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Breakthrough Genomics has partnered with myGenomics® to offer the first targeted Coronavirus Genetic Susceptibility Assessment (CGSA)* panel designed to assess your genetic susceptibility to SARS-CoV-2 infection and the development of acute respiratory distress syndrome (ARDS) and severe acute respiratory syndrome (SARS)

myGenomics® is a CLIA licensed Genomics Services laboratory that is using Breakthrough Genomics' ENLITER™ platform, a fully automated clinical genomic data interpretation platform.

ENLITER™ is powered by artificial intelligence and deep machine learning (ML) and the Breakthrough Genomics team used its proprietary ML knowledge base to comb through millions of published medical journals and curated databases and other information to identify genes and polymorphisms (also referred to as variants) that have been associated with SARS CoV-2 from 2019, SARS-CoV-1 from the SARS outbreak in 2003, as well as the middle east respiratory syndrome-related coronavirus (MERS-CoV) in 2012.

The polymorphisms selected for the CGSA panel provided a feasible mechanism of action at the molecular level that could translate into biological effects that can either impact viral infection or replication, or your immune response to viral infection, or were found to correlate with susceptibility to other coronavirus infections or SARS development. The CGSA polymorphisms may result in changes in the function or expression of these genes.

The CGSA panel covers 28 polymorphisms from 14 different genes. The genes can be categorized into 4 areas based their potential roles in SARS-CoV-2 infection and development of SARS (also referred to as COVID-19).

1 **Viral infection and replication.** 5 genes and 19 polymorphisms of the CGSA panel affect virus replication and antiviral machinery within host cells. 14 of the polymorphisms are associated with the ACE2 gene which encodes the receptor for SARS-CoV2. The SARS-CoV2 virus infects cells of the upper respiratory tract and lungs by binding to the angiotensin-converting enzyme (ACE2) molecule on the cell's surface. Upon binding, the spike protein is cleaved by a host protease (TMPRSS2) and internalized for further replication and subsequent amplification and spread of infection. Three ACE2 polymorphisms identified are suspected to disrupt binding to the SARS CoV-2 virus based on in vitro studies and should prevent or reduce virus infection.

The ACE2 gene is located on the X-chromosome, so men carry only one copy of the ACE2 gene while women carry two. Men (especially those over 50 years of age) are thought to be at higher risk of coronavirus-related hospitalization, mechanical ventilation, and death.

Alanyl aminopeptidase (ANPEP) is another angiogenic regulator which may serve as an alternate receptor for coronaviruses and SARS-CoV-2 infection and a polymorphism in this gene is part of the CGSA panel. The other polymorphisms of the CGSA panel in this category are part of the host cell machinery genes (IFITM3, OAS1, and MX1) responsible for viral replication, assembly and secretion of viruses and carrying these polymorphisms can disrupt the virus life cycle and limit the emerging viral infection.

** patent pending*

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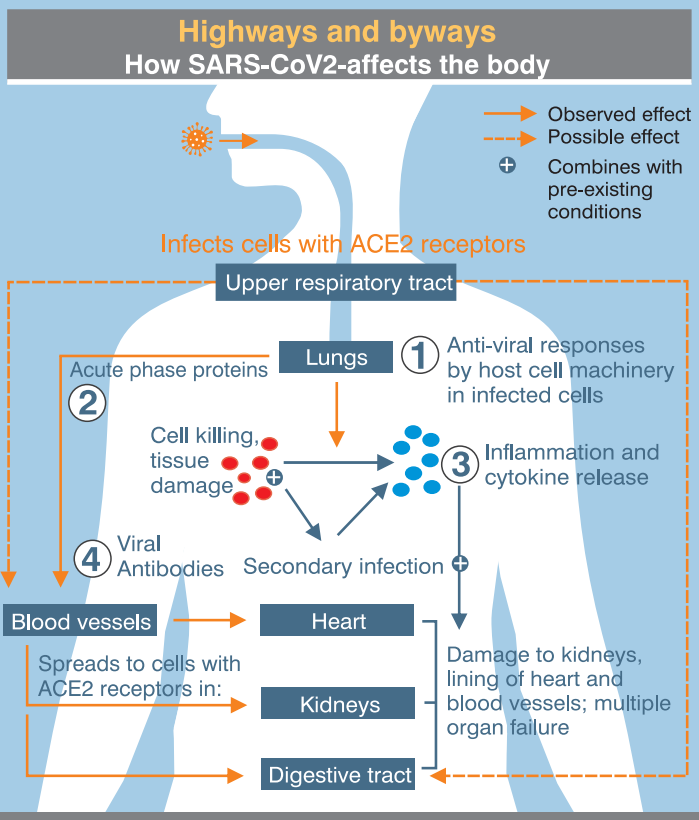
2 Innate Immunity and Antiviral Defense. Initial immune responses to virus infection are relatively non-specific and involves the recognition of distinct pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) which signals danger to cells and initiates a cascade of responses that direct host defense. Soluble PPRs like acute phase proteins are highly abundant proteins but polymorphisms in these genes are associated with decreased levels or functions which may contribute to virus amplification and a hyper immune response. The CGSA panels contains polymorphisms of three acute phase protein genes MBL2, ASHG, and Cd14 that have been associated with susceptibility to coronavirus infection and SARS.

3 Inflammatory Cytokines and Cytokine Storm. The coordinated recruitment and activation of the entire network of immune cells for the subsequent engagement of the adaptive immune response is mediated through cytokines, chemokines, and type 1 interferons. Their expression is typically transient and the amplitude and duration of their production limits the degree of inflammation. Prolonged and elevated expression of these molecules is the hallmark of severe and chronic inflammatory diseases and is referred to as a cytokine storm. Most COVID-19 patients will develop mild to moderate symptoms, while some infected people may face hyper-inflammation induced by massive cytokines/chemokines production which may lead to fatal pneumonia and acute respiratory distress syndrome. The CGSA panel contains polymorphisms for IFN-g, IL-4, CCL2 (MCP-1), and CCL5 (RANTES). These polymorphisms have been shown to correlate with changes in their relative expression levels as well as an individual's susceptibility to the development and severity of SARS including mortality.

4 Other immune related responses. Adaptive immunity to virus infection requires antibody production and subsequent binding of the antibody to the virus and clearance of the antibody-virus complexes by immune cells, a process called antibody-dependent cellular cytotoxicity (ADCC). This is a major mechanism of action for therapeutic monoclonal antibodies. A specific polymorphism in the Fc receptor gene, FCGR2A, is part of the CGSA panel and individuals carrying this polymorphism may have differential responses to therapeutic monoclonal antibodies such as cetuximab, rituximab, and trastuzumab and have also been shown to have susceptibility to inflammatory and infectious diseases including severe SARS-CoV infection.

Some of the most interesting CGSA polymorphisms are not within exons, commonly used SNP panels, or GWAS panels and would only be detected in whole genome sequencing. Although whole genome sequencing is the best method for identifying and understanding genetic susceptibility to COVID-19, the CGSA panel offers a cost-effective alternative and is aligned with our mission; to offer affordable and high quality genomic lab services to empower your personal health journey and to help you live a healthy and long life.



Disclaimer. The polymorphisms contained in the CGSA panel are speculative predictors of susceptibility and are based on limited information with less clinical information than is considered acceptable by clinical labs for a diagnostic test and are provided for informational purposes. The results may not necessarily predict how you will respond to SARS CoV-2 exposure and infection. You may want to consider the results of your CGSA results along with lifestyle, environmental factors, and pre-existing health conditions and consult your healthcare professional for the best precautionary measures against COVID-19.

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