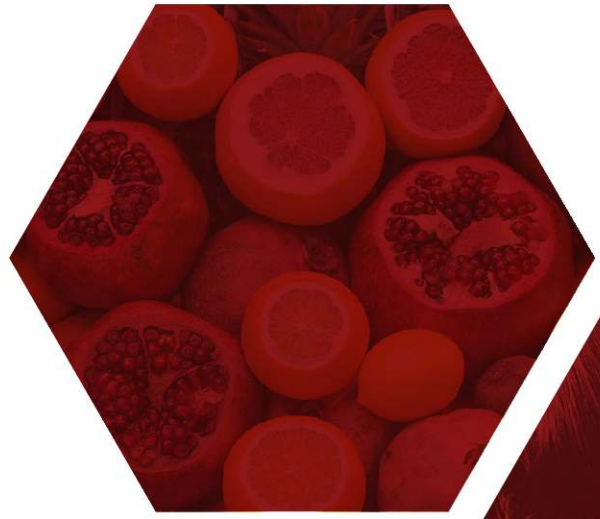
ImmuneHealth

Your personal genetic profile focused on **Immunity**

- Inflammation
- Vitamin D pathway
- Cardiovascular Health
- Gut Health and Methylation
- Metabolism of Lipids, Vitamin C, and Zinc



GENETIC PROFILE ID: 0000000

POWERED BY fitgenes

Name: Sample Client

Kit: 0-000-000-0

Introduction

Genetic variants (alterations in the DNA sequence) are what makes everyone unique.

Thank you for choosing Fitgenes and for your purchase of this report.

Fitgenes is a DNA-based healthtech company aiming at helping individuals achieve personalised goals in overall health, nutrition, and performance, by applying nutrigenetic and nutrigenomic evidence.

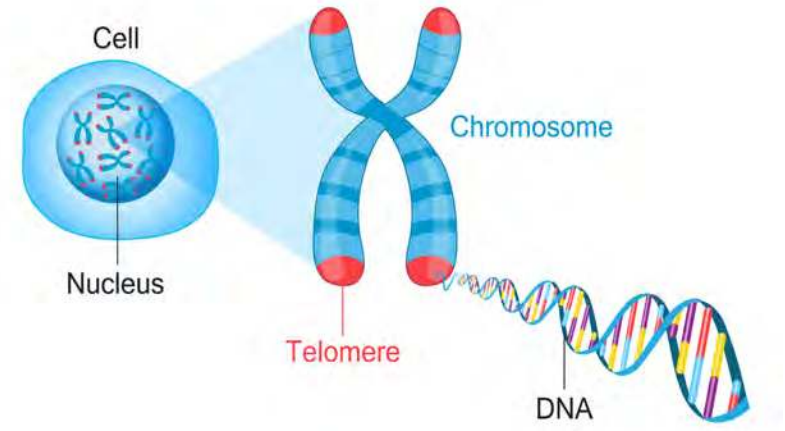
THE BASICS OF DNA

The human genome consists of 23 pairs of chromosomes found in the cell nuclei, which contain genes and other non-coding sequences. Overall, it is estimated that each individual has approximately 30,000 genes. A gene is, essentially, a sequence of DNA that codes for a molecule with a function. As chromosomes come in pairs, each individual has two copies of each gene, one inherited from each parent.

NUTRIGENOMICS

Nutrigenetics and nutrigenomics are the disciplines focused on the link between diet and genes. In particular, nutrigenetics is the science that studies genetic variants associated with a differential response to nutrients, as well as our health and wellbeing, while nutrigenomics is a whole system approach that investigates how nutrients can affect gene expression. Other lifestyle choices, including exercise, can also affect gene expression

A person cannot change their inherited genes, however they may be able to compensate for their influence. That is, one can modify gene expression and improve the functioning of genes by making the right nutrition, exercise, and other lifestyle choices.



THE GENETICS OF IMMUNITY

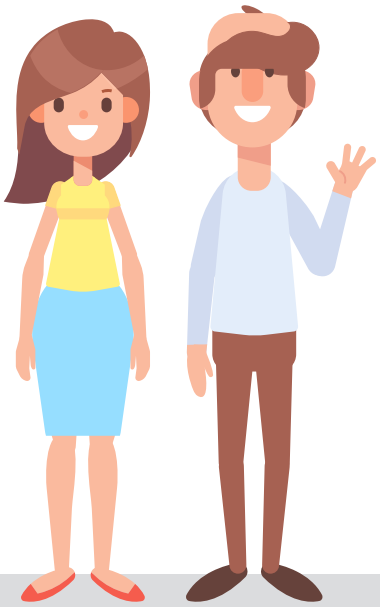
The immune response is a normal biological reaction to protect the body against foreign invaders, such as viruses, bacteria, and other substances that appear to be harmful. There are two main types of immune response that work together:

(i) innate immunity, which is the first line of defence and is present from birth, and

(ii) adaptive immunity, which is more specific and takes longer to activate.

The overall immune response can vary among individuals depending on environmental and genetic factors. In particular, there are genes with a direct role in immunity, but there are also other genes with multiple functions that have been shown to affect the immune response more directly.

Your ImmuneHealth Genetic Profile Report



This report presents a number of genes from different biological pathways that have been demonstrated to have a role in the immune system. Some of the genes have variants that have been associated with risk of varied immunity outcomes, while others belong to biological pathways relevant to immunity.

This may provide information regarding your ability to prevent and minimise the impact of disease and, where applicable, how your genes may be relevant to your ability to fight infections.

These genes have been grouped according to the primary biological effect that they have been demonstrated to have in the body, although some genes will impact multiple biological processes.

The groupings are:

- **Inflammation**
- **Vitamin D pathway**
- **Cardiovascular health**
- **Gut health and methylation**
- **Lipid metabolism**
- **Zinc metabolism, and**
- **Vitamin C metabolism**

For each gene, three different results are possible, as shown by the figure below.

Beneficial	Less Beneficial	Least Beneficial
One or both of the genes in the pair contributes to the normal healthy functioning of the gene product.	One of the genes in the pair is contributing to a situation that impairs the healthy functioning of the gene product.	Both of the genes in the pair are contributing to a situation that impairs healthy functioning of the gene product.

The result of a genetic test can be either the reference variant (that found in the human reference genome) or the alternative (that other than the reference found at the same position). As described earlier, genes in every human being exist as a pair. Variants in one or both of the genes, known as alleles, may result in three possible physiological outcomes as listed in the following table. The potential risk variants of each gene (denoted by orange or red dots) indicate an impaired or suboptimal physiological functioning of the gene product, or a less beneficial outcome from the available options.

Overall, the higher number of beneficial results in the report, the more efficient your immunity is likely to be, based on the genes tested in this report. Conversely, a higher number of less/least beneficial results suggest a possible "call for action" or greater scrutiny and assessment of your immunity risk. This information, combined with other assessments, can be used by an accredited health practitioner to design more personalised and targeted recommendations to optimise immunity.

More information and associated references and interventions can be found in Fitgenes' proprietary Pracware platform.

Note: when comparing results from Fitgenes with other sources, it is important to take into account whether testing was done on the forward or reverse strand. For this reason, it is possible that results do not match completely, but they are still the same (C=G, A=T). Caution should be taken with complementary changes (C>G, A>T).

Limitations: all genes and variants presented in this report, with their corresponding implications for your health, have gone through extensive scientific literature review. Nevertheless, genetic research is rapidly advancing, and our understanding of the information included in this report will increase over time, and so the content of future reports may vary from this one.

1 INFLAMMATION

Inflammation is a key biological response of the immune system triggered by pathogens, damaged cells or toxic substances. As a consequence of an injury or infection, immune cells travel to the necessary site to protect the area and cause inflammation. An efficient inflammatory response is controlled by an interplay between pro-inflammatory and anti-inflammatory cytokines, and variations in corresponding genes may impact that efficiency.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
IL-1α-1 (rs1800587)	Pro-inflammatory cytokine	Belong to the IL-1 family of cytokines Have a key role in inflammation and host response to pathogen infection Genetic variations in IL-1A and IL-1B have been associated with susceptibility to and/or severity of influenza virus infection	CC	🟢		
IL-1α-2 (rs17561)			GG	🟢		
IL-1-β (rs16944)			AG		🟡	
IL-1B-2 (rs1143627)			TC		🟡	
IL-6 (rs1800795)		Important mediator of the acute phase response Also acts as anti-inflammatory cytokine Genetic variation in IL-6 has been associated with spontaneous clearance of hepatitis C virus infections Overexpression leads to a favourable viral environment	GC		🟡	
IL-8 (rs4073)		Makes neutrophils and other granulocytes migrate to the site of infection and stimulates phagocytosis	AA			🔴
IL-17 (rs2275913)		Key cytokine whose role is linking T cell activation to neutrophil mobilization and activation Genetic variation in IL-17 has been associated with susceptibility to and/or severity of influenza virus infection	GG			🔴
IL-18 (rs1946518)		Augments natural killer cells and stimulates interferon-gamma production in T-helper type I cells	GG			🔴
IL-28B (rs8099917)		Cytokine member of the interferon (IFN)-λ family, reported to regulate B- and T-cell responses during influenza vaccination Genetic variation in IL-28B has been associated with susceptibility to and/or severity of influenza virus infection	GT		🟡	

❶ INFLAMMATION (cont.)

Inflammation is a key biological response of the immune system triggered by pathogens, damaged cells or toxic substances. As a consequence of an injury or infection, immune cells travel to the necessary site to protect the area and cause inflammation. An efficient inflammatory response is controlled by an interplay between pro-inflammatory and anti-inflammatory cytokines, and variations in corresponding genes may impact that efficiency.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
TNFα (rs1800629)	Pro-inflammatory cytokine (cont'd)	Its main role is the regulation of immune cells Also part of the acute phase reaction Has been shown to be a key negative regulator of type 1 immune activation following intracellular bacterial infection Genetic variation in TNFA has been associated with susceptibility to and/or severity of influenza virus infection	GA			
TNFA-2 (rs361525)			GG			
CRP-1 (rs2794520)		Acute-phase protein whose circulating concentrations increase in response to inflammation	CC			
CRP-2 (rs2592887)			GG			
CRP-3 (rs1205)			CC			
COX-2-1 (rs20417)		Plays a key role in chronic inflammatory events including infections Highly expressed during gammaherpesvirus directed malignancies	GG			
COX-2-3 (rs689466)			AA			
IL-10-1 (rs1800896)	Anti-inflammatory cytokine	Labelled as "the master regulator of immunity to infection" Can both prevent pathogen clearance and also improve immunopathology	AA			
IL-10-2 (rs1800871)			CC			
IL-10-3 (rs1800872)			CC			

❷ VITAMIN D PATHWAY

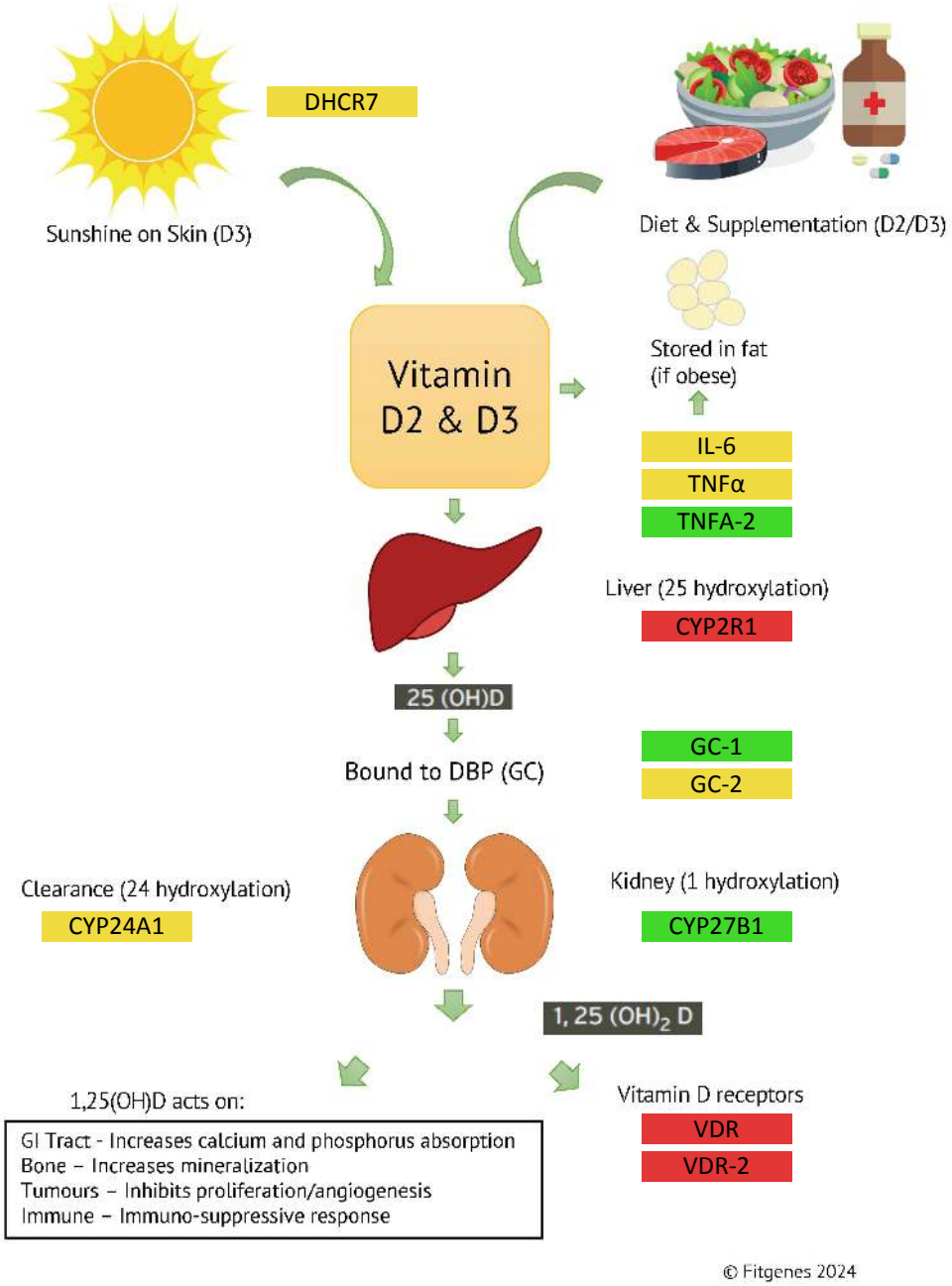
Vitamin D is a fat-soluble vitamin produced by the body in response to sunlight, and also found in some foods. In addition to its effect on calcium and bone health, vitamin D can also modulate both the innate and adaptive immunity, being essential for the proper functioning of the immune system. It exerts its function by binding the vitamin D receptor (VDR), which is expressed on immune cells (B cells, T cells and antigen presenting cells). Variations in VDRs may impact or limit the benefits of Vitamin D, necessary for immune-regulating role of the pro-inflammatory and anti-inflammatory cytokines. Accordingly, vitamin D deficiency has been associated with higher risk of several autoimmune diseases and viral infections.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
VDR (rs1544410)	Vitamin D receptor	Expressed by immune cells to allow vitamin D to participate in the regulation of innate immune responses	GG			🔴
VDR-2 (rs731236)		Has a role in the adaptive immune system by modulating antigen-presentation and T cells proliferation and phenotype	TT			🔴
DHCR7 (rs12785878)	7-dehydrocholesterol reductase	Inhibition of DHCR7 enzyme activity has been associated with a higher ability to clear multiple viruses through IRF3 activation and IFNβ production	TG		🟡	
CYP2R1 (rs10741657)	25-hydroxylase	CY2PR1 gene transcription has been associated with plasma levels of 1,25-dihydroxyvitamin D3 in Th cells, a type of T cell essential in immunity	GG			🔴
GC-1 (rs4588)	Vitamin D-binding protein	Plays a direct role in the inflammatory cascade, and a proximate role in innate immunity regulation	GG	🟢		
GC-2 (rs7041)		Genetic variation in GC has been associated with diverse outcomes in a range of infectious diseases	CA		🟡	
CYP27B1 (rs10877012)	1-alpha-hydroxylase	High expression of CYP27B1 occurs in response to innate immune stimuli to regulate immune responses Generates dihydroxyvitamin D in macrophages which has anti-mycobacterial and anti-viral effector functions	TT	🟢		
CYP24A1 (rs6013897)		Enzyme that converts 1,25(OH)2D to inactive 24,25 (OH)2D for clearance.	TA		🟡	

❷ VITAMIN D PATHWAY - DIAGRAM

The following diagram illustrates the biological process of vitamin D as it is processed by the skin, liver and kidneys and their associated genes highlighted in different colours according to your results. Some of the relevant genes are included in Inflammation. This visual representation helps to understand the pathway and the genetic variations affecting vitamin D metabolism.



❸ CARDIOVASCULAR HEALTH

Cardiovascular health relies on the healthy functioning of the heart, blood, and blood vessels. The heart can be defined as an immunological organ that activates an innate stress system following different types of injury to coordinate homeostatic responses. Cardiovascular disease has been proposed to be a risk factor for multiple autoimmune diseases and increased mortality following viral infections. At the same time, the immune system has an important contribution to cardiovascular health.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
ACE (rs4343)	Renin-angiotensin system protein	Part of the renin-angiotensin system, which is known to have a key role in the regulation of blood pressure, but also has an effect on the immune system and inflammation by modulating the cellular synthesis of several molecules such as cytokines, chemokines and transcription factors Genetic variation in ACE has been associated with the number of SARS-CoV-2 cases, and as a result this gene has been proposed to be a predictive marker for COVID-19 risk and severity	ID		🟠	
AGT (rs699)			TT	🟢		
AGTR1 (rs5186)			AA	🟢		
GNβ3 (rs5443)	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-3	Genetic variation in GNB3 has been associated with differential T cell response	CT		🟠	
eNOS3-2 (rs1799983)	Nitric oxide synthase 3	Its expression is important for the development of adaptive immune responses Nitric oxide is involved in the pathogenesis and control of infectious diseases and regulates dendritic cells immune function	GT		🟠	
NADPH-CYBA (rs4673)	Cytochrome b-245 alpha chain	Produces a protein part of the NADPH oxidase enzyme complex, which is essential in the immune system Especially active in phagocytes and regulates the activity of neutrophils	CC			🔴
PAI-1-S (rs2227631)	Plasminogen activator inhibitor 1	Has a critical role in protecting the host during the acute phase of infection by regulating interferon-gamma release	GG	🟢		
ADIPOQ (rs1501299)	Adiponectin	Produces adiponectin which has anti-inflammatory activity Has been labelled as "a versatile player in innate immunity" Genetic variation in ADIPOQ has been reported to result in higher adiponectin levels affecting the regulation of the immune response	CA		🟠	

4 GUT HEALTH AND METHYLATION

The microorganisms residing in the gastrointestinal tract have a role in regulating innate and adaptive immune homeostasis, not only in the local intestinal immune system but also in the systemic immune responses, being essential to host health. It has also been shown that host genetics has an effect on the composition of the gut microbiome, in combination with diet and lifestyle, with certain genetic variants leading to differences in the immune response through microbiome dysbiosis, among other mechanisms. On the other hand, gut microbiota composition is also associated with the global methylation pattern, having a specific role in the intestinal folate production.

YOUR RESULTS

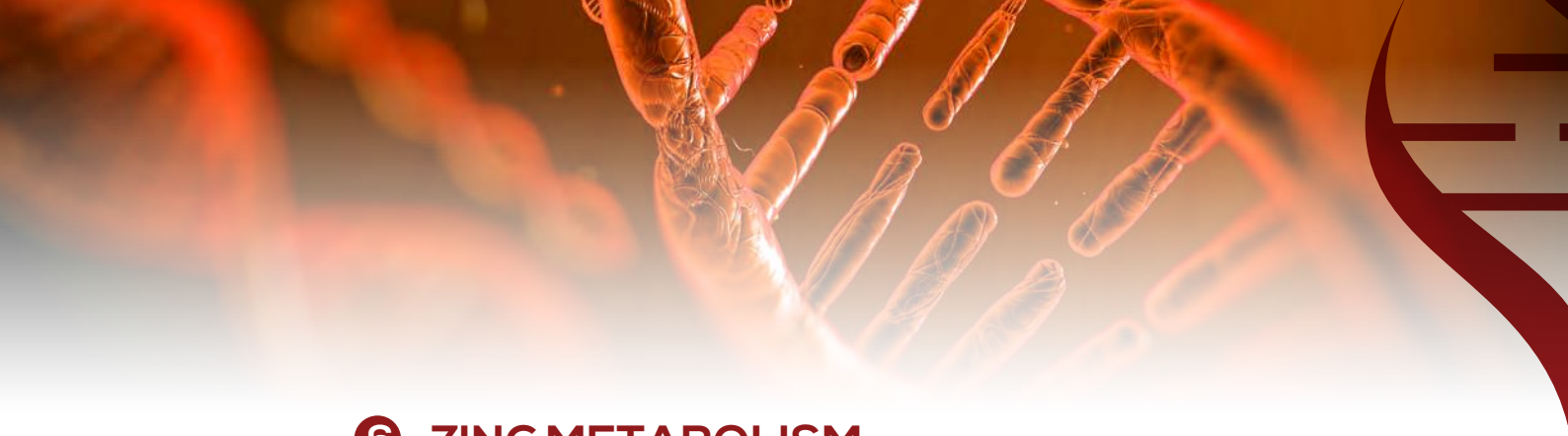
Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
FUT2 (rs602662)	Golgi stack membrane protein	Affects the HBGA (Histo-Blood Group Antigen) expression in intestinal epithelial cells Genetic variation in FUT2 determining the secretor or non-secretor status has been shown to modulate innate immune responses and may affect survival during different pathogen outbreaks	AA			
TLR1-1 (rs5743551)	Toll-like receptor	Expressed in the intestinal epithelial cells where it has a role in recognising harmful microorganisms and regulating the immune response Activation of TLR signalling leads to the production of inflammatory cytokines and chemokines Genetic variation in TLR1 has been associated with hyperinflammatory response, and consequently worse immunity outcomes, as well as differences in the ability to recognise harmful microorganisms Genetic variation in TLR4 has been associated with predisposition to many types of infectious diseases	CT			
TLR4 (rs4986790)			AA			
MY09B-2 (rs1545620)	Myosin IXB	Highly expressed in the human immune system Genetic variation in MY09B has been associated with risk of intestinal and autoimmune disorders, suggesting a defect in the primary intestinal barrier	CA			
MTHFR-1 (rs1801133)	Methylenetetrahydrofolate reductase	While genetic variation in MTHFR leads to reduced enzyme activity and therefore risk of impaired methylation and folate deficiency, this variation has also been reported to provide a survival advantage in the host response against pathogens and therefore might represent a beneficial outcome for immunity. Note: The genetic variant result will be the same, however the interpretation here (green versus orange/red) could therefore be expected to be different to that in the Fitgenes Health and Wellbeing Report.	CC			
MTHFR-2 (rs1801131)			CA			

5 LIPID METABOLISM

Lipid metabolism refers to the synthesis and degradation of lipids in cells. There is a complex interplay between lipid metabolism and the immune system by regulating each other. Specifically, lipids have immune functions to protect and modulate immune responses against infectious agents, which are attempting to exploit existing lipid signalling for cellular entry.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
PPARδ (rs2016520)	Member of the peroxisome proliferator-activated receptor subfamily of nuclear receptors	Has multiple functions in the immune system Expressed mostly by macrophages and dendritic cells Activation of PPARG has been proposed to be a potential effective therapeutic strategy following virus infections	TT			
PPARγ (rs1801282)	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-3	Has a role in in mediating responses to inflammation Expressed by many immune cells, including monocytes/macrophages, platelets, lymphocytes, and dendritic cells	CC			
LEPR-1 (rs1137101)	Leptin receptor	Inflammatory molecule that regulates both adaptive and innate immunity Links metabolism with the immune system Can enhance multiple immune functions and inhibit CD4+ T and NK cells	AA			
LEPR-2 (rs1137100)			AA			
ADRβ2 (rs1042714)	Beta-2-adrenergic receptor	ADRB2 signalling has been reported to regulate inflammation through IL-10 rapid induction and to have a role in adaptive T-cell responses to infection	GG			
CETP (rs708272)	Cholesteryl ester transfer protein	Has a role in decreasing the inflammatory response to bacterial endotoxins by interacting with the innate immune system and sequestrating pro-inflammatory lipopolysaccharide	TT			



6 ZINC METABOLISM

Zinc is an essential mineral naturally present in some foods. Zinc homeostasis is essential for the function of the immune system, given that zinc has a role in maintaining host immune function. Zinc deficiency has been shown to negatively affect both innate and adaptive immune responses, leading to an increased risk of infection.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
SLC39A14 (rs4872479)	Zinc transporter 14	Zinc importing protein with a role in glucose homeostasis Genetic variation in SLC39A14 has been associated with blood zinc concentrations	GG			
CA-1 (rs1532423)	Carbonic anhydrase	Carbonic anhydrases are zinc-containing enzymes that account for nearly all the zinc in erythrocytes Genetic variation in CA-1 has been associated with blood zinc concentrations	CT			
PPCDC (rs2120019)	Phosphopantothenoylcysteine decarboxylase	Part of the coenzyme A synthesis pathway Reported to affect zinc status through effects vitamin B5 metabolism Genetic variation in PPCDC has been associated with blood zinc concentrations	TT			
NBDY (rs4826508)	Negative Regulator Of P-Body Association	Human microprotein that interacts with the mRNA decapping complex Genetic variation in NBDY has been associated with blood zinc concentrations	TC			

7 VITAMIN C METABOLISM

Vitamin C is an essential macronutrient with many functions in the human body, including collagen formation, iron absorption, and proper functioning of the innate and adaptive immune system. Specifically, it supports epithelial barrier against pathogens and has a role in microbial killing. Research has shown a link between vitamin C deficiency and risk of infectious diseases and supplementation with vitamin C has been shown to prevent and treat respiratory and systemic infections.

YOUR RESULTS

Gene (variant)	Short description of the encoded molecule	Relation to immunity	Your Result			
SLC23A1 (rs33972313)	Vitamin C transporter	Key transporters involved in the absorption of vitamin C into the body	CC			
SLC23A2 (rs6053005)		Genetic variation in SLC23A1 and SLC23A2 has been associated with vitamin C levels	CC			

Summary

This report has been designed to identify variations in your genes involved in multiple biological pathways that could have an impact on your immunity. This and other information can be used by your health practitioner to design personalised interventions to boost your immunity.

#	Gene	Reported Variant	rsID	Your Result			
Inflammation - Pro-inflammatory cytokine							
1	IL-1α-1	-889C>T	rs1800587	CC	🟢		
2	IL-1α-2	+4845G>T	rs17561	GG	🟢		
3	IL-1β	-511G>A	rs16944	AG		🟡	
4	IL-1B-2		rs1143627	TC		🟡	
5	IL-6	-174 G>C	rs1800795	GC		🟡	
6	IL-8	-251T>A	rs4073	AA			🔴
7	IL-17		rs2275913	GG			🔴
8	IL-18	-607C>A (G>T)	rs1946518	GG			🔴
9	IL-28B		rs8099917	GT		🟡	
10	TNFα	-308 G>A	rs1800629	GA		🟡	
11	TNFA-2		rs361525	GG	🟢		
12	CRP-1	+0169171C>T	rs2794520	CC	🟢		
13	CRP-2	+0143294C>T (G>A)	rs2592887	GG			🔴
14	CRP-3	3872C>T	rs1205	CC			🔴
15	COX-2-1	(-765 G>C)	rs20417	GG			🔴
16	COX-2-3	-1195A>G	rs689466	AA			🔴
Inflammation - Anti-inflammatory cytokine							
17	IL-10-1	-1082G>A	rs1800896	AA			🔴
18	IL-10-2	-819C>T	rs1800871	CC	🟢		
19	IL-10-3	-592C>A	rs1800872	CC	🟢		
Methylation - Golgi stack membrane protein							
20	FUT2	A>G(T>C), (Ser258Gly)	rs602662	AA	🟢		
Methylation - Toll-like receptor							
21	TLR1-1		rs5743551	CT		🟡	
22	TLR4		rs4986790	AA	🟢		
Methylation - Myosin IXB							
23	MY09B-2		rs1545620	CA		🟡	
Methylation - Methylenetetrahydrofolate reductase							
24	MTHFR-1	+677 C>T	rs1801133	CC			🔴
25	MTHFR-2	+1298A>C	rs1801131	CA		🟡	
Vitamin D metabolism - Vitamin D receptor							
26	VDR	BsmI RFLP	rs1544410	GG			🔴
27	VDR-2	Taq1 C>T	rs731236	TT			🔴
Vitamin D metabolism - 7-dehydrocholesterol reductase							
28	DHCR7	T > G	rs12785878	TG		🟡	
Vitamin D metabolism - 25-hydroxylase							
29	CYP2R1	G > A	rs10741657	GG			🔴
Vitamin D metabolism - Vitamin D-binding protein							
30	GC-1	1307C>A, T436K	rs4588	GG	🟢		
31	GC-2	1296G>T, D432E	rs7041	CA		🟡	
Vitamin D metabolism - 1-alpha-hydroxylase							
32	CYP27B1	-1260C > A	rs10877012	TT	🟢		
33	CYP24A1	T > A	rs6013897	TA		🟡	

#	Gene	Reported Variant	rsID	Your Result			
Cardiovascular health - Renin-angiotensin system protein							
34	ACE	Ins. / Del.	rs4343	I/D		🟡	
35	AGT	M235T	rs699	TT	🟢		
36	AGTR1	+1166A>C	rs5186	AA	🟢		
Cardiovascular health - Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-3							
37	GNβ3	C825T	rs5443	CT		🟡	
Cardiovascular health - Nitric oxide synthase 3							
38	eNOS3-2	+894G>T	rs1799983	GT		🟡	
Cardiovascular health - Cytochrome b-245 alpha chain							
39	NADPH-CYBA	+242C>T	rs4673	CC			🔴
Cardiovascular health - Plasminogen activator inhibitor 1							
40	PAI-1-S	-844G>A	rs2227631	GG	🟢		
Cardiovascular health - Adiponectin							
41	ADIPOQ	+276 G>T (C>A)	rs1501299	CA		🟡	
Lipid metabolism - Member of the peroxisome proliferator-activated receptor subfamily of nuclear receptors							
42	PPARδ	+294T > C	rs2016520	TT	🟢		
Lipid metabolism - Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-3							
43	PPARγ	Pro12Ala	rs1801282	CC	🟢		
Lipid metabolism - Leptin receptor							
44	LEPR-1	Gln223Arg	rs1137101	AA	🟢		
45	LEPR-2	Lys109Arg	rs1137100	AA	🟢		
Lipid metabolism - Beta-2-adrenergic receptor							
46	ADRβ2	(Gln27Glu)	rs1042714	GG			🔴
Lipid metabolism - Cholesteryl ester transfer protein							
47	CETP	+279G>A (C>T)	rs708272	TT	🟢		
Zinc metabolism - Zinc transporter 14							
48	SLC39A14		rs4872479	GG			🔴
Zinc metabolism - Carbonic anhydrase							
49	CA-1		rs1532423	CT		🟡	
Zinc metabolism - Phosphopantothenoylcysteine decarboxylase							
50	PPCDC		rs2120019	TT	🟢		
Zinc metabolism - Negative Regulator Of P-Body Association							
51	NBDY		rs4826508	TC		🟡	
Vitamin C metabolism - Vitamin C transporter							
52	SLC23A1		rs33972313	CC	🟢		
53	SLC23A2		rs6053005	CC			🔴

Samples obtained after 18 Oct 2021 will test for all genes listed in this new ImmuneHealth Report. Older samples will only show genes which were available at the time of original testing (as listed in the previous version; the "Immunity Report"). Because of this, older samples may give a report with sections appearing blank as they were not present in the old panel.

The immune response is a very complex biological process controlled by genetic and environmental influences, and this report contains a subset of genes with a role in the immune response. A number of genetic variants included in this profile were originally selected based on outcomes related to the Fitgenes Health and Wellbeing profile, and therefore, unless indicated in the text, there are no reports specifically linking variation to immunity. If you have a serious concern about your immune system, please speak to your health practitioner.

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