Comprehensive Report v6

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SAMPLE REPORT

n all of the basic reports and a few more in addition, too.

bility and metabolism of micronutrients including vitamins D, C, B12, A, folate, omega-3, iron and nce metabolism including the response to various types of fat (saturated fat, polyunsaturated fat, complex carbohydrates vs. simple carbohydrates), which may influence blood pressure, blood triglycerides, obesity, cardiovascular risk, and more. It also focuses on SNPs relevant to cholesterol metabolism and HMG-CoA reductase inhibitors such as statins. It looks at certain SNPs involved in the inactivation of heterocyclic amines which are procarcinogens formed when meat is cooked at high temperatures. It looks at SNPs involved in exercise performance, sleep, and those that can have a direct or indirect influence on longevity.

Noteworthy

These genotypes are the ones that are potentially worth being aware of.

Gene	SNPs involved	Status	More information
SH2B3	rs3184504(T;T)	Increased risk for celiac disease.	SH2B adaptor protein 3 (SH2B3) is involved in signaling growth factors and cytokine receptors and plays a role in hematopoiesis (formation of blood cells). **This genotype, rs3184504(T;T), has been associated with an increased risk for celiac disease**. There are common polymorphisms in the *SH2B3* gene, which codes for the SH2B adaptor protein 3. The **T** allele is the variant form of the rs3184504 polymorphism and is located in the exonic region of the gene. In a genome-wide association study (GWAS) involving 778 celiac cases and 1,422 controls, the **T** allele was associated with celiac disease. Celiac disease is an autoimmune condition which occurs as a result of variations in genes involved in mounting an immune response in the gut when exposed to gluten. Gluten is a group of proteins found in wheat, oats, barley, and rye. While only one percent of the U.S. population has celiac disease, a further six percent may be sensitive to gluten. This gluten sensitivity may result from zonulin, a protein released into the gut after gluten is consumed. Individuals with the (**T;T**) genotype, particularly in combination with other SNPs influencing celiac risk, may choose to avoid gluten, which can exacerbate gut inflammation. **Note:** This SNP is only one of several polymorphisms that may affect celiac disease risk. Future versions of this report may include additional polymorphisms to provide a higher degree of accuracy than this SNP alone does. Generally speaking, a combination of both a genetic test and a blood test are needed to diagnose celiac disease and gluten sensitivity in a clinical setting. • Read more about rs3184504 on SNPedia SNPs Involved rs3184504(T;T)
GSTP1	rs1695(A;A)	Supplemental vitamin e may be harmful	The glutathione S-transferase enzyme plays a significant role in the detoxification of various harmful compounds (either from the environment or generated by normal metabolism and immune function). Glutathione is one of the most potent antioxidant systems that the body possesses and is orders of magnitude more powerful than supplemental vitamin E (alpha-tocopherol). **This genotype, rs1695(A;A), has been associated with possible harmful effects of supplemental vitamin E.** There are common polymorphisms in the *GSTP1* gene, which codes for the glutathione S-transferase enzyme. The variant form (**G**) of the rs1695 polymorphism, located in the coding region of the gene is thought to alter the activity of the enzyme. Individuals with the (**A;A**) genotype (approximately half of the population), have a form of the glutathione S-transferase enzyme with normal activity. In a study of 160 middle-aged men, subjects with the **A** allele had elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) in the blood when supplementing with vitamin E. However, those with the less active form of the GSTP1 enzyme (**G;G** genotype) had decreased IL-6 levels and thus, may receive an anti-inflammatory benefit from a low dose (75 IU) of supplemental vitamin E. • Read more about rs1695 on SNPedia SNPs Involved rs1695(A;A)

FTO	rs17817449(G;T)	Saturated fat may have a negative effect on blood glucose and insulin levels	The *FTO* gene, the major genetic risk factor for obesity, codes for the fat mass and obesity-associated protein. There is a cluster of polymorphisms in the FTO gene that increase obesity risk. **This genotype, rs17817449(G;T), has been associated with a 1.3-fold increased obesity risk and saturated fat may have a negative effect on blood glucose and insulin levels.** There are common polymorphisms in the *FTO* gene, which codes for the fat mass and obesity-associated protein. The rs17817449 polymorphism is located in the intronic region of the *FTO* gene This particular polymorphism is one of many in this gene that influence genetic obesity risk. Saturated fat may have a negative effect on blood glucose and insulin levels and increases type 2 diabetes risk in individuals with the (**G;T**) genotype. Other gene polymorphisms in the FTO gene are also associated with obesity, particularly in the context of a high saturated fat and low polyunsaturated fat intake. Saturated fat is found in fatty beef, pork, coconut oil, butter, cheese, and other dairy products, while polyunsaturated fats are found in foods like nuts and fatty fish such as salmon and herring. This research suggests that individuals at high risk of obesity due to FTO polymorphisms, such as this one, may benefit from having a higher polyunsaturated fat intake and a lower saturated fat intake. • Read more about rs17817449 on SNPedia. SNPs Involved rs17817449(G;T)
vitamin D binding protein	rs7041(G;T)	Possible genetic risk for vitamin d deficiency	GC Vitamin D binding protein is a member of the albumin family involved in the storage and transport of vitamin D throughout the body. The GC gene encodes for the vitamin D binding protei which affects the delivery of 25-hydroxyvitamin D (precursor to vitamin D hormone) and activated vitamin D (1,25-dihydroxyvitamin D) to target organs, as well as the clearance of vitamin D metabolites from circulation. **This genotype, rs7041(G;T), has been associated with low vitamin D levels.** There are common polymorphisms in the *GC* gene, which codes for the vitamin D binding protein. The variant form (**T**) of the rs7041 polymorphism, located in the coding region of the gene, is thought to result in a protein that binds less efficiently to vitamin D. The (**G;T**) genotype may increase the risk of vitamin D deficiency. Genetically low vitamin D levels have been associated with reduced longevity and higher all-cause mortality. In addition, people wi a genetic predisposition to low vitamin D levels have been shown to have a two-fold increased risk for multiple sclerosis as a consequence of low 25-hydroxyvitamin D levels. According to the endocrine society, blood levels of 25-hydroxyvitamin D below 20 ng/mL are considered deficient, while levels less than 30 ng/mL are considered inadequate. Individuals havin levels between 30-60 ng/mL are considered adequate. Meta-analyses have shown that people with serum levels of 25-hydroxyvitamin D between 40-60 ng/L have the lowest all-cause mortality. Regardless of an individual's genotype for this particular SNP, a 25-hydroxyvitamin D blood test, available from most health care providers, can provide insight into how to optimize vitamin D statu The best way to assess vitamin D levels is to get a blood test. Supplementing with 1,000 IU of vitamin D3 per day generally raises serum 25-hydroxyvitamin D levels by 5-10 ng/mL. However, individuals with the (**G;T**) genotype may require higher vitamin D supplementation doses to achie the same serum levels as individuals without this polymorphism. A blood test for 25-hydroxyvitam D levels following supplementation may help to guide optimal dosage. • Read more about rs7041 on SNPedia SNPs Involved rs7041(G;T)
CYP2R1	rs2060793(A;G)	Genetic risk for vitamin d deficiency	There are common polymorphisms in the CYP2R1 gene (called vitamin D 25-hydroxylase) that tha converts vitamin D3 into 25-hydroxyvitamin D, the major circulating form of vitamin D that gets converted into the active steroid hormone. This polymorphism can lower the conversion of D3 into 25-hydroxyvitamin D and, thus, is associated with lower circulating levels of 25-OHD. Other polymorphisms in this gene that are associated with lower circulating levels of vitamin D have bee associated with reduced longevity and higher all-cause mortality. The best way to assess vitamin D levels is to get a blood test. It is known that supplementing with 1,000 IU of vitamin D3 per day generally raises serum 25-hydroxy vitamin D levels by 5-10 ng/ml. This may not be the case for people with these polymorphisms and individuals with this genotype may require higher vitamin D supplementation doses to achieve the same serum levels as individuals without these polymorphisms. A 25-hydroxy vitamin D blood test after supplementatio may help indicate how much to supplement with. According to the endocrine society, blood levels of 25-hyroxyvitamin D below 20 ng/ml are considered deficient, less than 30 ng/ml is inadequate. Individuals with levels between 30-60 ng/m are considered adequate. Meta-analyses have shown that people with serum levels between 40-6 ng/ml have the lowest all-cause mortality. • Read more on SNPedia. • Read more about other SNPs that are associated with a higher all-cause mortality.

			SNPs Involved rs2060793(A;G)
FTO	rs9939609(A;T)	Possible increased risk for obesity and type-2 diabetes	The *FTO* gene, the major genetic risk factor for obesity, codes for the fat mass and obesity-associated protein. Ghrelin, often called the hunger hormone, is produced when the stomach is empty and is thought to stimulate appetite and desire to eat. **This genotype, rs9939609(A;T), has been associated with an intermediate increased ris of obesity and type 2 diabetes due to high production of ghrelin**. There are common polymorphisms in the *FTO* gene, which codes for the fat mass and obesity-associated protein. The rs9939609 polymorphism is located in the intronic region of the *FTO* gene. This particular polymorphism is one of many in this gene that influence genetic obesity risk. The **A** allele is associated with higher levels of the appetite-stimulating hormone ghrelin, as well a an increased risk of obesity and type-2 diabetes. Higher ghrelin levels are associated with over-eating due to lack of satiation. Macronutrient composition of the first meal of the day has been shown to affect ghrelin levels. Obese individuals who ate a meal high in fiber-rich carbohydrates and protein had significantly low postprandial ghrelin levels compared to those who ate an isocaloric diet that was low in carbohydrates. These results suggest that a breakfast high in carbohydrates and protein may help reduce ghrelin levels and facilitate greater satiety. Sleep has also been shown to be an important regulator of ghrelin levels. Sleep loss has been show to significantly increase ghrelin levels in healthy, normal weight individuals. This suggests that adequate sleep may be an important factor in maintaining normal ghrelin levels. The (**A;A**) genotype has been associated with obesity particularly in the context of a high saturate fat and low polyunsaturated fat intake. Saturated fat is found in fatty beef, pork, coconut oil, butte cheese, and other dairy products, while polyunsaturated fats are found in foods like nuts and fatty fish such as salmon and herring. This research suggests that individuals that are at high risk of obesity due to FTO polymorphisms, such as this one, may benefit by having a higher polyunsaturated fat intake and a lower saturated fat intake. • Read more about rs9939609 on SNPedia SNPs Involved rs9939609(A;T)
FTO	rs1121980(C;T)	1.67-fold increased risk for obesity particularly with saturated fat	The *FTO* gene, the major genetic risk factor for obesity, codes for the fat mass and obesity-associated protein. There is a cluster of polymorphisms in the *FTO* gene that increase obesity risk. **This genotype, rs1121980(C;T), has been associated with a 1.67-fold increased risk of obesity particularly with saturated fat.** There are common polymorphisms in the *FTO* gene, which codes for the fat mass and obesity-associated protein. The rs1121980 polymorphism is located in the intronic region of the *FTO* gene. This particular polymorphism is one of many in this gene that influence genetic obesity risk. The (**C;T**) genotype has been associated with a 1.67-fold increased risk for obesity particularly in t context of a high saturated fat and low polyunsaturated fat intake. Saturated fat is found in fatty beef, pork, coconut oil, butter, cheese, and other dairy products, while polyunsaturated fats are found in foods like nuts and fatty fish such as salmon and herring. This research suggests that individuals at high risk of obesity due to FTO polymorphisms, such as this one, may benefit from having a higher polyunsaturated fat intake and a lower saturated fat intake. • Read more about rs1121980 on SNPedia. • Read more about the association between this SNP and obesity. SNPs Involved rs1121980(C;T)
FADS2	rs1535(A;G)	~26.7% poorer conversion of ala into omega-3 epa	The fatty acid delta-6 desaturase (FADS2) enzyme is responsible for elongating the polyunsaturate fatty acid alpha-linolenic acid (ALA) and converting it into eicosapentaenoic acid (EPA). **This genotype, rs1535(A;G), has been associated with a 26.7% decrease in the efficienc at which ALA is converted into omega-3 EPA**. There are common polymorphisms in the *FADS2* gene, which codes for the fatty acid delta-6 desaturase enzyme. The **G** allele is the variant form of the rs1535 polymorphism and is located in the intronic region of the gene. In a meta-analysis of genome-wide association studies (GWAS) involving 8,866 individuals of European descent, the **G** allele was associated with elevated levels of ALA and reduced levels of EPA. These results suggest that subjects carrying the **G** allele convert ALA to EPA at a lower rate th individuals with the (**A;A**) genotype.

			predominantly on ALA (from flaxseed or chia seed, for example) as their source of EPA and DHA. A requires conversion into EPA by the FADS2 enzyme, whereas, fish or fish oil contains both EPA & DHA, and circumvents the need for conversion. Interestingly, curcumin has been demonstrated to increase the level of the FADS2 enzyme leading to an increase in brain DHA content. • Read more about rs1535 on SNPedia SNPs Involved rs1535(A;G)
FADS1	rs174548(C;G)	Associated with intermediate phosphatidylcholine levels	Phosphatidylcholine is a key component of cell membranes and plays an important role in the structure of the cell. It is also a precursor for the neurotransmitter acetylcholine, which has been shown to play a role in promoting REM sleep. Damage to the cholinergic system in the brain has been shown to be plausibly associated with the memory deficits associated with Alzheimer's disea and possibly other neurodegenerative diseases. For this reason it has been a therapeutic target through the action of acetylcholinesterase inhibitors, which prevent the enzymatic breakdown of acetylcholine. **This genotype, rs174548(C;G), has been associated with having intermediate phosphatidylcholine levels.** There are common polymorphisms in the *FADS1* gene, which codes for the fatty acid delta-5 desaturase enzyme. The variant form (**G**) of the rs174548 polymorphism, located in the intronic region of the gene, is thought to produce an enzyme with reduced efficiency. Study participants (n=1,644) were genotyped and a subset (n=284 males) were tested for various metabolic parameters. Researchers found that individuals carrying the **G** allele had lower phosphatidylcholine levels than individuals with the (**C;C**) genotype. Phosphatidylcholine can be found in supplement form and its precursor choline can be found in dietary sources, such as organ meats and egg yolk. *TMAO and choline supplementation* Recent research has suggested that nutrients such as choline, phosphatidylcholine, L-carnitine an betaine are metabolized by gut bacteria to generate trimethylamine (TMA), which is then converte into trimethylene N-oxide (TMAO) by the liver. Elevated plasma levels of TMAO may enhance plate aggregation (clotting) and increase heart disease risk. However, the metabolism of TMAO is compl and still poorly understood in humans. Furthermore, choline is an essential nutrient in the human diet. • Read more on SNPedia. SNPs Involved rs174548(C;G)
PEMT	rs7946(C;T)	Reduced phosphatidylcholine production	Phosphatidylethanolamine-N-methyltransferase (PEMT) is an enzyme that catalyzes the synthesis phosphatidylcholine and, thus, choline in the liver. Phosphatidylcholine is a fundamental compone in all cell membranes and plays an essential role in the structure and function of the cell. **This genotype, rs7946(C;T), has been associated with lower phosphatidylcholine production in the liver.** There are common polymorphisms in the *PEMT* gene, which codes for the phosphatidylethanolamine-N-methyltransferase enzyme. The variant form (**T**) of the rs7946 polymorphism is located in the coding region of the gene and results in an enzyme with partial los of activity. *Sleep* Phosphatidylcholine is a precursor for the neurotransmitter acetylcholine, which has been shown t play a role in promoting REM sleep. *Memory* Damage to the cholinergic system in the brain has been associated with memory deficits observed with Alzheimer's disease and other neurodegenerative diseases. Acetylcholinesterase inhibitors, which prevent the enzymatic breakdown of acetylcholine, are used as therapeutic targets in the treatment of dementia. *Fatty liver disease* In addition to the essential role that phosphatidylcholine plays in cell membranes (particularly in neurons), it is also necessary in the liver. Phosphatidylcholine is required for the liver to secrete triglycerides into very low-density lipoproteins (VLDL cholesterol). Decreased phosphatidylcholine can lead to reduced fat removal from the liver and, for that reason, may be associated with fatty liver disease. **Lifestyle interactions** *Dietary choline intake* Choline is found in foods such as eggs, meat, fish and cruciferous vegetables. Strict vegetarians m need to pay special attention to meeting their choline needs. The Food and Nutrition Board (FNB) the Institute of Medicine (IOM) has established the Adequate Intake (AI) for choline for men (550 m and for women (425 mg) during pregnancy (450 mg) and lactation (550 mg).

			Recent research has suggested that nutrients such as choline, phosphatidylcholine, L-carnitine an betaine are metabolized by gut bacteria to generate trimethylamine (TMA), which is then converte into trimethylene N-oxide (TMAO) by the liver. Elevated plasma levels of TMAO may enhance plate aggregation (clotting) and increase heart disease risk. However, the metabolism of TMAO is compl and still poorly understood in humans. Furthermore, choline is an essential nutrient in the human diet. • Read more about rs7946 on SNPedia SNPs Involved rs7946(C;T)
FTO	rs1421085(C;T)	1.3-fold increased obesity risk and decreased thermogenesis	The *FTO* gene, the major genetic risk factor for obesity, codes for the fat mass and obesity-associated protein. There is a cluster of polymorphisms in the FTO gene that increase obesity risk. **This genotype, rs1421085(C;T), has been associated with a 1.3-fold increased obesity r and decreased thermogenesis.** There are common polymorphisms in the *FTO* gene, which codes for the fat mass and obesity-associated protein. The rs1421085 polymorphism is located in the intronic region of the *FTO* gene. This particular polymorphism is one of many in this gene that influence genetic obesity risk. Approximately 43% of individuals of European ancestry carry one risk allele (**C**), and 20% possess two risk alleles (**C;C**). The (**C;T**) genotype is associated with a 1.3-fold increased risk of obesity as result of the body shifting from energy-burning adipocytes (brown adipose tissue) to energy-storin adipocytes (white adipose tissue). Consequently, adipocytes store more lipids, and the individual gains weight. This genotype is also associated with reduced thermogenesis (the burning of fat to produce heat) in response to cold exposure. Therefore, less fat is burned in adipose tissue during cold exposure. *Fish oil* Fish oil activates UCP1 and can increase thermogenesis, thus, fish oil supplementation may be beneficial for individuals with the (**C;T**) genotype. *Exercise* Regular exercise may also combat some of the negative effects of the (**C;T**) genotype. The effect FTO polymorphisms on obesity risk in general has been shown to be attenuated by approximately 30% in physically active individuals. • Read more about rs1421085 on SNPedia. • Read more about FTO and fat storage and decreased thermogenesis. SNPs Involved rs1421085(C;T)
MTRR	rs1801394(A;G)	Increased risk for hyperhomocysteinemia and altered choline metabolism	There are common polymorphisms in the MTRR gene that code for the enzymemethionine synthas reductase, which catalyzes the conversion of the inactive form of another enzyme, methionine synthase (MTR), to its active form using riboflavin (vitamin B2) as a cofactor. MTR is involved in th remethylation of homocysteine to methionine with cobalamin (vitamin B12) participating as a cofactor. This reaction is of utmost importance as MTR plays a pivotal role in folate metabolism an methionine cycling. **This genotype, rs1801394(A;G), may be associated with hyperhomocysteinemia and altered choline metabolism.** This polymorphism encodes for an MTRR enzyme with a reduced affinity for MTR resulting in less efficient reactivation of MTR, possibly resulting in elevated homocysteine levels. Some associations have been made between rs1801394 and hyperhomocysteinemia especially in combination with low vitamin B12 levels and the *MTHFR* rs1801133 variant. Individuals with this polymorphism may be at increased risk for neural tube defects (which can be circumvented by folate supplementation), meningioma (a form of brain cancer) 1.4X increased risl for the GG genotype (not this genotype) and altered choline metabolism. This polymorphism has been shown to influence the way choline is partitioned between the Cdp-choline pathway and betaine synthesis. At recommended adequate intake (AI) levels of choline, women with this variant shuttled more choline towards phosphatidylcholine synthesis at the exper of betaine synthesis. However, at levels above the AI, normal partitioning was restored, suggestin that women with this polymorphism may benefit from dietary choline intake above the current AI levels. These recent studies may prompt the Institute of Medicine (IOM) to refine the dietary recommendations to include individuals with increased choline needs. **Dietary choline intake.** Choline is found in foods such as eggs, meat, fish and cruciferous vegetables. Strict vegetarians may need to pay special attention to meeting their choline needs. T Food and Nutrition Board (FNB) of the Institute of Medicine (IOM) has established the Adequate Intake (AI) for choline for men (550 mg) and for women (425 mg) during pregnancy (450 mg) and lactation (550 mg). **Betaine and reductions in homocysteine.** One of the functions of choline is to serve as a precursor of a compound known as betaine or trimethylglycine. Betaine aids in the remethylation homocysteine to methionine via the enzyme betaine-homocysteine methyltransferase (BHMT), thu serving to lower homocysteine levels in the blood.

			associated with a slight *increase* in total and LDL cholesterol by 5 to 10 mg/dL in some studies. Ot studies have found that a more conservative and *dietarily* attainable dose of just 1.5 grams per da can also lower homocysteine levels by as much as 23% after six weeks. Foods rich in betaine inclu quinoa, spinach, and beets. **Vitamin B12 and B2.** Cobalamin (vitamin B12) and riboflavin (vitamin B2) balance is thought to an important factor in people with this polymorphism. When B12 status was low, those with the G allele had higher homocysteine levels than those with the (A;A) genotype. Individuals susceptible t low vitamin B12 status include older adults, those with digestive issues (Crohn's, colitis), post gast bypass patients and those following vegan diets. *TMAO and choline supplementation* Recent research has suggested that nutrients such as choline, phosphatidylcholine, L-carnitine an betaine are metabolized by gut bacteria to generate trimethylamine (TMA which is then converted into trimethylene N-oxide (TMAO) by the liver. Elevated plasma levels of TMAO may enhance platelet aggregation (clotting) and increase heart disease risk. However, the metabolism of TMAO is complex and still poorly understood in humans. Furthermore, choline is an essential nutrient in the human diet. • Read more on SNPedia SNPs Involved rs1801394(A;G)
APOC3	rs2542052(A;C)	May increase lifespan	**This genotype, rs2542052(A;C), may be associated with increased lifespan; however, scientific data for this particular variant are lacking.** It is noteworthy, however, that in a stud of more than 400 Ashkenazi Jewish centenarians and their offspring and an age-matched Ashkena control group, those who carried *both* of the APOC3 alleles **(C;C)** of the rs2542052 variant of the APOC3 gene tended to have healthy lipoprotein levels, better cardiovascular health, and increased insulin sensitivity, and were more likely to achieve older age. The effects of carrying a *single* allele a particular variant range from no easily observable effect to a lower magnitude of the effects see when carrying both alleles. • Read more about rs2542052 on SNPedia **APOC3** Apolipoprotein C-3 (APOC3) plays a key role in how the body metabolizes triglycerides. Mice that lack the APOC3 gene tend to have lower blood triglyceride levels, whereas mice that have high amounts of APOC3 tend to have higher blood triglyceride levels. In humans, some variants of APO are associated with having lower blood triglyceride levels and reduced risk for atherosclerosis and heart disease. SNPs Involved rs2542052(A;C)
CDKN2B-AS1	rs2811712(A;G)	Less risk of physical impairment with age	**This genotype, rs2811712(A;G), is associated withless risk for physical impairment with age.** In a study of nearly 3,000 older adults, those who carried the **A;G** form of the rs2811712 variant of the CDKN2B-AS1 gene had an approximately 1.5-fold lower risk of experiencing physical impairment with age. • Read more about rs2811712 on SNPedia **CDKN2B-AS1** CDKN2B-AS is a long, non-coding section of RNA. (Non-coding RNAs don't encode new proteins; rather, they regulate gene expression at the transcriptional and post-transcriptional level.) CDKN2 AS may play a role in several conditions associated with aging, including impaired physical functio cardiovascular disease, diabetes, and Alzheimer's disease. SNPs Involved rs2811712(A;G)
IL-6	rs1800795(G;G)	Associated with longer lifespan and increased risk of certain diseases	**This genotype, rs1800795(G;G), is associated with increased lifespan and increased ris of certain diseases.** In a study of 285 Finnish adults, those who carried one or more of the **G** alleles (**C;G** or **G;G**) of the rs1800795 variant of the IL-6 gene were more likely to achieve older age (between the ages of 90 and 95 years). In a meta-analysis of nearly 100 studies that investigated links between this genotype and cancer risk, 78 of the studies found that people who carried one or more of the **G** alleles (**C;G** or **G;G**) of th

G;G form of the rs1800795 variant of the IL-6 gene were nearly four times more likely to die within one year of the event.

In a study of more than 5,000 men and women that took place over a 9-year period those who carried one or more of the **G** alleles (**C;G** or **G;G**) of the rs1800795 variant of the IL-6 gene were more approximately 30% more likely to develop diabetes. (If they carried four or more diabetes-related variants, their risk increased by nearly 250%.)

- Read more about rs1800795 on SNPedia

IL-6

Interleukin-6, or IL-6, is a type of cell-signaling protein. It is produced by cells in the immune system in response to infection or trauma (such as burns). IL-6 plays both pro- and anti-inflammatory roles in the body, depending on the physiological context. For this reason, the rs1800795 variant of the 6 gene is both *directly* and *indirectly* associated with longevity.

For example, some studies *directly* link variants of this gene with increased lifespan. However, rs1800795 variants are also associated with heart disease, Kaposi's sarcoma, type-2 diabetes, stroke, obesity, Hodgkin's lymphoma, sudden infant death syndrome, cancer (including breast cancer, gastric cancer, and prostate cancer), high blood pressure, gum disease, and organ transplant rejection, all of which can *indirectly* shorten lifespan. In addition, the link between the variants and these conditions isn't always related to increased or decreased risk; rather, the link may be related to how a person does or does not respond to treatment.

Whereas the **C** allele is associated with *decreased* levels of IL-6, the **G** allele is associated with *increased* levels of IL-6.

SNPs Involved

rs1800795(G;G)

AKT1	rs3803304(G;G)	May increase lifespan	AKT serine/threonine kinase 1 (AKT1) is an enzyme that regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. It is a component of an intracellular signaling pathway called PI3K/AKT/mTOR, which plays roles in the cell cycle, cancer, and longevity. **This genotype, rs3803304(G;G), has been associated with increased lifespan.** There are common polymorphisms in the *AKT1* gene, which codes for AKT serine/threonine kinase enzyme. The variant form (**G**) of the rs3803304 polymorphism is located in the intronic region of th gene. In a study of elderly Caucasian men and women, individuals carrying one or more copies of the **G** allele (**C;G** or **G;G**) were more likely to reach older age, especially among female subjects. - Read more about rs3803304 on SNPedia * These alleles have been adjusted for consistency with SNP orientation. Read more about orientation.

SNPs Involved

rs3803304(G;G)

NPAS2	rs2305160(C;C)	Circadian-associated increased breast/prostate cancer risk	There has been increasing evidence that mutations in genes involved in circadian rhythm play a ro in cancer growth. The NPAS2 gene controls genes involved in cell growth, metabolism, and DNA repair. When these cellular processes become dysregulated this can allow cancer cells to form and proliferate. **This genotype, rs2305160(C;C), has been associated with *increased risk* of certain human cancers including breast cancer and prostate cancer.** One mechanism by which dysregulation of the *NPAS2* gene increases cancer risk is through its effe on metabolism and energy balance. Published data most strongly support fasting insulin, bioavailable estradiol, and C-reactive protein (CRP) as biomarkers of breast cancer risk. Individuall these biomarkers are associated with an approximate **two-fold** increased risk of incident or recurrent breast cancer. For each 10% increase in the proportion of calories consumed after 5pmwas associated with a 3% increase in the inflammatory biomarker CRP (c-reactive protein). For each 3-hour increase in night time fasting duration was linked to a 20% lower odds of elevated glycated hemoglobin (HbA1C). Studies have shown that consuming food earlier in the day and only during an11-hour window, can decrease breast cancer risk and recurrence by as much as 36%. Together, these data suggest that time-restricted eating is a viable option to lower biomarkers of inflammation and insu resistance and lower breast cancer risk and recurrence. **More Information** - More information about practical implications for time-restricted eating and breast cancer. - More information on time-restricted eating, circadian rhythm, and cancer risk. - Read more on SNPedia

SNPs Involved