Targeting SARS-CoV-2: A Comprehensive Mechanistic Approach

The SARS-CoV-2 virus, responsible for the COVID-19 pandemic, has posed an unprecedented global health challenge. Developing effective therapeutic interventions and diagnostic tools has become a top priority for researchers, pharmaceutical companies, and biotechnology firms worldwide.

Despite the immense efforts and resources dedicated to this endeavor, directly targeting the virus and its intricate mechanisms has proven to be a formidable task. However, recent advancements in our understanding of SARS-CoV-2 and its interactions with the host have paved the way for innovative strategies to combat this virus through various mechanisms of action (MoAs).

OniX AI's comprehensive report on SARS-CoV-2 therapeutic candidates and diagnostic platforms provides an in-depth analysis of these diverse approaches, offering a powerful tool for researchers, drug developers, and industry professionals in their quest to mitigate the impact of this pandemic.

OniX AI's Unparalleled Access to the Research Landscape

What sets OniX AI apart is its unparalleled access to the research landscape, which includes preclinical and clinical data on SARS-CoV-2 and COVID-19 interventions. OniX has one of the most extensive preclinical data repositories in the industry, including proprietary information not readily available in the public domain. By harnessing this wealth of fully standardized global data, OniX AI provides an unmatched window into the current and ongoing research landscape. This real-time intelligence can significantly impact strategic decision-making, R&D prioritization, partnership opportunities, go/no-go evaluations, and investment decisions – empowering each company to stay ahead of the curve in the rapidly evolving fight against COVID-19.

Mechanisms of Action for SARS-CoV-2 Potential Assets

In this comprehensive report, we highlight assets in several key MoAs being investigated for SARS-CoV-2 and COVID-19 treatments, including:

1. **Viral Entry Inhibitors**: Targeting the SARS-CoV-2 spike protein or host receptors like ACE2 and TMPRSS2 to block viral entry into host cells.
2. **Viral Replication Inhibitors**: Targeting viral enzymes essential for replication, such as 3C-like protease (3CLpro), RNA-dependent RNA polymerase (RdRp), and Papain-like protease (PLpro).

3. **Immune Modulators**: Enhancing or modulating the host immune response to SARS-CoV-2, including mucosal immunity and sex-biased immunity.
4. **Diagnostic Platforms**: Developing rapid, mobile, and point-of-care diagnostic tests for SARS-CoV-2, such as from saliva samples.

Actionable Intelligence for Strategic Advantage

Elevate your decision-making process with OniX AI's unparalleled ability to deliver actionable insights derived from the latest "live" preclinical and clinical data on SARS-CoV-2 and COVID-19 interventions. Whether you are a biotech entrepreneur, pharma executive, or academic researcher, OniX's AI-powered analysis empowers you with authoritative insights and a competitive edge in the quest to de-risk ongoing R&D, make informed go/no-go decisions, identify potential partnership opportunities, and uncover investment opportunities in the fight against the COVID-19 pandemic.

Research and development activity targeting SARS-CoV-2 and treating COVID-19

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Introduction to the gut microbiota-brain axis and its role in neurological disorders

- Overview of R&D activity targeting SARS-CoV-2

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Number of Projects/Assets/Companies

Mode of Action	Preclinical	Clinical	Biotech/Pharma
1. Viral Entry Inhibitors	100+	40+	40+
2. Viral Replication Inhibitors	150+	30+	20+
3. Immune Modulators	100+	20+	30+
4. Diagnostic Platforms	6K+	60+	800+

Viral Entry Inhibitors

Preclinical studies

Examples

Project: Targeting SARS-Related Coronaviruses with a D-peptide Entry Inhibitor

Organization: University Of Utah
Project Leader: Michael S Kay
Research Question:
Can D-peptides be developed as effective entry inhibitors to combat SARS-CoV-2 and other coronaviruses?
Stage:
This research is likely in the late pre-clinical stage, with a combination of in vitro (laboratory) and in silico (computer modeling) techniques.
Methods:

- Mirror-image phage display (MIPD) will be used to identify D-peptide inhibitors that target a conserved region (HR1) of the coronavirus spike protein.
- Surface plasmon resonance will be used to measure the binding affinity of D-peptides to the target.
- In vitro assays with pseudo viruses will be used to test the antiviral activity of D-peptides.

Drug Development:
This research focuses on developing D-peptides, mirror-image peptide drugs, as therapeutic agents against SARS-CoV-2 and related coronaviruses. D-peptides offer advantages like resistance to breakdown by enzymes and potentially lower immunogenicity.
The researchers plan to:

- Chemically synthesize promising D-peptide candidates identified through MIPD.
- Improve the potency of these D-peptides through further rounds of MIPD.
- Engineer the D-peptides for better binding and cellular uptake.
- Test the most effective D-peptides against authentic SARS-CoV-2 virus (in collaboration with another institution).
- Move the most promising D-peptide candidate to animal testing (hamsters) for efficacy studies.

The ultimate goal is to develop a D-peptide drug for treating or preventing SARS-CoV-2 and related coronaviruses.

Project: Structural Basis for T Cell Recognition of SARS-CoV-2

Organization: Univ Of Maryland, College Park
Project Leader: Roy A Mariuzza
Research Question:
This study focuses on understanding how T cells recognize SARS-CoV-2, the virus that causes COVID-19.
Stage:
This research is most likely in the early stage (pre-clinical) and relies on laboratory techniques (in vitro).
Methods:
The researchers will use X-ray crystallography to determine the 3D structure of molecules involved in T cell recognition of the virus. They will focus on structures from CD8+ T cells, which directly kill virus-infected cells.
Drug Development:
This study is not directly about drug development. However, understanding how T cells recognize the virus can help design vaccines and assess the risk of reinfection.

Project: Novel nanobodies to prevent and treat SARS-CoV-2 and other pathogenic human coronaviruses

Organization: New York Blood Center
Project Leader: Lanying Du
Research Question:
Can nanobodies (Nbs) be developed as effective therapeutic agents to neutralize SARS-CoV-2 and other coronaviruses?
Stage:
This research is most likely in the pre-clinical stage, possibly using a combination of in silico (computer modeling) and in vitro (laboratory) techniques.
Methods:
The researchers will use phage display, a laboratory technique, to identify Nbs that bind to specific parts of the SARS-CoV-2 spike protein. Structural biology will be used to understand how these Nbs interact with the virus.
Drug Development:
This study focuses on developing nanobodies (Nbs) as a potential treatment for SARS-CoV-2 and other coronaviruses. Nbs are single-domain antibodies with several advantages, including stability, good tissue penetration, and ease of production. The researchers aim to create Nbs that target both the receptor-binding domain (RBD) and the S2 region of the SARS-CoV-2 spike protein. They also hope to develop broad-spectrum Nbs that can neutralize a variety of coronaviruses.

Project: Targeting the SARS-CoV-2 spike protein to achieve hyperimmunicity and reduce infectivity

Organization: Angered Hospital, Sweden
Project Leader: Yang Weihong
Research Question:

- Can modulating the sugar content (glycosylation) of the SARS-CoV-2 spike protein and attaching an adjuvant directly to it improve the immunogenicity of a vaccine candidate?
- Can surfactant protein D (SP-D) prevent SARS-CoV-2 infection in cells?

Stage:
This research is likely in the early pre-clinical stage and relies on laboratory techniques (in vitro).
Methods:

- The researchers will produce the SARS-CoV-2 spike protein in cell cultures.
- They will modify the sugar content of the spike protein and attach an adjuvant molecule to it.
- They will evaluate the ability of the modified spike protein to induce an immune response in cells and mice.
- To investigate SP-D's antiviral effect, they will produce it in E. coli bacteria.
- They will then mix SP-D with SARS-CoV-2 before infecting cell cultures.
- Finally, they will measure the effect of SP-D on the virus using real-time PCR, plaque reduction assays, and cell viability experiments.

Drug Development:
This research focuses on developing a new concept for a SARS-CoV-2 vaccine. The approach involves modifying the spike protein and attaching an adjuvant to enhance the immune response.

- Project 1 aims to improve the toolbox for developing subunit vaccines, which could benefit future vaccine research and development.
- Project 2 investigates SP-D's potential as an antiviral treatment. While the focus is on SARS-CoV-2, SP-D might also be effective against other respiratory pathogens.

Clinical development: Ongoing trials, target indications, key companies involved

Examples

Project: Dose-Escalation Study Of Nanoparticle Carrier-Formulated Self- Replicating Replicon RNA (repRNA) SARS-CoV-2 Vaccine (HDT-301) Targeting A Variant Spike Protein In Unvaccinated Or Previously Vaccinated Healthy Adults

ID: NCT05132907
Phase: Phase 1
Intervention
This clinical trial is evaluating a vaccine candidate called **HDT-301**. It's a **self-replicating replicon RNA (repRNA) SARS-CoV-2 vaccine** delivered using a **nanoparticle carrier**. Replicon RNA is a type of genetic material that can be introduced into cells to create viral proteins, stimulating the immune system to respond. The specific SARS-CoV-2 variant targeted by the vaccine is not mentioned in the summary.
Route of Administration
The vaccine will be administered **intramuscularly (IM)**, likely into the upper arm.
Mode of Action
The vaccine is expected to work by introducing replicon RNA into cells. These cells will then produce copies of the viral spike protein, which the immune system will recognize as foreign.

This will trigger the immune system to develop antibodies and T cells specifically against the SARS-CoV-2 virus. If a person is later exposed to the virus, the immune system can rapidly respond to clear the infection.

Target

The target of the vaccine is the **spike protein** of the SARS-CoV-2 virus. The spike protein is what the virus uses to attach to and enter human cells.

Conditions

The study is focused on healthy adults who are either **unvaccinated or previously vaccinated** against COVID-19.

Sponsors

The sponsor of this clinical trial is **HDT Bio.**

Project: C144-LS and C135-LS) in Healthy Volunteers

ID: NCT04700163
Phase: Phase 1

Intervention

The intervention in this clinical trial is a combination of two monoclonal antibodies, C144-LS and C135-LS, that target the SARS-CoV-2 virus.

Route of Administration

The antibodies are administered via subcutaneous injection.

Mode of Action

The monoclonal antibodies are designed to neutralize the SARS-CoV-2 virus by binding to the spike protein, preventing the virus from entering and infecting host cells.

Target

The target of the intervention is the SARS-CoV-2 virus, the causative agent of COVID-19.

Conditions

This clinical trial is evaluating the safety and pharmacokinetics of the C144-LS and C135-LS antibodies in healthy volunteers.

Sponsors

The study is sponsored by the Rockefeller University in the United States.

Viral Replication Inhibitors

Preclinical research

Project: Synthesis of novel dual-inhibitors targeting SARS-CoV-2 Mpro

Organization: Universidade de São Paulo
Project Leader: Felipe Cardoso Prado Martins

Research Question:

Can existing Cathepsin L (CatL) and Cathepsin B (CatB) inhibitors be repurposed to target both these enzymes and the main protease (Mpro) of SARS-CoV-2?

Stage:

This research is likely in the early pre-clinical stage and relies on laboratory techniques (in vitro).

Methods:

- The researchers will modify existing CatL and CatB inhibitor molecules to increase their similarity to known SARS-CoV-2 Mpro inhibitors.
- Standard chemical synthesis techniques will be used to create the modified compounds.

- The researchers will then purify and characterize these new molecules.
- Finally, they will use biochemical assays to measure the affinity of the modified molecules for CatL, CatB, and SARS-CoV-2 Mpro.

Drug Development:
This research focuses on repurposing existing CatL and CatB inhibitors to inhibit SARS-CoV-2 Mpro as well. If successful, these modified molecules could become a new treatment for COVID-19.

- The project aims to develop a single drug that targets both CatL/CatB and Mpro, potentially offering a more effective treatment strategy.
- This approach relies on existing knowledge about CatL/CatB inhibitors, potentially accelerating the development process.

Project: Targeting SARS-CoV-2 PLpro for COVID-19 treatment

Organization: University Of Illinois At Chicago
Project Leader: Rui Xiong
Research Question:
Can novel binding sites on the SARS-CoV-2 papain-like protease (PLpro) be targeted with new drugs to inhibit viral replication?
Stage:
This research is likely in the late pre-clinical stage, with a combination of in vitro (laboratory) and in silico (computer modeling) techniques.
Methods:

- Structure-guided design and X-ray crystallography will be used to identify and validate novel drug binding sites on PLpro, away from the active site.
- The researchers will then develop and optimize new drug candidates targeting these novel binding sites.
- In vitro assays will be used to measure the antiviral potency of the new drugs in human cells infected with SARS-CoV-2.
- Additional tests will assess the drug-likeness properties, stability, and absorption, distribution, metabolism, and excretion (ADME) profile of the drugs.

Drug Development:
This research focuses on developing new drugs that target a novel site on the SARS-CoV-2 PLpro enzyme to inhibit viral replication.

- By targeting a site away from the active site, the researchers hope to overcome limitations associated with other approaches.
- The project aims to optimize lead compounds for potency and drug-like properties, making them more suitable for drug development.
- Successful completion of this research could lead to the development of new drugs to treat COVID-19.

Project: Novel small-molecule inhibitors of SARS-CoV-2 protease

Organization: Baylor College Of Medicine
Project Leader: Yongcheng Song
Research Question:
Can potent inhibitors of the SARS-CoV-2 main protease (Mpro) be developed as a therapeutic strategy for COVID-19?
Stage:

This research is likely in the early pre-clinical stage, with a combination of in vitro (laboratory) and in silico (computer modeling) techniques.

Methods:

- Medicinal chemistry will be used to design and synthesize new Mpro inhibitor molecules.
- X-ray crystallography will be used to determine the 3D structure of Mpro bound to the inhibitor molecules, helping to refine the design process.
- Biochemical assays will be used to measure the potency of the inhibitors against Mpro.
- In vitro antiviral activity testing will be used to assess the effectiveness of the inhibitors in blocking SARS-CoV-2 replication in cells.
- Cytotoxicity assays will be used to identify inhibitors that are not toxic to human cells.

Drug Development:

This research focuses on developing new drugs that target the SARS-CoV-2 Mpro enzyme to inhibit viral replication as a potential treatment for COVID-19.

- The project uses a combination of approaches to identify potent and specific Mpro inhibitors.
- X-ray crystallography will provide insights into how the drugs interact with the Mpro enzyme, aiding in further optimization.
- Successful development of these inhibitors could lead to novel drug candidates for treating SARS-CoV-2 infections.

Project: Broad-spectrum therapeutics against SARS-CoV-2 3CL protease

Organization: Emory University
Project Leader: Raymond Felix Schinazi
Research Question:
Can small molecule inhibitors of the SARS-CoV-2 3CL protease (3CLpro) be developed as antiviral drugs to treat COVID-19?
Stage:
This research is likely in the late pre-clinical stage, with a combination of in vitro (laboratory) and in vivo (animal) techniques.
Methods:

- The researchers will use two approaches to develop 3CLpro inhibitors:
  - Covalent peptidic inhibitors based on a lead compound (compound 3150).
  - Noncovalent nonpeptidic inhibitors identified through virtual screening and medicinal chemistry.
- In vitro enzyme assays will be used to measure the potency of the inhibitors against 3CLpro.
- In vitro viral assays will be used to assess the effectiveness of the inhibitors in blocking SARS-CoV-2 replication in cells.
- An animal model (golden hamster) will be used to test the efficacy of the most promising inhibitors.

Drug Development:

This research focuses on developing new antiviral drugs that target the SARS-CoV-2 3CLpro enzyme to inhibit viral replication as a treatment for COVID-19.

- The project utilizes two strategies to discover effective inhibitors.
- Successful development of these inhibitors could lead to a drug candidate for treating COVID-19, potentially paving the way for an investigational new drug (IND) application.
- The researchers envision this drug being used potentially in combination with other therapies like remdesivir and anti-inflammatory drugs.

Project: An interventional efficacy and safety, Phase 2/3, double-blind, 2 arm study to investigate orally administered PF07321332/Ritonavir compared with placebo in nonhospitalized symptomatic adult participants with COVID-19 who are at low risk of progressing to severe illness

ID: NCT05011513
Phase: Phase 2
Intervention
This clinical trial is evaluating the efficacy and safety of an investigational drug, **PF-07321332/ritonavir**, compared to a placebo.
Route of Administration
The drug (or placebo) will be administered **orally**, likely in the form of capsules or tablets.
Mode of Action
The specific mode of action of PF-07321332 is not provided in the summary. However, it is likely an antiviral drug that interferes with the replication of the SARS-CoV-2 virus. Ritonavir may be included to boost the blood levels of PF-07321332.
Target
The target of the drug is likely the SARS-CoV-2 virus.
Conditions
The study is focused on adult participants with **symptomatic COVID-19** who are considered **low risk** of developing severe illness.
Sponsors
The sponsor of this clinical trial is **Pfizer**.

Project: A National, Multi-Center, Open-Label, Three-Arm, Phase II Study to Investigate the Effect of Montelukast Between Emergency Room Visits and Hospitalizations in COVID-19 Pneumonia in Comparison With Standard Treatment

ID: NCT04718285
Phase: Phase 2
Intervention
This clinical trial is investigating the effect of **montelukast**, a medication typically used for asthma, compared to standard treatment for COVID-19 pneumonia.
Route of Administration
The route of administration for montelukast is not specified in the summary, but it is typically available as tablets or chewable tablets for adults and as granules for children.
Mode of Action
The summary doesn't specify how montelukast might influence COVID-19. Montelukast works by blocking leukotrienes, which are involved in inflammation.
Target
The target of montelukast in this study is likely the inflammatory response associated with COVID-19 pneumonia.
Conditions
The study is focused on patients with **COVID-19 pneumonia**.

Sponsors
The sponsors of this clinical trial

Immune Modulators

Preclinical data

Clinical development: Ongoing trials, target patient populations, companies involved

Diagnostic Platforms

Preclinical studies

Project:

Organization:
Project Leader:

Project:

Organization:
Project Leader:

Project:

Organization:
Project Leader:

Clinical trials: Current pipeline, trial designs, and early results

Project:

ID: NCT
Phase: Phase

Project:

ID: NCT
Phase: Phase

Competitive landscape and market potential

Key players in the SARS-CoV-2 and treating COVID-19 space (biotech, pharma, and academic institutions)

Biotech/Startup Companies

1. Moderna
2. BioNTech
3. Novavax
4. Vir Biotechnology
5. Regeneron

Pharmaceutical Companies

1. Pfizer
2. AstraZeneca
3. Johnson & Johnson
4. Merck
5. GlaxoSmithKline

Academic Institutions

1. University of Oxford
2. Harvard University
3. Imperial College London
4. University of Washington
5. Johns Hopkins University

Partnerships, collaborations, and licensing agreements

Market size and growth projections