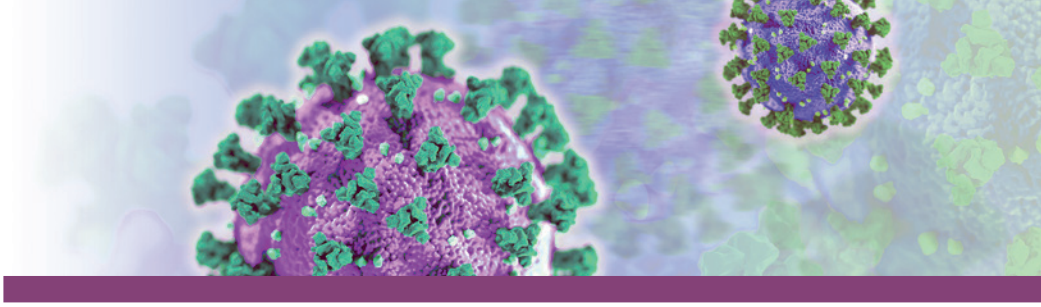
AdipoGen®
LIFE SCIENCES
insights



www.adipogen.com/covid-19

Latest Insight on COVID-19 Research

Coronaviruses (CoVs) – SARS-CoV & SARS-CoV-2 [2019-nCoV]

Coronaviruses (CoVs) are enveloped non-segmented positive-sense RNA viruses infecting human and vertebrates. They are classified into four types (genus), α-CoV, β-CoV, γ-CoV and δ-CoV. They can infect the respiratory, gastrointestinal, hepatic and central nervous system of human and many wild animals. The family of Coronaviridae constantly circulates within the human population and mainly causes mild respiratory diseases. Recently, a new severe acute respiratory syndrome β-coronavirus called SARS-CoV-2 (or 2019-nCoV) has emerged, which causes an epidemic of acute respiratory syndrome called coronavirus human disease 2019 or COVID-19. Typical clinical symptoms of these patients are dry cough, fever, breathing difficulties, anosmia, headache and pneumonia. Disease onset may result in progressive respiratory failure, heart tissue damage and even death.

SARS-CoV-2 shares 79.5% sequence identity with SARS-CoV and is 96.2% identical at the genome level to the bat coronavirus BatCoV RaTG133, suggesting it had originated in bats. Recent studies indicate that the lineage giving rise to SARS-CoV-2 has been circulating unnoticed in bats for decades. The coronaviral genome encodes four major structural proteins: the Spike (S) protein, Nucleocapsid (N) protein, Membrane/Matrix (M) protein and the Envelope (E) protein (see Figure 1). The SARS Envelope (E) protein plays a role in viral budding and virion envelope morphogenesis. The SARS Membrane/Matrix (M) protein is one of the major structural viral proteins. It is an integral membrane protein involved in the budding of the viral particles and interacts with SARS Spike (S) protein and the Nucleocapsid (N) protein. The N protein contains two domains, both of them bind the virus RNA genome via different mechanisms.

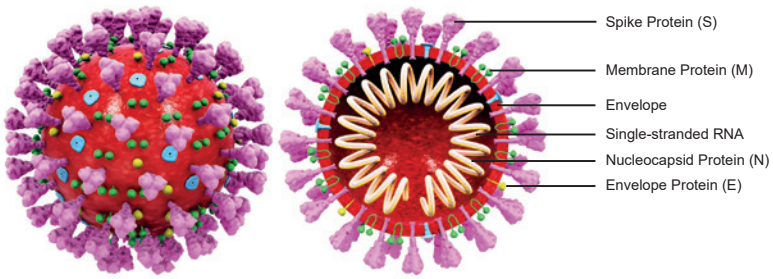


FIGURE 1: Schematic diagram of SARS-CoV-2.

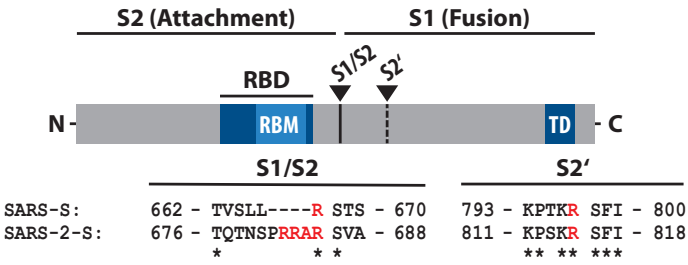


FIGURE 2: Domain comparison overview of Spike Protein S of SARS and SARS-CoV-2.

Schematic illustration of SARS-S including functional domains (RBD, receptor binding domain; RBM, receptor binding motif; TD, transmembrane domain) and proteolytic cleavage sites (S1/S2, S2', see arrows). Amino acid sequences around the two protease recognition sites (red) are shown for SARS-S and SARS-2-S (conserved residues are indicated as asterisks).

The CoV Spike (S) protein assembles as trimer and plays the most important role in viral attachment, fusion and entry. It is composed of a short intracellular tail, a transmembrane anchor and a large ectodomain that consists of a receptor binding S1 subunit and a membrane-fusing S2 subunit (see Figure 2, adapted from Cell, Hofmann, et al. (2020)). The S1 subunit contains a receptor binding domain (RBD), which binds to the cell surface receptor angiotensin-converting enzyme 2 (ACE2) present at the surface of epithelial cells.

LITERATURE REFERENCES: The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status: Y.R. Guo, et al.; Mil. Med. Res. **7,** 11 (2020) (Review) • SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor: M. Hoffmann, et al.; Cell **181,** 271 (2020) • Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine: W. Tai, et al.; Cell Mol. Immunol. **17,** 613 (2020) • Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2: R. Yan, et al.; Science **367,** 1444 (2020)

Contents

ACE2 & Functional Receptor for SARS Coronaviruses

Angiotensin-converting enzyme 2 (ACE2) is a type I transmembrane metallocarboxypeptidase within the renin-angiotensin system (RAS), which plays a key role in blood pressure regulation, fluid and electrolyte balance, thirst, cardiac/renal function and growth. ACE2 is expressed on the cell surface of type 2 alveolar epithelial cells in the lungs as well as on cells in many other tissues. ACE2 shares approx. 60% homology with ACE, the other key enzyme of the RAS system.

ACE2 converts angiotensin II (Ang II) into Ang(1–7), which acts on the Mas receptor and plays a role in cardiovascular disease to lower blood pressure through vasodilation and by promoting kidney sodium and water excretion, but also to lower inflammation. The effects of ACE2 directly oppose those induced by ACE–Ang II signaling, whereby ACE converts Ang I into Ang II, which increases blood pressure by inducing vasoconstriction, increasing kidney reabsorption of sodium and water and promoting inflammation.

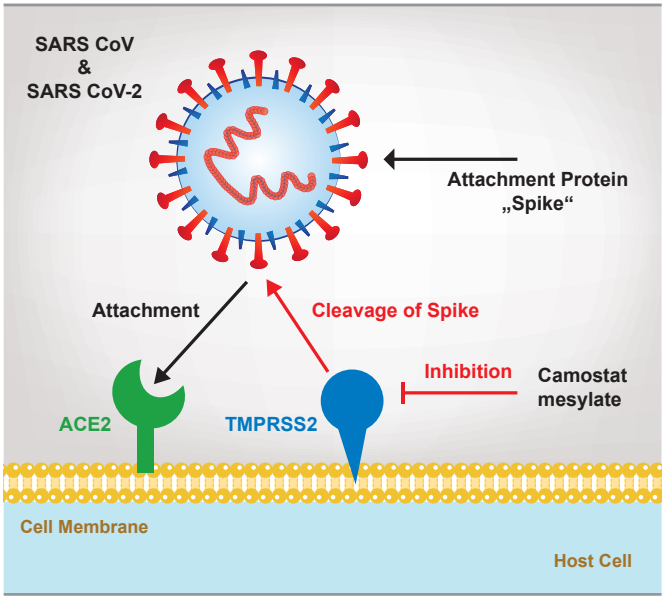


FIGURE 3: SARS-CoV-2 cell entry depends on ACE2 and the protease TMPRSS2.

ACE2 has been identified as a key receptor on target cells for SARS-CoV infections in 2002. ACE2 functions as the entry receptor of the new SARS-CoV-2 coronavirus that emerged in China in 2019 and is the cause of the new disease COVID-19. Strong binding of the spike protein of SARS-CoV-2 to ACE2, along with proteolytic cleavage of ACE2 by transmembrane serine protease 2 (TMPRSS2), facilitates entry of the virus into cells, viral replication and cell-to-cell transmission. The spike protein priming by the co-receptor serine protease TMPRSS2 is crucial for SARS-CoV-2 infection of target cells and spread of the coronavirus throughout the host (see Figure 3).

LITERATURE REFERENCES: Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System: M. Gheblawi, et al.; Circ. Res. **126,** 1456 (2020) • SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor: M. Hoffmann, et al.; Cell **181,** 271 (2020)

Biological Therapeutic Strategies against SARS-CoV-2 and COVID-19

18 years ago the SARS-CoV lead to respiratory diseases in infected people. To date there are no effective vaccines against any type of the coronavirus, which can cause pneumonia and possibly bronchitis. Nevertheless, there are several therapeutical strategies that are being pursued.

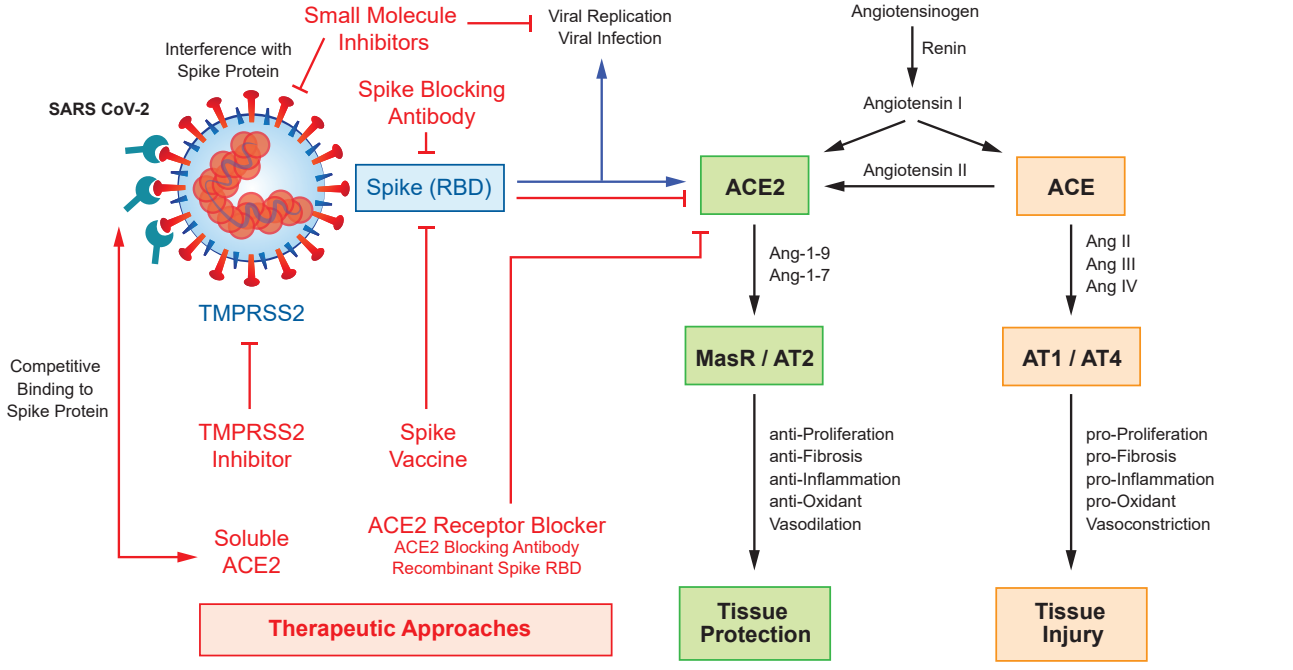


FIGURE 4: Biological Therapeutic Strategies against SARS-CoV-2 and COVID-19.

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Soluble Human ACE2:

The novel coronavirus uses membrane-bound ACE2 as the receptor. The soluble form of ACE2 lacks the membrane anchor and circulates in small amounts in the blood. This soluble form may act as a competitive interceptor of SARS-CoV-2 and other coronaviruses by preventing binding of the viral particle to the surface-bound, full-length ACE2.

ACE2 fused to the Fc portion of immunoglobulin has been reported to neutralize SARS-CoV-2 *in vitro*. Soluble recombinant human ACE2 protein could actually be beneficial as a novel biological therapeutic to combat or limit infection progression caused by coronaviruses that utilize ACE2 as a receptor.

Human ACE2 Blocking Antibodies:

Treatment with blocking anti-ACE2 antibodies disrupts the interaction between virus and receptor, neutralizing the spread of SARS-CoV-2.

Spike S (RBD) Protein:

The CoV Spike (S) protein plays the most important role in viral attachment, fusion and entry and serves as a target for development of antibodies, entry inhibitors and vaccines. The soluble recombinant RBD (receptor binding domain) of coronavirus (including SARS-CoV-2) Spike proteins exhibit significantly high binding affinity to ACE2 receptor and could block the binding by competing with the virus. Attachment of recombinant SARS-CoV-2 RBD to ACE2-expressing cells could inhibit the infection to host cells.

SARS-CoV-2 Antibodies:

SARS-CoV-2 specific antibodies react with SARS-CoV-2 proteins, mainly the Spike, but also the envelope, membrane and nucleocapsid proteins, and SARS-CoV-2 induced antisera could neutralize SARS-CoV-2, suggesting the potential to develop SARS-CoV-2 protein-based vaccines for prevention of SARS-CoV-2 and SARS-CoV infections. Spike (RBD) seems to be a strong immunogenic domain of coronaviruses with a large part of the antibody immune response that is directed against this region.

LITERATURE REFERENCES:

Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target: H. Zhang, et al.; Intensive Care Med. **46,** 586 (2020) (Review) • Therapeutic options for the 2019 novel coronavirus (2019-nCoV): G. Li & E. De Clercq; Nat. Rev. Drug Discov. **19,** 149 (2020) (Review) • SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor: M. Hoffmann, et al.; Cell **181,** 271 (2020) • Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2: J.M. Penninger, et al.; Cell **181,** 905 (2020) • Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy? D. Batlle, et al.; Clin. Sci. **134,** 543 (2020)

COVID-19 *in-vitro* & *in-vivo* Research

As the world is struggling to contain the novel coronavirus (COVID-19) outbreak, healthcare infrastructure and testing capacity have emerged as major issues. There is an urgent need for access to accurate and standardized diagnostics for SARS-CoV-2 (the causative agent of COVID-19). Laboratory testing for COVID-19 and the associated SARS-CoV-2 virus includes methods that detect the presence of the virus (PCR technology) and those that detect antibodies produced in response to infection. Detection of antibodies (serology) can be used both for clinical purposes and population surveillance. AdipoGen Life Sciences has an ongoing pipeline for detection of soluble ACE2, antibodies against SARS-CoV-2 and a HTS detection kit for the determination of SARS-CoV-2 blocking reagents.

LITERATURE REFERENCES: Detection of antibodies against SARS-CoV-2 in patients with COVID-19: Z. Du, et al.; J. Med. Virol. **(Epub ahead of print)** (2020)

MANUFACTURED IN SWITZERLAND

Validated SARS-CoV-2 Research Assays

NEW

QUALITATIVE IgG DETECTION

SARS-CoV-2 (Spike RBD) IgG Serological ELISA Kit

AG-45B-0020

This is a sensitive and specific ELISA Kit that can be used for the qualitative measurement of human Immunoglobulin G (IgG) against SARS-CoV-2 Spike (Receptor Binding Domain) protein in serum and plasma samples.

False Positive Control Plate:

Included in this assay kit and unique to the market for SARS-CoV-2 IgG assays, is a second plate (antigen non-coated Background Plate or False Positive Control Plate) to determine the sample specific background and to measure the amount of IgG antibodies non-specifically bound to the well. To measure presence of anti-SARS-CoV-2 human IgG antibodies in serum or plasma, net sample optical densities (Net ODs) are calculated by subtracting each sample Background Plate OD from the Spike (SARS-CoV-2) Antigen Plate (Spike Plate) OD.

Dry Blood Samples:

The Assay Kit can also be used with Dry Blood Samples, which is an inexpensive and easy alternative collecting blood!

VALIDATE SARS-CoV-2 IMMUNE RESPONSE

SARS-CoV-2 Neutralizing Antibodies Detection Kit

AG-48B-0002

This Assay Kit that can be used to detect the presence of neutralizing antibodies against SARS-CoV-2 in serum/plasma in about 2 hours independently of species and isotypes! It is an easy, safe, fast and scalable alternative to the classical neutralization assays using Vero E6 cells, such as virus neutralization test (VNT) and pseudo-virus neutralization test (pVNT) and does **not need** to follow **biosafety requirements**.

Useful Tool for SARS-CoV-2 Vaccine and Therapeutic Development:

The kit is useful in current COVID-19 investigations of seroprevalence, assessment of immune response, herd immunity, longevity of protective immunity, efficacy of different vaccine candidates as well as tracking infections in animals.

To Confirm & Characterize further SARS-CoV-2 Serological Assay Results:

This Neutralizing Antibody Detection Kit is ideal to further characterize the positive anti-SARS-CoV-2 IgG antibodies, detected with the SARS-CoV-2 IgG (Spike RBD) Serological ELISA Kit (Prod. No. AG-45B-0020).

DISCOVERY OF INHIBITORS

SARS-CoV-2 Inhibitor Screening Kit

AG-48B-0001

This is a High Throughput Screening (HTS) detection assay for the determination of SARS-CoV-2 blocking compounds.

The SARS-CoV-2 Inhibitor Screening Kit contains key reagents required to facilitate identification of SARS-CoV-2 biological or chemical inhibitors. This inhibitor screen is based on a colorimetric ELISA kit, which measures the binding of the RBD of the Spike S protein from SARS-CoV-2 to its human receptor ACE2.

Serum/Plasma Samples:

If you want to test your compounds in serum or plasma samples please use the Neutralizing Antibody Detection Kit (Prod. No. AG-48B-0002).

QUANTITATIVE SOLUBLE ACE2 DETECTION

ACE2 (human) ELISA Kit

AG-45B-0023

This is a sensitive and specific colorimetric sandwich ELISA Kit that can be used for the *in vitro* quantitative determination of soluble human ACE2 in cell culture supernatants, serum, plasma and urine.

Strong binding of the Spike protein of SARS-CoV-2 to ACE2, along with proteolytic cleavage of ACE2 by transmembrane serine protease 2 (TMPRSS2), facilitates entry of the virus into cells, viral replication and cell-to-cell transmission. Soluble ACE2 may act as a competitive interceptor of SARS-CoV-2 and other coronaviruses by preventing binding of the viral particle to the surface-bound, full-length ACE2.

A reliable ELISA Kit to determine circulating soluble human ACE2. Useful for testing developmental therapeutics.

APPLICATIONS: **FACS:** Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: **PF** = Preservative free

SPECIES: **Hu** = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Validated Recombinant Proteins for ACE2 & COVID-19 Research

PRODUCT NAME	PID	SOURCE	PURITY	APPLICATION/ACTIVITY
ACE2 (human) (rec.)	AG-40B-0192	HEK293 cells	≥95% (SDS-PAGE)	Soluble human ACE2 competitively inhibits SARS-CoV-2 infection.
ACE2 (human) (rec.) (Biotin)	AG-40B-0192B	HEK293 cells	≥95% (SDS-PAGE)	Soluble human ACE2 competitively inhibits SARS-CoV-2 infection.
ACE2 (human) (rec.) (His)	CHI-B232008	HEK293 cells	≥90% (SDS-PAGE)	Soluble human ACE2 competitively inhibits SARS-CoV-2 infection.
ACE2 (human):Fc (human) (rec.)	CHI-B232006	HEK293 cells	≥90% (SDS-PAGE)	Soluble human ACE2 competitively inhibits SARS-CoV-2 infection.
ACE2 (mouse) (rec.)	AG-40B-0193	HEK293 cells	≥95% (SDS-PAGE)	Soluble mouse ACE2 negative control.
SARS-CoV-2 Spike Protein S1 (RBD) (rec.) (His)	CHI-B232004	HEK 293 cells	≥90% (SDS-PAGE)	Soluble Protein S (RBD) competitively inhibits SARS-CoV-2 infection. For drug and antibody screening applications and immunization.
SARS-CoV-2 Spike Protein S1 (RBD) (rec.) (GST-His)	CHI-B249001	HEK 293 cells	≥95% (SDS-PAGE)	Soluble Protein S (RBD) competitively inhibits SARS-CoV-2 infection. For drug and antibody screening applications and immunization.
SARS-CoV-2 Spike Protein S1 (RBD):Fc (human) (rec.)	CHI-B232003	HEK 293 cells	≥95% (SDS-PAGE)	Soluble Protein S (RBD) competitively inhibits SARS-CoV-2 infection. For drug and antibody screening applications and immunization.
SARS-CoV-2 Spike Protein S1 (RBD):Fc (human) (rec.)	AG-40B-0194	HEK 293 cells	≥95% (SDS-PAGE)	Soluble Protein S (RBD) competitively inhibits SARS-CoV-2 infection. For drug and antibody screening applications and immunization.
SARS-CoV-2 Nucleocapsid Protein (rec.) (His)	CHI-B233501	E. coli	≥95% (SDS-PAGE)	For drug screening applications.
PLpro (SARS Coronavirus) (rec.) (His)	SBB-DE0024	E. coli	≥95% (SDS-PAGE)	Involved in the processing of the viral polyprotein.
ISG15 (human) (rec.) (Rhodamine 110)	SBB-PS0002	E. coli	≥97% (LCMS)	PLPro substrate. Inhibits viral budding and acts as IFNγ-inducing cytokine.

Validated Antibodies for ACE2 & COVID-19 Research

UNIQUE

UNIQUE Human ACE2 Monoclonal Blocking Antibody

AdipoGen Life Sciences' anti-ACE2 (human), mAb (blocking) (AC384) (preservative free) (Prod. No. AG-20A-0037PF) is a monoclonal antibody that recognizes human ACE2 and works specifically in ELISA, Western Blot and Functional Application. The antibody blocks the binding of human ACE2 to the Spike protein of SARS-CoV-2 without affecting the enzymatic activity of ACE2.

anti-ACE2 (human), mAb (blocking) (AC384) (preservative free)

AG-20A-0037PF Preservative Free 100 µg | 500 µg

Clone: AC384
Isotype: Mouse IgG1κ

Functional Application:
Blocks the binding of human ACE2 to the Spike protein of SARS-CoV-2.

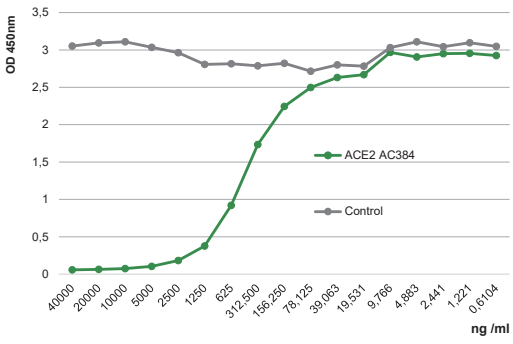

FIGURE: Binding of ACE2 (human) to the Spike protein of SARS-CoV-2 is inhibited by the antibody anti-ACE2 (human), mAb (blocking) (AC384) (AG-20A-0037PF).

METHODS: Spike (SARS-CoV-2):Fc (human) (RBD) (rec.) (AG-40B-0194) is coated on an ELISA plate at 1µg/ml. ACE2 (human), mAb (blocking) (AC384) (AG-20A-0037PF) or an unrelated mAb Control are added (starting at 40µg/ml with a two-fold serial dilution) together with 500ng/µl of ACE2 (human) (AG-40B-0192). After incubation for 1h at RT, the binding was detected using an anti-FLAG antibody (HRP).

UNIQUE

Flow Cytometry-Competent Human ACE2 Monoclonal Antibodies

AdipoGen Life Sciences' anti-ACE2 (human), mAb (AC18F) (**Prod. No. AG-20A-0032**) is a monoclonal antibody that recognizes human ACE2 and works specifically in Flow Cytometry (FACS). The antibody is available in different formats, unlabeled (**Prod. No. AG-20A-0032**) and Biotin-labeled (Prod. No. **AG-20A-0032B**), as well as labeled with the dyes ATTO 488 (Prod. No. **AG-20A-0032TD**) and ATTO 647N (Prod. No. **AG-20A-0032TS**). All variants are FACS-competent using the appropriate secondary reagents.

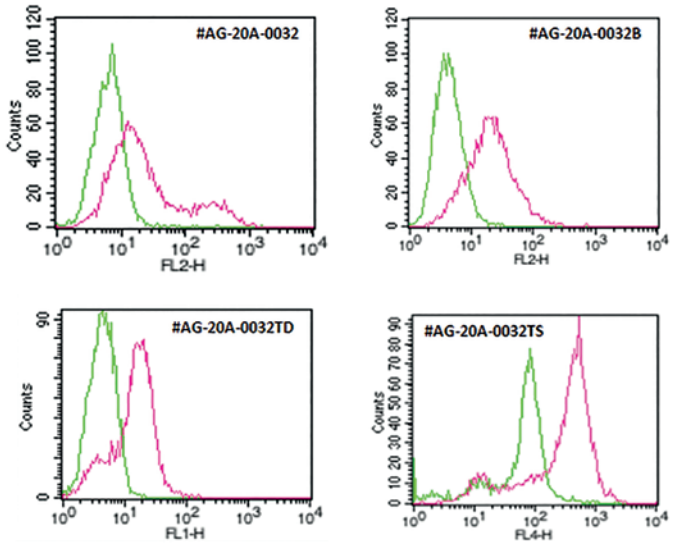

FIGURE: Detection of endogenous human ACE2 by different formats of anti-ACE2 (human), mAb (AC18F) (AG-20B-0032).

METHOD: HepG2 cell line is stained with anti-ACE2 (human), mAb (AC18F) (red line) or an appropriate isotype control at 1µg/106 cells each, revealed with a secondary reagent and then analyzed by flow cytometry.

ACE2 Antibodies Overview

PRODUCT NAME	PID	ISOTYPE	APPLICATIONS	SPECIES
anti-ACE2 (human), mAb (AC18F)	AG-20A-0032	Mouse IgG1κ	ELISA, FACS, WB	Human
anti-ACE2 (human), mAb (AC18F) (Biotin)	AG-20A-0032B	Mouse IgG1κ	ELISA, FACS, WB	Human
anti-ACE2 (human), mAb (AC18F) (ATTO 488)	AG-20A-0032TD	Mouse IgG1κ	FACS	Human
anti-ACE2 (human), mAb (AC18F) (ATTO 647N)	AG-20A-0032TS	Mouse IgG1κ	FACS	Human
anti-ACE2 (human), mAb (AC384)	AG-20A-0037	Mouse IgG1κ	ELISA, WB	Human
anti-ACE2 (human), mAb (AC384) (Biotin)	AG-20A-0037B	Mouse IgG1κ	ELISA, WB	Human
anti-ACE2 (human), mAb (blocking) (AC384) (PF)	AG-20A-0037PF	Mouse IgG1κ	ELISA, FUNC, WB	Human
anti-ACE2 (human), pAb	AG-25A-0042	Rabbit	ELISA, WB	Human

NEW

New SARS-CoV-2 Blocking Recombinant Antibodies

PRODUCT NAME	PID	ISOTYPE	APPLICATIONS	SPECIES
anti-SARS-CoV-2 Spike Protein S1, mAb (rec.) (blocking) (Covi-1) (PF)	AG-27B-6005PF	Human IgG1	ELISA, WB, FUNC (Blocking)	SARS CoV-2 RBD
anti-SARS-CoV-2 Spike Protein S1, mAb (rec.) (blocking) (Covi-2) (PF)	AG-27B-6006PF	Human IgG1	ELISA, WB, FUNC (Blocking)	SARS CoV-2 RBD

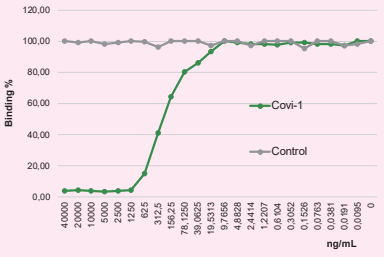

FIGURE: Binding of human ACE2 to the Spike protein of SARS-CoV-2 is inhibited by the antibody SARS-CoV-2 Spike Protein S1, mAb (rec.) (blocking) (Covi-1) (preservative free) (Prod. No. AG-27B-6005PF).

METHOD: SARS-CoV-2 Spike Protein S1 (RBD):Fc (human) (rec.) (Prod. No. AG-40B-0194) is coated on an ELISA plate at 1µg/ml. SARS-CoV-2 Spike Protein S1, mAb (rec.) (blocking) (Covi-1) (preservative free) (Prod. No. AG-27B-6005PF) or an unrelated recombinant mAb (Control) is added (starting at 40µg/ml with a two-fold serial dilution) together with 500ng/µl of ACE2 (human) (rec.) (Biotin) (Prod. No. AG-40B-0192B). After incubation for 1h at 37°C, the binding is detected using Streptavidin (HRP).

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APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: PF = Preservative free
SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Antiviral Compounds – Potential Small Molecule Therapeutics Against COVID-19

There are no approved drugs to treat the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that causes coronavirus disease 2019 (COVID-19). Existing drugs, that have a known favorable safety profile, are being examined for strategies to treat the disease and fast-track a treatment plan. Several influenza and HIV drugs are currently undergoing clinical trial in coronavirus patients. The rational selection of drugs already on the market is being made based on their ability to inhibit any proteins essential for virus-receptor interaction and/or viral life cycle.

LITERATURE REFERENCES: Recent discovery and development of inhibitors targeting coronaviruses: T. Pillaiyar, et al.; Drug Discov. Today **25,** 668 (2020) • Rapid Identification of Potential Inhibitors of SARS-CoV-2 Main Protease by Deep Docking of 1.3 Billion Compounds: A.T. Ton, et al.; Mol. Inform. **39,** 2000028 (2020) • Potential inhibitors against 2019-nCoV coronavirus M protease from clinically approved medicines: X. Liu & X.J. Wang; J. Genet. Genomics **47,** 119 (2020) • Structure of Mpro from COVID-19 virus and discovery of its inhibitors: Z. Jin, et al.; Nature **528,** 289 (2020)

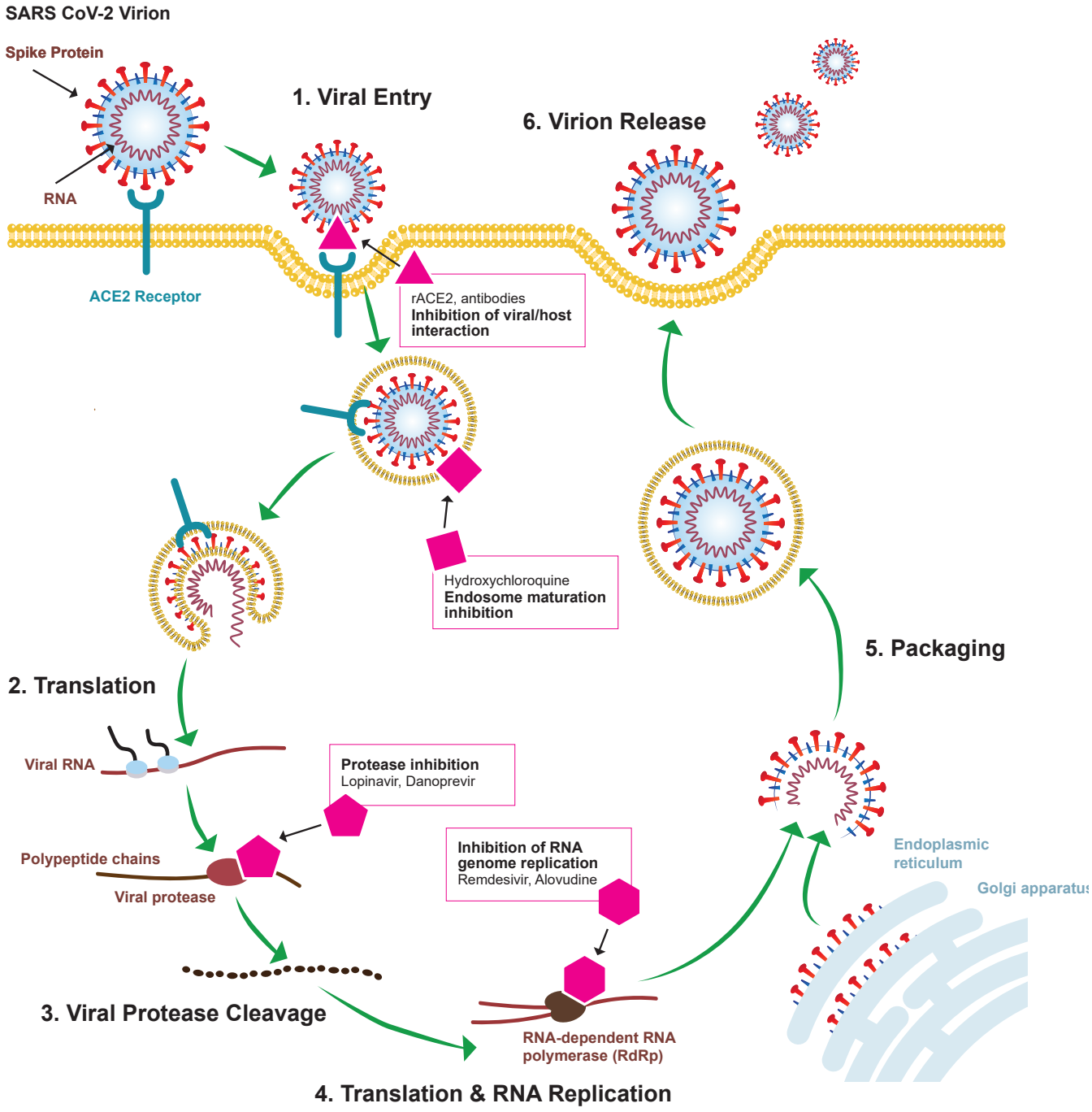

FIGURE 5: Schematic of the different physiological steps during an infection of SARS-CoV-2 with the potential blockade by small molecules and biologicals.

Antiviral Compounds for COVID-19 Research

BULK

PID	PRODUCT NAME
AG-CR1-3737	Aloxistatin [E-64d]
AG-CP3-7003	Amastatin . HCl
AG-CR1-3734	Baricitinib
AG-CR1-3735	Boceprevir
AG-CR1-3716	Camostat . mesylate
AG-CR1-3721	Chloroquine . diphosphate
AG-CR1-3720	Hydroxychloroquine . sulfate
AG-CR1-3736	Clevudine
AG-CR1-3712	Darunavir
AG-CR1-3724	Darunavir . ethanolate
AG-CR1-3742	Dexamethasone
AG-CR1-3744	Dexamethasone phosphate . disodium salt
AG-CR1-0031	Ebselen
AG-CR1-3733	EIDD-2801
AG-CR1-3729	Elbasvir
AG-CR1-3730	Famotidine
AG-CR1-3717	Favipiravir
AG-CR1-3738	Ibudilast
AG-CR1-3725	Imatinib . mesylate
AG-CR1-3715	Lopinavir
AG-CN2-0419	Mycophenolic acid
AG-CR1-3731	Nafamostat . mesylate

PID	PRODUCT NAME
AG-CR1-3726	Nelfinavir . mesylate
AG-CR1-3643	Niclosamide
AG-CR1-3644	Niclosamide . ethanolamine
AG-CR1-3723	Nitazoxanide
AG-CR1-3714	Oseltamivir . phosphate
AG-CR1-3739	PX-12
AG-CR1-3713	Remdesivir
AG-CR1-3722	GS-441524 (Remdesivir Metabolite)
AG-CR1-3719	Ribavirin
AG-CR1-3683	Ritonavir
AG-CR1-3728	Rosuvastatin . calcium salt
AG-CR1-3624	Ruxolitinib (free base)
AG-CR1-3645	Ruxolitinib . phosphate salt
AG-CR1-3727	Saquinavir . mesylate
AG-CN2-0487	Shikonin
AG-CR1-3575	Suramin . 6Na
AG-CR1-3740	TDZD-8
AG-CR1-3741	Telaprevir
AG-CR1-3625	Tofacitinib
AG-CR1-3732	Tofacitinib . citrate
AG-CR1-3718	Umifenovir . HCl [Arbidol]
AG-CP3-0041	VIP (human, mouse, rat) [RLF-100]

Cytokine Storm and Severity of COVID-19

The most critically ill COVID-19 patients are known to undergo a cytokine storm leading to poor prognosis and need of urgent anti-inflammatory treatment/hospitalization. There are many variations on this phenomenon and they go by many names: systemic inflammatory response syndrome, macrophage activation syndrome or cytokine release syndrome (CRS).

A cytokine storm is an overproduction of immune cells and their activating compounds, the cytokines. When SARS-CoV-2 enters the lungs, it triggers an immune response, attracting immune cells to the region to attack the virus, resulting in localized inflammation. But in some patients, excessive or uncontrolled levels of cytokines are released which then activate more immune cells, resulting in hyperinflammation. The resulting lung inflammation and fluid buildup can lead to respiratory distress and can be contaminated by a secondary bacterial pneumonia. This increases the risk of mortality in patients. Cytokine storms might explain why some people have a severe reaction to coronaviruses while others only experience mild symptoms. They could also be the reason why younger people are less affected, as their immune systems are less developed and so produce lower levels of inflammation-driving cytokines. Cytokine storms are a common complication not only of COVID-19 and flu but of other respiratory diseases caused by coronaviruses such as SARS and MERS. They are also associated with non-infectious diseases such as multiple sclerosis and pancreatitis.

Therefore the diagnostic detection and treatment of cytokine storms has become an important part of rescuing severe patients. Targets like IL-1, IL-6, IL-7, IL-10, IL-18, IL-33, IFN-γ, TNF-α or many others might play an important role in cytokine release syndrome (CRS). Detection of their levels and blockage of their signaling pathways with immunomodulatory agents (biologicals, small molecules) is expected to become a new method for the treatment of severe patients.

AdipoGen Life Sciences offers a broad range of Cytokine Immunoassays as well as recombinant cytokines and blocking antibodies, which are already being successfully used to research the various cytokine storm factors involved and to characterize the immune response.

LITERATURE REFERENCES: COVID-19: consider cytokine storm syndromes and immunosuppression: P. Mehta, et al. ; The Lancet 1033 (2020) • Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality: C. Zhang, et al.; Int. J. Antimicrob. Agents 55, 105954 (2020)

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