



Gene Comprehensive Nutrigenomic Report

Accession Number: #####

Specimen Collected: ###/###/####

Specimen Received: ###/###/####

Report Generated: November 16, 2022

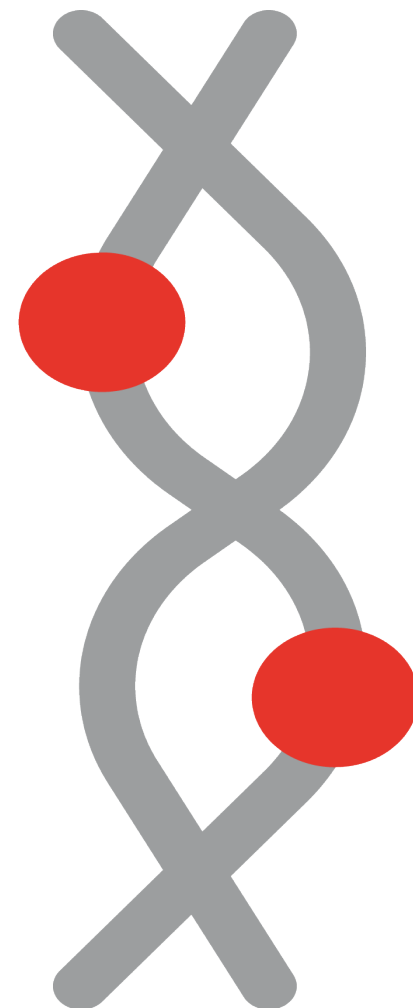
Specimen Type: Buccal Swab

Provider: #####

Patient Name: #####

Patient DOB: ###/###/####

Patient Gender: Female



Do not make any decisions about your health solely based on the information contained in this report.
Always consult with a licensed and experienced health practitioner when you receive this report.

– 8 – Female

(-/-) No clinical abnormality

(+/-) Heterozygous result

(+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Developmental							
Methylation							
rs651933	FOLR2	+/-	Methyltetrahydrofolate (5-MTHF)	Methyl Folate Plus™ Twice Daily			
rs1801131	MTHFR 1298	+/-					
rs1801133	MTHFR 677	+/-					
rs1801198	TCN2	-/-	Methyl B12, Adenosyl B12				
Neurotransmitters							
rs4680	COMT V158M	-/-	Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Methionine, SAME, Inositol				
rs769407	GAD1	-/-	Prescription Amantadine, Ketamine, Glycine, N-Acetyl-Cysteine (NAC), Zinc, Magnesium, Elderberry, L-Theanine, Melatonin		May benefit from Pro GAD Enhancer™ May Benefit from Calming Cream™ May Benefit from Melatonin if Sleep is an Issue		Consider Neurotransmitter Metabolite Testing
rs3828275	GAD1	+/-					
rs6323	MAO-A	-/-	B2 (Riboflavin), Methyl Donors (Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Inositol, Methionine		May Benefit from Full Focus+™ if you have Anxiety or Focus Issues		Consider Neurotransmitter Metabolite Testing
rs1799836	MAO-B	+/+					

rs1042173	SLC6A4	+/-	5-HTP (Hydroxytryptophan)		May Benefit from Mood Plus™ if you have Anxiety or Depression Issues	May Have Less Than Optimal Response To SSRIs	Consider Neurotransmitter Metabolite Testing
rs6313	HTR2	-/-					
rs4570625	TPH2	+/-	L-5-Methyl THF, Niacinamide, 5-HTP				Consider Neurotransmitter Metabolite Testing
rs1108580	DBH	+/-	Vitamin C Copper				

– 8 – Female

(-/-) No clinical abnormality

(+/-) Heterozygous result

(+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Neurotrophic Factors							
rs1142636	SYN1	-/-	RG3, Nicotinamide Riboside, Ginseng				
rs6265	BDNF	-/-	Curcumin, Lithium Orotate, D-Chiro-Inositol, Catechins, Resveratrol, Exercise				
Neuro-inflammation							
rs10402876	C3	+/+	Anti-Inflammatory Therapy: Curcumin, Omega 3s, Resveratrol, Quercetin, Low Dose Naltrexone (LDN), CBD Oil	CBD Oil PEA Soothe Support™ Prescription Low Dose Naltrexone (LDN)		Consider Low Inflammatory Diet	Consider Pregnenolone, Cortisol, T cell profile, Routine Thyroid Panel, Candida Titer, Food Allergy Panel, Environmental Allergy Testing
rs2569191	CD14	+/-					
rs2069812	IL5	+/-					
rs1800795	IL6	+/-					
rs1800925	IL13	-/-					
rs10181656	STAT4	+/-					
rs1800629	TNF	-/-					
rs231775	CTLA4	+/+					
rs1076560	DRD2	-/-	Increased Efficacy of Naltrexone				
Autophagy							
rs510432	ATG5	+/-	Curcumin, Lithium Orotate, D-Chiro-Inositol, Catechins, Resveratrol, Caffeine, 12 Hour Fasting	DCI 500 or Metabolic Stimulator™ N.A.S. Enhancer™		12-15 Hour Fasting if appropriate for age	Routine Blood Sugar, Insulin and Hb A1c
rs26538	ATG12	+/-					
rs10210302	ATG16L1	-/-					

– 8 – Female

(-/-) No clinical abnormality

(+/-) Heterozygous result

(+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Developmental							
Sugar Sensitivity and Mood							
rs1800544	ADRA2A	+/+	Increased Risk of Hyperactivity From Sugar and Anti-Psychotic Induced Weight Gain			High Risk of Major Weight Gain With Psychiatric Medications May Have Hyperactivity with Processed Sugar	
Detoxification							
rs1021737	CTH	-/-	N-Acetyl Cysteine (NAC), Glutathione				
rs7483	GSTM3	-/-	Glutathione				
rs1695	GSTP1 I105V	-/-					

– 8 – Female

(-/-) No clinical abnormality

(+/-) Heterozygous result

(+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Inflammatory Environmental							
rs10156191	AOC1	-/-	Poor Ability To Break Down Histamine in Foods				
rs11558538	HNMT	-/-					
rs12995000	HNMT	-/-					
rs492602	FUT2	+/+	Pre-biotics and Probiotics Needed		Biotic Boost Chews or Powder For Kids™		Consider Microbiome Testing If GI Inflammation Present
rs2187668	HLA DQA1	-/-	High Risk of Severe Gluten Sensitivity				
rs2858331	HLA DQA2	-/-					

Summary for Developmental

Highly Recommended Therapeutics

- Methyl Folate Plus™ Twice Daily
- CBD Oil
- PEA Soothe Support™
- Prescription Low Dose Naltrexone (LDN)
- DCI 500 or Metabolic Stimulator™
- N.A.S. Enhancer™

Provider Discretion: As Needed Formula Recommendations

- May benefit from Pro GAD Enhancer™
- May Benefit from Calming Cream™
- May Benefit from Melatonin if Sleep is an Issue
- May Benefit from Full Focus+™ if you have Anxiety or Focus Issues
- May Benefit from Mood Plus™ if you have Anxiety or Depression Issues
- Biotic Boost Chews or Powder For Kids™

Lifestyle Recommendations

- May Have Less Than Optimal Response To SSRIs
- Consider Low Inflammatory Diet
- 12-15 Hour Fasting if appropriate for age
- High Risk of Major Weight Gain With Psychiatric Medications
- May Have Hyperactivity with Processed Sugar

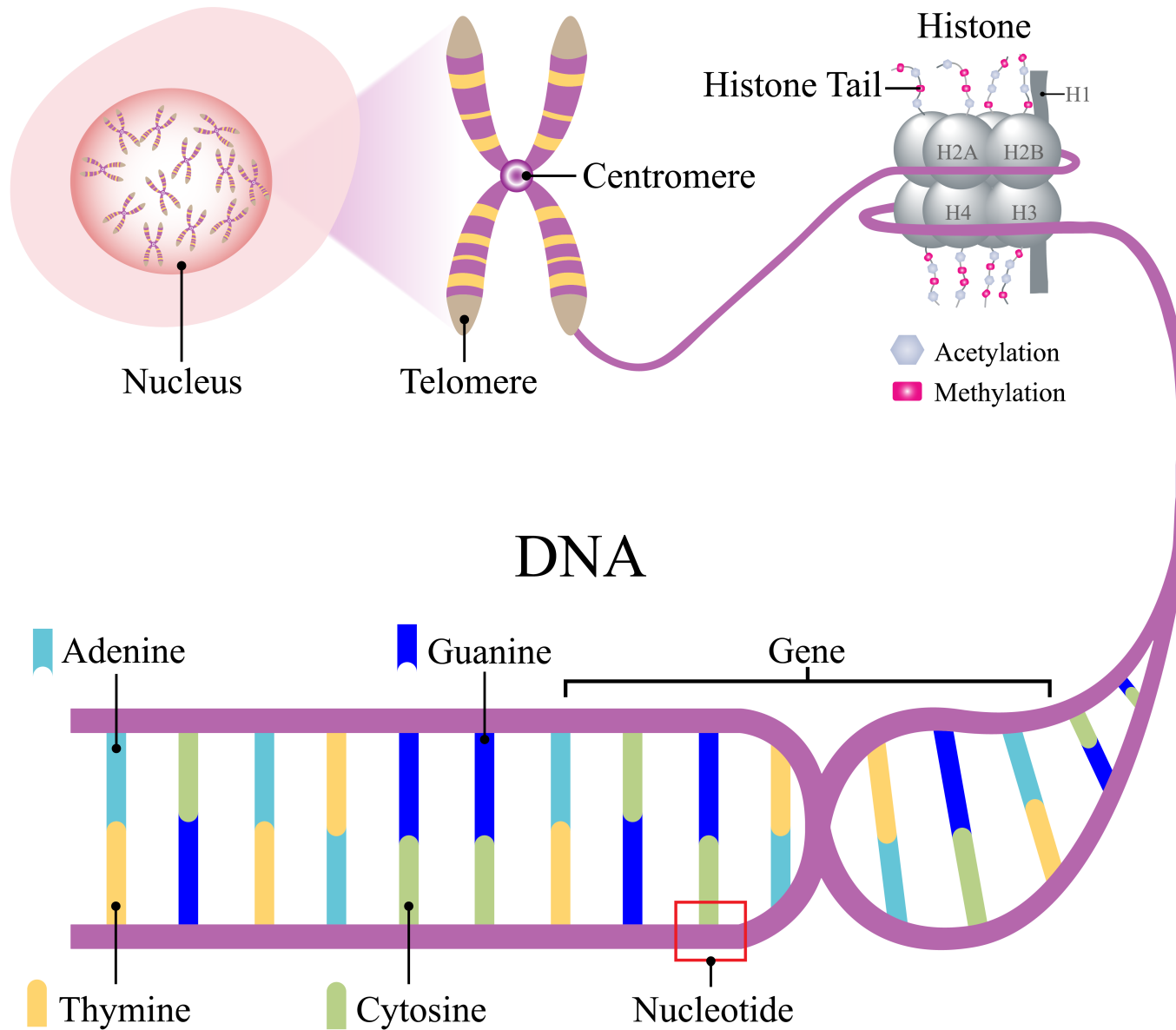
Laboratory Recommendations

- Consider Neurotransmitter Metabolite Testing
- Consider Pregnenolone
- Cortisol
- T cell profile
- Routine Thyroid Panel
- Candida Titer
- Food Allergy Panel
- Environmental Allergy Testing
- Routine Blood Sugar
- Insulin and Hb A1c
- Consider Microbiome Testing If GI Inflammation Present

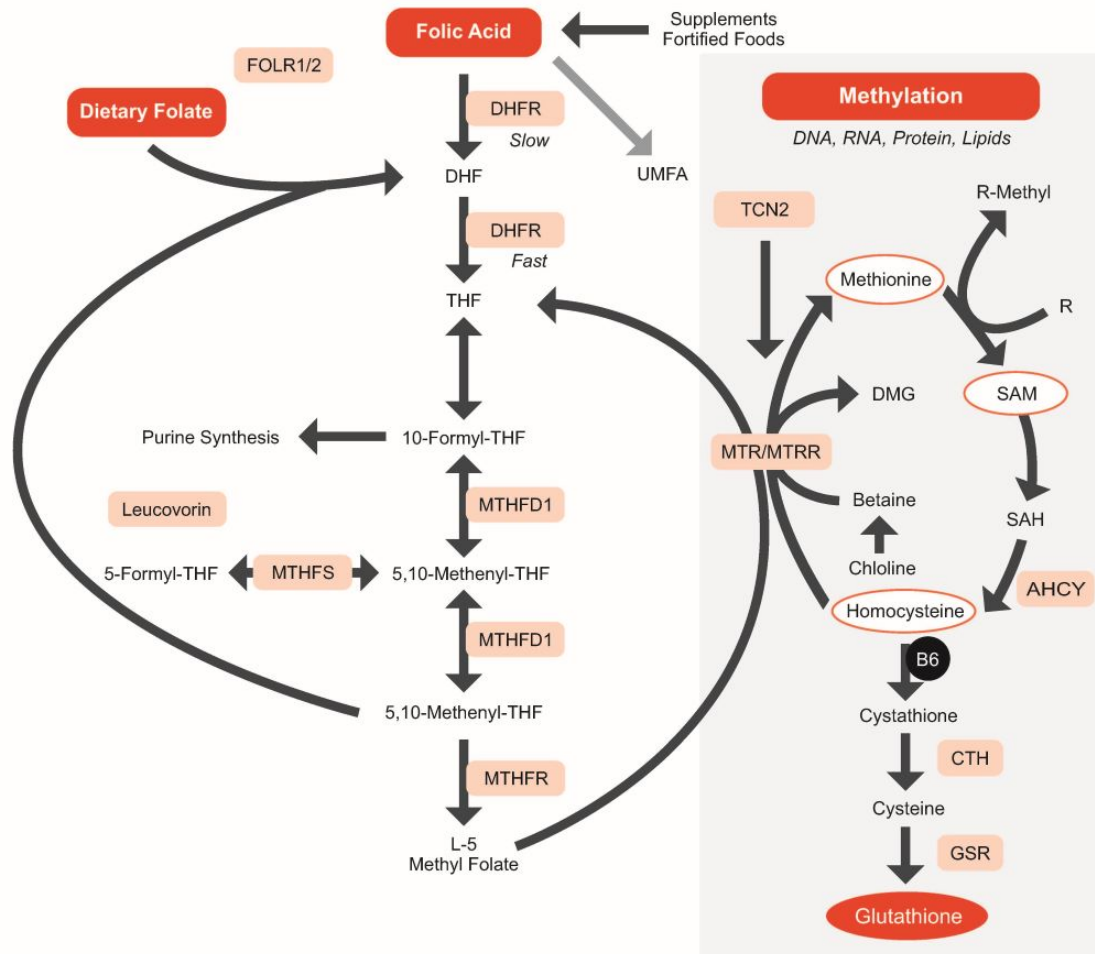
Cell

Chromosome

Nucleosome



METHYLATION



Methylation

- Involves the addition of a methyl group (CH₃)
- Regulates gene expression and repression
- Reduces or removes toxins that eliminate essential nutrients
- Provides nutrients needed for processes such as detoxification, immune regulation, gut health

Methionine

- Used in protein formation and stabilization
- Elevated levels are associated with risk for coronary heart disease, stroke & neurological diseases

Glutathione

- Important for chemical detoxification & proper mitochondrial functioning
- Genes relevant for production include: AHCY, CTH, CGTP1, GSTM1, GSTM3, GSR, MTRR & MTR

5-Methyl Folate

- Important for dopamine and serotonin formation, detoxification and mitochondrial strength
- Genes relevant for production include: DHFR, FOLR1/2, MTHFD1, MTHFR, MTHFS

Homocysteine

- Elevated levels are associated with risk for coronary heart disease, stroke, neurological diseases
- Variants in the methylation pathway can be associated with increased/decreased levels

FOLATE

FOOD SOURCES



Eggs



Citrus Fruits



Leafy Greens



Legumes



Broccoli



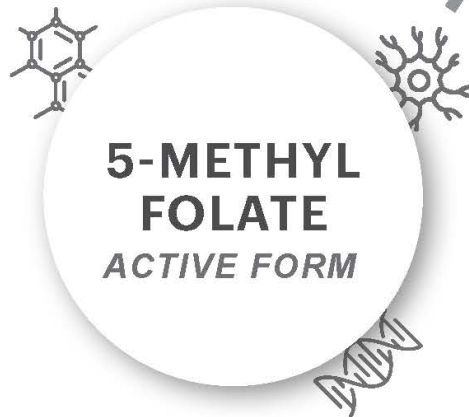
Brussel Sprouts



Breads, Cereal,
Pastas, Rice



**ABSORBABLE
FOLATE**
NATURAL B9



**5-METHYL
FOLATE**
ACTIVE FORM

FUNCTIONS (OR BENEFITS AS YOU AGE)

- Maintains structure & function of proteins
- Maintains structure & function of DNA
- Facilitates DNA replication, neurotransmitter production & detoxification

DEFICIENCY CAUSES

- Neural tube defects
- Cardiovascular disease
- Memory problems
- Depression
- Insomnia
- Irritability

NEUROTROPHIC FACTORS

VARIANTS IN THE SYN1, NGF & BDNF GENES CAUSE
DECREASED NEURON SYNTHESIS



Promote growth, development, survival, synaptic plasticity (strengthening) and repair of neurons



Regulate the development of the peripheral and central nervous systems



Regulate the formation of long-term memories

LOW LEVELS ARE CORRELATED WITH

- Neurodegenerative disorders
- Aging
- Chronic stress
- Mood disorders

WAYS TO INCREASE LEVELS



Exercise (physical or cognitive)



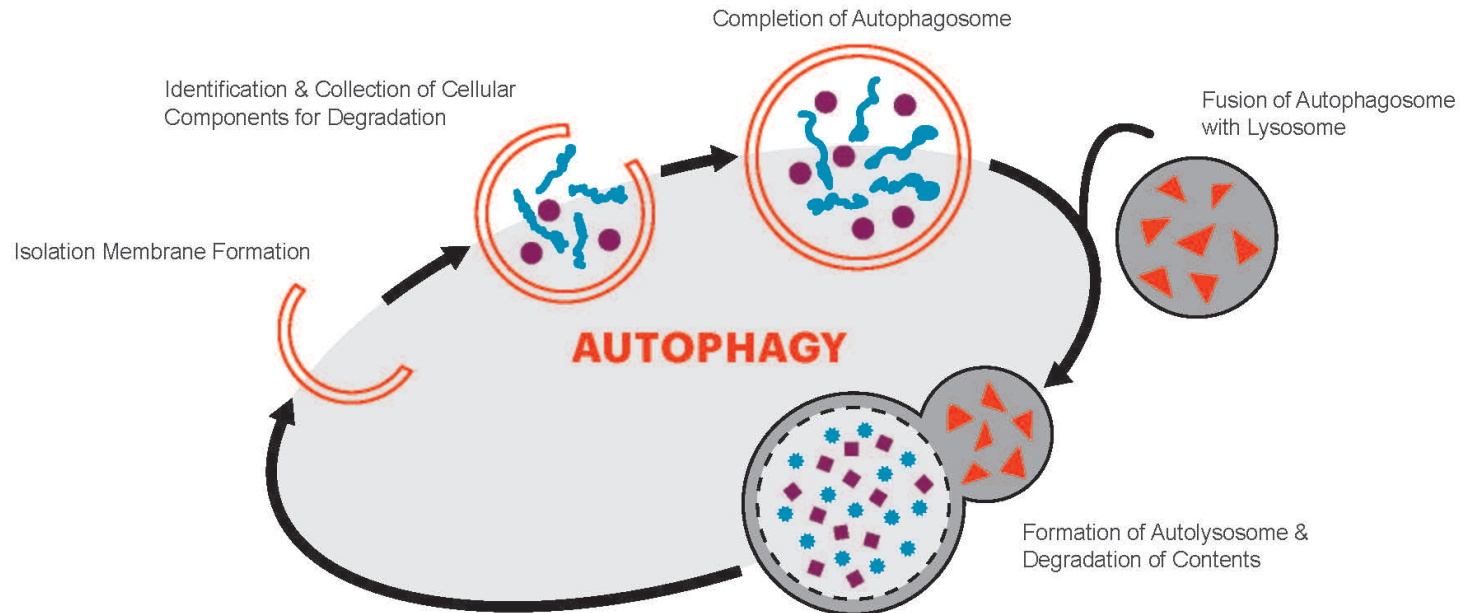
Social interactions



Reduce stress via breathing exercises and/or meditation

AUTOPHAGY

VARIANTS IN THE ATG GENES HAVE BEEN ASSOCIATED WITH CELLULAR BLOCKAGE



DEFECTS LEAD TO:

- Neurodegenerative Diseases
- Aging
- Heart Disease
- Developmental Disorders
- Type II Diabetes
- Insulin Resistance
- Fatty Liver
- Cancers



Intermittent fasting
or low-calorie diet



Routine Exercise



Ketogenic diets
(high fat, low carbs)



Medications &
Supplements
D-Chiro Inositol (B8)
Metformin

SUGAR SENSITIVITY & FOOD

VARIANTS IN THE ADRA2A GENE HAVE BEEN ASSOCIATED WITH A HIGHER RISK OF SUGAR-INDUCED HYPERACTIVITY AND ANTIPSYCHOTIC INDUCED WEIGHT GAIN

ADRA2A GENE



Causes inhibition of the sympathetic nervous system



Helps reduce sugar levels found in the body

SYMPATHETIC NERVOUS SYSTEM

Functions



"Fight or flight" system



Increases sugar levels in the body



Low activity has been associated with an increased risk for weight gain and obesity

POTENTIAL WAYS TO ALLEVIATE HYPERACTIVITY

Limit or avoid dietary intake of:



Sugar



Wheat



Dairy products/Eggs



Vegetables - corn, tomatoes



Fruits - grapes, oranges



Soy products



Beans



Beverages - caffeinated and/or sugar-sweetened drinks

WAYS TO COMBAT WEIGHT GAIN WITH ANTIPSYCHOTICS



Exercise



Low-calorie diet



Nutritional counseling



Cognitive strategies - understanding eating behaviors & physical well-being



Behavioral interventions - training in problem solving, goal setting, social support & monitoring exercise and eating habits

LOW-SUGAR DIET

BENEFITS



Weight management



Helps prevent diabetes, heart disease & stroke



Helps manage mood levels, inflammation & skin health



Improved mental health

FOODS TO AVOID



White potatoes



White grains



Refined sugars - breakfast cereals, ketchup, packaged sweets, candy, packaged snack foods



Beverages - sodas, juices, coffee drinks, energy drinks, sweetened smoothies, alcohol (champagne, dessert wine)



Green leafy vegetables (raw or cooked)



Fruits - oranges, grapefruit, berries



Whole grains



Beans and legumes



Sweet potatoes

FOODS TO EAT



Nuts/seeds - walnuts



Fatty fish - salmon, mackerel, sardines, tuna, anchovies, halibut, trout



Lean proteins



Herb/spices - cumin, turmeric, cinnamon

Gene Information Key

rsID	Gene	"-" variant	"+" variant
rs1800544	ADRA2A	G	C
rs10156191	AOC1	C	T
rs26538	ATG12	T	C
rs10210302	ATG16L1	C	T
rs510432	ATG5	C	T
rs6265	BDNF	C	T
rs10402876	C3	G	C
rs2569191	CD14	T	C
rs4680	COMT V158M	G	A
rs1021737	CTH	G	T
rs231775	CTLA4	A	G
rs1108580	DBH	A	G
rs1076560	DRD2	C	A
rs651933	FOLR2	A	G
rs492602	FUT2	A	G
rs3828275	GAD1	C	T
rs769407	GAD1	G	C
rs7483	GSTM3	C	T
rs1695	GSTP1:I105V	A	G
rs2187668	HLA-DQA1	C	T

rsID	Gene	"-" variant	"+" variant
rs2858331	HLA-DQA2	A	G
rs11558538	HNMT	C	T
rs12995000	HNMT	C	T
rs6313	HTR2	G	A
rs1800925	IL13	C	T
rs2069812	IL5	A	G
rs1800795	IL6	G	C
rs6323	MAO-A	T	G
rs1799836	MAO-B	T	C
rs1801131	MTHFR: 1298	T	G
rs1801133	MTHFR: 677	G	A
rs1042173	SLC6A4	A	C
rs10181656	STAT4	C	G
rs1142636	SYN1	A	G
rs1801198	TCN2	C	G
rs1800629	TNF	G	A
rs4570625	TPH2	G	T

Definitions

DETOXIFICATION	Detoxification enzymes are responsible for clearing environmental chemicals and metabolites from our body. Accumulation of these chemicals and by-products can damage intracellular biochemical functions. Alterations in these systems can have a significant negative effect on the nervous system and immune systems functions. These polymorphisms can result in decreased "quality of life" and even decreased "life-span".
CTH	Glutathione production is dependent on the function of the enzyme cystathionine gamma-lyase (CTH). CTH converts cystathionine to cysteine. Individuals with mutations in the CTH gene are predicted to have decreased glutathione-mediated detoxification.
GSTM3	Glutathione S-transferase mu 3 is an enzyme that detoxifies drugs, environmental toxins, and carcinogens by conjugating toxins to glutathione and subsequent excretion by the kidneys. Mutations in GSTM3 are associated with decreased clearance of toxins, anesthetics and drugs from the nervous system.
GSTP1	Glutathione S-transferases (GSTs) are a family of enzymes that play an important role in detoxification. The glutathione S-transferase pi gene (GSTP1) functions in chemical clearance and anti-inflammatory properties. High concentration of GST-p are found in the skin, lungs, sinuses, bladder and the intestinal tract. Polymorphisms of this enzyme allow for increased inflammatory activity in these areas that include eczema, asthma, chronic sinusitis, IBS, "leaky" gut and interstitial cystitis.
DEVELOPMENTAL	The SNPs in this category have been identified as potential areas of weakness in the recovery of developmental disorders.
ATG12	Autophagy-related 12 protein is part of the core autophagy machinery inside the cell. Autophagy, a form of cellular "recycling" is necessary for many cell functions. ATG12 is specifically involved in turning off the innate immune response. Mutations in the ATG12 gene are predicted to lead to increased activity of the innate immune response, and overall inflammation.
BDNF	The BDNF (Brain Derived Neurotrophic Factor) gene encodes for a member of the nerve growth factor family of proteins. BDNF acts on both the central nervous system and the peripheral nervous system helping to support the survival of existing neurons and encourage the growth and differentiation of new neurons and synapses. It is highly expressed in the brain, as well as, the retina, cochlear-vestibular system and motor neurons. Although the vast majority of neurons in the brain are formed prenatally, parts of the adult brain retain the ability to grow new neurons from neural stem cells in a process known as neurogenesis. BDNF helps to stimulate and control neurogenesis, as well as playing an important role in normal neural development. Binding of this protein to its cognate receptor promotes neuronal survival in the adult brain. Expression of this gene is reduced in Alzheimer's, Parkinson's and Huntington's disease. This gene may play a role in the regulation of the stress response and the biology of mood disorders. Several mechanisms to increase BDNF have been discovered. These mechanisms revolve around autophagy stimulation. These include Intermittent Fasting with a single meal of 600 calories on the fast day can increase BDNF production by 50-400%. Cognitive Stimulation, Calorie Restriction, Exercise, Hormone therapy and supplements including Quercetin, Caffeine, Curcumin, Niacinamide, Lithium Orotate, Magnesium Threonate, Resveratrol, Ginseng, Theanine, Olive Leaf Extract and NAC.
SYN1	SYN1 (Synapsin) codes for Synapsins that are responsible for synaptogenesis and the modulation of neurotransmitter release, suggesting a potential role in several neuropsychiatric diseases. This member of the synapsin family plays a role in regulation of axonogenesis and synaptogenesis. Mutations in this gene may be associated with X-linked disorders with primary neuronal degeneration such as Rett syndrome. Additionally, polymorphisms in this gene are associated with numerous neurological conditions, as well as, decreased recovery potential for neurological insults.
INFLAMMATORY	This Enzyme category has significant effects on the inflammatory state of a person's body. Polymorphisms in these specific enzymes will significantly increase the levels of inflammation in the body. By supplementing these enzyme deficiencies, the patient will effectively reduce inflammatory damage to the body.
AOC1	The SNP rs10156191 encodes a weaker form of the histamine degradation enzyme Amine Oxidase, Copper Containing 1 (AOC1). This mutation, Thr16Met, is predicted to produce an enzyme with less catalytic activity and associated higher levels of pro-inflammatory amines like histamine and putrescine.
ATG16L1 rs10210302	The ATG16L1 gene encodes a protein that is a vital component of a protein complex necessary for the cellular phenomena known as autophagy. Autophagy is the process of degrading and cleaning of inert debris of the cell. Weakness in autophagy leads to abnormal accumulation of cellular "garbage" that will eventually affect the cellular function and lead to autophagy-related disease states in including many neurological and immunological diseases, DM Type 2 and fatty liver disease.
ATG5	Autophagy-related 5 protein (ATG5) is an important intracellular mediator of the autophagy response. ATG5 is involved in a wide range of "quality control" features inside the cell: autophagy vesicle formation, innate immune system signaling, consumption of damaged mitochondria, and apoptosis. Mutations in the ATG5 gene are associated with numerous neurological, immunological and endocrine syndromes.
C3	Essential for the immune response, C3 is a protein involved in initiation of the complement system. C3 polymorphisms are associated with susceptibility to asthma and other inflammatory disorders.
CD14	The CD14 protein is a macrophage cell surface receptor that binds bacterial cell wall components. As one of the initiators of the innate immune response, fully functional CD14 is necessary for normal response to potential pathogens. Mutations in the CD14 gene are associated with susceptibility to asthma and other allergen-mediated inflammatory processes.
CTLA4	Cytotoxic T-lymphocyte Associated protein 4 (CTLA4) is an important inhibitor of T-cell activity: CTLA4 is part of the signaling cascade that turns off overactive T cells. Mutations in the gene that encodes CTLA4 are associated with a host of diseases characterized by a heightened immune state.

DRD2	Dopamine receptor D2 is an important component of the neuroinflammation process. Activation of DRD2 signaling is thought to decrease TNFalpha release from inflammatory mast cells. Polymorphisms associated with decreased DRD2 signaling activity are predicted to lead to pro-inflammatory phenotypes.
FUT2	Fucosyltransferase 2 (FUT2) is responsible for producing specific sugar groups that are secreted by the intestinal cells into the bowel to attract "good bacteria" . Polymorphisms in this gene produce "poor secreter" status. Lack of these sugars allows for gut dysbiosis and a higher risk of inflammatory bowel disease.
HLA-DQA1	Major histocompatibility complex, DQ alpha 1 (HLA-DQA1) is a human gene responsible for a cell surface receptor essential to the function of the immune system. Patients with a polymorphism in this gene are at higher risk for auto-immune based inflammatory disease including Celiac disease, Crohn's, Ulcerative Colitis, and gluten sensitivity.
HLA-DQA2	Major histocompatibility complex, DQ alpha 2 (HLA-DQA2) is a human gene responsible for a cell surface receptor essential to the function of the immune system. Patients with a polymorphism in this gene are at higher risk for auto-immune based inflammatory disease including Celiac disease, Crohn's, Ulcerative Colitis, and gluten sensitivity.
HNMT rs12995000	The HNMT gene encodes the histamine degradative enzyme, histamine N-methyltransferase. HNMT, in contrast to AOC1, requires the methyl donor S-adenosylmethionine and a complete methylation pathway for normal function. Polymorphisms in HNMT gene expression or protein-coding are predicted to prolong the pro-inflammatory effects of histamine signaling.
HNMT Thr105Ile	The HNMT gene encodes the histamine degradative enzyme, histamine N-methyltransferase. HNMT, in contrast to AOC1, requires the methyl donor S-adenosylmethionine and a complete methylation pathway for normal function. Polymorphisms in HNMT gene expression or protein coding are predicted to prolong the pro-inflammatory effects of histamine signaling.
IL13	IL13 (Interleukin 13) is a member of the interleukin family of chemical messengers of the immune system. Polymorphisms in this gene are associated with changes in IL13 gene expression and increase the risk of more severe inflammatory responses to allergens.
IL5	The protein product of the Interleukin 5 gene (IL5) is important for normal development of B lymphocytes and eosinophils (a pro-inflammatory white blood cell). Inactivating mutations in the IL5 gene are associated with susceptibility to certain viral infections and increased aggression of inflammatory response. These polymorphisms are also associated with increased aggression of allergies, asthma and eosinophilia.
IL6	Interleukin 6, IL6, is an important pro-inflammatory cytokine. Polymorphisms in this gene leads to a more aggressive inflammatory response. Patients with IL-6 mutations require assistance with inflammatory control.
STAT4	The Signal Transducer and Activator of Transcription 4 (STAT4) gene encodes a transcription factor that responds to extracellular growth factors and cytokines. Mutations in the STAT4 gene are associated with inflammatory disorders like lupus and rheumatoid arthritis.
TNF	Tumor necrosis factor, TNF, is an important pro-inflammatory signaling molecule. Polymorphisms in the protein coding part of this gene are associated with more severe pro-inflammatory responses and require supplementation for inflammatory control.
METHYLATION	Methylation is a primary biochemical process in the body that involves the addition of a "methyl" chemical group to a vitamin or neurotransmitter. The addition of the "methyl" group allows for very specific biochemical interactions. Poor "methylation" function alters the effectiveness, delivery and function of many vitamins and important chemicals in the cell.
FOLR2	Folate Receptor 2 (FOLR2) is a member of the folate receptor (FOLR) family. Members of this gene family have a high affinity for folic acid. Polymorphisms in this gene allow for poor delivery of folic acid to the interior of cells. This can create a high plasma folic acid. This polymorphism does create a methylation deficiency. This polymorphism is associated with many disorders of pregnancy. This receptor is found in high quantities on the placenta, thymus and bone marrow. Can be affiliated with immune disorders.
MTHFR A1298C	Methylenetetrahydrofolate reductase (MTHFR) catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the bioactive form of folic acid. Two significant polymorphism variants exist in this gene, the A1298C and the C677T. The 1298 confers a conversion weakness of 10% for one copy and approximately 20% for two copies. In contrast, the 677 variant is much more severe and conveys a 40% conversion weakness for one copy and 70% for two copies. A reduced level of MTHFolate produces significant biochemical effects including poor production of dopamine and serotonin, pregnancy complications, poor healing of the nervous system, weak mitochondrial function, reduced production of glutathione, poor cell turnover and poor function of T cell lymphocytes.
MTHFR C677T	Methylene tetrahydrofolate reductase (MTHFR) catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the bioactive form of folic acid. Two significant polymorphism variants exist in this gene, the A1298C and the C677T. The 1298 confers a conversion weakness of 10% for one copy and approximately 20% for two copies. In contrast, the 677 variant is much more severe and conveys a 40% conversion weakness for one copy and 70% for two copies. A reduced level of MTHFolate produces significant biochemical effects including poor production of dopamine and serotonin, pregnancy complications, poor healing of the nervous system, weak mitochondrial function, reduced production of glutathione, poor cell turnover and poor function of T cell lymphocytes.
TCN2	The protein product of the Transcobalamin 2 gene, TCN2, binds the active form of vitamin B-12. Individuals with the G/G phenotype at rs1801198 have decreased serum B-12 and increased homocysteine when compared to individuals with the C/C phenotype.
NEUROTRANSMITTER	Neurotransmitters are chemicals that are used to produce specific effects in the nervous system. These specific neurotransmitter genomics assess a person's risk for anxiety, depression and dysphoria.

ADRA2A	ADRA2A (Adrenergic Receptor Alpha 2A) gene that determines sensitivity of the adrenergic nervous system response. Individuals with the G allele at this location predicted to be at higher risk of sugar-induced hyperactivity, and better response to ADHD treatment with typical pharmacological interventions.
COMT V158M	Catechol-O-methyltransferase (COMT) is one of several enzymes that degrade catecholamine neurotransmitters such as dopamine, epinephrine, and norepinephrine. COMT's main function is to inactivate neurotransmitters (dopamine, epinephrine, and norepinephrine) by the addition of a methyl group to the catecholamine. Normal COMT function allows people to rapidly reverse feelings of anxiety or depression. COMT (+/-) patients have sluggish ability to alter anxiety or depression episodes. COMT (+/+) patients are more prone to prolonged episodes of anxiety, depression and OCD.
DBH	DBH (Dopamine Beta Hydroxylase) is an oxidoreductase belonging to the copper type II, ascorbate-dependent monooxygenase family. The encoded protein, expressed in neurosecretory vesicles catalyzes the conversion of dopamine to norepinephrine, which functions as both a hormone and sympathetic nervous system function. Polymorphisms in this gene lower the production of norepinephrine which causes poor autonomic and cardiovascular function, including hypotension and ptosis. Polymorphisms in this gene have also been linked to Autism, ADD, bipolar disorder and major depression.
GAD1 rs3828275	Glutamic Acid Decarboxylase (GAD 1) is the enzyme responsible for conversion of glutamic acid (a stimulant neurotransmitter) to GABA (a calming neurotransmitter). Deficiency of GABA from polymorphisms in this enzyme are associated with sleep disorders, "half glass empty" syndrome, dysphoria, and spasticity.
HTR2A	5-hydroxytryptamine receptor 2 (HTR2) is one of the neuronal receptors for the neurotransmitter serotonin. Mutations in the HTR2 gene are associated with individual response to antidepressants, appetite, and mood.
MAOA	Monoamine oxidase A (MAOA) is one of the classic neurotransmitter degradation enzymes. By degrading serotonin, dopamine, epinephrine, and norepinephrine, MAO-A ends neuronal signaling induced by those neurotransmitters. Mutations in the MAO-A gene leads to decreased degradation of these neurotransmitters and can be associated with increased aggression, mood disorders and drug addiction.
MAOB	Monoamine Oxidase B (MAO B) catalyzes the neuroactive amines, such as dopamine, epinephrine, norepinephrine, and plays a role in the stability of mood in the central nervous system,. MAO B's primary purpose is to degrade dopamine. Patients who possess polymorphisms of MAO B have a higher risk of clinical depression and mood disorders.
SLC6A4	The SLC6A4 gene encodes the serotonin transporter, also known as SERT. The serotonin transporter is responsible for clearing the serotonin neurotransmitter from the synaptic space. SERT is the target of many therapeutic drugs. Polymorphisms in the SLC6A4 gene are associated with increased risk of anxiety and depression and less effective response to SSRI medications.
TPH2	TPH2 (Tryptophan Hydroxylase 2) gene catalyzes the first and rate limiting step in the biosynthesis of serotonin (5HT), an important hormone and neurotransmitter. Mutations in this gene have been shown to be associated with psychiatric diseases such as bipolar affective disorder, anxiety and major depression. Polymorphisms in this gene are also correlated to an increased response rate to SSRI medications.

Disclaimers

METHODOLOGY AND LIMITATIONS:

Testing for genetic variation/mutation on listed genes was performed using ProFlex PCR and Real-Time PCR with TaqMan® allele-specific probes on the QuantStudio 12K Flex. All genetic testing is performed by GX Sciences, 4150 Freidrich Lane, Ste H, Austin, TX. 78744. This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Test results do not rule out the possibility that this individual could be a carrier of other mutations/variations not detected by this gene mutation/variation panel. Rare mutations surrounding these alleles may also affect our detection of genetic variations. Thus, the interpretation is given as a probability. Therefore, this genetic information shall be interpreted in conjunction with other clinical findings and familial history for the administration of specific nutrients. Patients should receive appropriate genetic counseling to explain the implications of these test results. Details of assay performance and algorithms leading to clinical recommendations are available upon request. The analytical and performance characteristics of this laboratory developed test (LDT) were determined by GX Sciences' laboratory pursuant to Clinical Laboratory Improvement Amendments (CLIA) requirements.

CLIA #: 45D2144988 Laboratory Director: James Jacobson, PhD

DISCLAIMER:

This test was developed and its performance characteristics determined by GX Sciences. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA and qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. rsIDs for the alleles being tested were obtained from the dbSNP database (Build 142).

DISCLAIMER:

UND Result: If you have received the result Variant undetermined (UND) this indicates that we were not able to determine your carrier status based on your raw data. Please refer to the GX Sciences genetic knowledge database for more information: https://www.gxsciences.com/kb_results.asp

DISCLAIMER:

Report contents and report recommendations are created and approved by GX Sciences. Sole responsibility for the proper use of the information on the GX Sciences report rests with the user, or those professionals with whom the user may consult. Nutrigenomic Testing and Dietary Supplements are not "Designated Health Services" covered by Medicare or Medicaid and may not be reimbursed under any state or Federal health care program.

DISCLAIMER:

These products are not approved by the Food and Drug Administration and are not intended to diagnose, treat, cure or prevent disease. These recommendations are for report purposes only and an individual is not required to use such products. These are recommendations only and do not replace the advisement of your own healthcare practitioner.

GX Sciences SNP References

DETOXIFICATION SNP References

CTH

• Huez-Diaz, P. et al. Association of Cth genetic variant with veno-occlusive disease in children receiving intravenous busulfan before hematopoietic stem cell transplantation. *Blood* 120, (2012). • Pizzorno, J. Glutathione! Integrative Medicine (Boulder) (2014). doi:10.5005/jp/books/13002_11 • Allocati, N., Masulli, M., Di Ilio, C. & Federici, L. Glutathione transferases: Substrates, inhibitors and pro-drugs in cancer and neurodegenerative diseases. *Oncogenesis* (2018). doi:10.1038/s41389-017-0025-3 • Hodges, R. E. & Minich, D. M. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism* (2015). doi:10.1155/2015/760689 • Wang, J. & Hegele, R. a. Genomic basis of cystathioninuria (MIM 219500) revealed by multiple mutations in cystathionine gamma-lyase (CTH). *Hum. Genet.* 112, 404–408 (2003). • Schrock, M. How Metabolic Detoxification Can Help You Live a Healthier Life. *Non Toxic Revolution* (2019). Available at: <https://www.nontoxicrevolution.org/blog/metabolic-detoxification>. • Whalen, R. & Boyer, T. D. Human glutathione S-transferases. *Seminars in Liver Disease* (1998). doi:10.1055/s-2007-1007169

GSTM3

• Patskovsky, Y. V, Huang, M. Q., Takayama, T., Listowsky, I. & Pearson, W. R. Distinctive structure of the human GSTM3 gene-inverted orientation relative to the mu class glutathione transferase gene cluster. *Arch. Biochem. Biophys.* (1999). doi:10.1006/abbi.1998.0964 • Maes, O. C., Schipper, H. M., Chong, G., Chertkow, H. M. & Wang, E. A GSTM3 polymorphism associated with an etiopathogenetic mechanism in Alzheimer disease. *Neurobiol. Aging* (2010). doi:10.1016/j.neurobiolaging.2008.03.007

GSTP1

• Sekine, I., Minna, J. D., Nishio, K., Tamura, T. & Saijo, N. A literature review of molecular markers predictive of clinical response to cytotoxic chemotherapy in patients with lung cancer. *J Thorac Oncol* (2006). doi:01243894-200601000-00008 [pii] • Buch, S. C., Notani, P. N. & Bhisey, R. A. Polymorphism at GSTM1, GSTM3 and GSTT1 gene loci and susceptibility to oral cancer in an Indian population. *Carcinogenesis* (2002). doi:10.1093/carcin/23.5.803 • Whalen, R. & Boyer, T. D. Human glutathione S-transferases. *Seminars in Liver Disease* (1998). doi:10.1055/s-2007-1007169 • Allocati, N., Masulli, M., Di Ilio, C. & Federici, L. Glutathione transferases: Substrates, inhibitors and pro-drugs in cancer and neurodegenerative diseases. *Oncogenesis* (2018). doi:10.1038/s41389-017-0025-3 • Pizzorno, J. Glutathione! Integrative Medicine (Boulder) (2014). doi:10.5005/jp/books/13002_11 • Schrock, M. How Metabolic Detoxification Can Help You Live a Healthier Life. *Non Toxic Revolution* (2019). Available at: <https://www.nontoxicrevolution.org/blog/metabolic-detoxification>. • Strange, R. C. & Fryer, A. A. The glutathione S-transferases: influence of polymorphism on cancer susceptibility. *IARC Sci. Publ.* (1999). • Hodges, R. E. & Minich, D. M. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism* (2015). doi:10.1155/2015/760689 • Kellen, E. et al. Pooled analysis and meta-analysis of the glutathione S-transferase P1 Ile 105Val polymorphism and bladder cancer: A HuGe-GSEC review. *American Journal of Epidemiology* (2007). doi:10.1093/aje/kwm003 • Gerhard, D. S. et al. The status, quality, and expansion of the NIH full-length cDNA project: The Mammalian Gene Collection (MGC). *Genome Res.* (2004). doi:10.1101/gr.2596504

DEVELOPMENTAL SNP References

ATG12

• Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing. in *Haschek and Rousseaux's Handbook of Toxicologic Pathology* (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. *Gene* 632, 36–42 (2017). • Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* 16, 268–278 (2008). • Mizushima, N. Autophagy: Process and function. *Genes and Development* (2007). doi:10.1101/gad.1599207 • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. *Cell* (2008). doi:10.1016/j.cell.2007.12.018 • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? *Clinics (Sao Paulo, Brazil)* (2018). doi:10.6061/clinics/2018/e8145 • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. *Autophagy* (2016). doi:10.1080/15548627.2016.1151597 • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. *Healthline* (2014). Available at: <https://www.healthline.com/health/autophagy#bottom-line>.

BDNF

• Brooks, S. J., Nilsson, E. K., Jacobsson, J. A., Stein, D. J., Fredriksson, R., Lind, L., & Schiöth, H. B. (2014). BDNF polymorphisms are linked to poorer working memory performance, reduced cerebellar and hippocampal volumes and differences in prefrontal cortex in a Swedish elderly population. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0082707> • Harrisberger, F., Spalek, K., Smieskova, R., Schmidt, A., Coynel, D., Milnik, A., ... Borgwardt, S. (2014). The association of the BDNF Val66Met polymorphism and the hippocampal volumes in healthy humans: A joint meta-analysis of published and new data. *Neuroscience and Biobehavioral Reviews*. <https://doi.org/10.1016/j.neubiorev.2014.03.011> • Zhao, X., Xi, B., Shen, Y., Wu, L., Hou, D., Cheng, H., & Mi, J. (2014). An obesity genetic risk score is associated with metabolic syndrome in Chinese children. *Gene*. <https://doi.org/10.1016/j.gene.2013.11.006> • Zivadinov, R., Weinstock-Guttman, B., Benedict, R., Tamaño-Blanco, M., Hussein, S., Abdelrahman, N., ... Ramanathan, M. (2007). Preservation of gray matter volume in multiple sclerosis patients with the Met allele of the rs6265 (Val66Met) SNP of brain-derived neurotrophic factor. *Human Molecular Genetics*. <https://doi.org/10.1093/hmg/ddm189> • Mitre, M., Mariga, A. & Chao, M. V. Neurotrophin signalling: Novel insights into mechanisms and pathophysiology. *Clinical Science* (2017). doi:10.1042/CS20160044 • Bathina, S. & Das, U. N. Brain-derived neurotrophic factor and its clinical Implications. *Archives of Medical Science* (2015). doi:10.5114/aoms.2015.56342 • Miranda, M., Morici, J. F., Zانونi, M. B. & Bekinshtein, P. Brain-Derived Neurotrophic Factor: A Key Molecule for Memory in the Healthy and the Pathological Brain. *Frontiers in Cellular Neuroscience* (2019). doi:10.3389/fncel.2019.00363 • Cheah, S. Y., Lawford, B. R., Young, R. M. D., Connor, J. P., Morris, C. P., & Voisey, J. (2014). BDNF SNPs are implicated in comorbid alcohol dependence in schizophrenia but not in alcohol-dependent patients without schizophrenia. *Alcohol and Alcoholism*. <https://doi.org/10.1093/alcac/agu040> • Harrisberger, F., Smieskova, R., Schmidt, A., Lenz, C., Walter, A., Wittfeld, K., ... Borgwardt, S. (2015). BDNF Val66Met polymorphism and hippocampal volume in neuropsychiatric disorders: A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews*. <https://doi.org/10.1016/j.neubiorev.2015.04.017> • Haslacher, H., Michlmayr, M., Batmyagmar, D., Perkmann, T., Ponocny-Seliger, E., Scheichenberger, V., ... Winker, R. (2015). Physical exercise counteracts genetic susceptibility to depression. *Neuropsychobiology*. <https://doi.org/10.1159/000381350> • Juhasz, G., Dunham, J. S., McKie, S., Thomas, E., Downey, D., Chase, D., ... Deakin, J. F. W. (2011). The CREB1-BDNF-NTRK2 pathway in depression: Multiple gene-cognition- environment interactions. *Biological Psychiatry*. <https://doi.org/10.1016/j.biopsych.2010.11.019> • Kambetitz, J. P., Bhattacharyya, S., Kambetitz-Irankovic, L. M., Valli, I., Collier, D. A., & McGuire, P. (2012). Effect of BDNF val66met polymorphism on declarative memory and its neural substrate: A meta-analysis. *Neuroscience and Biobehavioral Reviews*. <https://doi.org/10.1016/j.neubiorev.2012.07.002> • Laing, K. R., Mitchell, D., Wersching, H., Czira, M. E., Berger, K., & Baune, B. T. (2012). Brain-derived neurotrophic factor (BDNF) gene: A gender-specific role in cognitive function during normal cognitive aging of the MEMO-Study? *Age*. <https://doi.org/10.1007/s11357-011-9275-8> • Lester, K. J., Hudson, J. L., Tropeano, M., Creswell, C., Collier, D. A., Farmer, A., ... Eley, T. C. (2012). Neurotrophic gene polymorphisms and response to psychological therapy. *Translational Psychiatry*. <https://doi.org/10.1038/tp.2012.33> • McAllister, T. W., Tyler, A. L., Flashman, L. A., Rhodes, C. H., McDonald, B. C., Saykin, A. J., ... Moore, J. H. (2012). Polymorphisms in the Brain-Derived Neurotrophic Factor Gene Influence Memory and Processing Speed One Month after Brain Injury. *Journal of Neurotrauma*. <https://doi.org/10.1089/neu.2011.1930> • Niitsu, T., Fabbri, C., Bentini, F., & Serretti, A. (2013). Pharmacogenetics in major depression: A comprehensive meta-analysis. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. <https://doi.org/10.1016/j.pnpbp.2013.05.011> • Razavi, S. et al. Neurotrophic factors and their effects in the treatment of multiple sclerosis. *Adv. Biomed. Res.* (2015). doi:10.4103/2277-9175.151570 • Ursini, G., Cavalleri, T., Fazio, L., Angrisano, T., Iacovelli, L., Porcelli, A., ... Bertolino, A. (2016). BDNF rs6265 methylation and genotype interact on risk for schizophrenia. *Epigenetics*. <https://doi.org/10.1080/15592294.2015.1117736>

SYN1

• Mitre, M., Mariga, A. & Chao, M. V. Neurotrophin signalling: Novel insights into mechanisms and pathophysiology. *Clinical Science* (2017). doi:10.1042/CS20160044 • Fassio, A., Patry, L., Congia, S., Onofri, F., Piton, A., Gauthier, J., ... Cossette, P. (2011). SYN1 loss-of-function mutations in autism and partial epilepsy cause impaired synaptic function. *Human Molecular Genetics*. <https://doi.org/10.1093/hmg/ddr122> • Cruceanu, C., Kutsarova, E., Chen, E. S., Checknita, D. R., Nagy, C., Lopez, J. P., ... Turecki, G. (2016). DNA hypomethylation of Synapsin II CpG islands associates with increased gene expression in bipolar disorder and major depression. *BMC Psychiatry*. <https://doi.org/10.1186/s12888-016-0989-0> • Razavi, S. et al. Neurotrophic factors and their effects in the treatment of multiple sclerosis. *Adv. Biomed. Res.* (2015). doi:10.4103/2277-9175.151570 • Bathina, S. & Das, U. N. Brain-derived neurotrophic factor and its clinical Implications. *Archives of Medical Science* (2015). doi:10.5114/aoms.2015.56342 • Miranda, M., Morici, J. F., Zانونi, M. B. & Bekinshtein, P. Brain-Derived Neurotrophic Factor: A Key Molecule for Memory in the Healthy and the Pathological Brain. *Frontiers in Cellular Neuroscience* (2019). doi:10.3389/fncel.2019.00363 • Vasil'chenko, V. N. (1984). Effect of the cover factor unbalance of viscose rayon twill on its formation. <https://doi.org/10.1016/j.braindev.2013.04.013> • Lo-Castro, A., & Curatolo, P. (2014). Epilepsy associated with autism and attention deficit hyperactivity disorder: Is there a genetic link? *Brain and Development*. <https://doi.org/10.1016/j.braindev.2013.04.013> • Paonessa, F., Latifi, S., Scarongella, H., Cesca, F., & Benfenati, F. (2013). Specificity protein 1 (Sp1)-dependent activation of the synapsin I gene (SYN1) is modulated by RE1-silencing transcription factor (REST) and 5'-cytosine-phosphoguanine (CPG) methylation. *Journal of Biological Chemistry*. <https://doi.org/10.1074/jbc.M112.399782>

INFLAMMATORY SNP References

AOC1

• McGrath, A. P. et al. Structure and Inhibition of Human Diamine Oxidase - Biochemistry (ACS Publications). Biochemistry 48, 9810–22 (2009). • Maintz, L. & Novak, N. Histamine and histamine intolerance. Am. J. Clin. Nutr. (2007). doi:10.1093/ajcn/85.5.1185 • McGrath, A. P. et al. Structure and inhibition of human diamine oxidase. Biochemistry 48, 9810–9822 (2009). • Schwelberger, H. G. The origin of mammalian plasma amine oxidases. in Journal of Neural Transmission 114, 757–762 (2007). • Solismaa, A. et al. Histaminergic gene polymorphisms associated with sedation in clozapine-treated patients. Eur. Neuropsychopharmacol. 27, 442–449 (2017).

ATG16L1

• Mizushima, N. Autophagy: Process and function. Genes and Development (2007). doi:10.1101/gad.1599207 • Salem, M., Nielsen, O. H., Nys, K., Yazdanyar, S. & Seidelin, J. B. Impact of T300A Variant of ATG16L1 on antibacterial response, risk of culture positive infections, and clinical course of Crohn's disease. Clin. Transl. Gastroenterol. (2015). doi:10.1038/ctg.2015.47 • Begun, J. et al. Integrated Genomics of Crohn's Disease Risk Variant Identifies a Role for CLEC12A in Antibacterial Autophagy. Cell Rep. (2015). doi:10.1016/j.celrep.2015.05.045 • Cheng, J. F., Ning, Y. J., Zhang, W., Lu, Z. H. & Lin, L. T300A polymorphism of ATG16L1 and susceptibility to inflammatory bowel diseases: A meta-analysis. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i10.1258 • Kabat, A. M. et al. The autophagy gene Atg16l1 differentially regulates Treg and TH2 cells to control intestinal inflammation. Elife (2016). doi:10.7554/eLife.12444 • Lassen, K. G. et al. Atg16L1 T300A variant decreases selective autophagy resulting in altered cytokine signaling and decreased antibacterial defense. Proc. Natl. Acad. Sci. (2014). doi:10.1073/pnas.1407001111 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing, in Haschek and Rousseaux's Handbook of Toxicologic Pathology (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. Cell (2008). doi:10.1016/j.cell.2007.12.018 • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. Healthline (2014). Available at: <https://www.healthline.com/health/autophagy#bottom-line>. • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo, Brazil) (2018). doi:10.6061/clinics/2018/e814s • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. Autophagy (2016). doi:10.1080/15548627.2016.1151597 • Gazuoli, M. et al. NOD2/CARD15, ATG16L1 and IL23R gene polymorphisms and childhood-onset of Crohn's disease. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i14.1753 • Kuballa, P., Huett, A., Rioux, J. D., Daly, M. J. & Xavier, R. J. Impaired autophagy of an intracellular pathogen induced by a Crohn's disease associated ATG16L1 variant. PLoS One (2008). doi:10.1371/journal.pone.0003391 • Rosenthal, D. C. et al. Role of autophagy genetic variants for the risk of Candida infections. Med. Mycol. (2014). doi:10.1093/mmy/myt035 • Raju, D., Hussey, S. & Jones, N. L. Crohn disease ATG16L1 polymorphism increases susceptibility to infection with Helicobacter pylori in humans. Autophagy (2012). doi:10.4161/autophagy.21007 • Stappenbeck, T. C. et al. Crohn disease: A current perspective on genetics, autophagy and immunity. Autophagy (2011). doi:10.4161/auto.7.4.13074 • Csongéi, V. et al. Interaction of the major inflammatory bowel disease susceptibility alleles in Crohn's disease patients. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i12.176 • Boada-Romero, E. et al. A Crohn's disease risk polymorphism impairs function of the WD40 domain of ATG16L1. Nat. Commun. (2016). doi:10.1038/ncomms1821 • Glubb, D. M. et al. NOD2 and ATG16L1 polymorphisms affect monocyte responses in crohn's disease. World J. Gastroenterol. (2011). doi:10.3748/wjg.v17.i23.2829 • Salem, M., Ammitzboell, M., Nys, K., Seidelin, J. B. & Nielsen, O. H. ATG16L1: A multifunctional susceptibility factor in crohn disease. Autophagy (2015). doi:10.1080/15548627.2015.1017187 • Usategui-Martin, R. et al. Polymorphisms in autophagy genes are associated with paget disease of bone. PLoS One (2015). doi:10.1371/journal.pone.0128984 • Messer, J. S. et al. The Crohn's disease: Associated ATG16L1 variant and Salmonella invasion. BMJ Open (2013). doi:10.1136/bmjopen-2013-002790

ATG5

• Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. Healthline (2014). Available at: <https://www.healthline.com/health/autophagy#bottom-line>. • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. Autophagy (2016). doi:10.1080/15548627.2016.1151597 • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo, Brazil) (2018). doi:10.6061/clinics/2018/e814s • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. Cell (2008). doi:10.1016/j.cell.2007.12.018 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing, in Haschek and Rousseaux's Handbook of Toxicologic Pathology (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Mizushima, N. Autophagy: Process and function. Genes and Development (2007). doi:10.1101/gad.1599207 • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • White, K. A. M. et al. Variants in autophagy-related genes and clinical characteristics in melanoma: a population-based study. Cancer Med. 5, 3336–3345 (2016). • Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. Gene 632, 36–42 (2017). • Martin, L. J. et al. Functional Variant in the Autophagy-Related 5 Gene Promotor is Associated with Childhood Asthma. PLoS One 7, e33454 (2012).

C3

• Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. Frontiers in Human Neuroscience (2017). doi:10.3389/fnhum.2017.00316 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. Harvard Health (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Foods that fight inflammation. Harvard Health (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. in Annals of the New York Academy of Sciences (2009). doi:10.1196/annals.1393.013 • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. Frontiers in Neuroscience (2019). doi:10.3389/fnins.2019.00384 • Wei, M. Yoga could slow the harmful effects of stress and inflammation. Harvard Health Blog (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. Alzheimer's and Dementia (2014). doi:10.1016/j.jalz.2013.12.010 • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. International Journal of Biological Sciences (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? F1000 Medicine Reports 4, (2012). • Loos B, et al. Polymorphisms in an interferon-? receptor-1 gene marker and susceptibility to periodontitis. Acta Odontol. Scand. (2003). doi:10.1080/00016350310006168 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. Journal of Neurochemistry 139, 136–153 (2016). • Simpson, N. & Dinges, D. F. Sleep and Inflammation. Nutr. Rev. (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Kalođeropoulos, A. P., Georgiopolou, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. Heart Failure Clinics (2012). doi:10.1016/j.hfc.2011.08.002 • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. J. Exp. Neurosci. (2018). doi:10.1177/1179069518793639 • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Rasheed, H. et al. Replication of association of the apolipoprotein A1-C3-A4 gene cluster with the risk of gout. Rheumatol. (United Kingdom) (2016). doi:10.1093/rheumatology/kew057 • Nsaibia, M. J. et al. C3 Polymorphism Influences Circulating Levels of C3, ASP and Lipids in Schizophrenic Patients. Neurochem. Res. (2015). doi:10.1007/s11064-015-1543-z • Prechl, J. et al. Serological and genetic evidence for altered complement system functionality in systemic lupus erythematosus: Findings of the GAPAID consortium. PLoS One (2016). doi:10.1371/journal.pone.0150685 • Wu, Y. et al. Interactions of environmental factors and APOA1-APOC3-APOA4-APOA5 gene cluster gene polymorphisms with metabolic syndrome. PLoS One (2016). doi:10.1371/journal.pone.0147946 • Saksens, N. T. M. et al. Rare Genetic Variants Associated With Development of Age-Related Macular Degeneration. JAMA Ophthalmol. (2016). doi:10.1001/jamaophthalmol.2015.5592 • Bonyadi, M. et al. Association of polymorphisms in complement component 3 with age-related macular degeneration in an Iranian population. Ophthalmic Genet. (2016). doi:10.3109/13816810.2015.1126612 • Nakayama, Y. et al. C3 Promotes Expansion of CD8 + and CD4 + T Cells in a Listeria monocytogenes Infection . J. Immunol. (2009). doi:10.4049/jimmunol.0801191 • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease - Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>. • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>. • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. Healthline (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders#treatment>. • Wu, W. et al. Polymorphisms in complement genes and risk of preeclampsia in Taiyuan, China. Inflamm. Res. (2016). doi:10.1007/s00011-016-0968-4 • Li, Y., Li, C. & Gao, J. Apolipoprotein C3 gene variants and the risk of coronary heart disease: A meta-analysis. Meta Gene (2016). doi:10.1016/j.mgene.2016.04.004

CD14

• Loo, W. T. Y. et al. Clinical application of human ?-defensin and CD14 gene polymorphism in evaluating the status of chronic inflammation. J. Transl. Med. (2012). doi:10.1186/1479-5876-10-S1-S9 • Harvard Health Publishing. Foods that fight inflammation. Harvard Health (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. Harvard Health (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. Frontiers in Human Neuroscience (2017). doi:10.3389/fnhum.2017.00316 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. in Annals of the New York Academy of Sciences (2009). doi:10.1196/annals.1393.013 • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. Frontiers in Neuroscience (2019). doi:10.3389/fnins.2019.00384 • Wei, M. Yoga could slow the harmful effects of stress and inflammation. Harvard Health Blog (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. Alzheimer's and Dementia (2014). doi:10.1016/j.jalz.2013.12.010 • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. International Journal of Biological Sciences (2012). doi:10.7150/ijbs.4666 • Loos B, et al. Polymorphisms in an interferon-? receptor-1 gene marker and susceptibility to periodontitis. Acta Odontol. Scand. (2003). doi:10.1080/00016350310006168 • Simpson, N. & Dinges, D. F. Sleep and inflammation. Nutr. Rev. (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Kalođeropoulos, A. P., Georgiopolou, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. Heart Failure Clinics (2012). doi:10.1016/j.hfc.2011.08.002 • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>. • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? Autoimmune Disease: Why Is My Immune System Attacking Itself? Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>. • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. Healthline (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders#treatment>. • Turner, D. et al. Overexpression of a Novel Lymphocyte Population, Positive for an Intracellular CD14-Like Antigen, in Patients Positive for Human Immunodeficiency Virus Type 1. Clinical Diagnostic Laboratory Immunology 11, 1040–1044 (2004). • Zhang, A. Q. et al. Association between CD14 promoter -159C/T polymorphism and the risk of sepsis and mortality: a systematic review and meta-analysis. PLoS one (2013). doi:10.1371/journal.pone.0071237 • Misra, S. et al. Genetic association between inflammatory genes (IL-1?, CD14, LGALS2, PSMA6) and risk of ischemic stroke: A meta-analysis. Meta Gene (2016). doi:10.1016/j.mgene.2016.01.003 • Areeshi, M. Y., Mandal, R. K., Panda, A. K., Bishr, S. C. & Haque, S. CD14 -159 C>T Gene Polymorphism with Increased Risk of Tuberculosis: Evidence from a Meta-Analysis. PLoS One (2013). doi:10.1371/journal.pone.0064747 • Kim, E. J. et al. Helicobacter pylori infection enhances gastric mucosal inflammation in individuals carrying the 260-T allele of the CD14 gene. Gut Liver (2013). doi:10.5009/gnl.2013.7.3.317 • Wang, J. et al. Association between CD14 gene polymorphisms and cancer risk: A meta-analysis. PLoS One (2014). doi:10.1371/journal.pone.0100122 • Wang, S. et al. Racial differences in the association of CD14 polymorphisms with serum total IgE levels and allergen skin test reactivity. J. Asthma Allergy (2013). doi:10.2147/JAA.S42695 • Wang, Z., Hu, J., Fan, R., Zhou, J. & Zhong, J. Association between CD14 Gene C-260T Polymorphism and Inflammatory Bowel Disease: A Meta-Analysis. PLoS One (2012). doi:10.1371/journal.pone.0045144 • Liu, B. et al. CD14 ++ CD16 + Monocytes Are Enriched by Glucocorticoid Treatment and Are Functionally Attenuated in Driving Effector T Cell Responses. J. Immunol. (2015). doi:10.4049/jimmunol.1402409 • Cheah, M. T. et al. CD14-expressing cancer cells establish the inflammatory and proliferative tumor microenvironment in bladder cancer. Proc. Natl. Acad. Sci. (2015). doi:10.1073/pnas.1424795112 • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. J. Exp. Neurosci. (2018). doi:10.1177/1179069518793639 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. Journal of Neurochemistry 139, 136–153 (2016).

CTLA4

• Jeffery, L. E. et al. Vitamin D antagonises the suppressive effect of inflammatory cytokines on CTLA-4 expression and regulatory function. PLoS One (2015). doi:10.1371/journal.pone.0131539 • Tai, X. et al. Basis of CTLA-4 function in regulatory and conventional CD4 T cells. Blood 119, 5155–5163 (2012). • Wei, M. Yoga could slow the harmful effects of stress and inflammation. Harvard Health Blog (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Nie, W., Chen, J. & Xiu, Q. Cytotoxic T-lymphocyte associated antigen 4 polymorphisms and asthma risk: A meta-analysis. PLoS One (2012). doi:10.1371/journal.pone.0042062 • Patel, H. et al. Association of Cytotoxic T-Lymphocyte Antigen 4 (CTLA4) and Thyroglobulin (TG) genetic variants with autoimmune hypothyroidism. PLoS One (2016). doi:10.1371/journal.pone.0149441 • Wang, J. et al. Common variants on cytotoxic T lymphocyte antigen-4 polymorphisms contributes to type 1 diabetes susceptibility: Evidence based on 58 studies. PLoS One (2014). doi:10.1371/journal.pone.0085982 • Yan, Q., Chen, P., Lu, A., Zhao, P. & Gu, A. Association between CTLA-4 60G/A and -1661A/G polymorphisms and the risk of cancers: A meta-analysis. PLoS One (2013). doi:10.1371/journal.pone.0083710 • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. Frontiers in Neuroscience (2019). doi:10.3389/fnins.2019.00384 • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. Frontiers in Human Neuroscience (2017). doi:10.3389/fnhum.2017.00316 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. in Annals of the New York Academy of Sciences (2009). doi:10.1196/annals.1393.013 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is

in the details. Journal of Neurochemistry 139, 136–153 (2016). • Orrù, S. et al. Recipient CTLA-4*CT60-AA genotype is a prognostic factor for acute graft-versus-host disease in hematopoietic stem cell transplantation for thalassemia. Hum. Immunol. (2012). doi:10.1016/j.humimm.2011.12.014 • Wang, D. C., Tan, B. Y., Wang, F. & Yuan, Z. N. Association between CTLA-4 gene polymorphism and ankylosing spondylitis: A case-control study. Int. J. Clin. Exp. Pathol. (2015). • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Bour-Jordan, H. et al. Intrinsic and extrinsic control of peripheral T-cell tolerance by costimulatory molecules of the CD28/ B7 family. Immunol. Rev. (2011). doi:10.1111/j.1600-065X.2011.01011.x • Tector, M., Khatri, B. O., Kozinski, K., Dennert, K. & Oaks, M. K. Biochemical analysis of CTLA-4 immunoreactive material from human blood. BMC Immunol. (2009). doi:10.1186/1471-2172-10-51 • Karabon, L. et al. The CTLA-4 gene polymorphisms are associated with CTLA-4 protein expression levels in multiple sclerosis patients and with susceptibility to disease. Immunology (2009). doi:10.1111/j.1365-2567.2009.03083.x • AlFadhli, S. Overexpression and Secretion of the Soluble CTLA-4 Splice Variant in Various Autoimmune Diseases and in Cases with Overlapping Autoimmunity. Genet. Test. Mol. Biomarkers (2013). doi:10.1089/gtmb.2012.0391 • Wolff, A. S. B. et al. CTLA-4 as a genetic determinant in autoimmune Addison's disease. Genes Immun. (2015). doi:10.1038/gene.2015.27 • Zaletel, K. et al. Association of CT60 cytotoxic T lymphocyte antigen-4 gene polymorphism with thyroid autoantibody production in patients with Hashimoto's and postpartum thyroiditis. Clin. Exp. Immunol. (2010). doi:10.1111/j.1365-2249.2010.04113.x • Abdel Galil, S. M. & Hagrass, H. A. The role of CTLA-4 exon-1 49 A/G polymorphism and soluble CTLA-4 protein level in Egyptian patients with Behçet's disease. Biomed Res. Int. (2014). doi:10.1155/2014/513915 • Kalogeropoulos, A. P., Georgiopoulos, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. Heart Failure Clinics (2012). doi:10.1016/j.hfc.2011.08.002 • Simpson, N. & Dinges, D. F. Sleep and Inflammation. Nutr. Rev. (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Liu, J. & Zhang, H.-X. CTLA-4 polymorphisms and systemic lupus erythematosus: a comprehensive meta-analysis. Genet. Test. Mol. Biomarkers (2013). doi:10.1089/gtmb.2012.0302 • Du, L. et al. The associations between the polymorphisms in the CTLA-4 gene and the risk of Graves' disease in the Chinese population. BMC Med. Genet. (2013). doi:10.1186/1471-2350-14-46 • Esposito, L. et al. Investigation of Soluble and Transmembrane CTLA-4 Isoforms in Serum and Microvesicles. J. Immunol. (2014). doi:10.4049/jimmunol.1303389 • Walker, L. S. K. Treg and CTLA-4: Two intertwining pathways to immune tolerance. Journal of Autoimmunity (2013). doi:10.1016/j.jaut.2013.06.006 • Zhao, J. J., Wang, D., Yao, H., Sun, D. W. & Li, H. Y. CTLA-4 and MDR1 polymorphisms increase the risk for ulcerative colitis: A meta-analysis. World J. Gastroenterol. (2015). doi:10.3748/wjg.v21.i34.10025 • Harvard Health Publishing. Foods that fight inflammation. Harvard Health (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. Harvard Health (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Loos B, et al. Polymorphisms in an interferon-? receptor-1 gene marker and susceptibility to periodontitis. Acta Odontol. Scand. (2003). doi:10.1080/00016350310006168 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? F1000 Medicine Reports 4, (2012). • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. International Journal of Biological Sciences (2012). doi:10.7150/ijbs.4666 • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. Alzheimer's and Dementia (2014). doi:10.1016/j.jalz.2013.12.010 • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease - Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>. • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? Autoimmune Disease: Why Is My Immune System Attacking Itself? | Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>. • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? Autoimmune Disease: Why Is My Immune System Attacking Itself? | Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>. • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease - Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>.

DRD2

• Anton, R. F. et al. Pharmacogenomics. Nat. Genet. (2008). doi:10.1016/j.ejca.2015.06.122 • Disabato, D. J., Qian, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. Journal of Neurochemistry 139, 136–153 (2016). • Clarke, T. K. et al. The dopamine receptor D2 (DRD2) SNP rs1076560 is associated with opioid addiction. Ann. Hum. Genet. (2014). doi:10.1111/ahg.12046 • Sasabe, T., Furukawa, A., Matsusita, S., Higuchi, S. & Ishiura, S. Association analysis of the dopamine receptor D2 (DRD2) SNP rs1076560 in alcoholic patients. Neurosci. Lett. (2007). doi:10.1016/j.neulet.2006.10.064

FUT2

• FUT2 fucosyltransferase 2 (secretor status included) [Bos taurus (cattle)] - Gene - NCBI. Current neurology and neuroscience reports. Available at: <https://www.ncbi.nlm.nih.gov/gene/281175>. • Kimura, K. et al. Diversification of transcriptional modulation: Large-scale identification and characterization of putative alternative promoters of human genes. Genome Res. (2006). doi:10.1101/gr.4039406 • Strausberg, R. L. et al. Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences. Proc. Natl. Acad. Sci. U. S. A. (2002). doi:10.1073/pnas.242603899 • Koda, Y., Soejima, M., Wang, B. & Kimura, H. Structure and expression of the gene encoding secretor-type galactoside 2-alpha-L-fucosyltransferase (FUT2). Eur. J. Biochem. (1997). doi:10.1111/j.1432-1033.1997.t01-1-00750.x • Reguigne-Armoud, I. et al. Relative positions of two clusters of human ?-L-fucosyltransferases in 19q (FUT1–FUT2) and 19p (FUT6–FUT3–FUT5) within the microsatellite genetic map of chromosome 19. Cytogenet. Genome Res. (1995). doi:10.1159/000134098 • BALL, S. P. et al. The human chromosome 19 linkage group FUT1 (H), FUT2 (SE), LE, LU, PEPD, C3, APOC2, D19S7 and D19S9. Ann. Hum. Genet. (1991). doi:10.1111/j.1469-1809.1991.tb00417.x

HLA-DQA1

• Kao, H. T. et al. Molecular analysis of the HLA class II genes in two DRw6-related haplotypes, DRw13 DQw1 and DRw14 DQw3. J. Immunol. (1989). • Todd, J. a, Fukui, Y., Kitagawa, T. & Sasazuki, T. The A3 allele of the HLA-DQA1 locus is associated with susceptibility to type 1 diabetes in Japanese. Proc. Natl. Acad. Sci. U. S. A. (1990). • Marsh, S. G. & Bodmer, J. G. HLA class II nucleotide sequences, 1992. Immunogenetics (1993). • Liu, C. P., Bach, F. H. & Wu, S. K. Molecular studies of a rare DR2/LD-5a/DQw3 HLA class II haplotype. Multiple genetic mechanisms in the generation of polymorphic HLA class II genes. J Immunol (1988). • Histocompatibility complex - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/primer/genefamily/hla>. • Schmidt, H., Williamson, D. & Ashley-Koch, A. HLA-DR15 haplotype and multiple sclerosis: A HuGe review. American Journal of Epidemiology (2007). doi:10.1093/aje/kwk118 • Horn, G. T., Bugawan, T. L., Long, C. M., Manos, M. M. & Erlich, H. A. Sequence analysis of HLA class II genes from insulin-dependent diabetic individuals. Hum. Immunol. (1988). doi:10.1016/0198-8859(88)90034-1 • Schiffenbauer, J. et al. Complete sequence of the HLA DQ alpha and DQ beta cDNA from a DR5/DQw3 cell line. J. Immunol. (1987). • Jonsson, A.-K. et al. Class II genes of the human major histocompatibility complex. Comparisons of the DQ and DX ? and ? genes. J. Biol. Chem. (1987). • Blum, A. & Miller, H. The major histocompatibility complex and inflammation. Southern Medical Journal (2000). doi:10.1097/00007611-200002000-00002 • Mangalam, A. K., Taneja, V. & David, C. S. HLA Class II Molecules Influence Susceptibility versus Protection in Inflammatory Diseases by Determining the Cytokine Profile. J. Immunol. (2013). doi:10.4049/jimmunol.1201891

HLA-DQA2

• Khalil, I. et al. Trans-encoded DQ alpha beta heterodimers confer susceptibility to myasthenia gravis disease. C.R.Acad.Sci.III (1993). • Kwok, W. W. et al. Polymorphic DQ alpha and DQ beta interactions dictate HLA class II determinants of allo-recognition. Journal Of Experimental Medicine (1990). doi:10.1084/jem.171.1.85 • Hall, M. A., Lanchbury, J. S. S., Bolsover, W. J., Welsh, K. I. & Ciclitira, P. J. Celiac disease is associated with an extended HLA-DR3 haplotype which includes HLA-DPw1. Hum. Immunol. (1990). doi:10.1016/0198-8859(90)90052-Q • Solild, L. M. Evidence for a primary association of celiac disease to a particular HLA-DQ alpha/beta heterodimer. J. Exp. Med. (1989). doi:10.1084/jem.169.1.345 • Wang, H. & He, R. HLA-DQA and DQB alleles contribute to susceptibility to insulin-dependent diabetes mellitus. Chinese Med. Sci. J. = Chung-kuo I hshueh k'o hshueh ts'a chih (1993). • Bolsover, W. J., Hall, M. A., Vaughan, R. W., Welsh, K. I. & J. Ciclitira, P. A family study confirms that the HLA-DP associations with celiac disease are the result of an extended HLA-DR3 haplotype. Hum. Immunol. (1991). doi:10.1016/0198-8859(91)90012-X • Yu, L. & Sheehy, M. The cryptic HLA-DQA2 (DX alpha) gene is expressed in human B cell lines. J Immunol. (1991). • Olerup, O. & Hillert, J. HLA class II-associated genetic susceptibility in multiple sclerosis: a critical evaluation. Tissue Antigens (1991). doi:10.1111/j.1399-0039.1991.tb02029.x • HLA-DQA2 major histocompatibility complex, class II, DQ alpha 2 [Homo sapiens (human)] - Gene - NCBI. Current neurology and neuroscience reports. Available at: <https://www.ncbi.nlm.nih.gov/gene/3118>. • Histocompatibility complex - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/primer/genefamily/hla>. • Blum, A. & Miller, H. The major histocompatibility complex and inflammation. Southern Medical Journal (2000). doi:10.1097/00007611-200002000-00002 • Mangalam, A. K., Taneja, V. & David, C. S. HLA Class II Molecules Influence Susceptibility versus Protection in Inflammatory Diseases by Determining the Cytokine Profile. J. Immunol. (2013). doi:10.4049/jimmunol.1201891 • Khalil, I. et al. A combination of HLA-DQ beta Asp57-negative and HLA DQ alpha Arg52 confers susceptibility to insulin-dependent diabetes mellitus. J. Clin. Invest. (1990). doi:10.1172/JCI114569

HNMT

• The Food List. Histamine Intolerance Available at: <https://www.histamineintolerance.org.uk/about/the-food-diary/the-food-list/>. • Reference SNP (refSNP) Cluster Report: rs12995000. National Center for Biotechnology Information Available at: https://www.ncbi.nlm.nih.gov/SNP/snp_ref.cgi?rs=rs12995000. • Keeling, B. H. et al. Histamine N-methyltransferase Thr105ile is not associated with Parkinson's disease or essential tremor. Parkinsonism Relat. Disord. (2010). doi:10.1016/j.parkreldis.2009.08.011 • Maintz, L. & Novak, N. Histamine and histamine intolerance. Am. J. Clin. Nutr. (2007). doi:10.1093/ajcn/85.5.1185 • Sighi. Normal histamine metabolism in healthy people. HIT > Histaminosis > Histamine metabolism (2020). Available at: https://www.histaminintoleranz.ch/en/histaminosis_histaminemetabolism.html. • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. (2008). doi:10.1016/j.ejca.2015.06.122

IL-13

• Gervas-Arruga, J. et al. The influence of genetic variability and proinflammatory status on the development of bone disease in patients with Gaucher disease. PLoS One (2015). doi:10.1371/journal.pone.0126153 • Harvard Health Publishing. Foods that fight inflammation. Harvard Health (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. Harvard Health (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. Frontiers in Human Neuroscience (2017). doi:10.3389/fnhum.2017.00316 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. in Annals of the New York Academy of Sciences (2009). doi:10.1196/annals.1393.013 • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. Frontiers in Neuroscience (2019). doi:10.3389/fnins.2019.00384 • Wei, M. Yoga could slow the harmful effects of stress and inflammation. Harvard Health Blog (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. Alzheimer's and Dementia (2014). doi:10.1016/j.jalz.2013.12.010 • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. International Journal of Biological Sciences (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? F1000 Medicine Reports 4, (2012). • Loos B, et al. Polymorphisms in an interferon-? receptor-1 gene marker and susceptibility to periodontitis. Acta Odontol. Scand. (2003). doi:10.1080/00016350310006168 • Simpson, N. & Dinges, D. F. Sleep and Inflammation. Nutr. Rev. (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Kalogeropoulos, A. P., Georgiopoulos, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. Heart Failure Clinics (2012). doi:10.1016/j.hfc.2011.08.002 • Accordini, S. et al. An Interleukin 13 polymorphism is associated with symptom severity in adult subjects with asthma. PLoS One (2016). doi:10.1371/journal.pone.0151292 • Chen, P., Chen, C., Chen, K., Xu, T. & Luo, C. Polymorphisms in IL-4/IL-13 pathway genes and glioma risk: an updated meta-analysis. Tumour Biology (2014). doi:10.1007/s13277-014-2895-8 • Liu, Z. et al. A meta-analysis of IL-13 polymorphisms and pediatric asthma risk. Medical science monitor : international medical journal of experimental and clinical research. (2014). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25502839>. • Egli, A. et al. IL-28B is a Key Regulator of B- and T-Cell Vaccine Responses against Influenza. PLoS Pathog. (2014). doi:10.1371/journal.ppat.1004556 • Seyfzadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients to multiple sclerosis. Am. J. Clin. Exp. Immunol. (2014). • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. Curr. Opin. Gastroenterol. (2015). doi:10.1097/MOG.0000000000000186 • Sonntag, K. et al. Chronic graft-versus-host-disease in CD34+humanized NSG mice is associated with human susceptibility HLA haplotypes for autoimmune disease. J. Autoimmunity. (2015). doi:10.1016/j.jaut.2015.06.006 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. Cytokine (2015). doi:10.1016/j.cyto.2015.05.023 • Cianferoni, A. & Spergel, J. M. From genetics to treatment of eosinophilic esophagitis. Current Opinion in Allergy and Clinical Immunology (2015). doi:10.1097/ACI.0000000000000200 • Narozna, B. et al. Polymorphisms in the interleukin 4, interleukin 4

receptor and interleukin 13 genes and allergic phenotype: A case control study. *Adv. Med. Sci.* (2016). doi:10.1016/j.advms.2015.07.003 • Shamran, H. A. et al. Single nucleotide polymorphisms in IL-10, IL-12p40, and IL-13 genes and susceptibility to glioma. *Int. J. Med. Sci.* (2015). doi:10.7150/ijms.12609 • Mitchell, J. A. et al. IL-13 Augments Compressive Stress-Induced Tissue Factor Expression in Human Airway Epithelial Cells. *Am. J. Respir. Cell Mol. Biol.* (2016). doi:10.1165/rncmb.2015-0252OC • Nicodemus-Johnson, J. et al. Genome-wide methylation study identifies an IL-13-induced epigenetic signature in asthmatic airways. *Am. J. Respir. Crit. Care Med.* (2016). doi:10.1164/rccm.201506.12430C • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Becher, B., Spath, S. & Goverman, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. *J. Exp. Neurosci.* (2018). doi:10.1177/1179069518793639 • DiSabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016).

IL5

• Wei, M. Yoga could slow the harmful effects of stress and inflammation. *Harvard Health Blog* (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. *Frontiers in Neuroscience* (2019). doi:10.3389/fnins.2019.00384 • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. *J. Exp. Neurosci.* (2018). doi:10.1177/1179069518793639 • Simpson, N. & Dinges, D. F. Sleep and Inflammation. *Nutr. Rev.* (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. In *Annals of the New York Academy of Sciences* (2009). doi:10.1196/annals.1393.013 • Becher, B., Spath, S. & Goverman, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. *Frontiers in Human Neuroscience* (2017). doi:10.3389/fnhum.2017.00316 • Kalogeropoulos, A. P., Georgiopoulos, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. *Heart Failure Clinics* (2012). doi:10.1016/j.hfc.2011.08.002 • Simpson, N. & Dinges, D. F. Sleep and Inflammation. *Nutr. Rev.* (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Loos B, et al. Polymorphisms in an interferon- γ receptor-1 gene marker and susceptibility to periodontitis. *Acta Odontol. Scand.* (2003). doi:10.1080/00016350310006168 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? *F1000 Medicine Reports* 4, (2012). • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. *Alzheimer's and Dementia* (2014). doi:10.1016/j.jalz.2013.12.010

IL6

• Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. *J. Exp. Neurosci.* (2018). doi:10.1177/1179069518793639 • Becher, B., Spath, S. & Goverman, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • DiSabato, D. J., Quan, N., & Godbout, J. P. (2016). Neuroinflammation: the devil is in the details. *Journal of neurochemistry*, 139 Suppl 2(Suppl 2), 136–153. <https://doi.org/10.1111/jnc.13607> • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Kalogeropoulos, A. P., Georgiopoulos, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. *Heart Failure Clinics* (2012). doi:10.1016/j.hfc.2011.08.002 • Simpson, N. & Dinges, D. F. Sleep and Inflammation. *Nutr. Rev.* (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Loos B, et al. Polymorphisms in an interferon- γ receptor-1 gene marker and susceptibility to periodontitis. *Acta Odontol. Scand.* (2003). doi:10.1080/00016350310006168 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? *F1000 Medicine Reports* 4, (2012). • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. *Alzheimer's and Dementia* (2014). doi:10.1016/j.jalz.2013.12.010 • Wei, M. Yoga could slow the harmful effects of stress and inflammation. *Harvard Health Blog* (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. *Frontiers in Neuroscience* (2019). doi:10.3389/fnins.2019.00384 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. In *Annals of the New York Academy of Sciences* (2009). doi:10.1196/annals.1393.013 • Fishman, D. et al. The effect of novel polymorphisms in the interleukin-6 (IL-6) gene on IL-6 transcription and plasma IL-6 levels, and an association with systemic-onset juvenile chronic arthritis. *J. Clin. Invest.* (1998). doi:10.1172/JCI2629 • Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* (2008). doi:10.1016/j.ejca.2015.06.122 • Illig, T. et al. Significant association of the interleukin-6 gene polymorphisms C-174G and A-598G with type 2 diabetes. *J. Clin. Endocrinol. Metab.* (2004). doi:10.1210/jc.2004-0355 • Baumer, P., Lake, M. J., Stewart, C. E., Drust, B. & Erskine, M. Genetic variation and exercise-induced muscle damage: implications for athletic performance, injury and ageing. *European Journal of Applied Physiology* (2016). doi:10.1007/s00421-016-3411-2 • Buixens, A. et al. Can we predict top-level sports performance in power vs endurance events? A genetic approach. *Scand. J. Med. Sci. Sport.* (2011). doi:10.1111/j.1600-0838.2009.01079.x • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. *Frontiers in Human Neuroscience* (2017). doi:10.3389/fnhum.2017.00316 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. *Harvard Health* (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget* (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>.

STAT4

• Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget* (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. *Harvard Health* (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. *Frontiers in Human Neuroscience* (2017). doi:10.3389/fnhum.2017.00316 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. In *Annals of the New York Academy of Sciences* (2009). doi:10.1196/annals.1393.013 • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. *Frontiers in Neuroscience* (2019). doi:10.3389/fnins.2019.00384 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. In *Annals of the New York Academy of Sciences* (2009). doi:10.1196/annals.1393.013 • DiSabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • Sigurdsson, S. et al. A risk haplotype of STAT4 for systemic lupus erythematosus is over-expressed, correlates with anti-dsDNA and shows additive effects with two risk alleles of IRF5. *Hum. Mol. Genet.* (2008). doi:10.1093/hmg/ddn184 • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. *Frontiers in Human Neuroscience* (2017). doi:10.3389/fnhum.2017.00316 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. *Harvard Health* (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • O'Shea, J. J., Lahesmaa, R., Vahedi, G., Laurence, A. & Kanno, Y. Genomic views of STAT function in CD4 + T helper cell differentiation. *Nature Reviews Immunology* (2011). doi:10.1038/nri2958 • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? *Autoimmune Disease: Why Is My Immune System Attacking Itself?* | Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>. • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. *Healthline* (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders#treatment>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget* (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. *J. Exp. Neurosci.* (2018). doi:10.1177/1179069518793639 • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>. • Lamana, A. et al. The minor allele of rs1754865 in the STAT4 gene is associated with increased mRNA and protein expression. *PLoS One* (2015). doi:10.1371/journal.pone.0142683 • Wang, Y., Qu, A. & Qu, A. Signal transducer and activator of transcription 4 in liver diseases. *International Journal of Biological Sciences* (2015). doi:10.7150/ijbs.11164 • Yan, N. et al. Association between STAT4 Gene Polymorphisms and Autoimmune Thyroid Diseases in a Chinese Population. *Int. J. Mol. Sci.* (2014). doi:10.3390/ijms150712280 • McWilliams, I. L., Rajbhandari, R., Nozell, S., Benveniste, E. & Harrington, L. E. STAT4 controls GM-CSF production by both Th1 and Th17 cells during EAE. *J. Neuroinflammation* (2015). doi:10.1186/s12974-015-0351-3 • Jabeen, R. et al. Altered STAT4 Isoform Expression in Patients with Inflammatory Bowel Disease. *Inflamm. Bowel Dis.* (2015). doi:10.1097/MIB.0000000000000495 • Namjou, B. et al. High-density genotyping of STAT4 reveals multiple haplotypic associations with Systemic lupus erythematosus in different racial groups. *Arthritis Rheum.* (2009). doi:10.1002/art.24387 • Glas, J. et al. Evidence for STAT4 as a common autoimmune gene: Rs7574865 is associated with colonic Crohn's disease and early disease onset. *PLoS One* (2010). doi:10.1371/journal.pone.0010373 • Lamana, A. et al. The TT genotype of the STAT4 rs7574865 polymorphism is associated with high disease activity and disability in patients with early arthritis. *PLoS One* (2012). doi:10.1371/journal.pone.0043661 • Gourh, P. et al. Polymorphisms in TBX21 and STAT4 increase the risk of systemic sclerosis: Evidence of possible gene-gene interaction and alterations in Th1/Th2 cytokines. *Arthritis Rheum.* (2009). doi:10.1002/art.24958 • Sugiura, T. et al. Association between a C8orf13-BLK polymorphism and polymyositis/dermatomyositis in the Japanese population: An additive effect with STAT4 on disease susceptibility. *PLoS One* (2014). doi:10.1371/journal.pone.0090019 • Svensson, A. et al. STAT4 Regulates Antiviral Gamma Interferon Responses and Recurrent Disease during Herpes Simplex Virus 2 Infection. *J. Virol.* (2012). doi:10.1128/JVI.00947-12

TNF

• Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. *Healthline* (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders#treatment>. • Idriess, H. T. & Naismith, J. H. TNF γ and the TNF receptor superfamily: Structure-function relationship(s). *Microsc. Res. Tech.* (2000). doi:10.1002/1097-0029(20000801)50:3<3.0.CO;2-H • Kalogeropoulos, A. P., Georgiopoulos, V. V. & Butler, J. From Risk Factors to Structural Heart Disease: The Role of Inflammation. *Heart Failure Clinics* (2012). doi:10.1016/j.hfc.2011.08.002 • Tanaka, T. & Kishimoto, T. Targeting interleukin-6: All the way to treat autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Ferreira, S. T., Clarke, J. R., Bomfim, T. R. & De Felice, F. G. Inflammation, defective insulin signaling, and neuronal dysfunction in Alzheimer's disease. *Alzheimer's and Dementia* (2014). doi:10.1016/j.jalz.2013.12.010 • Wei, M. Yoga could slow the harmful effects of stress and inflammation. *Harvard Health Blog* (2020). Available at: <https://www.health.harvard.edu/blog/yoga-could-slow-the-harmful-effects-of-stress-and-inflammation-2017101912588>. • Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. *Frontiers in Neuroscience* (2019). doi:10.3389/fnins.2019.00384 • Oke, S. L. & Tracey, K. J. The inflammatory reflex and the role of complementary and alternative medical therapies. In *Annals of the New York Academy of Sciences* (2009). doi:10.1196/annals.1393.013 • Liu, Y. Z., Wang, Y. X. & Jiang, C. L. Inflammation: The common pathway of stress-related diseases. *Frontiers in Human Neuroscience* (2017). doi:10.3389/fnhum.2017.00316 • Harvard Health Publishing. Take steps to prevent or reverse stress-related health problems. *Harvard Health* (2017). Available at: <https://www.health.harvard.edu/stress/take-steps-to-prevent-or-reverse-stress-related-health-problems>. • Chen, L. et al. Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget* (2018). doi:10.18632/oncotarget.23208 • Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • DiSabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • Simpson, N. & Dinges, D. F. Sleep and Inflammation. *Nutr. Rev.* (2007). doi:10.1111/j.1753-4887.2007.tb00371.x • Chen, S. et al. Associations between TNF- γ 308A/G Polymorphism and Susceptibility with Dermatomyositis: A Meta-Analysis. *PLoS ONE* 9, (2014). • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? *F1000 Medicine Reports* 4, (2012). • Chen, M. et al. Tumor Necrosis Factor (TNF) -308G>A, Nitric Oxide Synthase 3 (NOS3) +894G>T polymorphisms and migraine risk: A meta-analysis. *PLoS One* (2015). doi:10.1371/journal.pone.0129372 • Lee, J. et al. Genetic polymorphisms in codon 10 of the transforming growth factor- γ 1 gene in patients with alcoholic liver cirrhosis. *Korean J. Hepatol.* (2011). doi:10.3350/kjhep.2011.17.1.37 • Zeng, X., Zhang, L., Gu, H. & Gu, Y. Association between TNF- γ 308 A/G polymorphism and COPD susceptibility: a meta-analysis update. *International Journal of Chronic Obstructive Pulmonary Disease* 1367 (2016). doi:10.2147/copd.s105394 • Li, M., Han, Y., Wu, T. T., Feng, Y. & Wang, H. B. Tumor Necrosis Factor Alpha rs1800629 Polymorphism and Risk of Cervical Lesions: A Meta-Analysis. *PLoS One* (2013). doi:10.1371/journal.pone.0069201 • Guo, X. F. et al. TNF- γ 308 polymorphism and risk of digestive system cancers: A meta-analysis. *World J. Gastroenterol.* (2013). doi:10.3748/wjg.v19.i48.9461 • Ma, Zhang & Baloch. Pathogenetic and Therapeutic Applications of Tumor Necrosis Factor- γ (TNF- γ) in Major Depressive Disorder: A Systematic Review. *Int. J. Mol. Sci.* (2016). doi:10.1016/j.cherd.2012.09.019 • Khan, S. et al. TNF- γ 308 G>?A (rs1800629) Polymorphism is Associated with Celiac Disease: A Meta-analysis of 11 Case-Control Studies. *Scientific Reports* 6, (2016). • Li, H. H. et al. Tumor Necrosis Factor- γ Gene Polymorphism is Associated with Metastasis in Patients with Triple Negative Breast Cancer. *Sci. Rep.* (2015). doi:10.1038/srep10244 • Aghyan, G. et al. Relation between inflammatory cytokine levels in serum and bronchoalveolar lavage fluid and gene polymorphism in young adult patients with bronchiectasis. *J. Thorac. Dis.* (2014). doi:10.3978/j.issn.272-1439.2014.04.14 • Loos B, et al. Polymorphisms in an interferon- γ receptor-1 gene marker and susceptibility to periodontitis. *Acta Odontol. Scand.* (2003). doi:10.1080/00016350310006168 • Laddha, N. C., Dwivedi, M., Gani, A. R., Mansuri, M. S. & Begum, R. Tumor Necrosis Factor B (TNFB) genetic variants and its increased expression are associated with vitiligo susceptibility. *PLoS One* (2013). doi:10.1371/journal.pone.0081736 • Yang, J.-K., Wu, W.-J., Qi, J., He, L. & Zhang, Y.-P. TNF-308 G/A Polymorphism and Risk of Acne Vulgaris: A Meta-Analysis. *PLoS ONE* 9, (2014). • Feng, R. N., Zhao, C., Sun, C. H. & Li, Y. Meta-analysis of TNF 308 G/A polymorphism and type 2 diabetes mellitus. *PLoS One* (2011). doi:10.1371/journal.pone.0018480 • Delongui, F. et al. Association of tumor necrosis factor β genetic polymorphism and sepsis susceptibility. *Exp. Ther. Med.* (2011). doi:10.3892/etm.2011.213 • Western, K. A. Overview of the Immune System | National Institute of Allergy and Infectious Diseases (NIAID): An Overview. National Institute of Allergy and Infectious Diseases, NIH 3–8 (2008). doi:10.1007/978-1-59745-569-5_1 • Johns Hopkins Medicine Pathology. Definition of Autoimmunity & Autoimmune Disease. Definition of Autoimmunity & Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmune/definitions>. • Orbai, A.-M. Autoimmune Disease: Why Is My Immune System Attacking Itself? *Autoimmune Disease: Why Is My Immune System Attacking Itself?* | Johns Hopkins Medicine Available at: <https://www.hopkinsmedicine.org/health/wellness-and-prevention/autoimmune-disease-why-is-my-immune-system-attacking-itself>.

METHYLATION SNP References

FOLR2

• Scaglione, F. & Panzavolta, G. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. *Xenobiotica* (2014). doi:10.3109/00498254.2013.845705 • Freisheim, J. H., Price, E. M. & Ratnam, M. Folate coenzyme and antifolate transport proteins in normal and neoplastic cells. *Adv. Enzyme Regul.* (1989). doi:10.1016/0065-2571(89)90091-5 • Ragoussis, J., Senger, G., Trowsdale, J. & Campbell, I. G. Genomic organization of the human folate receptor genes on chromosome 11q13. *Genomics* (1992). doi:10.1016/S0888-7543(05)80236-8 • Voutilainen, S., Rissanen, T. H., Virtanen, J., Lakka, T. A. & Salonen, J. T. Low dietary folate intake is associated with an excess incidence of acute coronary events: The Kuopio Ischemic Heart Disease Risk Factor Study. *Circulation* (2001). doi:10.1161/01.CIR.103.22.2674 • Nakashima-Matsushita, N. et al. Selective expression of folate receptor beta and its possible role in methotrexate transport in synovial macrophages from patients with rheumatoid arthritis. *Arthritis Rheum.* (1999). doi:10.1002/1529-0131(199908)42:83.0.CO;2-L • Suzuki, Y., Yoshitomo-Nakagawa, K., Maruyama, K., Suyama, A. & Sugano, S. Construction and characterization of a full length-enriched and a 5'-end-enriched cDNA library. *Gene* (1997). doi:10.1016/S0378-1119(97)00411-3 • Page, S. T., Owen, W. C., Price, K. & Elwood, P. C. Expression of the Human Placental Folate Receptor Transcript is Regulated in Human Tissues. *Journal of Molecular Biology* 229, 1175–1183 (1993). • Shen, F., Ross, J. F., Wang, X. & Ratnam, M. Identification of a novel folate receptor, a truncated receptor, and receptor type beta in hematopoietic cells: cDNA cloning, expression, immunoreactivity, and tissue specificity. *Biochemistry* (1994). doi:10.1021/bi00171a021 • Ratnam, M., Marquardt, H., Duhning, J. L. & Freisheim, J. H. Homologous membrane folate binding proteins in human placenta: cloning and sequence of a cDNA. *Biochemistry* (1989). • 5-Methyltetrahydrofolate. National Center for Biotechnology Information. PubChem Compound Database (2004). Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/135483998>. • Office of Dietary Supplements - Folate. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/> • Link, R. 15 Healthy Foods That Are High in Folate (Folic Acid). *Healthline* (2020). Available at: <https://www.healthline.com/nutrition/foods-high-in-folate-folic-acid/#6.-Citrus-fruits>. • Strausberg, R. L. et al. Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences. *Proc. Natl. Acad. Sci. U. S. A.* (2002). doi:10.1073/pnas.242603899 • Ducker, G. S. & Rabinowitz, J. D. One-Carbon Metabolism in Health and Disease. *Cell Metabolism* (2017). doi:10.1016/j.cmet.2016.08.009 • Henderson, G. B. Folate-binding proteins. *Annu. Rev. Nutr.* (1990). doi:10.1146/annurev.nutr.10.1.319 • Abu Seman, N., Wan Mohamad, W. N., Östenson, C. G., Brismar, K. & Gu, H. F. Increased DNA methylation of the slc30a8 gene promoter is associated with type 2 diabetes in a malay population. *Clin. Epigenetics* (2015). doi:10.1186/s13148-015-0049-5 • Tanaka, T. et al. Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations. *Am. J. Hum. Genet.* (2009). doi:10.1016/j.ajhg.2009.02.011 • Moore, L. D., Le, T. & Fan, G. DNA methylation and its basic function. *Neuropsychopharmacology* (2013). doi:10.1038/npp.2012.112

MTHFR

• Mischoulon, D. & Raab, M. F. The role of folate in depression and dementia. *Journal of Clinical Psychiatry* (2007). • Goyette, P. et al. Human methylentetrahydrofolate reductase: Isolation of cDNA, mapping and mutation identification. *Nat. Genet.* (1994). doi:10.1038/ng0694-195 • Hua, Y., Zhao, H., Kong, Y. & Lu, X. Association between Alzheimer's disease and the NOS3 gene Glu298Asp polymorphism. *Int. J. Neurosci.* (2004). doi:10.3109/00207454.2013.834336 • Tran, P. et al. Multiple transcription start sites and alternative splicing in the methylentetrahydrofolate reductase gene result in two enzyme isoforms. *Mamm. Genome* (2002). doi:10.1007/s00335-002-2167-6 • Födinger, M., Hörl, W. H. & Sunder-Plassmann, G. Molecular biology of 5,10-methylenetetrahydrofolate reductase. *Journal of Nephrology* (2000). doi:10.5860/CHOICE.39-4838 • E. Trimmer, E. Methylentetrahydrofolate Reductase: Biochemical Characterization and Medical Significance. *Curr. Pharm. Des.* (2013). doi:10.2174/13816128113139140008 • Wu, X. et al. Association Between the MTHFR C677T Polymorphism and Recurrent Pregnancy Loss: A Meta-Analysis. *Genet. Test. Mol. Biomarkers* (2012). doi:10.1089/gtmb.2011.0318 • Voutilainen, S., Rissanen, T. H., Virtanen, J., Lakka, T. A. & Salonen, J. T. Low dietary folate intake is associated with an excess incidence of acute coronary events: The Kuopio Ischemic Heart Disease Risk Factor Study. *Circulation* (2001). doi:10.1161/01.CIR.103.22.2674 • Ducker, G. S. & Rabinowitz, J. D. One-Carbon Metabolism in Health and Disease. *Cell Metabolism* (2017). doi:10.1016/j.cmet.2016.08.009 • Papakostas, G. I. et al. Effect of adjunctive L-methylfolate 15 mg among inadequate responders to SSRIs in depressed patients who were stratified by Biomarker levels and genotype: Results from a randomized clinical trial. in *Journal of Clinical Psychiatry* (2014). doi:10.4088/JCP.130808947 • Schneider, J. A., Rees, D. C., Liu, Y.-T. & Clegg, J. B. Worldwide Distribution of a Common Methylentetrahydrofolate Reductase Mutation. *The American Journal of Human Genetics* 62, 1258–1260 (1998). • Moore, L. D., Le, T. & Fan, G. DNA methylation and its basic function. *Neuropsychopharmacology* (2013). doi:10.1038/npp.2012.112 • Scaglione, F. & Panzavolta, G. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. *Xenobiotica* (2014). doi:10.3109/00498254.2013.845705 • 5-Methyl-tetrahydrofolate. National Center for Biotechnology Information. PubChem Compound Database (2004). Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/135483998>. • Office of Dietary Supplements - Folate. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/> • Sibani, S. et al. Characterization of six novel mutations in the methylentetrahydrofolate reductase (MTHFR) gene in patients with homocystinuria. *Hum. Mutat.* (2000). doi:10.1002/(SICI)1098-1004(200003)15:33.0.CO;2-I • Goyette, P. et al. Human methylentetrahydrofolate reductase: Isolation of cDNA, mapping and mutation identification. *Nat. Genet.* (1994). doi:10.1038/ng0694-195 • Abu Seman, N., Wan Mohamad, W. N., Östenson, C. G., Brismar, K. & Gu, H. F. Increased DNA methylation of the slc30a8 gene promoter is associated with type 2 diabetes in a malay population. *Clin. Epigenetics* (2015). doi:10.1186/s13148-015-0049-5 • Link, R. 15 Healthy Foods That Are High in Folate (Folic Acid). *Healthline* (2020). Available at: <https://www.healthline.com/nutrition/foods-high-in-folate-folic-acid/#6.-Citrus-fruits>. • Matthews, R. G. & Daubner, S. C. Modulation of methylentetrahydrofolate reductase activity by S-adenosylmethionine and by dihydrofolate and its polyglutamate analogues. *Adv. Enzyme Regul.* (1982). doi:10.1016/0065-2571(82)90012-7 • Yamada, K., Strahler, J. R., Andrews, P. C. & Matthews, R. G. Regulation of human methylentetrahydrofolate reductase by phosphorylation. *Proc. Natl. Acad. Sci.* (2005). doi:10.1073/pnas.0504786102 • Tanaka, T. et al. Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations. *Am. J. Hum. Genet.* (2009). doi:10.1016/j.ajhg.2009.02.011 • Schwahn, B. & Rozen, R. Polymorphisms in the methylentetrahydrofolate reductase gene: Clinical consequences. *American journal of pharmacogenomics / genomics-related research in drug development and clinical practice* (2001). doi:10.2165/00129785-200101030-00004 • Yamada, K., Chen, Z., Rozen, R. & Matthews, R. G. Effects of common polymorphisms on the properties of recombinant human methylentetrahydrofolate reductase. *Proc. Natl. Acad. Sci.* (2001). doi:10.1073/pnas.261469998 • Voutilainen, S., Rissanen, T. H., Virtanen, J., Lakka, T. A. & Salonen, J. T. Low dietary folate intake is associated with an excess incidence of acute coronary events: The Kuopio Ischemic Heart Disease Risk Factor Study. *Circulation* (2001). doi:10.1161/01.CIR.103.22.2674 • Bailey, L. B. Folate, Methyl-Related Nutrients, Alcohol, and the MTHFR 677C>T Polymorphism Affect Cancer Risk: Intake Recommendations. *J. Nutr.* (2003). doi:10.1093/jn/133.11.3749S • Nishiyama, M., Kato, Y., Hashimoto, M., Yukawa, S. & Omori, K. Apolipoprotein E, Methylentetrahydrofolate Reductase(MTHFR) Mutation and the Risk of Senile Dementia. An Epidemiological Study Using the Polymerase Chain Reaction(PCR) Method. *J. Epidemiol.* (2000). doi:10.2188/jea.10.163 • Reilly, R., McNulty, H., Pentieva, K., Strain, J. J. & Ward, M. MTHFR 677TT genotype and disease risk: Is there a modulating role for B-vitamins?. *Proc. Nutr. Soc.* (2014). doi:10.1017/S0029665113003613

TCN2

• Regec, A., Quadros, E. V., Platica, O. & Rothenberg, S. P. The cloning and characterization of the human transcobalamin II gene. *Blood* (1995). • Linnebank, M. et al. Association of transcobalamin c. 776C>G with overall survival in patients with primary central nervous system lymphoma. *Br. J. Cancer* (2012). doi:10.1038/bjc.2012.476 • Martinelli, M. et al. A candidate gene study of one-carbon metabolism pathway genes and colorectal cancer risk. *Br. J. Nutr.* (2013). doi:10.1017/S0007114512002796 • Moore, L. D., Le, T. & Fan, G. DNA methylation and its basic function. *Neuropsychopharmacology* (2013). doi:10.1038/npp.2012.112 • Tanaka, T. et al. Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations. *Am. J. Hum. Genet.* (2009). doi:10.1016/j.ajhg.2009.02.011 • Koushik, A. et al. Nonsynonymous polymorphisms in genes in the one-carbon metabolism pathway and associations with colorectal cancer. *Cancer Epidemiol. Biomarkers Prev.* (2006). doi:10.1158/1055-9965.EPI-06-0624 • Semeco, A. Top 12 Foods That Are High in Vitamin B12. *Healthline* (2020). Available at: <https://www.healthline.com/nutrition/vitamin-b12-foods/#10.-Fortified-nondairy-milk>. • Mills, J. L. et al. Folate-related genes and omphalocele. *Am. J. Med. Genet.* (2005). doi:10.1002/ajmg.a.30772 • Martinelli, M. et al. Idiopathic pulmonary fibrosis and polymorphisms of the folate pathway genes. *Clin. Biochem.* (2013). doi:10.1016/j.clinbiochem.2012.10.009 • Office of Dietary Supplements - Vitamin B12. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/#:~:text=Vitamin%20B12%20is%20naturally%20found,5%2C13%2D15%5D>. • Miller, A. L. The methionine-homocysteine cycle and its effects on cognitive diseases. *Alternative Medicine Review* (2003). • Teplitzky, V. et al. Hereditary partial transcobalamin II deficiency with neurologic, mental and hematologic abnormalities in children and adults. *Isr. Med. Assoc. J.* (2003). • Refsum, H., Johnston, C., Guttormsen, A. B. & Nexø, E. Holotranscobalamin and total transcobalamin in human plasma: Determination, determinants, and reference values in healthy adults. *Clin. Chem.* (2006). doi:10.1373/clinchem.2005.054619 • Seetharam, B., Bose, S. & Li, N. Cellular Import of Cobalamin (Vitamin B-12) 1,2. *J. Nutr* (1999). • Winkelmayer, W. C., Skoupy, S., Eberle, C., Födinger, M. & Sunder-Plassmann, G. Effects of TCN2 776C>G on vitamin B, folate, and total homocysteine levels in kidney transplant patients. *Kidney international*. (2004). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15086930> • Hoffbrand, A. V., Tripp, E., Jackson, B. F., Luck, W. E. & Frater-Schroder, M. N. Hereditary Abnormal Transcobalamin II Previously Diagnosed as Congenital Dihydrofolate Reductase Deficiency. *New England Journal of Medicine* 310, 789–790 (1984). • Garg, G. et al. Polymorphisms in transcobalamin II gene is associated with coronary artery disease in Indian population. *Biomarkers* (2012). doi:10.3109/1354750X.2011.642408 • Cascalha, J. F. et al. Association of the transcobalamin II gene 776C>G polymorphism with Alzheimer's type dementia: dependence on the 5, 10-methylenetetrahydrofolate reductase 1298A>C polymorphism genotype. *Ann. Clin. Biochem.* (2015). doi:10.1177/0004563214561770

NEUROTRANSMITTER SNP References

ADRA2A

• Attention-deficit/hyperactivity disorder (ADHD) in children. Mayo Clinic (2019). Available at: <https://www.mayoclinic.org/diseases-conditions/adhd/diagnosis-treatment/drc-20350895#:~:text=Standard treatments for ADHD in,works best for your child.> • Amanda Capritto, A. C. E.-C. P. T. What Is the Low Sugar Diet? Verywell Fit Available at: <https://www.verywellfit.com/low-sugar-diet-pros-cons-and-how-it-works-4689214#:~:text=The low sugar diet involves, and vital vitamins and antioxidants.> • S.N., R. et al. Association of ADRA2A and MTHFR gene polymorphisms with weight loss following antipsychotic switching to aripiprazole or ziprasidone. *Human Psychopharmacology* (2014). • Zhang, J. P. et al. Pharmacogenetic Associations of Antipsychotic Drug-Related Weight Gain: A Systematic Review and Meta-analysis. *Schizophren. Bull.* (2016). doi:10.1093/schbul/sbw058 • Kumar, S. et al. Significant role of ADRB3 rs4994 towards the development of coronary artery disease. *Coron. Artery Dis.* 25, 29–34 (2014). • Comings, D. E. et al. Additive effect of three noradrenergic genes (ADRA2A, ADRA2C, DBH) on attention-deficit hyperactivity disorder and learning disabilities in Tourette syndrome subjects. *Clin. Genet.* 55, 160–172 (1999). • Thorp, A. A. & Schlaich, M. P. Relevance of sympathetic nervous system activation in obesity and metabolic syndrome. *J. Diabetes Res.* (2015). doi:10.1155/2015/341583 • Davy, K. P. & Orr, J. S. Sympathetic nervous system behavior in human obesity. *Neuroscience and Biobehavioral Reviews* (2009). doi:10.1016/j.neubiorev.2008.05.024 • Attention-deficit/hyperactivity disorder (ADHD) in children. Mayo Clinic (2019). Available at: <https://www.mayoclinic.org/diseases-conditions/adhd/diagnosis-treatment/drc-20350895#:~:text=Standard treatments for ADHD in,works best for your child.>

COMT

• Lotta, T. et al. Kinetics of Human Soluble and Membrane-Bound Catechol O-Methyltransferase: A Revised Mechanism and Description of the Thermolabile Variant of the Enzyme. *Biochemistry* (1995). doi:10.1021/bi00013a008 • Stein, M. B., Fallin, M. D., Schork, N. J. & Gelernter, J. COMT polymorphisms and anxiety-related personality traits. *Neuropsychopharmacology* (2005). doi:10.1038/sj.npp.1300787 • Lee, L. O. & Prescott, C. A. Association of the catechol-O-methyltransferase val158met polymorphism and anxiety-related traits: A meta-analysis. *Psychiatr. Genet.* (2014). doi:10.1097/YPG.000000000000018 • Ulanen, I. et al. Expression and intracellular localization of catechol O-methyltransferase in transfected mammalian cells. *Eur. J. Biochem.* (1997). doi:10.1111/j.1432-1033.1997.0452a.x • Axelrod, J. O-methylation of epinephrine and other catechols in vitro and in vivo. *Science* (80-.). (1957). doi:10.1126/science.126.3270.400 • Tai, C. H. & Wu, R. M. Catechol-O-methyltransferase and Parkinson's disease. *Acta Medica Okayama* (2002). • Grossman, M. H., Emanuel, B. S. & Budarf, M. L. Chromosomal mapping of the human catechol-O-methyltransferase gene to 22q11.1? q11.2. *Genomics* (1992). doi:10.1016/0888-7543(92)90316-K • Golan, D. E., Armstrong, E. J. & Armstrong, A. W. Principles of pharmacology: the pathophysiologic basis of drug therapy. (Wolters Kluwer Health, 2017). • Bonifácio, B. L., Palma, P. N., Almeida, L. & Soares-Da-Silva, P. Catechol-O-methyltransferase and its inhibitors in Parkinson's disease. *CNS Drug Reviews* (2007). doi:10.1111/j.1527-3458.2007.00020.x • Wichers, M. et al. The Catechol-O-methyl transferase Val158Met polymorphism and experience of reward in the flow of daily life. *Neuropsychopharmacology* (2008). doi:10.1038/sj.npp.1301520 • Diamond, A., Briand, L., Fossella, J. & Gehlbach, L. Genetic and Neurochemical Modulation of Prefrontal Cognitive Functions in Children. *Am. J. Psychiatry* (2004). doi:10.1176/appi.ajp.161.1.125 • Robinson, S., Goddard, L., Dritschel, B., Wisley, M. & Howlin, P. Executive functions in children with Autism Spectrum Disorders. *Brain Cogn.* (2009). doi:10.1016/j.bandc.2009.06.007 • Bruder, G. E. et al. Catechol-O-methyltransferase (COMT) genotypes and working memory: Associations with differing cognitive operations. *Biol. Psychiatry* (2005). doi:10.1016/j.biopsych.2005.05.010 • Chen, J. et al. Functional analysis of genetic variation in catechol-O-methyltransferase (COMT): Effects on mRNA, protein, and enzyme activity in postmortem human brain. *Am. J. Hum. Genet.* (2004). doi:10.1086/425589

DBH

• Rahman, M. K., Rahman, F., Rahman, T. & Kato, T. Dopamine-?-hydroxylase (DBH), its cofactors and other biochemical parameters in the serum of neurological patients in Bangladesh. Int. J. Biomed. Sci. (2009). doi:10.1016/j.ijcard.2009.09.092 • Barrie, E. S., Weinshenker, D., Verma, A., Pendergrass, S. A., Lange, L. A., Ritchie, M. D., ... Sadee, W. (2014). Regulatory polymorphisms in human DBH affect peripheral gene expression and sympathetic activity. Circulation Research. <https://doi.org/10.1161/CIRCRESAHA.116.304398> • Das, M., Bhowmik, A. Das, Bhaduri, N., Sarkar, K., Ghosh, P., Sinha, S., ... Mukhopadhyay, K. (2011). Role of gene-gene/gene-environment interaction in the etiology of eastern Indian ADHD probands. Progress in Neuro-Psychopharmacology and Biological Psychiatry. <https://doi.org/10.1016/j.pnpbp.2010.12.027> • Das Bhowmik, A., Sarkar, K., Ghosh, P., Das, M., Bhaduri, N., Sarkar, K., ... Mukhopadhyay, K. (2017). Significance of Dopaminergic Gene Variants in the Male Biasness of ADHD. Journal of Attention Disorders. <https://doi.org/10.1177/1087054713494004> • Fang, Y., Ji, N., Cao, Q., Su, Y., Chen, M., Wang, Y., & Yang, L. (2015). Variants of Dopamine Beta Hydroxylase Gene Moderate Atomoxetine Response in Children with Attention-Deficit/Hyperactivity Disorder. Journal of Child and Adolescent Psychopharmacology. <https://doi.org/10.1089/cap.2014.0178> • Parasuraman, R., de Visser, E., Lin, M. K., & Greenwood, P. M. (2012). Dopamine beta hydroxylase genotype identifies individuals less susceptible to bias in computer-assisted decision making. PLoS ONE. <https://doi.org/10.1371/journal.pone.0039675> • Sezer, S., Kurt, S., & Ates, O. (2016). Analysis of dopamine beta hydroxylase gene polymorphisms in migraine. Clinical Neurology and Neurosurgery. <https://doi.org/10.1016/j.clineuro.2016.02.002> • Sun, Z., Ma, Y., Li, W., He, J., Li, J., Yang, X., ... Tang, Y. L. (2018). Associations between the DBH gene, plasma dopamine ?-hydroxylase activity and cognitive measures in Han Chinese patients with schizophrenia. Schizophrenia Research. <https://doi.org/10.1016/j.schres.2017.06.028> • Sundararajan, R. (2013). Effect of DBH, DRD2 and ADRA2A gene variants on human working memory. Dissertation Abstracts International: Section B: The Sciences and Engineering.

GAD1

• GAD1 glutamate decarboxylase 1 [Homo sapiens (human)] - Gene - NCBI. National Center for Biotechnology Information (2020). Available at: <https://www.ncbi.nlm.nih.gov/gene/2571>. • KELLY, C. D. et al. Nucleotide sequence and chromosomal assignment of a cDNA encoding the large isoform of human glutamate decarboxylase. Ann. Hum. Genet. (1992). doi:10.1111/j.1469-1809.1992.tb01150.x • Giordà, R., Peakman, M., Tan, K. C., Vergani, D. & Trucco, M. Glutamic acid decarboxylase expression in islets and brain. The Lancet (1991). doi:10.1016/0140-6736(91)92781-V • Dirx, R. et al. Targeting of the 67-kDa isoform of glutamic acid decarboxylase to intracellular organelles is mediated by its interaction with the NH2- terminal region of the 65-kDa isoform of glutamic acid decarboxylase. J. Biol. Chem. (1995). doi:10.1074/jbc.270.5.2241 • Bu, D. F. & Tobin, A. J. The exon-intron organization of the genes (gad1 and gad2) encoding two human glutamate decarboxylases (gad67 and gad65) suggests that they derive from a common ancestral gad. Genomics (1994). doi:10.1006/geno.1994.1246 • Demakova, E. V, Korobov, V. P. & Lemkina, L. M. Determination of gamma-aminobutyric acid concentration and activity of glutamate decarboxylase in blood serum of patients with multiple sclerosis. Klin. Lab. Diagn. (2003). • Asada, H. et al. Mice lacking the 65 kDa isoform of glutamic acid decarboxylase (GAD65) maintain normal levels of GAD67 and GABA in their brains but are susceptible to seizures. Biochem. Biophys. Res. Commun. (1996). doi:10.1006/bbrc.1996.1898 • McHale, D. P. et al. A Gene for Autosomal Recessive Symmetrical Spastic Cerebral Palsy Maps to Chromosome 2q24-25. Am. J. Hum. Genet. (1999). doi:10.1086/302237

HTR2

• Anton, R. F. et al. Pharmacogenomics. Nat. Genet. (2008). doi:10.1016/j.ejca.2015.06.122 • Unschuld, P. G. et al. Polymorphisms in the serotonin receptor gene HTR2A are associated with quantitative traits in panic disorder. Am. J. Med. Genet. Part B Neuropsychiatr. Genet. (2007). doi:10.1002/ajmg.b.30412 • Kling, a et al. Genetic variations in the serotonin 5-HT2A receptor gene (HTR2A) are associated with rheumatoid arthritis. Ann. Rheum. Dis. (2008). doi:10.1136/ard.2007.074948 • HTR2A gene - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/gene/HTR2A>.

MAO-A

• Kim, S. K. et al. Association study between monoamine oxidase A (MAOA) gene polymorphisms and schizophrenia: Lack of association with schizophrenia and possible association with affective disturbances of schizophrenia. Mol. Biol. Rep. (2014). doi:10.1007/s11033-014-3207-5 • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • Karmakar, A. et al. Pilot study indicate role of preferentially transmitted monoamine oxidase gene variants in behavioral problems of male ADHD probands. BMC Med. Genet. (2017). doi:10.1186/s12881-017-0469-5 • Bortolato, M. & Shih, J. C. Behavioral outcomes of monoamine oxidase deficiency: Preclinical and clinical evidence. in International Review of Neurobiology (2011). doi:10.1016/B978-0-12-386467-3.00002-9

MAO-B

• Ukrainitseva, S. V., Arbeev, K. G., Michalsky, A. I. & Yashin, A. I. Antiaging treatments have been legally prescribed for approximately thirty years. in Annals of the New York Academy of Sciences (2004). doi:10.1196/annals.1297.014 • Shih, J. C. & Chen, K. MAO-A and -B gene knock-out mice exhibit distinctly different behavior. Neurobiology (Budapest, Hungary). (1999). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10591056>. • Riederer, P. & Laux, G. MAO-inhibitors in Parkinson's Disease. Exp. Neurobiol. (2011). doi:10.5607/en.2011.20.1.1 • Saura, J. et al. Increased monoamine oxidase b activity in plaque-associated astrocytes of Alzheimer brains revealed by quantitative enzyme radioautography. Neuroscience (1994). doi:10.1016/0306-4522(94)90311-5 • Mallajosyula, J. K., Chinta, S. J., Rajagopalan, S., Nicholls, D. G. & Andersen, J. K. Metabolic control analysis in a cellular model of elevated MAO-B: Relevance to parkinson's disease. Neurotox. Res. (2009). doi:10.1007/s12640-009-9032-2 • Nagatsu, T. & Sawada, M. Molecular mechanism of the relation of monoamine oxidase B and its inhibitors to Parkinson's disease: possible implications of glial cells. J. Neural Transm. Suppl. (2006). doi:10.1007/978-3-211-33328-0_7 • Kumar, M. J. & Andersen, J. K. Perspectives on MAO-B in Aging and Neurological Disease: Where Do We Go From Here? Mol. Neurobiol. (2004). doi:10.1385/MN:30:1:077 • Shih, J. C., Chen, K. & Ridd, M. J. MONOAMINE OXIDASE: From Genes to Behavior. Annu. Rev. Neurosci. (1999). doi:10.1146/annurev.neuro.22.1.197 • MAOB monoamine oxidase B [Homo sapiens (human)] - Gene - NCBI. National Center for Biotechnology Information Available at: <https://www.ncbi.nlm.nih.gov/gene/4129>. • Bortolato, M. & Shih, J. C. Behavioral outcomes of monoamine oxidase deficiency: Preclinical and clinical evidence. in International Review of Neurobiology (2011). doi:10.1016/B978-0-12-386467-3.00002-9 • Bortolato, M., Godar, S. C., Davarian, S., Chen, K. & Shih, J. C. Behavioral disinhibition and reduced anxiety-like behaviors in monoamine oxidase b-deficient mice. Neuropsychopharmacology (2009). doi:10.1038/npp.2009.118 • Miller, G. M. The emerging role of trace amine-associated receptor 1 in the functional regulation of monoamine transporters and dopaminergic activity. Journal of Neurochemistry (2011). doi:10.1111/j.1471-4159.2010.07109.x • Edmondson, D. E., Binda, C. & Mattevi, A. Structural insights into the mechanism of amine oxidation by monoamine oxidases A and B. Archives of Biochemistry and Biophysics (2007). doi:10.1016/j.abb.2007.05.006 • Nolen, W. A., Hoencamp, E., Bouvy, P. F. & Haffmans, P. M. Reversible Monoamine Oxidase-A Inhibitors In Resistant Major Depression. Clinical Neuropharmacology 15, (1992).

SLC6A4

• Johnson, B. A. et al. Pharmacogenetic approach at the serotonin transporter gene as a method of reducing the severity of alcohol drinking. Am. J. Psychiatry 168, 265–275 (2011). • SLC6A4 gene - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/gene/SLC6A4>. • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • Ait-Daoud, N. et al. Preliminary Evidence for cue-induced Alcohol Craving Modulated by Serotonin Transporter Gene Polymorphism rs1042173. Front. Psychiatry 3, 6 (2012). • Landgren, S. et al. Genetic Variation of the Ghrelin Signaling System in Females With Severe Alcohol Dependence. Alcohol. Clin. Exp. Res. 34, 1519–1524 (2010).

TPH2

• Bragatti, J. A., Bandeira, I. C., de Carvalho, A. M., Abujamra, A. L., Leistner-Segal, S., & Bianchin, M. M. (2014). Tryptophan hydroxylase 2 (TPH2) gene polymorphisms and psychiatric comorbidities in temporal lobe epilepsy. Epilepsy and Behavior. <https://doi.org/10.1016/j.yebeh.2014.01.007> • Zhang, X., Beaulieu, J. M., Gainetdinov, R. R. & Caron, M. G. Functional polymorphisms of the brain serotonin synthesizing enzyme tryptophan hydroxylase-2. Cellular and Molecular Life Sciences (2006). doi:10.1007/s00018-005-5417-4 • Plemenitis, A., Kores Plesni?ar, B., Kastelic, M., Porcelli, S., Serretti, A., & Do?an, V. (2015). Genetic variability in tryptophan hydroxylase 2 gene in alcohol dependence and alcohol-related psychopathological symptoms. Neuroscience Letters. <https://doi.org/10.1016/j.neulet.2015.07.037> • Natarajan, R., Einarasdottir, E., Riutta, A., Hagman, S., Raunio, M., Mononen, N., ... Elovaaara, I. (2012). Melatonin pathway genes are associated with progressive subtypes and disability status in multiple sclerosis among Finnish patients. Journal of Neuroimmunology. <https://doi.org/10.1016/j.jneuroim.2012.05.014> • Kim, Y. K., Lee, H. J., Yang, J. C., Hwang, J. A., & Yoon, H. K. (2009). A tryptophan hydroxylase 2 gene polymorphism is associated with panic disorder. Behavior Genetics. <https://doi.org/10.1007/s10519-008-9254-8> • Gao, J., Pan, Z., Jiao, Z., Li, F., Zhao, G., Wei, Q., ... Evangelou, E. (2012). TPH2 gene polymorphisms and major depression - a meta-analysis. PLoS ONE. <https://doi.org/10.1371/journal.pone.0036721> • Baehne, C. G., Ehli, A. C., Plichta, M. M., Conzelmann, A., Pauli, P., Jacob, C., ... Fallgatter, A. J. (2009). Tph2 gene variants modulate response control processes in adult ADHD patients and healthy individuals. Molecular Psychiatry. <https://doi.org/10.1038/mp.2008.39> • Pae, C. U., Chiesa, A., Porcelli, S., Han, C., Patkar, A. A., Lee, S. J., ... De Ronchi, D. (2012). Influence of BDNF variants on diagnosis and response to treatment in patients with major depression, bipolar disorder and schizophrenia. Neuropsychobiology. <https://doi.org/10.1159/000327605> • Walitza, S., Renner, T. J., Dempfle, A., Konrad, K., Wewetzer, C., Halbach, A., ... Lesch, K. P. (2005). Transmission disequilibrium of polymorphic variants in the tryptophan hydroxylase-2 gene in attention-deficit/hyperactivity disorder. Molecular Psychiatry. <https://doi.org/10.1038/sj.mp.4001734> • Singh, A. S., Chandra, R., Guhathakuria, S., Sinha, S., Chatterjee, A., Ahmed, S., ... Rajamma, U. (2013). Genetic association and gene-gene interaction analyses suggest likely involvement of ITGB3 and TPH2 with autism spectrum disorder (ASD) in the Indian population. Progress in Neuro-Psychopharmacology and Biological Psychiatry. <https://doi.org/10.1016/j.pnpbp.2013.04.015> • Reuter, M., Kuepper, Y., & Hennig, J. (2007). Association between a polymorphism in the promoter region of the TPH2 gene and the personality trait of harm avoidance. International Journal of Neuropsychopharmacology. <https://doi.org/10.1017/S1461145706007073> • Su, Y. A., Li, J. T., Dai, W. J., Liao, X. M., Dong, L. C., Lu, T. L., ... Si, T. M. (2016). Genetic variation in the tryptophan hydroxylase 2 gene moderates depressive symptom trajectories and remission over 8 weeks of escitalopram treatment. International Clinical Psychopharmacology. <https://doi.org/10.1097/YIC.000000000000115> • Serretti, A., Liappas, I., Mandelli, L., Albani, D., Forloni, G., Malitas, P., ... Kaloufitis, A. (2009). TPH2 gene variants and anxiety during alcohol detoxification outcome. Psychiatry Research. <https://doi.org/10.1016/j.psychres.2007.12.006>