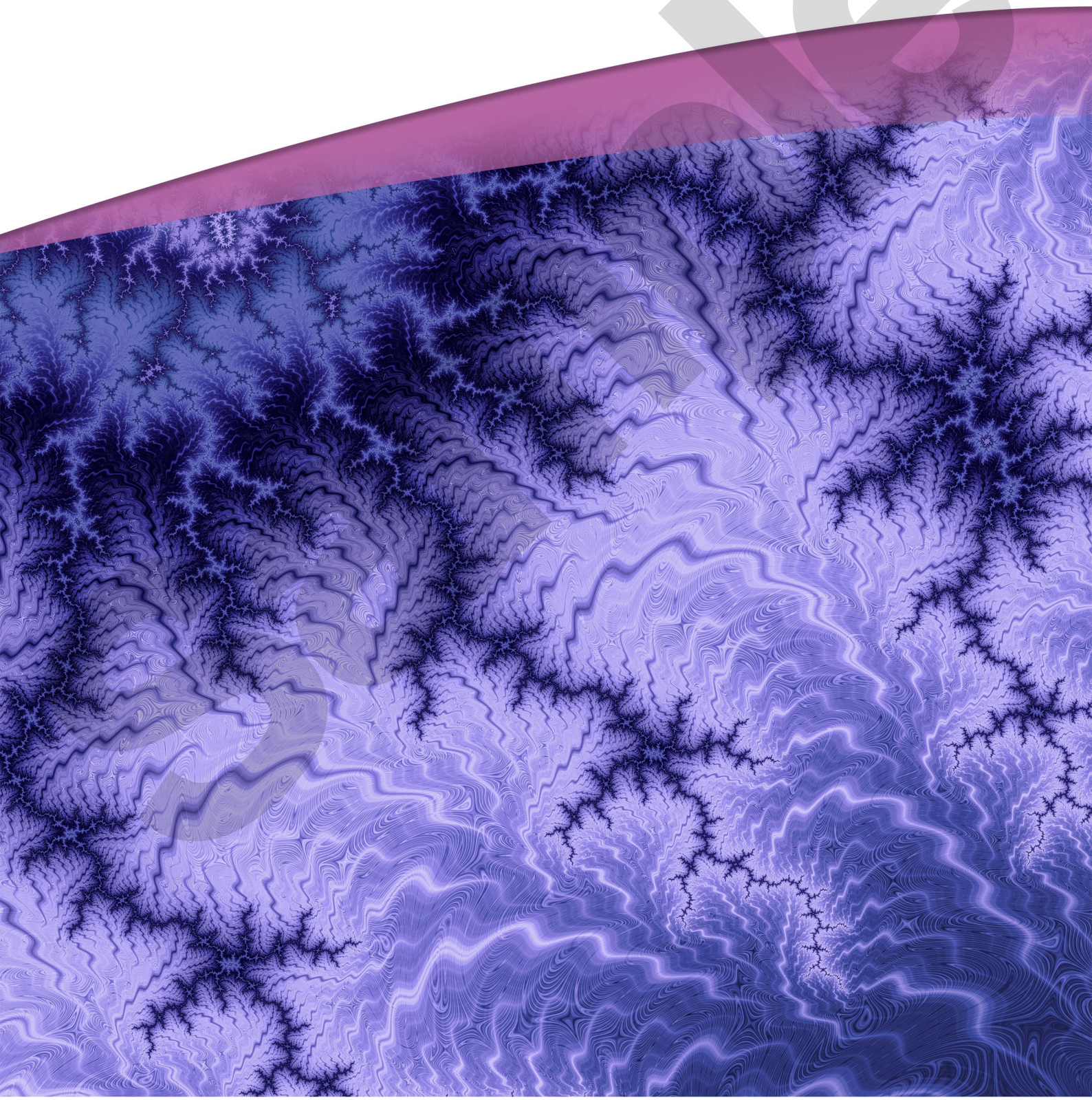
Lifecode GX ®
— Professional Genotype Analysis —

APOE Report



Apolipoprotein E (APOE) is a protein that is best known for its role in lipid metabolism by helping to remove cholesterol from the blood stream. It can exist in three main forms known as E2, E3 and E4. Variances on the APOE gene determine which forms of the APOE protein are present. The different forms of APOE work in different ways.

The E4 (epsilon 4) form of the APOE gene has been associated with disorders of lipid metabolism (increased plasma cholesterol and triglyceride levels), susceptibility to cardiovascular disease (heart attacks or strokes due to atherosclerosis), insulin resistance and Alzheimer's disease.

Having the genetic variant that creates the APOE E4 version of the protein is one of many risk factors and does not mean you will get any disease associated with it. If you have a higher risk version of APOE you can reduce your risk of developing cardiovascular disease or Alzheimer's disease by making changes to your diet and lifestyle.

Your APOE Result

APOE Genotypes

The APOE gene has three common versions which are determined by examining the DNA present at two specific locations in the genome. The locations are identified by the references rs429358 (Cys130Arg) and rs7412 (Arg158Cys).

Risk Assessment

The risk assessment below shows the relative susceptibility of different APOE types to Alzheimer's disease. As described elsewhere in this report, many other factors can influence this risk, including other genetic variances and lifestyle.

Your APOE Type

APOE type is determined by examining the alleles inherited from each parent - the left hand and then the right hand alleles for each SNP. A 'TT' result codes for E2, 'TC' for E3 and 'CC' for E4.

According to the methodology described, your APOE type is: **E3/E3**

APOE Type	rs429358 Cys130Arg	rs7412 Arg158Cys	Alzheimer's Disease Risk Assessment*
E2/E2	TT	TT	least risk x 0.6
E2/E3	TT	TC	low risk x 0.6
E3/E3	TT	CC	most common and neutral odds ratio 1
E2/E4	TC	TC	above average risk x 2.6
E3/E4	TC	CC	elevated risk x 3.2
E4/E4	CC	CC	highest risk x 14.9

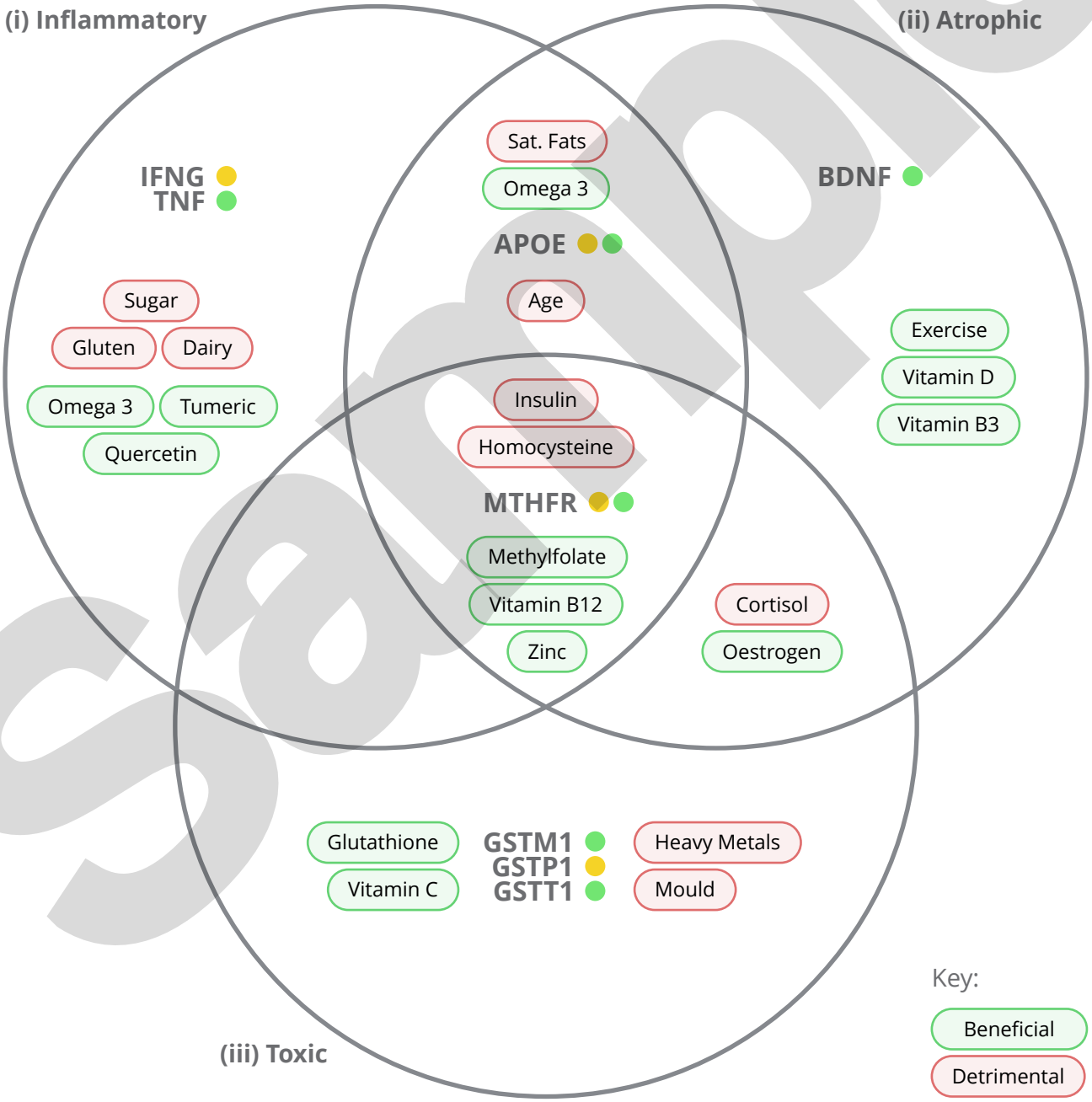
The combinations rs429358 CC and rs7412 TC or TT are very rare and are not reported.

* Global average risk odds - Farrer LA et al, 1997

APOE and Alzheimer's disease

Whilst APOE E4 alleles represent the strongest single genetic risk factor for Alzheimer's disease, examination of additional genetic variances can be helpful in considering the different sub-types.

According to Dale Bredesen MD, an expert in the mechanisms of neurodegenerative diseases, Alzheimer's disease is not a single disease but has three major subtypes:
(i) hot (inflammatory);
(ii) cold (atrophic); and
(iii) vile (toxic).



Detailed Results for type (i) Inflammatory

IFN-gamma
rs2430561

AT ▲

The T allele is associated with increased IFNG expression which helps defend against viral infection. However, over-expression of IFNG has been associated with increased inflammation and a slight increase in Alzheimer's disease risk.

MTHFR
[redacted]

TT

Neutral genotype. No impact on 5-MTHF or BH4 levels - needed for neurotransmitter synthesis.
Methylation can be supported by adequate consumption of folate containing foods (such as green leafy vegetables, citrus fruits, beans and liver) and cofactors (vitamins B2 and B3).

MTHFR
[redacted]

AG ▼

Up to 40% reduction in gene function which may impact supply of methyl-folate (5-MTHF) needed for homocysteine metabolism. Associated with a broad range potential health impacts, although many people are asymptomatic.
It is important to examine this variant in the context of the methylation cycle as a whole. Consider other genetic variants and environmental conditions that may affect 5-MTHF levels.
Methylation can be supported through a diet rich in folate and other B vitamins (B2, B3, B6 B12) and co-factors including magnesium and zinc.

TNF
[redacted]

GG

No variance. Normal TNF levels and normal inflammatory response. Not associated with increased risk of Alzheimer's disease.

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omitted in the sample

A Guide to APOE and Alzheimer's disease

(i) Hot (Inflammatory)

An up-regulated immune system can increase inflammation and the risk of cardiovascular disease, insulin resistance, arthritis and the 'hot' sub-type of Alzheimer's disease.

Variants on APOE, TNF (Tumour Necrosis Factor) and IFN-gamma (Interferon Gamma) genes can up-regulate carriers' immune and inflammatory response.

(ii) Cold (Atrophic)

The 'cold' sub-type of Alzheimer's is associated with reduced support from hormones - thyroid (T3), adrenal (cortisol), sex hormones (oestrogen, progesterone, testosterone) - and Vitamin D, and is often accompanied by increased homocysteine (see Methylation) and insulin resistance.

APOE E4 alleles are a risk factor for this sub-type. In addition, variants on BDNF (Brain Derived Neurotrophic Factor) can reduce support for neuronal and synaptic growth, survival and protection.

(iii) Vile (Toxic)

The 'toxic' sub-type of Alzheimer's disease is atypical, partly in that it occurs at a younger age, with no family history, and more often in APOE E3 carriers (risk is not elevated by APOE A4). Symptom onset usually follows a period of stress, sleep loss, anaesthesia or menopause.

It is characterised by hypothalamic-pituitary-adrenal axis (HPA) disfunction, metal toxicity (mercury, lead or iron), high homocysteine and low zinc (and elevated copper) and/ or chronic inflammatory response syndrome (CIRS) - a reaction to mycotoxins (found in mould).

The GST (Glutathione S-Transferase) family of genes play an important part in detoxification and individual responses to these toxins.

Methylation

Methylation is a process by which methyl-groups (CH3) are added to molecules, contributing to numerous biological functions including cell division and repair, inflammation control, neurotransmitter synthesis and detoxification.

MTHFR (Methylenetetrahydrofolate Reductase) gene variants can result in reduced availability of methyl-folate (B9) needed for homocysteine metabolism - a factor in all three sub-types of Alzheimer's disease, and synthesis of SAMe - the master methyl-donor.

Nutrition and Lifestyle

The risk of developing Alzheimer's disease (AD) can be reduced by adopting healthy lifestyle behaviours.

Reduce Inflammation

Inflammation is a significant risk factor for the 'hot' subtype of AD. Anti-inflammatory supplements such as turmeric, fish oil, quercetin and resveratrol can be useful, particularly for those who are genetically predisposed.

It is also vital to identify and remove the root cause(s) such as dietary sugars or damaging trans-fats, leaky gut, insulin resistance, viral or bacterial infections (including oral bacteria and Lyme disease) and psychological or physical stress.

Avoid Insulin Resistance

Insulin resistance is perhaps the single greatest metabolic contributor to AD risk. To reduce risk experts recommend:

- Minimising intake of simple carbohydrates (sugar) found in processed foods, starchy foods and alcohol
- Consuming unsaturated fats sourced from fatty fish, avocados, nuts and olive oil (preferably extra-virgin, cold pressed)
- Fasting for at least 12 hours between your last meal of the day and the first the next morning
- Maintaining a healthy body weight

Balance Hormones

Hormone optimisation can help prevent or reverse cognitive decline associated with the 'cold' and 'toxic' subtypes of AD.

Thyroid hormones can get out of balance (hyper or hypo) due to genetic variances, insufficient or excess of cofactors (iodine or selenium), inhibitors (cortisol), or damage or disruption to the thyroid gland.

Oestrogen and Progesterone have protective effects on the brain and in many cases onset of cognitive changes can be linked with menopause.

Testosterone (males and females) is critical for maintenance of synapses.

Whilst cortisol is protective against pathogens, high levels (due to stress) can damage neurons and can also deplete the pregnelolone needed to make oestrogen and testosterone.

As this is a complex topic, you are advised to work with a health professional.

Detoxify

Exposure to toxic substances can contribute to cognitive decline associated with 'toxic' AD. Toxins such as heavy metals - lead, iron and mercury (found in predatory fish, paint and amalgam fillings), medications (including proton pump inhibitors), pesticides, alcohol, general anaesthetic, Lyme disease (tick bites), (endogenous) homocysteine, and mould (found in water damaged buildings) can contribute to toxic load.

Optimise Methylation

Homocysteine can be a factor in all three sub-types of Alzheimer's. Homocysteine is a toxin that can damage blood vessels and increase inflammation.

High homocysteine levels can be indicative of impaired methylation. To optimise methylation ensure sufficient supply of B6, B9, B12 (bioactive, or 'methylated' forms), magnesium and zinc.

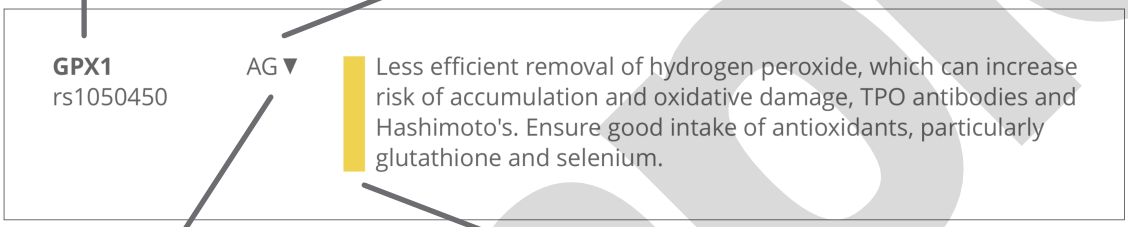
How to Read the Report

Genes

Results are listed in order of the gene short name. The 'rs' number is the reference sequence number that identifies a specific location on the genome. It is also known as a SNP (Single Nucleotide Polymorphism) pronounced 'snip', polymorphism or mutation.

Personalised Result

Your genotype result is shown as two letters (A,G,T or C) which represent the DNA bases present at that location.



Arrow Direction

The direction of the arrow indicates the potential effect of the SNP on gene expression, where applicable - it can increase or decrease activity, or neither.

▲ up-regulates or increases the activity and effect on the gene

▼ down-regulates or decreases the activity and effect on the gene

No arrow - no effect on the activity of the gene

Highlight Colour

The genotype result highlight indicates the potential effect of the SNP on gene function in a particular context.

RED the effect of the variant is negative

AMBER the effect of the variant is somewhat negative

GREEN no variation, or the effect of the variant is positive

References

APOE Apolipoprotein E

Bu G. Apolipoprotein E and its receptors in Alzheimer's disease: pathways, pathogenesis and therapy. Nature reviews Neuroscience. 2009;10(5):333-344. doi:10.1038/nrn2620. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2908393/)

Fallaize R, Carvalho-Wells AL, Tierney AC, et al. APOE genotype influences insulin resistance, apolipoprotein CII and CIII according to plasma fatty acid profile in the Metabolic Syndrome. Scientific Reports. 2017;7:6274. doi:10.1038/s41598-017-05802-2. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5524844/)

Giri M, Shah A, Upreti B, Rai JC. Unraveling the genes implicated in Alzheimer's disease. Biomedical Reports. 2017;7(2):105-114. doi:10.3892/br.2017.927. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5526178/#b56-br-0-0-927)

Kim J, Basak JM, Holtzman DM. The Role of Apolipoprotein E in Alzheimer's Disease. Neuron. 2009;63(3):287-303. doi:10.1016/j.neuron.2009.06.026. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3044446/)

BDNF Brain Derived Neurotrophic Factor

Coelho F. G., Vital T. M., Stein A. M., et al. Acute aerobic exercise increases brain-derived neurotrophic factor levels in elderly with Alzheimer's disease. Journal of Alzheimer's Disease. 2014;39(2):401–408. doi: 10.3233/JAD-131073. (https://www.ncbi.nlm.nih.gov/pubmed/24164734)

Park et al. (2017). The BDNF Val66Met Polymorphism Affects the Vulnerability of the Brain Structural Network. Frontiers in Human Neuroscience, 2017; 11: 400. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541016/)

Wu A, Ying Z, Gomez-Pinilla F. DHA dietary supplementation enhances the effects of exercise on synaptic plasticity and cognition. Neuroscience. 2008;155(3):751-759. doi:10.1016/j.neuroscience.2008.05.061. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3208643/#___abstractidm140630145270736title)

GSTM1 Glutathione S-Transferase Mu 1

Wang, M., Li, Y., Lin, L. et al. Mol Neurobiol (2016) 53: 1355. https://doi.org/10.1007/s12035-015-9092-7 (https://www.ncbi.nlm.nih.gov/pubmed/25633095)

GSTP1 Glutathione S-Transferase Pi 1

Bernardini S, Bellincampi L, Ballerini S, Federici G, Iori R, Trequattrini A, et al. (2005) Glutathione S-transferase P1 *C allelic variant increases susceptibility for late-onset Alzheimer disease: association study and relationship with apolipoprotein E epsilon4 allele. Clin Chem 51: 944–951. (https://www.ncbi.nlm.nih.gov/pubmed/15805147)

Pocernich CB, Butterfield DA. Elevation of Glutathione as a Therapeutic Strategy in Alzheimer Disease. Biochimica et Biophysica Acta. 2012;1822(5):625-630. doi:10.1016/j.bbadis.2011.10.003. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3277671/)

GSTT1 Glutathione S-Transferase (GST) Theta 1

Zahra Jafarian, Kioomars Saliminejad, Koorosh Kamali, Mina Ohadi, Ali Kowsari, Leila Nasehi & Hamid Reza Khorram Khorshed. Association of glutathione S-transferases M1, P1 and T1 variations and risk of late-onset Alzheimer's disease. Neurological Research Vol. 40, Iss. 1, 2018 (https://www.ncbi.nlm.nih.gov/pubmed/29072550)

IFN-gamma Interferon Gamma

TNFalpha plus IFNgamma induce the production of Alzheimer beta-amyloid peptides and decrease the secretion of APPs. Blasko I, Marx F, Steiner E, Hartmann T, Grubeck-Loebenstein B FASEB J. 1999 Jan; 13(1):63-8. (https://www.ncbi.nlm.nih.gov/pubmed/9872930/)

a M., Rafa H., Medjeber O., et al. IFN- and TNF- are involved during Alzheimer disease progression and correlate with nitric oxide production: a study in Algerian patients. Journal of Interferon and Cytokine Research. 2014;34(11):839–847. doi: 10.1089/jir.2013.0085. (https://www.ncbi.nlm.nih.gov/pubmed/24831467)

MTHFR Methylenetetrahydrofolate Reductase (NAD(P)H)

Rai, V. (2017), Methylenetetrahydrofolate Reductase (MTHFR) C677T Polymorphism and Alzheimer Disease Risk: a Meta-Analysis; Mol Neurobiol (2017) 54: 1173. https://doi.org/10.1007/s12035-016-9722-8 (https://www.ncbi.nlm.nih.gov/pubmed/26820674)

Bhatia, P. and Singh, N. (2015), Homocysteine excess: delineating the possible mechanism of neurotoxicity and depression. Fundam Clin Pharmacol, 29: 522–528. doi:10.1111/fcp.12145 (https://www.ncbi.nlm.nih.gov/pubmed/26376956)

Mansoori, Nasim et al. MTHFR (677 and 1298) and IL-6-174 G/C genes in pathogenesis of Alzheimer's and vascular dementia and their epistatic interaction. Neurobiology of Aging , Volume 33 , Issue 5 , 1003.e1 - 1003.e8 (https://www.ncbi.nlm.nih.gov/pubmed/22015309)

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