Whitepaper

Cerba Research

COVID-19 Therapy Development and Clinical Diagnostics

Revised January 2022

A clinical approach to a multifaceted, evolving disease

Executive summary

The SARS-CoV-2 virus, the causative agent for COVID-19, and the approach to diagnosis, vaccination, and treatment, have all evolved since the start of the pandemic. In response, researchers and drug developers have shifted focus from a prophylactic to a therapeutic approach. Regardless of emphasis, these experts must tackle the disease from every angle to make progress.

As scientists discover new variants, new questions become more relevant: How will variants impact vaccine efficacy? Who will need booster shots? Will we need new vaccines?

Targeting a multifaceted disease such as COVID-19 requires a diverse team of infectious disease experts. It also requires a central lab and clinical diagnostics partner with the expertise and portfolio of testing to serve sponsors' varied needs.

Studying COVID-19, a multifaceted disease, requires a comprehensive approach to further increase our understanding of the virus and the disease from a clinical point of view.

This knowledge will in turn provide us with more tools to battle the SARS-CoV-2 virus in the form of prophylactics, to prevent infection and/or therapeutics to treat the virus' downstream effects.

The approach to diagnose SARS-CoV-2 infection, vaccinate people, and treat COVID-19 patients has evolved since the start of the pandemic. In response to the evolving situation, the focus of researchers and drug developers has progressed from a prophylactic to a prophylactic and/or therapeutic approach to combat the disease. Regardless of emphasis, these experts must tackle the disease from every angle.

As scientists discover new variants, new questions become more relevant: How will variants impact vaccine efficacy? Who will need booster shots? Will we need new vaccines? How will new variants impact the epidemiology and the natural history of the disease?

Targeting a multifaceted disease such as COVID-19 not only requires a diverse team of infectious disease and immunology experts, it also requires a central lab and clinical diagnostics partner with the expertise and portfolio to serve sponsors' varied needs.

The many facts of COVID-19

Coronaviruses are infectious viral disease agents of zoonotic origin that can infect humans.

The diseases caused by human coronaviruses used to be so mild that there was no research done on them. This lasted up until the emergence of pathogenic coronaviruses two decades ago, with the first one (SARS-CoV-1) causing severe acute respiratory syndrome in 2002. This outbreak was quickly contained in 2003. However, the next outbreak causing a severe acute respiratory syndrome by a coronavirus, SARS-CoV-2, in December 2019, is not contained to this day and is responsible for the pandemic we still face.

Clinicians have described SARS-CoV-2 as a "COVID Planet" because of the large number of organs and tissues it affects and the wide clinical spectrum of COVID-19 ranging from asymptomatic, mild, moderate, severe, to critical disease.[1] While most patients only develop mild (40%) or moderate (40%) symptoms, about 15% develop severe symptoms requiring supplemental oxygen. And even 5% progress to critical disease with severe complications such as acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure.

Patients with underlying comorbidities are at a higher risk of progressing to severe or critical COVID-19. Comorbidities include being over age 65; having cardiovascular disease, chronic lung disease, sickle cell disease, diabetes, cancer, obesity, or chronic kidney disease; being a cigarette smoker; and receiving immunosuppressive therapy.[2]

Initially it was thought that SARS-CoV-2 infection caused purely a respiratory disease, it is now known that infected individuals can rapidly progress to a multiple organ dysfunction syndrome (MODS). The latter can be expressed in different organs and systems, such as lung, liver, kidney, heart, gastrointestinal, hematological, and nervous system.[3]

The study of such a multifaceted disease requires a comprehensive approach for diagnostics and multitarget therapeutics to reduce or even prevent SARS-CoV-2 infection and its downstream effects.

COVID-19 pathogenesis

The pathogenic phases of COVID-19 are not entirely understood. It has generally been hypothesized that the course of infection follows the viremia phase, dysregulated immune response, multiple organ damage, and recovery.

SARS-CoV-2 is an enveloped β-coronavirus, with high genetic similarity to SARS-CoV-1 (80%). The viral envelope is coated by spike (S) glycoprotein, envelope (E), and membrane (M) proteins. The S protein mediates host cell binding and entry, which is the first step in infection. The S1 sub-unit of the S protein contains the receptor binding domain (RBD) that binds to the angiotensin-converting enzyme 2 (ACE 2), the host target cell receptor.[3] During the viremia phase, the virus enters the host cells where it replicates, assembles, and is released extracellularly to target cells. At the same time, the host cell lyses or form syncytia and other lesions occur. This is the **direct cytopathic effect** of SARS-CoV-2, and it directly causes damage to cells such as alveolar epithelial cells.[4]

At the same time, the **antiviral innate immune response is stimulated**, meaning that the host immune cells produce antiviral and proinflammatory cytokines and chemokines to eliminate the invading viruses. The intensity of this response is related to the viral load, the age, and immune status of the host. In controlled disease, alveolar macrophages, cytotoxic T lymphocytes, and specific antibodies work to neutralize and eliminate infected cells.[4]

In the case of uncontrolled disease, there is an excessive immune response reaction to the virus triggered by inflammatory cell infiltration in the lungs, activation of T-helper 1 reactions, and abundant release of proinflammatory cytokines, including interleukin 6, into circulation. This can result in fatal uncontrolled systemic inflammatory response, known as the cytokine storm (CS). The CS syndrome can lead to ARDS, sepsis, and MODS. Researchers can monitor this severe immune response in a laboratory by quantifying the main proinflammatory cytokines like interleukin 6, interleukin-1 beta, interferon gamma, and TNF alpha.[5]

There are various long-term outcomes observed in patients with COVID-19, including recovery, organ fibrosis and dysfunction, chronic critical illness or persistent inflammation, immunosuppression and catabolism syndrome, and possibly even death.

Note: Patients with COVID-19 can relapse or become reinfected. Relapsed patients show reappearance of symptoms during recovery. Reinfected people are survivors susceptible to acquiring new infections after recovery.[6]

The many manifestations of COVID-19

Accurate diagnosis is necessary whether treating patients in clinical trials or in traditional healthcare settings. COVID-19 manifests in multiple ways, from asymptomatic to severe disease accompanied by life-threatening lung complications.

Acute COVID-19:

As mentioned above, about 80% of COVID-19 patients develop mild to moderate symptoms. The most common COVID-19 symptoms include headache, fever, fatigue, and lung problems. SARS-CoV-2 also causes damage to olfactory cells, which explains the loss of taste and smell that some COVID-19 patients experience.[1] Fifteen percent of patients experience severe respiratory symptoms requiring supplemental oxygen. In rare cases (5%), COVID-19 patients experience acute respiratory distress syndrome (ARDS) – the primary reason for intensive care unit admission. These severe cases often culminate in multiorgan dysfunction and death.

As the study of this virus requires a comprehensive approach for diagnostics and therapeutics, Cerba Research has prioritized implementing techniques to benefit research-driven projects and clinical research. On a research level, Cerba Research has contributed to identifying predictive biomarkers to help researchers gain a better understanding of the acute disease. On a clinical level, Cerba Research has developed the whole range of techniques to identify and characterize the virus and it infectious process, including NGS as well as PCR and antigen test for diagnosis, PCR and qPCR for viral load, mutation screening and NGS for variant typing, anti-N and anti-S serology, T-SPOT.COVID, etc.

Long COVID:

While most people with COVID-19 recover within a few weeks, a notable percentage experience symptoms that last for 12 weeks or longer. A survey conducted by the U.K. Office for National Statistics that followed 20,000 COVID-positive individuals over four weeks found that 13.7% experienced the lingering symptoms known as long COVID.[7]

Researchers have identified 205 long COVID symptoms that affect 10 organ systems.[8] These symptoms range from fatigue and shortness of breath to joint pain and cognitive dysfunctions. The sole cause of long COVID remains unknown. Researchers hypothesize that the virus causes the immune system to overreact and attack healthy tissue as well as the virus. Others suspect fragments of the virus could remain in the body, lie dormant, and then reactivate.

COVID-19 associated pulmonary aspergillosis (CAPA):

Viral pneumonia, such as COVID-19, increases patients' susceptibility to bacterial and fungal superinfections, including invasive pulmonary aspergillosis (IPA). Respiratory viruses cause direct damage to the airway epithelium. This enables Aspergillus species to invade tissues. On top of that, viral infection hampers ciliary clearance and leads to immune dysfunction or dysregulation. The extent of dysregulation is not yet fully understood; however, it can facilitate bacterial and fungal superinfection.

Since the emergence of COVID-19 in December 2019, there have been several reports of CAPA.[9] This is concerning as this superinfection can be an additional contributing factor to mortality, meaning that proper diagnosis of these patients is crucial to properly treat them. CAPA is associated with severe mortality rates, yet it remains difficult to diagnose and treat.[9]

The most sensitive diagnostic for aspergillosis in the intensive care unit, bronchoalveolar lavage fluid alactomannan testing and culture, requires a bronchoscopy. Physicians rarely perform this procedure in COVID-19 patients due to the risk of transmission. Drug-drug interactions and kidney damage caused by COVID-19 hinder treatment with broad spectrum azoles and liposomal amphotericin B.

COVID-19 diagnostic support

A multifaceted disease requires an arsenal of diagnostics with varying levels of speed, sensitivity, and specificity. While polymerase chain reaction (PCR) remains the most common testing method, companion diagnostics provide further information when addressing false positives and negatives. They also help researchers comprehensively monitor the virus and track disease progression.

Molecular diagnostics (RT-PCR and TMA):

Reverse transcription polymerase chain reaction (RT-PCR) is the gold standard for SARS-CoV-2 testing methods. In clinical trials, researchers use PCR tests to check whether a sample from a patient contains genetic material (RNA) of the virus.

The RNA will first be converted to complementary DNA (cDNA). This conversion is called reverse transcription (RT). The cDNA is then amplified using polymerase chain reactions until the reaction rate is no longer exponential. The amplification is monitored by fluorescent signals. The threshold, known as the Ct value, is the number of cycles required for the fluorescent signal to be detected. This Ct value inversely corresponds with the amount of genetic material present in the sample. By evaluating the Ct value, researchers can differentiate between the presence of virus or lack of it (qualitative).

RT-PCR tests have the added advantage of allowing virologists to target multiple genes, which can be achieved with multiplex PCR. This helps circumvent the possibility of false negative results due to variants. However, PCR experiments require attention when setting up the right threshold in terms of Ct value. PCR experiments can detect pathogens in very small amounts. It is therefore paramount that researchers select a clinically significant threshold value for the presence of the virus. There needs to be a clear distinction between contamination of a sample/remnant viral particle weeks after infection and the potential onset of symptoms. This is in practice, however, not always as straightforward as in theory.

There are two types of PCR platforms to test for SARS-CoV-2: the mass production PCR platforms with results in hours, and the rapid PCR tests that yield results in less than an hour. Because of their higher cost and lower throughput, the latter are recommended in situations where a quick result is required, such as in medical care or airports.

In the United States, virologists also use qualitative transcription-mediated amplification (TMA), a testing platform that uses a similar nucleic acid amplification technique. Both offer high levels of sensitivity and specificity.

Rapid antigen tests:

Rapid antigen tests detect COVID-19-causing proteins on the surface of the virus. The test is considered accurate for individuals already exhibiting COVID-19 symptoms and can be administered by a clinician or patients.

Rapid antigen tests are less expensive and faster than the gold standard PCR tests – some tests give results in 15 minutes – but tend to produce variable sensitivity and specificity. Compared to PCR, rapid antigen tests are much less sensitive for lower viral loads (high Ct), which can lead to false negative results. In clinical trials, researchers can use rapid antigen tests to screen participants and throughout the study as point of care. Generally, this antigen test is only significant after several days of infection because it cannot detect a very low viral load.

Serology:

Serological assays detect antibodies in patients that were exposed to SARS-CoV-2. The assays are used to delineate possible past infection or previous vaccination. They can also be used to assess disease prevalence and monitor the dynamics of individual immunological responses over time. Serological assays for SARS-CoV-2 are widely available and include lateral flow assays (LFAs), enzyme-linked immunosorbent assays (ELISAs), and virus neutralization assays.

LFAs and ELISAs are performed with recombinant antigens, such as the spike (S) protein – the key surface glycoprotein that interacts with host cell response; the receptor-binding domain (RBD) – which is part of the spike protein; or the viral nucleocapsid (N) protein.

In humans, the humoral response includes antibodies directed against the above-mentioned proteins. These antibodies – including IgM, IgG, and IgA – can be detected in serum within one to three weeks after infection. In theory, IgM and IgG antibodies can arise nearly simultaneously; however, IgM and IgA antibodies decay more rapidly than IgG. The clinical significance of measuring serum IgA in SARS-CoV-2 infection is unknown; however, it plays a role in protecting mucosal surfaces against pathogens, including SARS-CoV-2. In clinical trial settings, either total antibody is measured (IgA, IgM, and IgG) or IgG and/or IgM separately in either a qualitative or quantitative manner.

The LFAs are used as a diagnostic device to confirm the presence or absence of SARS-CoV-2 antibodies. The antigens against IgG and IgM are immobilized on a nitrocellulose membrane. After binding of the antibodies to the antigens, a colored band appears, meaning that antibodies are present in the patient's sample. The advantages of this test are that it is rapid (15 minutes) and easy; there is no automation needed and it can be performed in difficult to access places (point of care). The disadvantages are that LFAs only provide qualitative results – meaning that no antibody kinetics can be measured, and they have only a low throughput.

ELISAs can provide qualitative/semi-quantitative/quantitative results depending on the kit and platform that are used. ELISAs are more specific and sensitive than LFAs. They have a medium throughput and are less rapid (hours). Besides ELISA, another common (and faster – minutes to hours) technique to measure SARS-CoV-2 antibodies is using chemiluminescent assays (CLIAs). CLIAs provide specific and very sensitive quantitative results and has a high throughput.

Various commercial anti-spike SARS-CoV-2 antibody tests are used for studies and in clinical settings after vaccination. Those tests are highly variable, due to their different characteristics and to the lack of reference materials. The World Health Organization's (WHO) first International Standard (IS) for anti-SARS-CoV-2 immunoglobulin is the harmonization of humoral immune response assessment after natural infection or vaccination, and recommends reporting the results for binding activity in binding antibody units (BAUs).[10] Binding antibodies are the ones that bind the S proteins, whereas neutralizing antibodies are produced only against the RBD, and therefore can neutralize the virus from entering the human host.

As ELISA and CLIA are both LFAs, they are not able to differentiate binding antibodies from neutralizing antibodies. The latter can be detected using neutralization assays. In a neutralization test, serum and virus are reacted together in equal volumes and inoculated into a cell culture. If antibodies to the virus are present, then there are no changes in the cells observed, meaning that viral replication will be inhibited, and virus is neutralized.

Due to the recombinant nature of the selected antigens, LFA, ELISA, and CLIA can be handled at biosafety level 1 or 2. Neutralization assays, however, use live SARS-CoV-2 and therefore must be performed in biosafety level 3 facilities, which limits their application. Researchers use ELISAs/CLIAs and LFAs during participant screening and throughout a clinical trial. Virus neutralization assay, however, is generally performed during clinical trials and not for participant screening.

COVID-19 clinical trial support

As the effort to develop more effective COVID-19 treatments and vaccines and protect the global public continues, therapy and vaccine developers must partner with central labs that offer a broad scope of services. A diverse portfolio of exploratory tools and tests is paramount when studying an unpredictable virus.

To detect the level of infection (viral load):

In addition to qualitatively measuring the presence of viruses, researchers can also quantify the viral load using PCR techniques. More specifically with quantitative RT-PCR (qRTPCR) and droplet digital PCR (ddPCR).

The principle of qRT-PCR is the same as for RT-PCR. The genetic material is first converted to cDNA and then amplified until the reaction rate is no longer exponential. This test will yield a qualitative result. To measure the exact quantity, the scientist sets up a calibration curve of Ct values with known concentration of genetic material. This is known as qRT-PCR.

ddPCR provides direct measurements and does not require calibration curves. Instead of performing one reaction per well, ddPCR involves partitioning the PCR solution into tens of thousands of nano-liter sized droplets, each consisting of either one target molecule or none.

Fluorescence is measured as being present or not, allowing scientists to calculate the fraction of positive droplets to predict the number of target copies per droplet.

Viral viability and infectivity:

Cell-based assays and viral cultures allow researchers to measure changes in host cells that indicate virus viability and infectivity. Direct cultures measure neutralizing antibodies. Cerba Research uses the plaque reduction neutralization test (PRNT) to measure neutralizing antibodies in vitro.

To detect immune response:

Serology tests suit immunosurveillance, vaccine clinical trials, and diagnostics in a variety of study types. On top of the above mentioned serological assays, Cerba Research has a variety of assays that can evaluate different aspects from the immune response.

The Meso Scale Discovery (MSD) platform detects cytokines, which allows researchers to monitor cytokine release syndrome. Cerba Research also has Centers of Excellence for flow cytometry around the world. Flow cytometry is being used to immunophenotype cells. The flow cytometry panels are customizable so that they can be a perfect fit for the client's needs.

Cerba Research recently introduced the T spot COVID (ELISpot assay), a sensitive test used to identify individuals with an adaptive immune response to SARS-CoV-2, specifically the T-cell response. This assay is used in patients who tested negative for COVID-19 using PCR methods and have either a negative or suspicious serology. The sensitivity of the ELISpot assay in these seronegative infected patients is between 50 and 80%. ELISpot measures specific cellular response against more than 250 peptides of the SARS-CoV-2 S and N proteins by quantifying the number of interferon producing T cells. The lymphocytes of recovered or vaccinated patients are isolated and then brought into contact with the virus antigens. After 20 hours of incubation, scientists measure the production of interferon.[11]

A positive assay allows for differentiating the immunity related to infection with the virus (testing positive for anti-SARS-CoV-2 S-protein and N-protein antibodies) from the immunity related to vaccination (testing positive only for anti-SARS-CoV-2 S-protein antibodies).

Genetic analysis:

Genomic assays such as next-generation sequencing (NGS) help researchers understand the mechanism of the virus as well as its progression. Studying the host helps researchers screen targets for potential COVID-19 therapeutics as well as study immune responses in people with COVID-19. Studying the viral genome provides precise information to help scientists track global transmission routes, design vaccine candidates, detect co-infections, and identify and control mutations not visible on molecular diagnostic assays. Genetic analysis is used in research, medical care, in clinical, and for epidemiological purposes.

Cerba Research recently implemented a pan respiratory viral sequencing panel that can detect multiple viruses from one single sample. This allows researchers to detect co-infecting viruses within patients (influenza and SARS-CoV-2, for example) to not only improve the diagnosis but also to track emerging viral infections.

CAPA diagnostics:

Early detection and treatment is critical in cases of suspected CAPA. Although diagnostics have their limitations, mycology capabilities may provide clues. Examples include fungal culture, galactomannan, and aspergillus qPCR.

For predictive research:

Few biomarkers predict the severity of COVID-19. Cerba HealthCare has two in development:

- Serum calprotectin – Studies show serum calprotectin levels were significantly higher in people hospitalized with COVID-19.[12] Evaluating immunosuppressive phenotypes of monocytes and neutrophils, together with the calprotectin plasma level, could provide robust biomarkers for severe COVID-19.
- Anti-interferon alpha-2 – Research shows SARS-CoV-2 replicates despite the presence of interferon alpha-2 in the presence of autoantibodies against interferon alpha-2.[12] Quantification of these antibodies may predict severe COVID-19. They can also be used to predict adverse reactions with some live viral vaccines while potentially playing a role in some autoimmune diseases, but this has yet to be demonstrated.

Biomarker identification and immune profiling:

IHC: Research-use-only studies can use immunohistochemistry (IHC) assays to evaluate novel biomarkers and to analyze immune profiling. Cerba Research can customize these assays to suit research into novel drug therapies. Examples of readily available IHC assays on lung tissues from healthy and SARS-CoV-2 infected patients can be seen in Figure 1.

The infiltration and spatial distribution of natural killer cells, M1/M2 macrophages, cytotoxic T cells, and tissue resident memory T cells can be appreciated. There is a clear increase of macrophages and T cells in viral infected lungs while the classic first line innate cell response of NK cells in COVID-19 patients appears to be stunted to a baseline level.

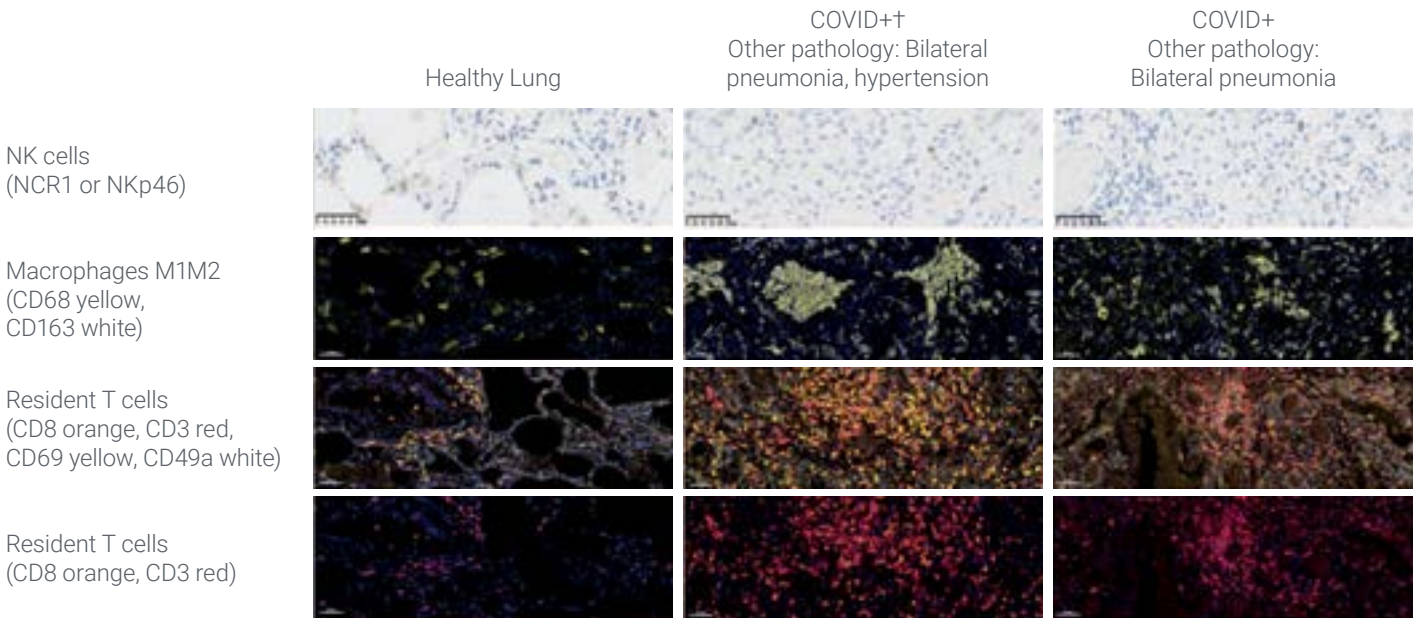

Figure 1: Representative images of infiltrating immune cells in healthy lung (left column) and SARS-CoV-2 infected lungs (middle and right columns). The following populations can be identified with readily available panels at Cerba Research for mechanistic studies: Innate natural killer cells (NK, detected with NKp46 antibody, top row), Macrophage phenotypes (CD68 in yellow, CD163 (white), 2nd row from the top), Resident memory T cells (CD8 in orange, CD3 in red, CD69 in yellow, CD49a in white, 2nd row from bottom), and Cytotoxic T cells (CD8 in orange, CD3 in red, bottom row).

Pave the way for novel drug therapies. Cerba Research provides mechanistic information on risk factors and biomarkers related to variable clinical presentation, organ and system injury and outcomes. There is a clear request for this type of work, based on the calls for applications by government agencies.



Partner with an expert infectious disease central lab

Cerba Research has remained at the forefront of COVID-19 clinical research support by contributing to Operation Warp Speed for development and subsequent FDA approval of a COVID vaccine. They also provided support to French and Belgium government task forces.

Since the start of the pandemic, Cerba Research has developed new tools and expanded its existing portfolio to enhance infectious disease research. We have performed high-throughput sequencing of SARS-CoV-2 since July 2020, contributing data to a variety of studies. Cerba Research began offering digital droplet PCR and whole genome sequencing in the summer of 2020. The systematic approach to high-throughput sequencing of the virus means we can build a refined and real-time picture of the epidemiology and viral circulation.

Cerba Research also has several predictive biomarkers in development. All these advancements enhance Cerba Research's comprehensive portfolio of state-of-the-art tests in virology, bacteriology, and parasitology. This demonstrates that the company is a strong player in all aspects of the market and can offer support from research to clinical trials.

As infectious diseases, antimicrobial resistance, and the continuous emergence of new and old pathogens gain prevalence, count on Cerba Research for integrated clinical laboratory and diagnostic solutions that help you succeed in developing effective treatments and vaccines.

Cerba Research

About Cerba Research

Cerba Research is a leading specialty laboratory services provider with the capacity and breadth of a global central laboratory network. Our highly qualified scientists provide insight on the latest biomarkers, assays, and testing approaches and develop innovative solutions for unique challenges across all research phases for pharmaceutical, biotechnology, medical device, government, public health, and CRO organizations.

Cerba Research's extensive capability in laboratory testing and global logistics, including Bioanalysis, Flow Cytometry, HistoCytopathology, and Next-Generation Sequencing, enables us to drive operational agility at scale in a wide range of therapeutic areas, with recognized expertise in Virology, Immunology, Oncology, and Cell & Gene Therapy.

Cerba Research is part of the Cerba HealthCare Group with 15,000 employees on five continents, driven to advance diagnosis and health.

Interested in how we can shape your laboratory strategy for better outcomes?

Get in touch today and see how Cerba Research will support your next program.

cerbaresearch.com

© Cerba Research 2026

2026-05-29_WP_C19TDCD_V1



References

1. Contini C, Caselli E, Martini F, et al. COVID-19 Is a Multifaceted Challenging Pandemic Which Needs Urgent Public Health Interventions. Microorganisms. 2020;8(8):1228. Published 2020 Aug 12. doi:10.3390/microorganisms8081228
2. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed November 3, 2021
3. Lopes-Pacheco M, Silva PL, Cruz FF, Battaglini D, Robba C, Pelosi P, Morales MM, Caruso Neves C and Rocco PRM (2021) Pathogenesis of Multiple Organ Injury in COVID-19 and Potential Therapeutic Strategies. Front. Physiol. 12:593223. doi: 10.3389/fphys.2021.59322
4. Chao L. et al. Overview of the pathogenesis of COVID-19 (review); Experimental and Therapeutic Medicine 22: 1101, 2021
5. Aslani et al. Cytokine storm in the pathophysiology of COVID-19: Possible functional disturbances of miRNAs. Internal immunopharmacology. Volume 101. 2021; Cappanera et al. When Does the Cytokine Storm Begin in COVID-19 Patients? A Quick Score to Recognize It. J Clin Med. 2021 Jan; 10(2): 297
6. Cappanera et al. When Does the Cytokine Storm Begin in COVID-19 Patients? A Quick Score to Recognize It. J Clin Med. 2021 Jan; 10(2): 297
7. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the U.K. Press release, Office of National Statistics, April 1, 2021
8. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021;38:101019. doi:10.1016/j.eclinm.2021.101019
9. Arastehfar A, Carvalho A, van de Veerdonk FL, et al. COVID-19 Associated Pulmonary Aspergillosis (CAPA)–From Immunology to Treatment. J Fungi (Basel). 2020;6(2):91. Published 2020 Jun 24. doi:10.3390/jof6020091
10. Infantino M, Pieri M, Nuccetelli M, et al. The WHO International Standard for COVID-19 serological tests: towards harmonization of anti-spike assays. Int Immunopharmacol. 2021;100:108095. doi:10.1016/j.intimp.2021.108095
11. Clinical trials during a pandemic – lessons from COVID-19. News-Medical.Net. July 23, 2021.
12. Kaya T, Yaylacı S, Nalbant A, et al. Serum calprotectin as a novel biomarker for severity of COVID-19 disease [published online ahead of print, 2021 Feb 27]. Ir J Med Sci. 2021;1-6. doi:10.1007/s11845-021-02565-8