has a molecular weight of 43000 Daltons which associates with high-density lipoprotein (HDL) in the circulation. Serum PON1 is secreted mainly by the liver, although local synthesis occurs in several tissues and PON1 protein is found in almost all tissues.(4)

PON1 is responsible for hydrolysing organophosphate pesticides and nerve gases. It metabolizes toxic oxidized lipids associated with both low-density lipoprotein (LDL) and HDL; and it can hydrolyze a number of lactone-containing pharmaceutical compounds, inactivating some, while activating others. Serum PON1 activity in a given population can vary by 40-fold. Though most of this variation can be explained by polymorphisms in the coding region (Q192R) and the 5' regulatory region (T-108C), rs705379, modulation of PON1 by a variety of other factors should be taken into account. (5,6)

Polymorphisms in the PON1 gene significantly affect the catalytic ability of the enzyme.(7) The "natural" substrates for PON1 appear to be lactones. (8)

However, PON1 has evolved to be a highly promiscuous enzyme capable of hydrolysing a wide variety of substrates such as lactones (including a number of important pharmaceutical agents such as statins), glucuronide drugs, thiolactones, arylesters, cyclic carbonates, organophosphorus pesticides and nerve gases such as sarin, soman and VX, oestrogen esters and lipid peroxides (oxidised lipids).

Major factors (environmental chemicals, drugs, smoking, alcohol, diet, age, disease conditions) have been shown to modulate PON1 activity in either direction. As PON1 plays a protective role in organophosphate toxicity, and, because of its antioxidant capacity, in cardiovascular disease, a better understanding of how PON1 can be modulated by environmental factors has potential toxicological and clinical consequences. (5,6)

References:

- "PARATHION". Pesticide Information Profiles. Extension Toxicology Network. Sep 1993. Archived from the original on 2007-07-22.
- Historical CDC Document: https://www.cdc.gov/nceh/clusters/fallon/organophosfaq.htm
- Mackness B, Durrington PN, Mackness MI (Sep 1998). "Human serum paraoxonase". General Pharmacology. 31 (3): 329–36. doi:10.1016/s0306-3623(98)00028-7. PMID 9703197
- Harel M, Aharoni A, Gaidukov L, Brumshtein B, Khersonsky O, Meged R, Dvir H, Ravelli RB, McCarthy A, Toker L, Silman I, Sussman JL, Tawfik DS (May 2004). "Structure and evolution of the serum paraoxonase family of detoxifying and anti-atherosclerotic enzymes". Nature Structural & Molecular Biology. 11 (5): 412–9. doi:10.1038/nsmb767. PMID 15098021
- Costa LG, Vitalone A, Cole TB, Furlong CE (Feb 2005). "Modulation of paraoxonase (PON1) activity". Biochemical Pharmacology. 69 (4): 541–50. doi:10.1016/j.bcp.2004.08.027. PMID 15670573
- Costa LG, Giordano G, Furlong CE. Pharmacological and dietary modulators of paraoxonase 1 (PON1) activity and expression: the hunt goes on. Biochem Pharmacol. 2011 Feb 1;81(3):337-44. doi: 10.1016/j.bcp.2010.11.008. Epub 2010 Nov 18. Review. PubMed PMID: 21093416; PubMed Central PMCID: PMC3077125.
- Costa LG, Cole TB, Vitalone A, Furlong CE (Feb 2005). "Measurement of paraoxonase (PON1) status as a potential biomarker of susceptibility to organophosphate toxicity". Clinica Chimica Acta; International Journal of Clinical Chemistry. 352 (1–2): 37–47. doi:10.1016/j.cccn.2004.09.019. PMID 15653099
- Khersonsky O, Tawfik DS (Apr 2005). "Structure-reactivity studies of serum paraoxonase PON1 suggest that its native activity is lactonase". Biochemistry. 44 (16): 6371–82. doi:10.1021/bi047440d. PMID 15835926

SNP outcomes in gene PON1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs854571 *(832A>G)*	T	R	**CC**	--		ORGANOPHOSPHATE METABOLIZER, MAJOR ANTIATHEROSCLEROTIC COMPONENT OF HDL
rs662 *(Q192R, Gln192Arg, 575A>G)*	T	R	**TT**	++		R-FORM ORGANOPHOSPHATE METABOLIZER, Q-FORM REMOVES OXIDIZED LIPIDS, REDUCES RISK IN VENOUS THROMBOEMBOLISM, CORONARY HEART DISEASE, CANCER, MACULAR DEGENERATION, RHEUMATOID DISEASE, HIV-INFECTION

New concepts:

- A *metabolite* is a product of metabolism; a substance essential to the metabolism of a particular organism or to a particular metabolic process.

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *PON1*:

- *Olive Oil*
- *Vitamin C (ascorbic acid)*
- *Vitamin B-9 (folic acid)*
- *Quercetin*
- *Selenium*
- *Caloric restriction*
- *Vitamin B-12 (cobalamin)*

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.

Activation of PPARA reduces triglyceride levels.[PMID: 22247890]

SNP outcomes in gene PPARA relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs4253623	G	R	**AA**	--		
rs4253772	T	R	**CC**	--		
rs135549 *(-43+5435C>T)*	T	B	**TC**	+-		REDUCED FAT AND SATURATED FAT ESP DAIRY FAT REDUCES TRIGLYCERIDES AND LDL CHOLESTEROL, SKIMMED MILK ESP BENEFICIAL FOR HOMOZYGOUS TT
rs1800206	G	R	**CC**	--		
rs4253776	G	R	**AA**	--		LDL, CHOLESTEROL
rs135539 *(A>C)*	A	R	**AA**	++		

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *PPARA*:

- *Resveratrol*
- *beta-Carotene*
- *Gynostemma pentaphyllum*
- *N-acetylcysteine (NAC)*
- *Linoleic acid*
- *Ivermectin*
- *Pterostilbene*
- *High Fat Diet*
- *Vitamin B-6 (pyridoxine)*
- *Genistein*
- *Caloric restriction*
- *Co-enzyme Q10*
- *Nicotinamide mononucleotide (NMN)*
- *Ursolic acid*
- *Quercetin*
- *Zinc*

PPARG

peroxisome proliferator-activated receptor gamma

This gene encodes a member of the peroxisome proliferator-activated receptor (PPAR) subfamily of nuclear receptors. PPARs form heterodimers with retinoid X receptors (RXRs) and these heterodimers regulate transcription of various genes. Three subtypes of PPARs are known: PPAR-alpha, PPAR-delta, and PPAR-gamma. The protein encoded by this gene is PPAR-gamma and is a regulator of adipocyte differentiation. Additionally, PPAR-gamma has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis and cancer.

PPARG agonists may reduce edema.[PMID: 18794727]

PPARG causes insulin sensitization and enhances glucose metabolism.[PMID: 22247890]

SNP outcomes in gene PPARG relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs3856806 *(*143C>T C161T His449)*	T	R	**TC**	**+-**		TRANSCRIPTION, TT OR TC ALLELES RISK OF TYPE 2 DIABETES, T2D, HIGHER TNF-ALPHA AND IGE LEVELS AND LOWER PEAK NASAL INSPIRATORY FLOW IN ALLERGIC RHINITIS, NON-ALCOHOLIC FATTY LIVER DISEASE, ESSENTIAL HYPERTENSION, MORTALITY IN END-STAGE RENAL DISEASE, CORONARY HEART DISEASE, CAROTID ARTERY ATHEROSCLEROSIS, HIGH-CHO DIET AND RATIOS OF PLASMA LIPIDS AND APOLIPOPROTEINS AND THE ASSOCIATION OF THE RATIOS WITH PLASMA GLUCOSE AND BMI, ALTITUDE ADAPTATION, LOW PEAK BONE MASS, REDUCED BONE MINERAL DENSITY
rs17036170	A	R	**GG**	**--**		TRANSCRIPTION ELEVATED RISK FOR DRUG INDUCED LIVER INJURY WITH DICLOFENAC
rs1801282 *(-2-28078C>G Pro12Ala)*	G	B	**CG**	**-+**		REDUCED TRANSCRIPTION, MONOUNSATURATED FATS ASSOCIATED WITH REDUCED BMI, PUFA, LOWER T2D RISK, POLYUNSATURATED FATS ARE BENEFICIAL
rs1151999 *(T>G)*	G	R	**GG**	**++**		INCREASED BMD BONE MINERAL DENSITY ON A HIGH-FAT DIET, BUT T ALLELE INCREASED BMD ON A LOW-FAT DIET

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *PPARG*:

- *beta-Carotene*
- *Omega 3 Fatty Acids*
- *Gynostemma pentaphyllum*
- *High Fat Diet*
- *Krill oil*
- *Nicotinamide mononucleotide (NMN)*
- *Resveratrol*
- *Ginkgo (Ginkgo biloba)*
- *Milk thistle (Silybum marianum)*
- *Linoleic acid*
- *Sulforaphane*
- *Cannabidiol*
- *Citral*
- *Genistein*
- *Salacia oblonga*
- *Curcumin*
- *Quercetin*
- *Berberine*

PSMA6

proteasome (prosome, macropain) subunit, alpha type, 6

The proteasome is a multicatalytic proteinase complex with a highly ordered ring-shaped 20S core structure. The core structure is composed of 4 rings of 28 non-identical subunits; 2 rings are composed of 7 alpha subunits and 2 rings are composed of 7 beta subunits. Proteasomes are distributed throughout eukaryotic cells at a high concentration and cleave peptides in an ATP/ubiquitin-dependent process in a non-lysosomal pathway. An essential function of a modified proteasome, the immunoproteasome, is the processing of class I MHC peptides. This gene encodes a member of the peptidase T1A family, that is a 20S core alpha subunit. Multiple transcript variants encoding several different isoforms have been found for this gene. A pseudogene has been identified on the Y chromosome.

SNP outcomes in gene PSMA6 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2277459	G	R	**GG**	**++**		MYOCARDIAL INFARCTION

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 gene PSRC1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs599839	A	R	**AG**	**+-**		

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.

SHMT2

serine hydroxymethyltransferase 2 (mitochondrial)

The SHMT2 gene provides instructions for the form of a pyridoxal phosphate-dependent enzyme that catalyzes the reversible reaction of serine and tetrahydrofolate to glycine and 5,10-methylene tetrahydrofolate in the mitochondria (the power-producing parts of the cell). The protein is primarily responsible for making glycine, and may be the main source of glycine in the cell.

SHMT2 is inhibited by 5-formyltetrahydrofolate (a form of folate) in when proteins are needed, transferring serine to glycine, which significantly reduces the availability of serine as a necessary component for breaking down the toxic protein homocysteine by cystathionine beta synthase (CBS). SHMT2 is also responsible for the conversion of glycine to serine, and is shown to be a crucial factor in the serine/glycine metabolism of several types of cancer cell, including colon and breast. SHMT2 also shifts the methylation (1-carbon) cycle towards producing DNA.

This gene is found on chromosome 12. The gene which encodes the form of this enzyme that enables the same reaction inside the cell rather than in mitochondria (SHMT1) is located on chromosome 17.

SNP outcomes in gene SHMT2 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs34095989	A	R	**AG**	**+-**		GLYCINE DEPENDENT CANCER PROLIFERATING, CANCER RISK, LUNG CANCER
rs12319666 *(229G>T)*	T	R	**GG**	**--**		

THOC5

THO complex 5

THOC5 (THO Complex 5) is a Protein Coding gene. Among its related pathways are RNA transport. GO annotations related to this gene include RNA binding. Acts as component of the THO subcomplex of the TREX complex which is thought to couple mRNA transcription, processing and nuclear export, and which specifically associates with spliced mRNA and not with unspliced pre-mRNA. TREX is recruited to spliced mRNAs by a transcription-independent mechanism, binds to mRNA upstream of the exon-junction complex (EJC) and is recruited in a splicing- and cap-dependent manner to a region near the 5 end of the mRNA where it functions in mRNA export to the cytoplasm via the TAP/NFX1 pathway. The TREX complex is essential for the export of Kaposis sarcoma-associated herpesvirus (KSHV) intronless mRNAs and infectious virus production. THOC5 in conjunction with ALYREF/THOC4 functions in NXF1-NXT1 mediated nuclear export of HSP70 mRNA; both proteins enhance the RNA binding activity of NXF1 and are required for NXF1 localization to the nuclear rim. Involved in transcription elongation and genome stability. Involved in alternative polyadenylation site choice by recruiting CPSF6 to 5 region of target genes; probably mediates association of the TREX and CFIm complexes Regulates the expression of myeloid transcription factors CEBPA, CEBPB and GAB2 by enhancing the levels of phosphatidylinositol 3,4,5-trisphosphate. May be involved in the differentiation of granulocytes and adipocytes. Essential for hematopoietic primitive cell survival and plays an integral role in monocytic development

SNP outcomes in gene THOC5 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs17482753	T	R	**GG**	--		CARDIOVASCULAR

New concepts:

- *Introns* are sections of DNA in-between the protein-coding sequences of a gene; these sequences are transcribed into RNA but are cut out of the message before it is translated into protein. Sometimes (erroneously) called 'Junk DNA'.
- *Cytoplasm* is the material or protoplasm within a living cell, excluding the nucleus.
- *Exons* are sections of DNA that contain the protein-coding sequences of a gene.

TNC

tenascin C

This gene encodes an extracellular matrix protein with a spatially and temporally restricted tissue distribution. This protein is homohexameric with disulfide-linked subunits, and contains multiple EGF-like and fibronectin type-III domains. It is implicated in guidance of migrating neurons as well as axons during development, synaptic plasticity, and neuronal regeneration.

SNP outcomes in gene TNC relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs2104772 *(T>A)*	T	R	**TT**	++		T ALLELE RISK OF HAMSTRING INJURY, NOT 100PCT CLEAR IF ORIENTATION IS CORRECT
rs3789875	A	R	**CC**	--		

New concepts:

- the *extracellular matrix* is a collection of extracellular (outside of the cell) molecules secreted by cells that provides structural and biochemical support to the surrounding cells.

ZNF259

zinc finger protein 259

The protein encoded by this gene is found in the cytoplasm of quiescent cells but translocates to the nucleolus in proliferating cells. The encoded protein interacts with survival motor neuron protein (SMN1) to enhance pre-mRNA splicing and to induce neuronal differentiation and axonal growth. Defects in this gene or the SMN1 gene can cause spinal muscular atrophy. Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Nov 2015]

SNP outcomes in gene ZNF259 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs6589566	G	R	**AG**	-+		CARDIOVASCULAR

ZPR1

ZPR1 Zinc Finger

ZPR1 (ZPR1 Zinc Finger) is a Protein Coding gene. Among its related pathways are Translational Control and EGFR1 Signaling Pathway. Acts as a signaling molecule that communicates proliferative growth signals from the cytoplasm to the nucleus. Plays

a role for the localization and accumulation of the survival motor neuron protein SMN1 in sub-nuclear bodies, including gems and Cajal bodies. Induces neuron differentiation and stimulates axonal growth and formation of growth cone in spinal cord motor neurons. Plays a role in the splicing of cellular pre-mRNAs. May be involved in H(2)O(2)-induced neuronal cell death. rs964184 (C→G) of the ZPR1 zinc finger gene (ZPR1) was significantly associated (P=0.0017; FDR=0.050) with type 2 DM.

SNP outcomes in gene ZPR1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs964184	G	R	**CG**	**-+**		HYPERTRIGLYCERIDEMIA, DYSLIPIDEMIA

New concepts:

- The *nucleus* is the central part of most cells that contains genetic material and is enclosed in a membrane

ANTI-AGING

MULTI-SNP MACROS

AMD/ antioxidant response genotype group 4

Genes	CFH,ARMS2
Repute:	RISK
Magnitude:	3
Frequency:	23%

INTERPRETATION: This client is AMD/antioxidant response genotype group 3 (GTG3). These clients are non-responsive to antioxidant therapy for AMD. For the patients in GTG 4 (high CFH and high ARMS2 risk; 23% of the study population), no AREDS-assigned treatment (beta carotene, lutein plus zeaxanthin, vitamin C, vitamin E, zinc zinc) appears beneficial, and these patients can avoid the cost and infrequent adverse effects associated with nutritional supplements.

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

Your results: rs3766405 (**TC**) rs1048663 (**GG**) rs10490924 (**TG**)

Age related macular degeneration

Genes	CFH
Repute:	RISK
Magnitude:	3
Frequency:	N/A

INTERPRETATION: (Age-related macular degeneration ARMD) is the leading cause of blindness for people over 50. Your genotype places you at increased risk of ARMD. This is due to having both the rs380390(CC) and rs3793784 (GG) genotypes and/or the rs1061170(C) allele.

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

Your results: rs3793784 (**CC**) rs380390 (**N/A**) rs1061170 (**TC**)

Younger, healthier kidney function

Genes	MMP20
Repute:	BENEFIT
Magnitude:	2.4
Frequency:	47%

INTERPRETATION: The 'T' allele of the rs1711437 SNP in the MMP20 gene is correlated with clearance of creatinine, a waste product of metabolism that is excreted in the urine. Creatinine is a byproduct of the metabolism of creatine, and is used in muscle contraction. Measurement of blood creatinine is associated with the health of the kidneys and their ability to remove creatinine from the blood. Creatinine clearance is a marker of kidney function. Mutation in the rs1711437 SNP explains 2.1% of the variation in creatinine clearance, with 'T' being the protective allele. For an individual who carries the 'T' allele, his or her creatinine clearance is approximately the same as that of someone 4–5 years younger who does not carry the 'T' allele.

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

Your results: rs1711437 (**TC**)

Effect of FOXO3 and CFH polymorphisms on longevity

Genes	FOXO3,CFH
Repute:	SEE CHART
Magnitude:	2
Frequency:	N/A

INTERPRETATION: A study of 5 genes in 3,741 Japanese men, some of whom lived significantly longer than average (centenarians), concluded that the FOXO3 gene (Forkhead box 03) harbors several SNPs linked to longevity, including SNPs rs2802292 and rs2764264. Benefits are conveyed by having the genotype rs2802292(G) and/or rs2764264(CC) In the Finnish Vitality 90+ study, people with rs1061170(TT) in the CFH (Factor H) gene generally lived longer than (C) allele carriers.

Your results:

NEUTRAL FOXO3 rs2802292 TT No benefit to lifespan
NEUTRAL FOXO3 rs2764264 TT No benefit to lifespan
NEUTRAL CFH rs1061170 TC No benefit to lifespan

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

Your results: rs2802292 (**TT**) rs2764264 (**TT**) rs1061170 (**TC**)

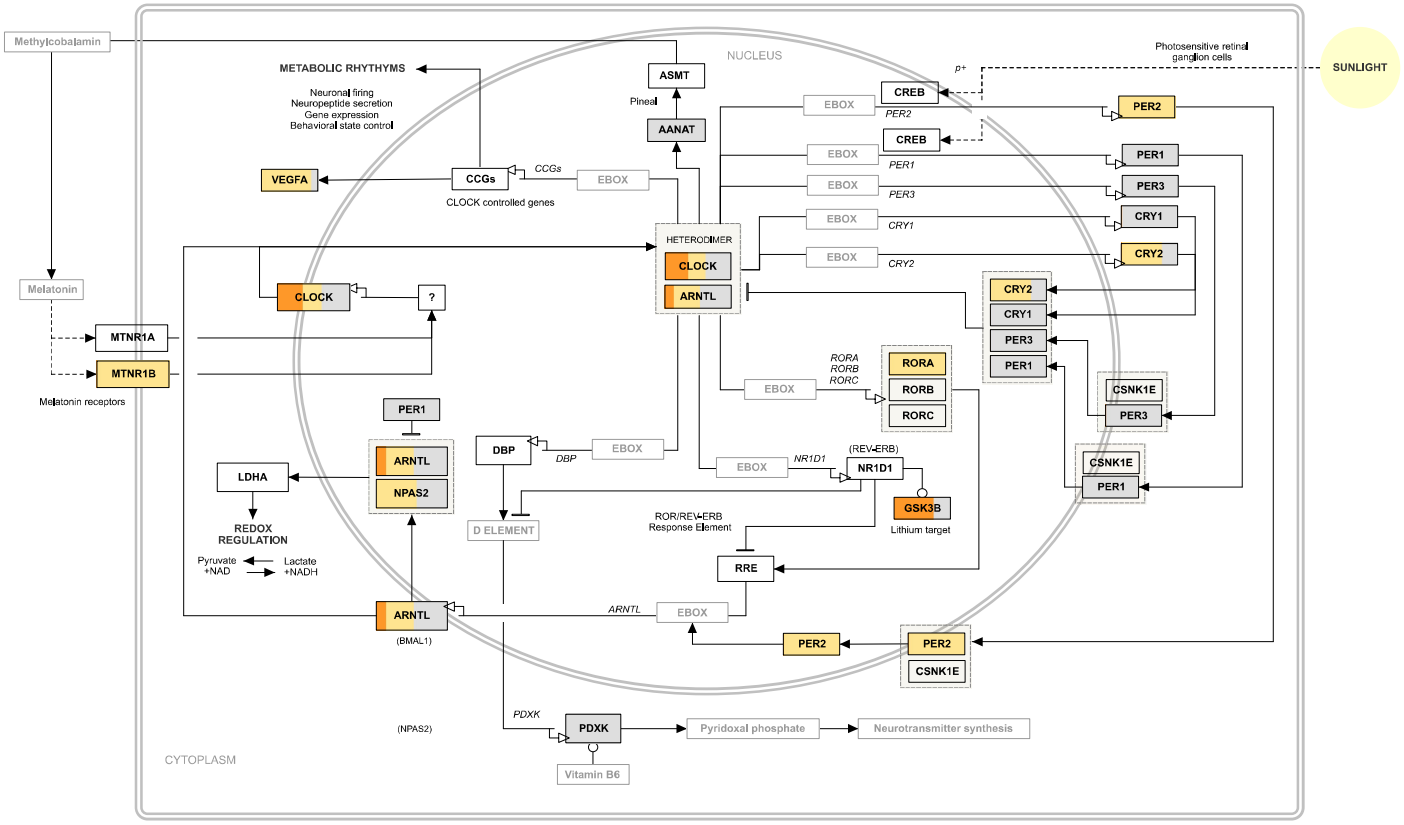
ANTI-AGING

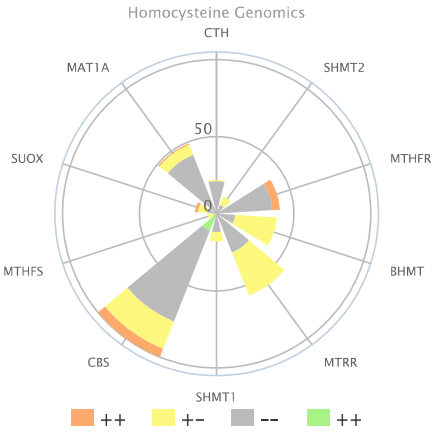
NETWORK MAPS

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).

Circadian Oscillator Network

Daily rotation of the Earth on its axis and yearly revolution around the Sun have significant effects on our 'biological rhythms'. We have developed endogenous molecular circadian clocks to synchronize our behavioral, biological, and metabolic rhythms to environmental cues, with the aim to perform at their best over a 24-h span. The coordinated circadian regulation of sleep/wake, rest/activity, fasting/feeding, and catabolic/anabolic cycles is crucial for optimal health. Circadian rhythms in gene expression synchronize biochemical processes and metabolic fluxes with the external environment, allowing the organism to function effectively in response to predictable physiological challenges. A loss of synchronization may alter the physiological array of rhythms, leading to metabolic derangement and disease, i.e., chronopathology.



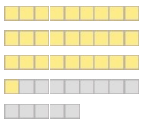


CARDIOMETABOLIC

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.

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.

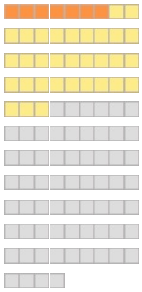
SNP outcomes in gene BHMT relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs617219 *(04)*	C	R	**AC**	**-+**		FOLATES, FOLATE METABOLISM
rs651852 *(-08)*	T	R	**TC**	**+-**		IMPAIRED HOMOCYSTEINE RECYCLING, NEURAL TUBE DEFICIT
rs6875201 *(c.34-1026A>>G)*	G	R	**AG**	**-+**		LIVER, METHYLATION
rs567754 *(02)*	T	R	**TC**	**+-**		FOLATE METABOLISM, FOLATES, HOMOCYSTEINURIA
rs585800 *(01)*	T	R	**AA**	**--**		FOLATES, FOLATE METABOLISM, FOLATE
rs3733890 *(716G>A Arg239Gln R239Q)*	A	R	**GG**	**--**		CHOLINE, OMPHALOCELE, NEURAL TUBE DEFECTS, NSCL, NSCP, CLEFT LIP, CLEFT PALATE, NONSYNDROMIC, SHORTER TELOMERES, REDUCED RISK OF CORONARY ARTERY DISEASE
rs16876512	T	R	**TC**	**+-**		FOLATE METABOLISM, LIVER, FOLATES,

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *BHMT*:

- *Vitamin B-9 (folic acid)*
- *Selenium*
- *Zinc*

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 gene CBS relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
i5003396 *(rs121964964 A114V)*	A	R	**GG**	--		
rs234715 *(C224A)*	T	R	**TG**	+-		AUTISM NTD RISK IN HYPOMETHYLATION
rs121964967 *(rs121964967 K384E)*	C	R	**TT**	--		
rs121964962 *(G307S)*	T	R	**CC**	--		PYRIDOXINE RESISTANT HOMOCYSTEINURIA
rs234709 *(317-477G>A)*	T	R	**TT**	++		METABOLISM, ARSENIC METABOLISM, LUNG CANCER
i5003397 *(rs121964963 P145L)*	A	R	**GG**	--		
i5003393 *(rs121964967 K384E)*	C	R	**TT**	--		
rs121964970 *(V168M rs121964970)*	T	R	**CC**	--		MILD HOMOCYSTEINURIA B-6 REPSONSIVE
rs2851391 *(A13637G)*	T	R	**TC**	+-		BLOOD, METABOLITES, HOMOCYSTEINE, OBESITY
rs28934892 *(P422L)*	A	R	**GG**	--		
rs121964963 *(rs121964963 P145L)*	A	R	**GG**	--		
rs121964972 *(T353M rs121964972)*	A	R	**GG**	--		B6 UNRESPONSIVE
rs1801181 *(C1080T, A360A, G>A)*	A	B	**AG**	+-		TRANSSULFATION NO REDUCTION OF ACTIVITY, BUT INCREASED HOMOCYSTEINURIA
rs4920037 *(1039+530C>T, C19150T)*	A	R	**AG**	+-		SLOW TRANSSULFATION
i5003391 *(V168M rs121964970)*	T	R	**CC**	--		MILD HOMOCYSTEINURIA B-6 REPSONSIVE
rs28934891 *(D444N)*	T	R	**CC**	--		NORMAL CBS ACTIVITY
rs234706 *(C699T Y233Y)*	A	B	**AG**	+-		INCREASED ACTIVITY, VIT B6 RESPONSIVE, AND RESPONSIVE TO HOMOCYSTEINE LOWERING EFFECTS OF FOLIC ACID, REDUCED RISK OF CLEFT LIP AND NON-HODGKIN LYMPHOMA
rs6586282 *(G134A)*	T	R	**CC**	--		HOMOCYSTEINURIA
i5003389 *(T353M rs121964972)*	A	R	**GG**	--		B6 UNRESPONSIVE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CBS*:

- *Linoleic acid*
- *Vitamin B-9 (folic acid)*
- *Vitamin B-6 (pyridoxine)*
- *Omega 3 Fatty Acids*
- *Copper*
- *Magnesium*
- *Vitamin B-12 (cobalamin)*

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 gene CTH relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs28941786 *(rs28941786 622C>G, 718C>G, 586C>G Gln196Glu)*	G	R	**CC**	**--**		CYSTATHIONINURIA,
rs681475 *(T8763C)*	T	R	**TC**	**+-**		
rs10889869 *(G6010A)*	A	R	**GG**	**--**		
rs12723350 *(T16147C)*	C	R	**TT**	**--**		
rs1021737 *(S4031I)*	T	R	**GG**	**--**		CLEFT PALATE WITH HOMOZYGOUS RISK ALLELE, HIGHER HOMOCYSTEINE, AGING
rs663649 *(G25229T)*	T	R	**GG**	**--**		
i5004013 *(rs28941786 622C>G, 718C>G, 586C>G Gln196Glu)*	G	R	**CC**	**--**		CYSTATHIONINURIA

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *CTH*:

- *Copper*
- *Vitamin B-6 (pyridoxine)*

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 gene MAT1A relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs118204005 *(rs118204005 790C>T ARG264CYS)*	A	R	**GG**	--		HYPERMETHIONINEMIA
i5007206 *(rs118204003 1070C>T Pro357Leu)*	A	R	**GG**	--		HYPERMETHIONINEMIA
i5007205 *(rs118204006 164C>A Ala55Asp, Gly336Arg)*	T	R	**CC**	--		HYPERMETHIONINEMIA AUTOSOMAL RECESSIVE
rs118204006 *(rs118204006 164C>A Ala55Asp, Gly336Arg)*	T	R	**CC**	--		HYPERMETHIONINEMIA AUTOSOMAL RECESSIVE
rs118204003 *(rs118204003 1070C>T Pro357Leu)*	A	R	**GG**	--		HYPERMETHIONINEMIA
rs4934028 *(C15656T, 549+1150C>T)*	A	R	**AG**	+-		CHINESE MALE GENDER ASSOCIATED LOW SAM LEVELS
rs72558181	T	R	**CC**	--		SAME
rs756208	G	R	**GG**	++		
i5007208 *(rs118204005 790C>T ARG264CYS)*	A	R	**GG**	--		HYPERMETHIONINEMIA
rs118204004 *(rs118204004 914T>C Leu305Pro)*	G	R	**AA**	--		HYPERMETHIONINEMIA
i5007207 *(rs118204004 914T>C Leu305Pro)*	G	R	**AA**	--		HYPERMETHIONINEMIA
rs2993763 *(C1131T, Tyr377=, Y377=)*	A	R	**AG**	+-		BENIGN ALLELE

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MAT1A*:

- *Omega 3 Fatty Acids*

MTHFS

5,10-methenyltetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)

The MTHFS gene provides instructions for making the 5,10-methenyltetrahydrofolate synthetase enzyme. This protein enables the conversion of 5-formyltetrahydrofolate to 5,10-methenyltetrahydrofolate, a precursor of reduced folates involved in the 1-carbon metabolism pathway. This metabolic pathway is a series of steps which enable a molecule of carbon from serine or glycine to be transferred to tetrahydrofolate (THF) to form methylene-THF. An increased activity of the MTHFS protein can result in an increased rate of folate use and folate depletion (monitor MCV, RDW and the need for folic acid after response to other methionine and folate cycle cofactor supplementation). Magnesium, the cofactor of MTHFS may be depleted. Test thyroid function (comprehensive thyroid panel) and liver conversion (rT3). Temporary magnesium supplementation should be replaced when thyroid hormone activity is restored. Supplementing the SHMT carbon-donor with its cofactor, B6 and regulating cellular Magnesium with exogenous thyroid may be indicated.

SNP outcomes in gene MTHFS relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs6495446 *(Thr202Ala, ST20, G39646A)*	T	R	**TC**	+-		FOLATE METABOLISM GENE CHRONIC KIDNEY DISEASE, SMALL CELL CANCER

MTR

5-methyltetrahydrofolate-homocysteine methyltransferase

Methionine synthase (MTR) is responsible for the regeneration of methionine from homocysteine. In humans it is encoded by the MTR gene (5-methyltetrahydrofolate-homocysteine methyltransferase). Methionine synthase forms part of the S-adenosylmethionine (SAMe) biosynthesis and regeneration cycle. Mutations in MTR have been identified as the underlying cause of methylcobalamin (a form of vitamin B12) deficiency. Deficiency or deregulation of the enzyme in early age due to deficient methionine synthase reductase can directly result in elevated levels of homocysteine, which is associated with blindness, neurological symptoms and birth defects. Methionine synthase is inhibited by lead, arsenic, mercury and aluminum toxicity.

Noteworthy: A mutation in MTR A2756G, rs1805087 causes increase function and increased methyl group depletion and a possible increased need for methylated B12. This can be made worse by MTRR mutations.

SNP outcomes in gene MTR relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs10925260	C	R	**AC**	-+		B-12 RESPONSIVE
rs1770449	C	R	**TC**	-+		B-12 RESPONSIVE
rs1805087 *(↑ 2756A>G A2756G Asp919Gly)*	G	R	**AG**	-+		UPREGULATED ACTIVITY, B12-RESPONSIVE DEMENTIA DEPRESSION HOMOCYSTEINE, LONGER TELOMERES

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MTR*:

- *Vitamin B-9 (folic acid)*
- *Vitamin B-2 (riboflavin)*
- *Vitamin B-12 (cobalamin)*

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.

Methionine synthase reductase (MTRR) is a vital enzyme of the homocysteine/methionine metabolic pathway and is required for the conversion of the inactive form of methionine synthase (MTR) to its active form. MTRR helps recycle B12.

The MTRR enzyme places a methyl group on B12 so it can be used by MTR to convert homocysteine into methionine and requires B2. Variants here may hamper this function. When combined with other variants that impact the absorption and transport of B12, and if the MTR variant exists (which is trying to make it go faster), this function may be impaired.

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 gene MTRR relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs10520873	C	R	**TC**	**-+**		
rs162036 *(↓ 1049A>G Lys350Arg K350A)*	G	R	**AA**	**--**		
rs2303080 *(↓ 769T>>A Ser257Thr S257T)*	A	R	**AT**	**+-**		CLEFT LIP AND PALATE
rs7703033 *(↓ 780+1515G>A)*	A	R	**AG**	**+-**		HOMOCYSTEINE ASSOCIATION, B12 UTILIZATION
rs1802059 *(↓ 1911G>A Ala637= A664A)*	A	R	**GG**	**--**		
rs162049	G	R	**AG**	**-+**		
rs3776467	G	R	**AA**	**--**		
rs2287780 *(↓ 243C>T R415T)*	T	R	**TC**	**+-**		
rs1801394 *(↓ A66G Ile22Met)*	G	R	**AG**	**-+**		NEURAL TUBE DEFECT, MENINGIOMA, LOW SERUM FOLATE, REDUCED RISK PSA ELEVATION
rs1532268 *(↓ C524T Ser175Leu)*	T	R	**CC**	**--**		FOLATE METABOLISM, CANCER
rs9332	A	R	**GG**	**--**		
rs10380 *(↓ 1783C>T His595Tyr H595Y)*	T	R	**CC**	**--**		METHIONINE REGENERATION

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *MTRR*:

- *Omega 3 Fatty Acids*
- *Vitamin B-9 (folic acid)*
- *Vitamin B-6 (pyridoxine)*
- *Vitamin B-2 (riboflavin)*
- *Vitamin B-12 (cobalamin)*

SHMT1

serine hydroxymethyltransferase 1 (soluble)

The SHMT1 gene provides instructions for making a form of the serine hydroxymethyltransferase protein, an enzyme that contains pyridoxal phosphate, a form of vitamin B6. The enzyme helps to convert the amino acid serine and a form of folic acid (tetrahydrofolate) to the amino acid glycine and another form of folic acid (5,10-methylene tetrahydrofolate). The results of this reaction provides the ingredients for making the amino acid methionine and some of the components for making DNA.

Variation in C1420T (rs1979277) of the SHMT1 gene can affect the risk of mothers having a Down syndrome baby, with the G allele being protective against Down syndrome. SHMT1 is important in the development of cancer resulting from damage to the repair mechanisms of DNA because it is responsible for a change in the balance of the DNA components uracil and thymidine during replication of DNA.

SNP outcomes in gene SHMT1 relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs9909104 *(105+27894A>G)*	C	R	**TT**	--		EPITHELIAL OVARIAN CANCER, CONGENITAL HEART DEFECTS IN OFFSPRING OF MOTHERS TAKING SSRIS, REDUCED SURVIVAL IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA
rs17806333 *(+74A>G)*	C	R	**TT**	--		
rs1979277 *(C1420T Leu474Phe)*	A	R	**AG**	+-		DOWN'S SYNDROME, COLON BREAST PROSTATE CANCER, THYMIDINE GENERATION ERRORS, INCREASED PSA ELEVATION RISK
rs9902498	T	R	**CC**	--		

Selected natural products: Your clinician has curated a natural product that may exert an effect on the expression of *SHMT1*:

- *Omega 3 Fatty Acids*
- *Vitamin B-9 (folic acid)*
- *Vitamin B-6 (pyridoxine)*
- *Vitamin B-1 (thiamine)*
- *Vitamin B-12 (cobalamin)*

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 gene SUOX relevant to Robert Pfoff:

SNP ID	Risk	Type	You	Outcome	Magnitude	Keywords
rs705703 *(C5444T -158C>T)*	T	R	**CC**	--		POOR SULFITE TO SULFATE CONVERSION, RISK FOR ISCHEMIC HEART DISEASE
i5000976 *(rs753217781)*	G	R	**GG**	++		
rs7297662 *(A628C -10-618G>A)*	A	R	**AG**	+-		LEUKEMIAS IN TUNGSTEN AND ARSENIC TOXICITY
rs753217781 *(rs753217781)*	G	R	**GG**	++		

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.

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.

CARDIOMETABOLIC

MULTI-SNP MACROS

Celera GRS: Risk of coronary artery disease.

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

INTERPRETATION: *Unable to calculate Celera GRS Risk.* This algorithm requires a minimum of 4 reported SNP results. Opus Explorer could only find 3.

Although you did not have enough risk alleles to allow for a conclusion, you have variants that still independently increase your risk of CAD by 137 %.

Gene	SNP	Genotype
PALLD	rs7439293	AA

This algorithm has **insufficient data** but has partial observations that apply to you

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

Significant risk of salt-sensitive hypertension

Genes	SLC4A5,GRK4,DRD2
Repute:	RISK
Magnitude:	4.5
Frequency:	N/A

INTERPRETATION: Studies of high blood pressure resulting from salt consumption found relevant SNPs in three genes: SLC4A5 (a sodium bicarbonate transporter), DRD2 (a dopamine receptor) and GRK4 (an enzyme that deactivates cellular sensing mechanisms). Of these, the AA mutation of rs7571842 in SLC4A5 was highly significant. , with the G allele conferring protection. Lesser effects were observed for the risk alleles of rs2960306 in GRK4 and rs6276 in DRD2. The effects of these mutations were relevant regardless of body mass index (BMI) and age.

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

Your results: rs7571842 (**AA**) rs2960306 (**N/A**) rs6276 (**TT**)

Lower HDL levels

Genes	PLTP
Repute:	RISK
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 (**TC**)

Risk of carotid artery occlusion

Genes	CHR1-LOC109818530,TOMM40
Repute:	RISK
Magnitude:	
Frequency:	N/A

INTERPRETATION: The carotid artery is the large blood vessel in the sides of the neck that carries blood to the brain. The amount and size of LDL (low density lipoprotein, 'bad' cholesterol) particles in the blood may cause blockage of these arteries. The C allele of the intergenic rs646776 SNP on chromosome 1p13.3 near the CELSR2 and PSRC1 genes has been shown to influence the number of LDL particles. The G allele of the rs2075650 SNP in TOMM40 havs been shown to influence LDL particle size. You have the following genotype: rs2075650(AA), rs646776(TC).

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

Your results: rs2075650 (**AA**) rs646776 (**TC**)

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 (**GG**) rs1800775 (**AA**)

Cardiometabolic macro algorithms returning as false:

- Increased risk of Atrial Fibrillation
- Risk of myocardial infarction
- 300% increased risk of venous thrombosis
- Celera GRS: Reduced risk of coronary artery disease
- Lower risk (35%) of a heart attack or cardiovascular incident

CARDIOMETABOLIC

NETWORK MAPS

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

NATURAL PRODUCTS

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

RANK	AGENT	INDICATION VALUE
1.	Omega 3 Fatty Acids	
2.	Omega 6 Fatty Acids	
3.	Vitamin B-9 (folic acid)	
4.	Betaine	
5.	Curcumin	
6.	Vitamin B-12 (cobalamin)	
7.	Methionine	
8.	Vitamin B-2 (riboflavin)	
9.	Docosahexaenoic acid (DHA)	
10.	Vitamin B-6 (pyridoxine)	
11.	Choline	
12.	Rhodiola rosea	
13.	Phosphatidylcholine	
14.	Multivitamin	
15.	S-Adenosyl Methionine (SAMe)	
16.	Pyridoxal 5' phosphate	
17.	Zinc	
18.	Salacia oblonga	
19.	Copper	
20.	Resveratrol	
21.	Quercetin	
22.	Theanine	
23.	Eicosapentaenoic acid (EPA)	
24.	Alpha-Linolenic acid ALA	
25.	Linoleic acid	

Your clinician has elected to include recommendations from the Designs For Health® product line. Here are the top 10 recomended products based on your genomic results.

RANK	DFH FORMULA	DESCRIPTION
1.	***OmegAvail Hi-Po*** 	OmegAvail Hi-Po provides a potent 1500 mg of EPA/DHA per serving (two softgels), and also includes lipase, a digestive aid to ensure maximum absorption. Lipase also helps to prevent any fishy aftertaste, known as 'repeat', that sometimes occurs with fish oil supplements.
2.	***BioFizz Immune*** 	BioFizz® Immune provides 1,000 mg of vitamin C, along with targeted amounts of the bioflavonoids quercetin and resveratrol, 50 mcg (2,000 IU) of vitamin D, 100 mg of vitamin E isomers (as DeltaGold® delta- and gamma-tocotrienols), 50 mg of geranylgeraniol (as GG-Gold®), and 20 mg of zinc in each serving of 4 grams.
3.	***Quercetin-Ascorbate*** 	Quercetin Ascorbate powder is a powerful flavonoid and antioxidant blend. Quercetin is one of several flavonoids that have effects on mast cells and basophils. Vitamin C helps regulate histamine levels and supports a healthy inflammatory response.
4.	***HistaEze*** 	HistaEze is a synergistic blend of nutrients that provides natural support to help balance the immune response during environmental challenges.* It features Tinofend®, a patented and clinically researched extract derived from the plant Tinospora cordifolia, which has been shown to regulate key immune mediators and support the activity of macrophages. Tinofend® supports the immune response by promoting a balance of phagocytic white blood cells and eosinophils.* HistaEze also contains quercetin, nettle leaf, and vitamin C, which have been historically used during allergy season to support immune balance.* Additionally, bicarbonate salts are included for their role in maintaining normal histamine metabolism.
5.	***Quercetin + Nettles*** 	Quercetin + Nettles contain 600 mg quercetin and 600 mg nettles. Research suggests that nettle's anti-inflammatory actions are attributed to its ability to interrupt the production and actions of inflammation-producing cytokines, prostaglandins and leukotreines.
6.	***CannabOmega*** 	CannabOmega is a unique omega-3 formulation, combining a 1:1 ratio of EPA/DHA, along with standardized phytocannabinoids found in hemp oil. The omega-3 fatty acids found in this product are best known for their neuro-protective properties and their roles in brain health, including support for healthy mood and cognition. CannabOmega also provides synergistic support for cardiovascular, metabolic, and immune health. The fish oils in this product are in the triglyceride (TG) form for superior absorption and bioavailability. Their presence in this product help to increase the bioavailability of the phytocannabinoids
7.	***Vitamin B-6 Liquid*** 	Vitamin B-6 Liquid tastes great with a natural raspberry flavor, absorbs easily, and is the perfect solution for people who need higher doses of this often-lacking vitamin. This unique formula works synergistically to support numerous bodily reactions, such as neurotransmitter production, hormone metabolism and much more.
8.	***P-5-P 120*** 	Vitamin B6 is found in three forms – pyridoxine hydrochloride, pyridoxal, and pyridoxamine – all of which must be converted into activated pyridoxal-5-phosphate (P-5-P) by the liver. P-5-P is the form of vitamin B6 the body ultimately uses and is necessary for a wide range of actions, including the production of GABA, the conversion of 5-HTP to serotonin, and also in the decarboxylation of L-Dopa to dopamine. It is also needed for glucose production as well as amino acid and lipid metabolism.
9.	***OmegAvail Ultra DHA*** 	OmegAvail Ultra DHA contains highly concentrated DHA (docosahexaenoic acid) from fish oil in its natural TG (triglyceride) form. As with all Designs for Health TruTG fish oil products, OmegAvail Ultra DHA is comprised of a minimum 90% natural TG-bound omega-3 oils. Each softgel provides 500 mg DHA + 110 mg EPA for optimal DHA status. As always, our fish oils are molecularly distilled and filtered to ensure purity and to maximize the removal of heavy metals, pesticides, solvents, PCBs, and other contaminants.
10.	***Homocysteine Supreme*** 	Homocysteine Supreme contains synergistic nutrients known to facilitate the efficient metabolism of homocysteine. Homocysteine Supreme maintains a healthy homocysteine pathway, allowing for the normal production of its necessary and important end products. These include the sulfur-containing amino acids taurine and cysteine, and the neurotransmitters norepinephrine and dopamine.* An optimally functioning homocysteine pathway provides methyl and sulfur groups for biochemical reactions such as detoxification, healthy immune function, ideal joint and cartilage structure, and brain and cardiovascular health.