Viral Report v1

Source: genome_Elizabeth_Owen_v4_Full_20190520235434.zip

Created at June 10 at 5:34 PM PST

This report includes some of the SNPs that have been studied in the context of SARS-CoV-2, SARS-CoV-1, ACE2 gene expression, acute respiratory distress syndrome (ARDS), flu risk, and more.

Noteworthy

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

Gene	SNPs involved	Status	More information
IL1A	rs1800587(C;T)	Associated with slight increased viral load in sars-cov-1 infection	Interleukin 1 alpha (IL1A) is a proinflammatory cytokine located both intracellularly and bound to cell membranes. IL1A performs several roles in the immune response. Functioning as an alarmin, IL1A alerts the host to infection or cell damage and triggers an inflammatory response. While much remains unknown about 1L1A, some research suggests that it gauges the level of infection or damage and signals other immune response molecules to launch the appropriate response. **This genotype, rs1800587(C;T), has been associated with slightly increased viral load in SARS-CoV-1 infection.** There are common polymorphisms in the *IL1A* gene, which codes for the interleukin 1 alpha protein. The variant form (**T**) of the rs1800587 polymorphism (also known as -889 C>T), is located in the 5 prime untranslated region of the gene and may alter the level of gene expression. In the SARS-CoV-1 outbreak of 2003, patients experienced inter-individual differences in nasopharyngeal viral loads, with higher viral load predicting poor prognosis. To determine whether host genetic factors accounted for some of these differences, researchers analyzed immunity related genes in 94 SARS CoV-1 patients. Investigators observed that patients with the **T** allele of the rs1800587 polymorphism exhibited increased risk of virus shedding as compared to those with the (**C;C**) genotype. The authors suggest that in a pandemic where no preexisting immunity exists, the host's innate immunity will be important to decrease viral burden and potentially influence the clinical outcome. • Read more about rs1800587 on SNPedia SNPs Involved rs1800587(C;T)
MBL2	rs1800450(A;G)	Associated with susceptibility to sars-cov-1 infection	Mannose-binding lectin (MBL) is a protein in the blood that plays a critical role in the innate immune response and is considered to be a first-line host defense against pathogens. Repeating mannose and N-acetylglucosamine sugar motifs are found on the surfaces of bacterial and fungal cells and viruses, but not on mammalian cells. The SARS-CoV-1 S protein, believed to play a critical role in infection, also exhibits these repeating mannose units. The MBL protein binds to an invader via these motifs activating the complement system and initiating opsonophagocytosis (a process that signals the immune system to engulf and destroy a pathogen). **This genotype, rs1800450(A;G), has been associated with susceptibility to SARS-CoV-1 infection.** There are common polymorphisms in the *MBL2* gene, which codes for the mannose-binding lectin protein. The variant form (**A**) of the rs1800450 polymorphism (also known as Gly54Asp), located in the exonic region of the gene, leads to an altered protein structure which degrades more rapidly, resulting in lower plasma concentrations of the MBL protein. In a study of 352 SARS1 patients and 392 healthy control subjects, individuals with the **A** allele had a higher risk of becoming infected with the SARS-CoV-1 virus as compared to those with the (**G;G**) genotype. However, researchers did not find an association between the **A** allele and disease severity. The authors suggest that this polymorphism may play a role in activating the innate immune response. Individuals with the (**A;G**) genotype exhibit one-tenth the level of MBL protein as compared to those with the (**G;G**) genotype. Individuals with the (**A;A**) genotype had undetectable MBL plasma levels. A deficient level of MBL protein may be a critical factor in determining the susceptibility to SARS1 during the initial phase of infection before the production of antibodies. Researchers replicated these findings in a study including 4 case-control populations (n = 932 patients with SARS1 and 982 control subjects). Subjects with low serum MBL levels were at greater risk of SARS-CoV-1 infection as compared to individuals with the (**G;G**) genotype. Again, no association was found between this polymorphism and disease severity. The authors suggest that a deficiency in MBL may be a factor influencing the susceptibility to SARS-CoV-1 infection. The adaptive immune response involves pathogen recognition and the production of specific antibodies. However, this process takes time, often several days. The innate immune response is vital during the early phase of infection before the production of sufficient antibodies. The capability of an individual's innate immune response may partly explain the variable response to the SARS-CoV-1 virus. • Read more about rs1800450 on SNPedia

			SNPs Involved rs1800450(A;G)
OAS1	rs2660(G;G)	Associated with a protective role against sars1	Oligoadenylate synthetase 1 (OAS1) is an interferon-induced protein with antiviral properties. OAS1 activates latent RNase L, a ribonuclease enzyme capable of degrading viral RNA and inhibiting replication. **This genotype, rs2660(G;G), has been associated with a protective role against SARS1.** There are common polymorphisms in the *OAS1* gene, which codes for the 2',5'-oligoadenylate synthetase 1 enzyme. The variant form (**G**) of the rs2660 polymorphism (also known as Arg397Gly), located in the exonic region of the gene, is thought to affect a splicing site resulting in an OAS1 enzyme with higher activity. In a case-control study of Chinese subjects (n = 66 confirmed SARS1 patients and 64 serologically negative close contacts), this polymorphism was associated with SARS-CoV-1 infection. Carriers of the **G** allele were more likely to be in the control group than the case group, suggesting a possible protective effect of the **G** allele. The authors suggest that among Chinese individuals the **G** allele confers protection against SARS-CoV-1 infection. The estimated frequencies of the **G** allele are 41.7% among European-Americans, 10.9% among African-Americans, 18.2% among Japanese, and 36.4% among Chinese individuals. • Read more about rs2660 on SNPedia SNPs Involved rs2660(G;G)
IL17A	rs2275913(A;G)	Associated with a reduced risk of developing acute respiratory distress syndrome	Interleukin 17 (IL17), also known as IL17A is a proinflammatory cytokine produced by activated memory CD4 + and T-cells. Some patients with acute respiratory distress syndrome have elevated levels of IL17. IL17 amplifies the inflammatory response by attracting other immune cells. While IL17 is useful to defend against pathogens, excessive IL17 may pose problems. The cytokine storm, a characteristic feature of severe COVID-19, involves the expression of mass amounts of proinflammatory cytokines like IL17. **This genotype, rs2275913(A;G), has been associated with a reduced risk of developing acute respiratory distress syndrome.** There are common polymorphisms in the *IL17A* gene, which codes for the interleukin 17 protein. The variant form (**A**) of the rs2275913 polymorphism (also known as G197A), located in the promoter region of the gene may affect gene expression. Acute respiratory distress syndrome (ARDS) is a serious form of respiratory failure that occurs in some critically ill patients due to uncontrolled inflammation in the lungs. In a study of 210 patients with ARDS and 210 at-risk patients without ARDS, carriers of the **A** allele exhibited a reduced risk of ARDS as compared to patients with the (**G;G**) genotype. Furthermore, patients with the **A** allele had a decreased 30-day mortality risk compared to patients with the (**G;G**) genotype. The authors note that **A** allele carriers had lower IL17 serum levels, which they suggest may provide the patient with some protection from developing ARDS. paper While further studies are needed, the regulation of IL17 might be involved in the initiation and progression of ARDS, and this polymorphism may be a marker to predict the risk of ARDS. • Read more about rs2275913 on SNPedia SNPs Involved rs2275913(A;G)

Less noteworthy

These genotypes are normal.

Gene	SNPs involved	Status	More information
ACE2	rs2158082(A;A)	Higher tissue expression of the ace2 gene which may have implications for covid-19 disease symptoms	Angiotensin-converting enzyme-2 (ACE2) is a transmembrane protein that is involved in the renin-angiotensin system that regulates blood pressure, inflammation and body fluid homeostasis. The SARS-CoV-2 virus exploits the ACE2 receptor to gain entry into host cells. **This genotype, rs2158082(A;A), has been associated witha higher tissue expression of the *ACE2* gene which may have implications for COVID-19 disease symptoms.** There are common polymorphisms in the *ACE2* gene, which codes for the angiotensin-converting enzyme-2. The variant form (**G**) of the rs2158082 polymorphism, located in the intron region of the gene, is thought to decrease gene expression. Researchers examined the expression levels of the *ACE2* gene in various tissues and found that

			individuals with the **G** allele had lower expression of the gene as compared to those with the **A;A**) genotype. The authors propose that the expression level of the *ACE2* gene may be a factor in susceptibility or severity of SARS-CoV-2 infection. They suggest that an increase in ACE2 expression may be associated with a more severe clinical outcome, while lower expression may result in a milder form of the disease. It is important to note that these findings are preliminary, and research is evolving rapidly in this area. This agrees with previous research using SARS-CoV-1 infected transgenic mice, where overexpressing the human *ACE2* gene increased disease severity. ACE2 is necessary for viral entry into the host cell, however upon infection, ACE2 expression is down-regulated leading to an unbalanced renin-angiotensin system and lung damage. Thus, ACE2 is thought to have a dual role, involved both in viral entry and protecting the lung from damage. Investigators analyzed 1,700 polymorphisms found in the *ACE2* gene to determine whether their frequency differed across populations. They found that variants associated with higher ACE2 tissue expression are more common in East Asian populations as compared to Europeans and propose that this may alter susceptibility or severity to the SARS-CoV-2 virus. The authors did not identify any variations in the *ACE2* gene that would predict a weakened binding of the coronavirus S-protein, which might confer resistance. A promising study in human organoid tissue revealed that a recombinant form of the human ACE2 receptor was able to neutralize the SARS-CoV-2 virus by binding to it, thus blocking it from infecting the cell. The recombinant receptor reduced viral load by a factor of 1,000 to 5,000 and may diminish excessive inflammation, limiting lung injury. A randomized, double-blind Phase II trial in 200 severely infected SARS-CoV-2 patients will begin soon. SNPs Involved rs2158082(A;A)
IL18	rs1946518(G;G)	Associated with lower viral load in sars-cov-1 infection	Interleukin 18 (IL18) is a potent proinflammatory cytokine expressed in the lung. IL18 performs several functions in the immune response, including stimulation of interferon-gamma (IFN-γ) release from natural killer cells and T lymphocytes. Interestingly, IFN-γ has been shown to directly inhibit the replication of certain viruses, including SARS CoV-1. **This genotype, rs1946518(G;G), has been associated with a lower viral load in SARS-CoV-1.** There are common polymorphisms in the *IL18* gene, which codes for the interleukin 18 protein. The variant form (**T**) of the rs1946518 polymorphism, located in the promoter region of the gene, is thought to disrupt a transcription factor-binding site and lead to reduced IL18 production. In the SARS-CoV-1 outbreak of 2003, patients experienced inter-individual differences in nasopharyngeal viral loads, with higher viral load predicting poor prognosis. To determine whether host genetic factors accounted for some of these differences, researchers analyzed immunity related genes in 94 SARS CoV-1 patients. Investigators observed that patients with the **T** allele of the rs1946518 polymorphism exhibited increased risk of virus shedding as compared to those with the (**G;G**) genotype. The authors suggest that in a pandemic where no preexisting immunity exists, the host's innate immunity will be important to decrease viral burden and potentially influence the clinical outcome. • Read more about rs1946518 on SNPedia SNPs Involved rs1946518(G;G)
MX1	rs17000900(C;C)	Associated with normal susceptibility to sars-cov-1 infection	Myxovirus resistance A (MxA) is an intracellular protein with antiviral properties. Levels of MxA protein in the cells of healthy individuals are low, however, upon viral infection, these proteins are induced by interferons. **This genotype, rs17000900(C;C), has been associated with normal susceptibility to SARS 1 coronavirus infection.** There are common polymorphisms in the *MX1* gene, which codes for the myxovirus resistance A protein. The variant form (**A**) of the rs17000900 polymorphism (also known as -123 C>A), located in the promoter region of the gene, increases promoter activity leading to higher gene expression and production of the myxovirus resistance A protein. In a case-control genetic-association study (n = 817 SARS1 patients and 422 seronegative household members), researchers observed that carriers of the **A** allele had a lower risk of SARS-CoV-1 infection than those with the (**C;C**) genotype. The authors propose that the **A** allele of this polymorphism enhances the basal expression of the *MX1* gene without requiring induction by interferon, which may be significant in a disease such as SARS1 where the virus suppresses interferons. In this study, **A** allele carriers exhibited a decreased susceptibility to SARS-CoV-1 infection, however the polymorphism was not associated with clinical outcomes. The authors conclude that this SNP may be useful in assessing susceptibility to infectious diseases, particularly those that are similar to SARS CoV-1. • Read more about rs17000900 on SNPedia SNPs Involved rs17000900(C;C)

AHR	rs2066853(G;G)	Associated with a decreased risk of ards in patients with pneumonia	Aryl hydrocarbon receptor (AhR) is a transcription factor that controls several genes involved in diverse cellular processes, including inflammation, immune regulation, and the detoxification of xenobiotic substances. A mounting body of evidence suggests that AhR plays a critical role in the intersection between the innate and adaptive immune system, helping to maintain immune homeostasis. Furthermore, AhR may be involved in controlling pathways that protect the lungs from oxidative stress. **This genotype, rs2066853(G;G), has been associated with a decreased risk of ARDS in patients with nosocomial pneumonia.** There are common polymorphisms in the *AHR* gene, which codes for the aryl hydrocarbon receptor. The variant form (**A**) of the rs2066853 polymorphism (also known as Arg554Lys) is located in the coding region of the gene and is thought to decrease gene expression. Nosocomial (hospital-acquired) pneumonia is a complication of trauma that can progress to acute respiratory distress syndrome (ARDS), a serious form of respiratory failure due to excessive inflammation in the lungs. Researchers conducted a prospective study to evaluate if host genetic factors affect whether individuals progress from pneumonia to ARDS. They studied 419 hospitalized patients at high risk of critical illness and 331 healthy controls. Of the hospitalized patients, 268 developed pneumonia, and 151 patients did not. Investigators observed that in patients with hospital-acquired pneumonia, carriers of the **A** allele were more likely to develop ARDS than patients with the (**G;G**) genotype. The authors propose that variants in the*AHR* gene may be involved with increasing lung inflammation and the development of ARDS. • Read more about rs2066853 on SNPedia SNPs Involved rs2066853(G;G)
CD55	rs2564978(C;C)	Associated with normal influenza a disease severity	Complement regulatory protein CD55 (CD55), also known asdecay accelerating factor (DAF), occurs as both a membrane-bound and soluble protein that is involved in regulating the complement system of the innate immune response. The complement system is a host-defense strategy against invading pathogens. CD55 binds to complement proteins and induces an accelerated decay, thus keeping the complement system in check so that it does not damage host cells. **This genotype, rs2564978(C;C), has been associated with normal influenza A disease severity.** There are common polymorphisms in the *CD55* gene, which codes for the cmplement regulatory protein CD55. The variant form (**T**) of the rs2564978 polymorphism, located in the intronic region of the gene, decreases gene expression and results in lower CD55 protein synthesis. This SNP serves as a proxy for a 21 base pair insertion/deletion that occurs in the promoter region of the gene. Individuals with the **C** allele possess the insertion, and those with the**T** allele carry the deletion. The influenza H1N1 pandemic of 2009 typically produced mild infection, however, some patients developed severe pneumonia. To investigate whether host genetic factors influenced disease severity, researchers performed a small genome-wide association study (GWAS) involving 25 patients with severe H1N1 infection and 26 controls with mild symptoms. They identified polymorphisms in the *CD55* gene that strongly associated with disease severity. In a second study of 425 Chinese patients with severe (n = 177) or mild (n = 248) disease, investigators observed that the (**T;T**) genotype associated with severe disease as compared to carriers of the**C** allele. Moreover, the investigators report that individuals with the (**T;T**) genotype had lower monocyte CD55 levels compared to **C** allele carriers. The authors propose that CD55 plays a role in determining the severity of H1N1 by protecting respiratory epithelial cells from complement damage. Since **T** allele carriers have lower CD55 levels, they are more prone to severe disease. In another gene association study (n = 275 patients with avian H7N9 or pandemic H1N1 influenza) the (**T;T**) genotype was associated with an increased incidence of the need for hospitalization. In a study of European individuals from northern Greece with severe (*n* = 59) or mild (*n* = 51) H1N1 infection, the (**T;T**) genotype was associated with an increased mortality risk as compared to carriers of the **C** allele. CD55 inhibits an overactive complement system. The researchers propose that individuals with the (**T;T**) genotype who have a deletion in the promoter of the *CD55* gene, and thus lower CD55 levels, may generate a stronger complement activation, which may damage respiratory epithelial cells leading to worse outcomes. The authors state that their findings are preliminary and that more research is needed. • Read more about rs2564978 on SNPedia SNPs Involved rs2564978(C;C)
TLR4	rs4986790(A;A)	Associated with normal risk for septic shock	Toll-like receptor 4 (TLR4) is a member of a family of receptors found on the surfaces of macrophages and dendritic cells. As part of the innate immune response, TLRs recognize specific bacterial and viral proteins and target them for destruction. The interaction of TLR4 and a viral protein leads to the production of pro-inflammatory cytokines. Uncontrolled activation of the TLR4 pathway is a feature of sepsis and cytokine storm. **This genotype, rs4986790(A;A), has been associated with normal risk for septic shock.** There are common polymorphisms in the *TLR4* gene, which codes for the toll-like receptor 4 protein. The variant form (**G**) of the rs4986790 polymorphism (also known as Asp299Gly) is located in the coding region of the gene.

			In a study of 91 patients in the ICU with septic shock as a result of a bacterial infection and 73 healthy controls, the **G** allele of this polymorphism was only observed in septic shock patients The authors propose that individuals with the **G** allele might be predisposed to develop septic shock when infected with gram-negative bacteria. Investigators examined 99 hospitalized infants with severe respiratory syncytial virus (RSV) bronchiolitis, 88 infants with mild RSV bronchiolitis, and 90 healthy adults. They observed that the **G** allele was associated with severe RSV bronchiolitis. Animal studies show that deleting the TLR4 gene in mice renders the animals resistant to a lethal influenza virus. • Read more about rs4986790 on SNPedia SNPs Involved rs4986790(A;A)
TMPRSS2	rs12329760(C;C)	Predicted to have normal susceptibility to the a2a (d614g) strain of sars-cov-2	Transmembrane serine protease 2 (TMPRSS2) is an enzyme expressed in cells of the lung, ileum, and nasal passage, that participates in both physiological and pathological activities. In some viral infections, including influenza and the coronavirus diseases, SARS1 (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), this protease cleaves a viral protein, facilitating its entry into the host cell. The SARS-CoV-2 spike (S) glycoprotein exploits the ACE2 receptor to gain entry into host cells. For the viral and cell membranes to fuse, a protease, such as TMPRSS2, must cleave the spike (S) protein in a process known as priming. SARS-CoV-2 was recently shown to use the ACE2 receptor for binding and the TMPRSS2 protease for S protein priming. **This genotype, rs12329760(C;C), has been predicted to have normal susceptibility to the A2a (D614G) strain of SARS-CoV-2.** There are common polymorphisms in the TMPRSS2 gene, which codes for the transmembrane serine protease 2 enzyme. The variant form (**T**) of the rs12329760 polymorphism (also known as V160M), located in the coding region of the gene, is thought to disrupt a pathogen interaction site. Viruses are constantly mutating, and only changes that do not affect essential viral functions persist in the population. SARS-CoV-2 has mutated into at least 10 subtypes, with subtype A2a spreading widely across Europe and North America, but not East Asia. Subtype A2a, also known as D614G, has a mutation in the spike protein that creates an additional enzyme site where the S protein can be cut and activated. This mutation may allow the virus to more easily enter host cells. The **T** variant of this polymorphism is predicted to cleave the spike protein of the A2a strain less effectively (than the **C** allele), thus limiting the virus's entry into cells. The **T** allele is negatively correlated (r^2 = -0.4) with the frequency of the A2a viral subtype, suggesting that individuals with the (**T;T**) genotype might have some protection against this strain of the virus The allele frequencies of this polymorphism differ between populations, with ~19 percent of East Asians having the (**T;T**) genotype, while only ~7 percent of Europeans and ~4 percent of North Americans possess the (**T;T**) genotype. These varying frequencies may partly explain why the A2a strain spread less rapidly in East Asia. Further research is needed to determine if these preliminary findings are validated in other studies. • Read more about rs12329760 on SNPedia SNPs Involved rs12329760(C;C)

Unavailable

Depending on the dataset you provided for report generation, not all possible report entries may be available. *This is normal.* In this case, the following groups were excluded because the data you upload did not contain the requisite SNPs:

IFITM3, ACE2, FGL2, TLR1