



Gene Comprehensive Nutrigenomic Report

Accession Number: #####

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

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

Report Generated: September 9, 2020

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.

– 40 – 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
Neurological / Psych							
Neurotransmitters							
rs4680	COMT V158M	+/-	Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Methionine, SAME, Inositol		May Benefit from Full Focus+™ for anxiety, depression or focus issues		
rs769407	GAD1	-/-	Prescription Amantadine, Glycine, Beta Phenyl GABA, Zinc, Magnesium, Elderberry, L-Theanine, Melatonin	Consider Pro GAD Enhancer™ If Anxiety or Depression is Present May benefit from Prescription Amantadine		Be cautious with MSG (Monosodium Glutamate) Be cautious with Glutamine Supplementation	
rs3828275	GAD1	+/+					
rs6323	MAO-A	-/-	B2 (Riboflavin)		Consider Full Focus™ if Focus or Anxiety Present	Higher Risk of Depression / Anxiety during stressful events	
rs1799836	MAO-B	+/+	Methyl Donors (Taurine, Choline, TMG, DMG, Inositol, SAME)				
rs6313	HTR2	+/-	5-HTP (Hydroxytryptophan)				
rs1042173	SLC6A4	+/-					
rs4570625	TPH2	+/-	L-5-Methyl THF Niacinamide 5-HTP		Consider 5-HTP or Mood Plus™ if Depression or Anxiety Present		

rs1108580	DBH	+/-	Phenylpropanolamine Pseudoephedrine Vitamin C Strattera			
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rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Neurological / Psych							
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, Progesterone, Testosterone
rs2569191	CD14	+/-					
rs1143634	IL1B	-/-					
rs2069812	IL5	-/-					
rs1800795	IL6	-/-					
rs1800925	IL13	-/-					
rs10181656	STAT4	-/-					
rs1800629	TNF	-/-					
rs231775	CTLA4	+/-					
rs1076560	DRD2	-/-	Increased Efficacy of Naltrexone				

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rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Neurological / Psych							
Neurotrophic Factors							
rs1142636	SYN1	-/-	RG3, Nicotinamide Riboside, Ginseng				
rs6265	BDNF	-/-	D-Chiro-Inositol, 12 Hour Fasting, Exercise				
rs6330	NGF	-/-	Intravenous Stem Cells should be Highly Beneficial				
Autophagy Efficacy							
rs10210302	ATG16L1	-/-	Curcumin, Lithium Orotate, D-Chiro-Inositol, Catechins, Resveratrol, Caffeine, 12-15 Hour Fasting	N.A.S. Enhancer™ DCI 500 twice daily		Consider Intermittant Fasting (12-15 Hours) Routine Exercise	Routine Blood Sugar, Insulin and Hb A1c
rs26538	ATG12	+/-					
rs510432	ATG5	+/-					
rs3798963	PARK2 (Parkin)	-/-	Curcumin, Lithium Orotate, D-Chiro-Inositol, Catechins, Resveratrol, 12-15 Hour Fasting				
rs7412	APOE	-/-	Increased Risk of Memory Disorders			Discuss APOE findings with Physician	Routine Lipid Panel
rs429358	APOE	+/-					
Detoxification							
rs1021737	CTH	-/-	N-Acetyl Cysteine (NAC)				
rs819147	AHCY	+/-					

rs7483	GSTM3	-/-	Glutathione NRF2 Enhancers				
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Summary for Neurological / Psych

Highly Recommended Therapeutics

- Consider Pro GAD Enhancer™ If Anxiety or Depression is Present
- May benefit from Prescription Amantadine
- CBD Oil
- PEA Soothe Support™
- Prescription Low Dose Naltrexone (LDN)
- N.A.S. Enhancer™
- DCI 500 twice daily

Provider Discretion

- May Benefit from Full Focus+™ for anxiety
- depression or focus issues
- Consider Full Focus™ if Focus or Anxiety Present
- Consider 5-HTP or Mood Plus™ if Depression or Anxiety Present

Lifestyle Recommendations

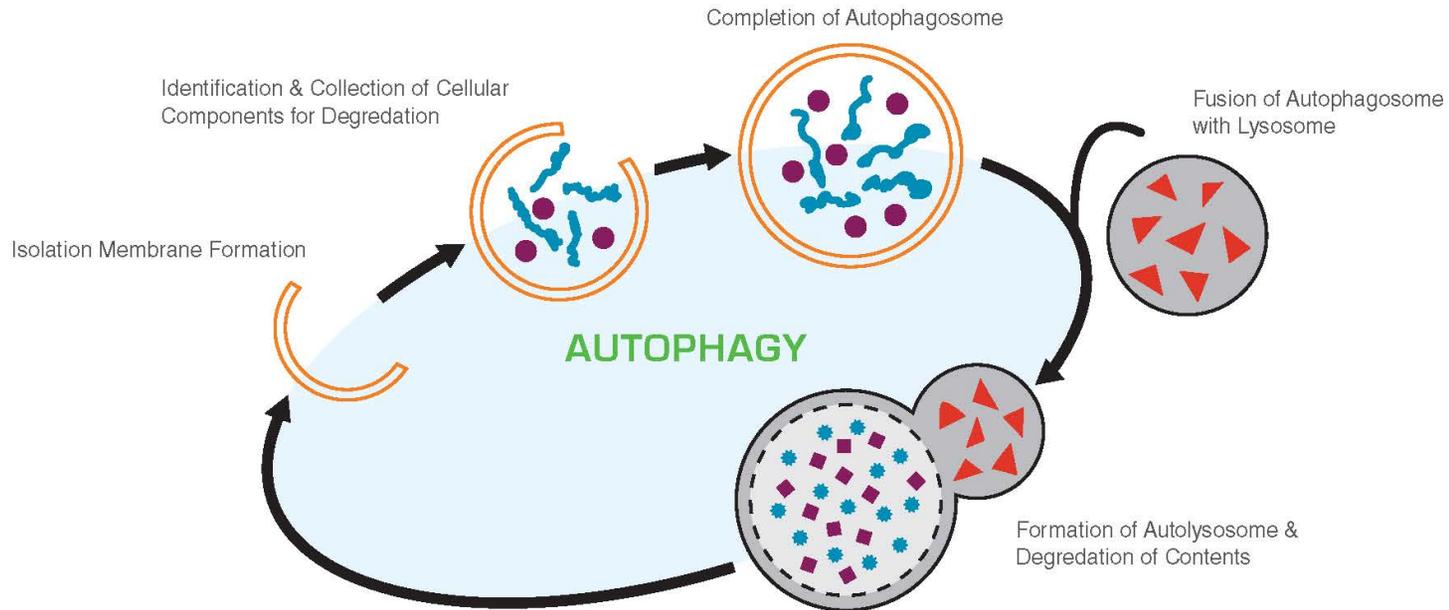
- Be cautious with MSG (Monosodium Glutamate)
- Be cautious with Glutamine Supplementation
- Higher Risk of Depression / Anxiety during stressful events
- Consider Low Inflammatory Diet
- Consider Intermittant Fasting (12-15 Hours)
- Routine Exercise
- Discuss APOE findings with Physician

Laboratory Recommendations

- Consider Pregnenolone
- Cortisol
- Progesterone
- Testosterone
- Routine Blood Sugar
- Insulin and Hb A1c
- Routine Lipid Panel

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

WAYS TO INCREASE

DETOXIFICATION

GLUTATHIONE IN DETOXIFICATION

Relevant genes for production are AHCY, CTH, GSTP1, GSTM1, GSTM3, GSR, MTRR & MTR

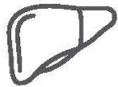
WHY IS IT IMPORTANT?



Maintains health by protecting the body from toxins



Regulates cell production and programmed cell death



Critical role in chemical detoxification



Vital for proper mitochondrial function

DEFICIENCY CAUSES

- Auto-immune diseases
- Cardiovascular diseases
- Neurodegenerative diseases
- Cell death
- Poor mitochondrial function

WAYS TO INCREASE GLUTATHIONE

- Limit alcohol intake
- N-acetyl-cysteine (NAC)
- Glutathione therapies
- (ie. IV Glutathione, Glutathione suppository, Liposomal Glutathione)
- Include whey in diet, unless allergic or intolerant
- Methylation Support - if necessary

SUPEROXIDES & ANTIOXIDANTS

- SOD1, SOD2, SOD3 genes are important to transform superoxides to protect against mitochondrial damage
- Reactive Oxygen Species (ROS) can damage mitochondria and cause cell death.
- Antioxidants such as Vitamin A, Vitamin C and Vitamin E act as a defense against ROS



LOW-INFLAMMATORY

FOODS TO EAT



Fruits: strawberries, blueberries, cherries, oranges



Fatty fish: salmon, mackerel, tuna, sardines



Spices - turmeric, ginger



Green leafy vegetables & tomatoes



Dark chocolate



Olive oil



LOW-INFLAMMATORY DIET

FOODS TO AVOID



Soda & other sugar-sweetened drinks



Dairy products



Fried foods



Red & Processed meats (hotdogs, sausage)



Refined carbohydrates: white bread, pastries



Margarine, shortening, lard

BENEFITS



Reduces inflammation



Reduces risk for cardiovascular disease & Type II diabetes

NEURO-INFLAMMATION

INFLAMMATION OF THE BRAIN & SPINAL CORD

RELEVANT GENES

- Variants have been associated with increased inflammatory aggression and the inability to “shut down” neuro-inflammation
 - Interleukins (IL-1B, IL5, IL6, IL13) stimulate the immune response
 - C3 & STAT4 activate, form and/or differentiate T-cells
 - CTLA4 & CD14 are involved in the suppression of T-cells
 - TNF triggers inflammation
 - DRD2 suppresses neuroinflammation

WAYS TO DECREASE NEUROINFLAMMATION



Meditation/Yoga & breathing exercises



Therapeutic massages with herbalized oils (ex. Sesame oil)



Mediterranean Diet



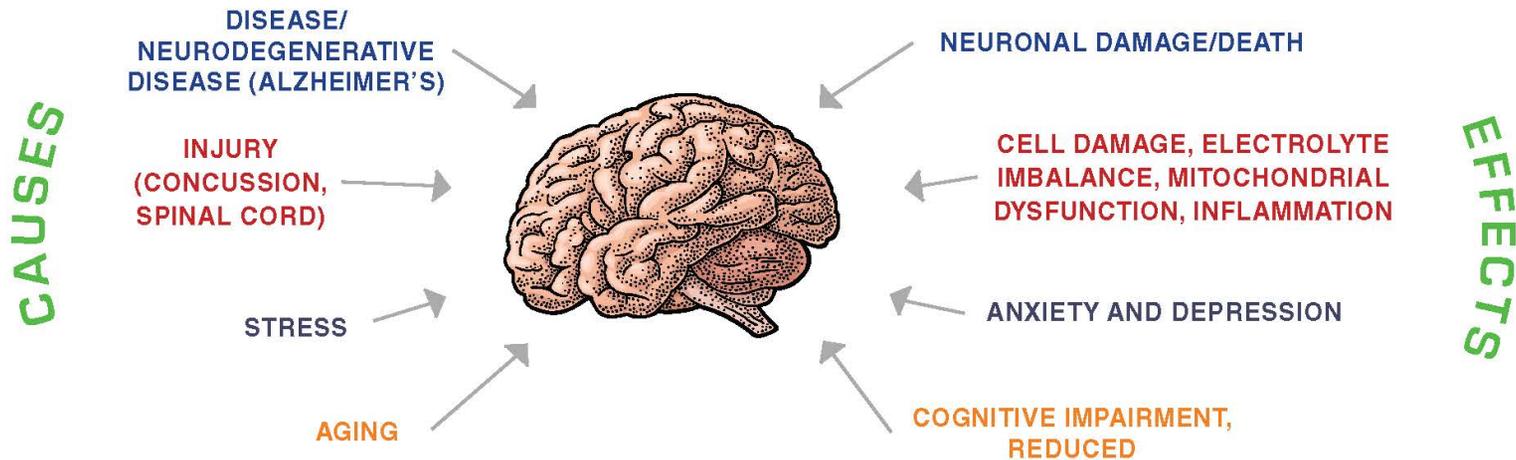
Medications & Supplements
CBD, LDN, PEA



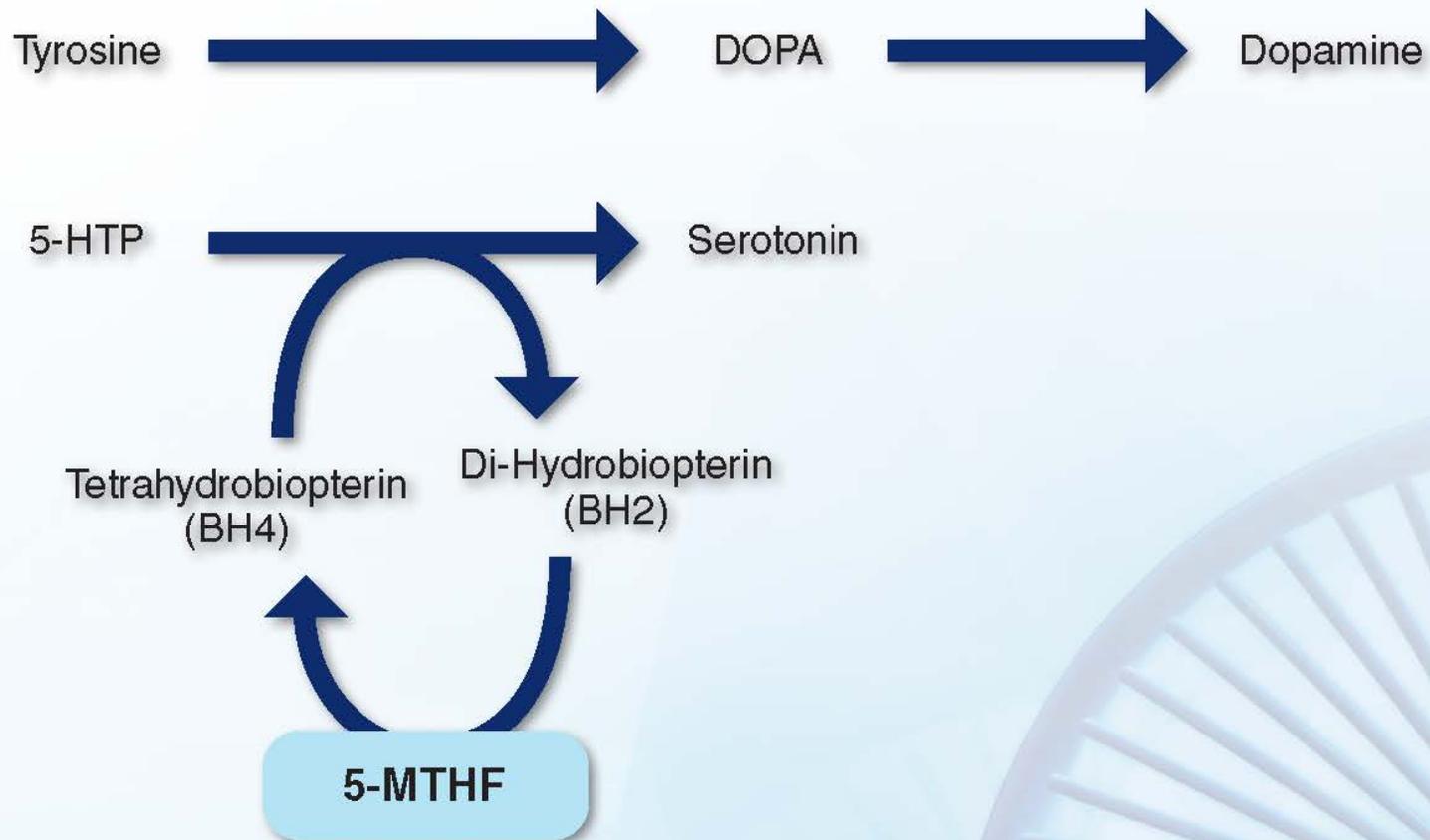
Curcumin, Bacopa herb



Anti-inflammatory Diet

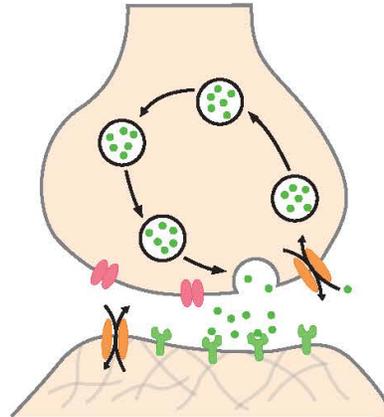


5-MTHF & Neurotransmitter Production



NEUROTRANSMITTERS & PATHWAY

TRANSMIT INFORMATION FOR ESSENTIAL PROCESSES
DIGESTION, BREATHING, HEARTBEAT, MOVEMENT, PAIN REGULATION, ETC.



RELEVANT GENES

- **HTR2, TPH2, SLC6A4, MAO-A** genes are important in the synthesis, breakdown, transport and/or functioning of serotonin
- **COMT, MAO-A, MAO-B** genes are important for the breakdown of serotonin, norepinephrine and/or dopamine
- The **DBH** gene is important for norepinephrine synthesis
- The **GAD1** gene is important for GABA synthesis
- Variants in **COMT, MAO-A, MAO-B** and **GAD1** genes have been associated with mood, anxiety and focus issues

WAYS TO INCREASE LEVELS



Supplements
Methyl donors, 5-HTP,
5-MTHF, PPA, Strattera



Mediation/Yoga



Aerobic Exercise



Dietary Factors



Increase Sun Exposure

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 formation of long-term memories



Regulate the development of the peripheral and central nervous systems

LOW LEVELS ARE CORRELATED WITH

- Neurodegenerative disorders
- Aging
- Chronic stress
- Mood disorders

WAYS TO INCREASE LEVELS



Medications & Supplements
RG3, Nicotinamide Riboside,
Ginseng, D-Chiro-Inositol



Exercise (physical
or cognitive)



Social interactions



Reduce stress via
breathing exercises
and/or meditation

Gene Information Key

rsID	Gene	"-" variant	"+" variant
rs819147	AHCY	T	C
rs7412	APOE	C	T
rs429358	APOE	T	C
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
rs3828275	GAD1	C	T
rs769407	GAD1	G	C
rs7483	GSTM3	C	T

rsID	Gene	"-" variant	"+" variant
rs6313	HTR2	G	A
rs1800925	IL13	C	T
rs1143634	IL1B	G	A
rs2069812	IL5	A	G
rs1800795	IL6	G	C
rs6323	MAO-A	T	G
rs1799836	MAO-B	T	C
rs6330	NGF	G	A
rs3798963	PARK2 (Parkin)	A	T
rs1042173	SLC6A4	A	C
rs10181656	STAT4	C	G
rs1142636	SYN1	A	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".
AHCY	Adenosylhomocysteinase (AHCY) is an enzyme that breaks down S-adenosylhomocysteine (SAH) to homocysteine and adenosine. Polymorphisms in this gene will lead to lower levels of homocysteine and glutathione.
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.
DEVELOPMENTAL	The SNPs in this category have been identified as potential areas of weakness in the recovery of developmental disorders.
APOE Arg176Cys	Individuals homozygous for T/T at rs7412 are assumed to have the E2 allele of the gene APOE. APOE encodes a protein involved in cholesterol and lipid transport and metabolism
APOE Cys130Arg	Individuals homozygous for the C/C allele at rs429358 may harbor the APOE E4 allele. Consult with a provider to determine APOE risk allele status.
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.
NGF	This gene encodes a member of the nerve growth factor family of proteins. Alternative splicing results in multiple transcript variants, at least one of which encodes a preproprotein that is proteolytically processed to generate the mature protein. 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 patients. This gene may play a role in the regulation of the stress response and in the biology of mood disorders
PARK2	PARK2 is a protein involved in normal turnover of damaged or old proteins inside the cell. Mutations in the PARK2 gene are associated with heritable Parkinson's disease.
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.
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.
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.
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.
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.
IL1B	Interleukin 1B is the pro-inflammatory cytokine responsible for inducing cyclooxygenase-2 (COX2) expression in the central nervous system. COX2 enzymatic function leads to prostanoid signaling that increases pain sensation associated with inflammation. Mutations in the IL1B gene are associated with many chronic inflammation disorders.
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

TESTING:

Testing Performed By: TY

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

AHCY

• 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>. • 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 • Motzek, A. et al. Abnormal hypermethylation at imprinting control regions in patients with S-adenosylhomocysteine hydrolase (AHCY) deficiency. *PLoS One* 11, (2016). • Vugrek, O., Beluži?, R. & Naki?, N. S-adenosylhomocysteine hydrolase (AHCY) deficiency: Two novel mutations with lethal outcome. *Hum. Mutat.* 30, (2009). • 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/ip/books/13002_11

CTH

• 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 • Huezo-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). • 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 • 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 • Pizzorno, J. Glutathione! *Integrative Medicine (Boulder)* (2014). doi:10.5005/ip/books/13002_11 • 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).

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 etiopathogenic mechanism in Alzheimer disease. *Neurobiol. Aging* (2010). doi:10.1016/j.neurobiolaging.2008.03.007

DEVELOPMENTAL SNP References

APOE: Arg176Cys

• Ruano, G. et al. Physiogenomic comparison of weight profiles of olanzapine- and risperidone-treated patients. *Mol. Psychiatry* 12, 474–482 (2007). • Tejedor, M. T., Garcia-Sobreviela, M. P., Ledesma, M. & Arbones-Mainar, J. M. The apolipoprotein E polymorphism rs7412 associates with body fatness independently of plasma lipids in middle aged men. *PLoS One* 9, e108605 (2014).

APOE Cys130Arg

• Rubinsztein, D. C. & Easton, D. F. Apolipoprotein E Genetic Variation and Alzheimer's Disease. *Dement. Geriatr. Cogn. Disord.* 10, 199–209 (1999). • Takei, N. et al. Genetic association study on and around the APOE in late-onset Alzheimer disease in Japanese. *Genomics* 93, 441–448 (2009). • Tejedor, M. T., Garcia-Sobreviela, M. P., Ledesma, M. & Arbones-Mainar, J. M. The apolipoprotein E polymorphism rs7412 associates with body fatness independently of plasma lipids in middle aged men. *PLoS One* 9, e108605 (2014).

ATG12

• Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. *Gene* 632, 36–42 (2017). • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. *Healthline* (2014). Available at: <https://www.healthline.com/health/autophagy#bottom-line>. • 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 • 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 • 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).

BDNF

• Mitre, M., Mariga, A. & Chao, M. V. Neurotrophin signalling: Novel insights into mechanisms and pathophysiology. *Clinical Science* (2017). doi:10.1042/CS20160044 • 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 • Kambaitz, J. P., Bhattacharyya, S., Kambaitz-Ilanovic, 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> • 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/alcal/agu040> • 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> • 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> • 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> • Zivadnov, 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> • Miranda, M., Morici, J. F., Zanoni, M. B. & Bekinschtein, 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 • Bathina, S. & Das, U. N. Brain-derived neurotrophic factor and its clinical Implications. *Archives of Medical Science* (2015). doi:10.5114/aoms.2015.56342 • Harrisberger, F., Spalek, K., Smieskova, R., Schmidt, A., Coyne, 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> • 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-Seligler, 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> • 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>

NGF

• Miranda, M., Morici, J. F., Zanoni, M. B. & Bekinschtein, 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 • 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 • 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*

PARK2

• Benitez, B. A. et al. Resequencing analysis of five Mendelian genes and the top genes from genome-wide association studies in Parkinson's Disease. *Mol. Neurodegener.* 11, 29 (2016). • Xu, L., Lin, D., Yin, D. & Koefler, H. P. An emerging role of PARK2 in cancer. *J. Mol. Med.* 92, 31–42 (2014).

SYN1

• 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> • Miranda, M., Morici, J. F., Zanoni, 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 • Bathina, S. & Das, U. N. Brain-derived neurotrophic factor and its clinical Implications. *Archives of Medical Science* (2015). doi:10.5114/aoms.2015.56342 • Mitre, M., Mariga, A. & Chao, M. V. Neurotrophin signalling: Novel insights into mechanisms and pathophysiology. *Clinical Science* (2017). doi:10.1042/CS20160044 • 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 • 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> • 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> • Cureauu, 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>

INFLAMMATORY SNP References

ATG16L1

• Messer, J. S. et al. The Crohn's disease: Associated ATG16L1 variant and Salmonella invasion. *BMJ Open* (2013). doi:10.1136/bmjopen-2013-002790 • Salem, M., Amritzboell, 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 • 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 • Gazouli, 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 • Boada-Romero, E. et al. The T300A Crohn's disease risk polymorphism impairs function of the WD40 domain of ATG16L1. *Nat. Commun.* (2016). doi:10.1038/ncomms11821 • 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 • Mizushima, N. *Autophagy: Process and function*. *Genes and Development* (2007). doi:10.1101/gad.1599207 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing. in *Haschek and Rousseau's Handbook of Toxicologic Pathology* (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • 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 • 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 • 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 • 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 • 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 • Stappenbeck, T. S. et al. Crohn disease: A current perspective on genetics, autophagy and immunity. *Autophagy* (2011). doi:10.4161/auto.7.4.13074 • 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/auto.21007 • Rosentul, D. C. et al. Role of autophagy genetic variants for the risk of *Candida* infections. *Med. Mycol.* (2014). doi:10.1093/mmy/myt035 • 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 • Csöngöi, 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.i2.176 • Usategui-Martín, R. et al. Polymorphisms in autophagy genes are associated with paget disease of bone. *PLoS One* (2015). doi:10.1371/journal.pone.0128984

ATG5

• 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). • Martin, L. J. et al. Functional Variant in the Autophagy-Related 5 Gene Promoter is Associated with Childhood Asthma. *PLoS One* 7, e33454 (2012). • Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. *Genet* 632, 36–42 (2017). • Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* 16, 268–278 (2008). • 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 • Lindberg, S. *Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More*. *Healthline* (2014). Available at: <https://www.healthline.com/health/autophagy#bottom-line>. • 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 Rousseau'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

C3

• Maydych, V. The interplay between stress, inflammation, and emotional attention: Relevance for depression. *Frontiers in Neuroscience* (2019). doi:10.3389/fnins.2019.00384 • 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 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • 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>. • 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/jamaophthol.2015.5592 • 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 • 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 • 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 • 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>. • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. *Healthline* (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders/#treatment>. • 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 • 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 • Nsaiba, 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 • 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? *World 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 • 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>. • 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>.

CD14

• 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). • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. *Healthline* (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders/#treatment>. • 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>. • 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 • 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). • 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 • 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>. • 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 • 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 • 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

CTLA4

• 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 • 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 • Tai, X. et al. Basis of CTLA-4 function in regulatory and conventional CD4 T cells. *Blood* 119, 5155–5163 (2012). • 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>. • 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>. • 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 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • 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. 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 • 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). • 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 • 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., Khatiri, 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 • Karaban, 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 Gallil, 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 • 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. 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>. • 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

DRD2

• 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 • 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 • Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* (2008). doi:10.1016/j.ejca.2015.06.122 • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016).

IL-13

• Becher, B., Spath, S. & Goverman, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • 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>. • 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>. • 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.201506-1243OC • Mitchel, 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/rcmb.2015-0252OC • 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. 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh, J. Y. & Sin, 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 • Oh, J. Y. & Sin, 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 • Sharan, 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 • 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.advm.2015.07.003 • 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 • McCormick, S. M. & Heller, N. M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine* (2015). doi:10.1016/j.cyt.2015.05.023 • 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. Autoimmun.* (2015). doi:10.1016/j.jaut.2015.06.006 • Blanchard, C. Molecular pathogenesis of eosinophilic esophagitis. *Curr. Opin. Gastroenterol.* (2015). doi:10.1097/MOG.0000000000000186 • Gervas-Aruga, 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 • Seyfizadeh, N. et al. Association of IL-13 single nucleotide polymorphisms in Iranian patients with autoimmune and inflammatory diseases. *International Journal of Biological Sciences* (2012). doi:10.7150/ijbs.4666 • Oh,

• 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 • 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 • 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 • 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>. • 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>. • Research Area. Neuroinflammation - Creative Diagnostics (2020). Available at: <https://www.creative-diagnostics.com/neuroinflammation.htm>. • 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 • 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> • Becher, B., Spath, S. & Gorman, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • 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/ijc.2004-0355 • Baumert, P., Lake, M. J., Stewart, C. E., Drust, B. & Erskine, R. M. Genetic variation and exercise-induced muscle damage: implications for athletic performance, injury and ageing. *European Journal of Applied Physiology* (2016). doi:10.1007/s00421-016-3411-1 • Buxens, 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 • Lurie, D. I. An integrative approach to neuroinflammation in psychiatric disorders and neuropathic pain. *J. Exp. Neurol.* (2018). doi:10.1177/1179069518793639 • Kalogeropoulos, A. P., Georgiopolou, V. Y. & 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

STAT4

• 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>. • Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • 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/autoimmunity/definitions>. • 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 • Jabeen, R. et al. Altered STAT4 Isoform Expression in Patients with Inflammatory Bowel Disease. *Inflamm. Bowel Dis.* (2015). doi:10.1097/MIB.0000000000000495 • 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>. • Disabato, D. J., Quan, N., & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • 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 • 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 • 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 • 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 • 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. Neurol.* (2018). doi:10.1177/1179069518793639 • 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 • 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 • 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 T10 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 C8orf13-BLK polymorphism and polyomysitis/dermatomyositis in the Japanese population: An additive effect with STAT4 on disease susceptibility. *PLoS One* (2014). doi:10.1371/journal.pone.0090019 • 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 • Lamana, A. et al. The minor allele of rs7574865 in the STAT4 gene is associated with increased mRNA and protein expression. *PLoS One* (2015). doi:10.1371/journal.pone.0142683 • McWilliams, I. L., Rajbhandari, R., Nozelli, 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 • 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 • 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 • Watson, S. Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. *Healthline* (2002). Available at: <https://www.healthline.com/health/autoimmune-disorders#treatment>. • 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>. • 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>.

TNF

• Harvard Health Publishing. Foods that fight inflammation. *Harvard Health* (2018). Available at: <https://www.health.harvard.edu/staying-healthy/foods-that-fight-inflammation>. • 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 • 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 • Yang, J.-K., Wu, W.-J., Qi, J., He, L. & Zhang, Y.-P. TNF- β 308 G/A Polymorphism and Risk of Acne Vulgaris: A Meta-Analysis. *PLoS ONE* 9, (2014). • 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 • Ayhan, 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.2072-1439.2014.04.14 • Li, H. H. et al. Tumour Necrosis Factor- β Gene Polymorphism Is Associated with Metastasis in Patients with Triple Negative Breast Cancer. *Sci. Rep.* (2015). doi:10.1038/srep10244 • Khan, S. et al. TNF- β 308 G>A (rs1800629) Polymorphism is Associated with Celiac Disease: A Meta-analysis of 11 Case-Control Studies. *Scientific Reports* 6, (2016). • Ma, Zhang & Baloch. Pathogenetic and Therapeutic Applications of Tumor Necrosis Factor- β (TNF- β) in Major Depressive Disorder: A Systematic Review. *Int. J. Mol. Sci.* (2016). doi:10.1016/j.ijch.2012.09.019 • Guo, X. F. et al. TNF- β 308 polymorphism and risk of digestive system cancers: A meta-analysis. *World J. Gastroenterol.* (2013). doi:10.3748/wjg.v19.i48.9461 • 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 • Zeng, X., Zhang, L., Gu, H. & Gu, Y. Association between TNF- β 308 G/A polymorphism and COPD susceptibility: a meta-analysis update. *International Journal of Chronic Obstructive Pulmonary Disease* 1367 (2016). doi:10.2147/copd.s105394 • Oh, J. Y. & Sin, D. D. Lung inflammation in COPD: why does it matter? *F1000 Medicine Reports* 4, (2012). • Lee, J. J. et al. Genetic polymorphism at codon 10 of the transforming growth factor- β 1 gene in patients with alcoholic liver cirrhosis. *Korean J. Hepatol.* (2011). doi:10.3350/kjhep.2011.17.1.37 • 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 • Chen, S. et al. Associations between TNF- β 308A/G Polymorphism and Susceptibility with Dermatomyositis: A Meta-Analysis. *PLoS ONE* 9, (2014). • 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 • Kalogeropoulos, A. P., Georgiopolou, V. Y. & 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 - Autoimmune Disease | Johns Hopkins Pathology (2020). Available at: <https://pathology.jhu.edu/autoimmunity/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>. • 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 • 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 • 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 • Disabato, D. J., Quan, N., & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016). • Idriss, H. T. & Naismith, J. H. TNF- β and the TNF receptor superfamily: Structure-function relationship(s). *Microsc. Res. Tech.* (2000). doi:10.1002/1097-0029(20000801)50:33.0.CO;2-H • 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>. • Simpson, N. & Dinges, D. F. Sleep and Inflammation. *Nutr. Rev.* (2007). doi:10.1111/j.1753-4887.2007.tb00371.x

NEUROTRANSMITTER SNP References

COMT

• 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 • Grossman, M. H., Emanuel, B. S. & Budarf, M. L. Chromosomal mapping of the human catechol-O-methyltransferase gene to 22q11.1?qt11.2. *Genomics* (1992). doi:10.1016/0888-7543(92)90316-K • Bonifácio, M. J., 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.1527-3458.2007.00200.x • Wichers, M. et al. The catechol-O-methyl transferase Val158Met polymorphism and experience of reward in the fruit 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 • Golan, D. E., Armstrong, E. J. & Armstrong, A. W. Principles of pharmacology: the pathophysiology basis of drug therapy. (Wolters Kluwer Health, 2017). • Tai, C. H. & Wu, R. M. Catechol-O-methyltransferase and Parkinson's disease. *Acta Medica Okayama* (2002). • Axelrod, J. O-methylation of epinephrine and other catechols in vitro and in vivo. *Science* (80-). (1957). doi:10.1126/science.126.3270.400 • Ulanman, 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 • 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 • 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 • 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 • 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.0000000000000108

DBH

• Rahman, M. K., Rahman, F., Rahman, T. & Kato, T. Dopamine- β -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 • Sun, Z., Ma, Y., Li, W., He, J., Li, J., Yang, X., ... Tang, Y. L. (2018). Associations between the DBH gene, plasma dopamine β -hydroxylase activity and cognitive measures in Han Chinese patients with schizophrenia. *Schizophrenia Research*. <https://doi.org/10.1016/j.schres.2017.06.028> • 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> • 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> • Barrie, E. S., Weinschenker, 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> • 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

• 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 • 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 • Giorda, 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 • 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 • 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> • 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). • 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 • Bu, D. F. & Tobin, A. J. The exon-intron organization of the genes (gad1 and gad2) encoding two human glutamate decarboxylases (gad67and gad65) suggests that they derive from a common ancestral gad. *Genomics* (1994). doi:10.1006/geno.1994.1246

HTR2

• 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.2007.047948 • HTR2A gene - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/gene/HTR2A> • 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

IL1B

• Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* (2008). doi:10.1016/j.ejca.2015.06.122 • 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> • Becher, B., Spath, S. & Governan, J. Cytokine networks in neuroinflammation. *Nature Reviews Immunology* (2017). doi:10.1038/nri.2016.123 • Carter, K. W. et al. Association of Interleukin-1 gene polymorphisms with central obesity and metabolic syndrome in a coronary heart disease population. *Hum. Genet.* (2008). doi:10.1007/s00439-008-0540-6 • Licastro, F. et al. Gene polymorphism affecting alpha1-antichymotrypsin and interleukin-1 plasma levels increases Alzheimer's disease risk. *Ann. Neurol.* (2000). doi:3.0.CO:2-G • Disabato, D. J., Quan, N. & Godbout, J. P. Neuroinflammation: the devil is in the details. *Journal of Neurochemistry* 139, 136–153 (2016).

MAO-A

• Anton, R. F. et al. Pharmacogenomics. *Nat. Genet.* 16, 268–278 (2008). • 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 • 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 • 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

MAO-B

• 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 • Riederer, P. & Laux, G. MAO-inhibitors in Parkinson's Disease. *Exp. Neurol.* (2011). doi:10.5607/en.2011.20.1.1 • 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 • 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> • MAOB monoamine oxidase B [Homo sapiens (human)] - Gene - NCBI. National Center for Biotechnology Information Available at: <https://www.ncbi.nlm.nih.gov/gene/4129> • 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 • Ukrainitseva, S. V., Arbeev, K. G., Michalsky, A. I. & Yashin, A. I. Antiging 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 • 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 • 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 • 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 • 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 • 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 • Nolen, W. A., Hoencamp, E., Bouvy, P. F. & Haffmans, P. M. Reversible Monoamine Oxidase-A Inhibitors In Resistant Major Depression. *Clinical Neuropharmacology* 15, (1992). • 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

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). • 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). • SLC6A4 gene - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: <https://ghr.nlm.nih.gov/gene/SLC6A4> • 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., Abujaama, 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> • 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> • 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> • Natarajan, R., Einarsdottir, E., Riutta, A., Hagman, S., Raunio, M., Mononen, N., ... Elovaara, 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> • 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> • Plemenitaš, A., Kores Plesničar, B., Kastelic, M., Porcelli, S., Serretti, A., & Dolžan, 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> • Serretti, A., Liappas, I., Mandelli, L., Albani, D., Forloni, G., Malitas, P., ... Kalofoutis, A. (2009). TPH2 gene variants and anxiety during alcohol detoxification outcome. *Psychiatry Research*. <https://doi.org/10.1016/j.psychres.2007.12.006> • 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/10.1017/S1461145706007073> • Singh, A. S., Chandra, R., Guhathakurta, 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> • 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> • 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 • Baehne, C. G., Ehlis, 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>