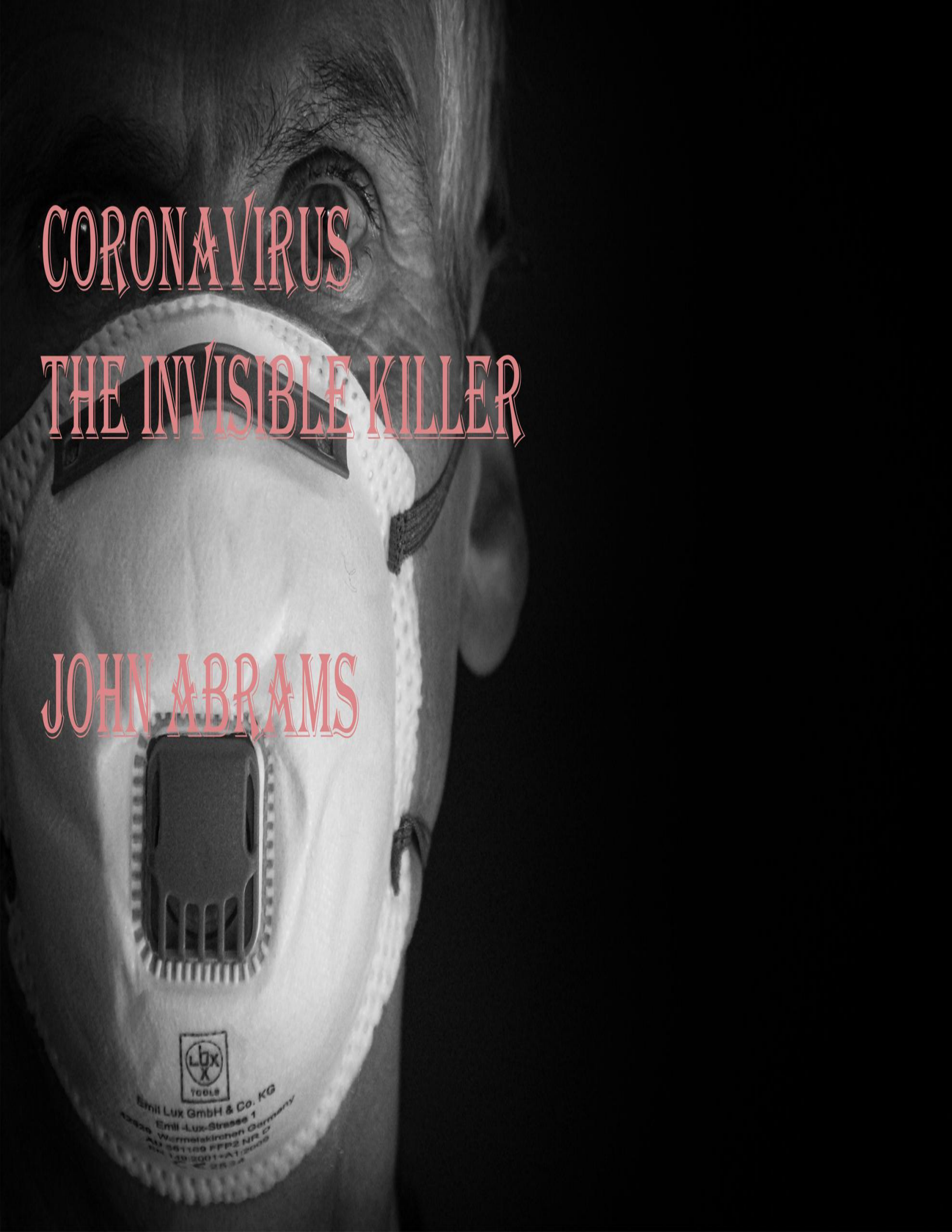
CORONAVIRUS
THE INVISIBLE KILLER
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# CONTENTS

High-risk healthcare and mortuary workplaces

### Management

Medications
Personal protective equipment
Mechanical ventilation
Acute respiratory distress syndrome

### Experimental treatment

Information technology
Psychological support

## Part Four

## Prevention and management of mental health conditions

### Reinfection
### History
### Epidemiology
### Society and culture

US biological weapon
Anti-Muslim
Antisemitic
Spy operation
Population control scheme

### Statistics
### Medical
### Government

Bat soup
*Simpsons* prediction
Corona beer misassociation
Hospital conditions
Return of wildlife
Lions freed on the streets

### Research

Drug design and laboratory testing

CORONAVIRUS (THE INVISIBLE KILLER)
**First edition. April 15, 2020.**

Written by John Abrams.

# Coronavirus
## *The Invisible Killer*
John Abrams

With so much uncertainty and concern surrounding the recent novel coronavirus, it’s easy to feel helpless—but there is something we can all do to help the fight against it. Aside from keeping safe and following guidelines from medical experts, we can all do our part to get help to people and regions that have been affected.

By fundraising for coronavirus relief efforts, or donating to a coronavirus relief fund, we can all do our part and provide much-needed support and aid. With the growing number of quarantined areas, individuals in these areas need vital medical help and day-to-day items to pull through this new threat.

Getting ahead and helping now is key to making sure everyone is prepared for new developments. It’s important to do something now. Just $1 or less can help us continue our work.

Support Us through PayPal Here:
https://bit.ly/paypal-covid-19

Make a Donation to PayPal with Scanning of QR Code Below

# Part one

## *Severe Acute Respiratory Syndrome Coronavirus*

**Severe acute respiratory syndrome coronavirus** (**SARS-CoV** or **SARS-CoV-1**)is a strain of virus that causes severe acute respiratory syndrome (SARS).It is an enveloped, positive-sense, single-stranded RNA virus which infects the epithelial cells within the lungs. The virus enters the host cell by binding to the ACE2 receptor.It infects humans, bats, and palm civets. [6]

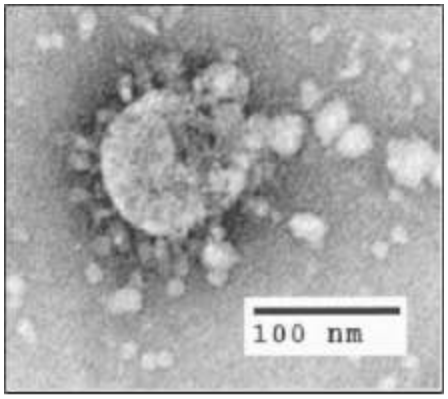
On 16 April 2003, following the outbreak of SARS in Asia and secondary cases elsewhere in the world, the World Health Organization (WHO) issued a press release stating that the coronavirus identified by a number of laboratories was the official cause of SARS. The Centers for Disease Control and Prevention (CDC) in the United States and National Microbiology Laboratory (NML) in Canada identified the SARS-CoV genome in April 2003.Scientists at Erasmus University in Rotterdam, the Netherlands demonstrated that the SARS coronavirus fulfilled Koch's postulates thereby confirming it as the causative agent. In the experiments, macaques infected with the virus developed the same symptoms as human SARS victims.

A pandemic due to novel coronavirus disease in 2019 showed many similarities to the SARS outbreak, and the viral agent was identified as yet another strain of the SARS-related coronavirus, SARS-CoV-2.

# SARs

SARS, OR SEVERE ACUTE respiratory syndrome, is the disease caused by SARS-CoV. It causes an often severe illness and is marked initially by systemic symptoms of muscle pain, headache, and fever, followed in 2–14 days by the onset of respiratory symptoms,mainly cough, dyspnea, and pneumonia. Another common finding in SARS patients is a decrease in the number of lymphocytes circulating in the blood.

In the SARS outbreak of 2003, about 9% of patients with confirmed SARS-CoV infection died.The mortality rate was much higher for those over 60 years old, with mortality rates approaching 50% for this subset of patients.




electron microscope image of SARS virion

**Virus classification**

| | |
|---|---|
| (unranked): | Virus |
| *Realm*: | *Riboviria* |
| Phylum: | *incertae sedis* |
| Order: | *Nidovirales* |
| Family: | *Coronaviridae* |
| Genus: | *Betacoronavirus* |
| Species: | *Severe acute respiratory syndrome-related coronavirus* |
| Strain: | **Severe acute respiratory syndrome coronavirus** |

## Synonyms

- SARS coronavirus
- SARS-related coronavirus
- Severe acute respiratory syndrome coronavirus

# HISTORY

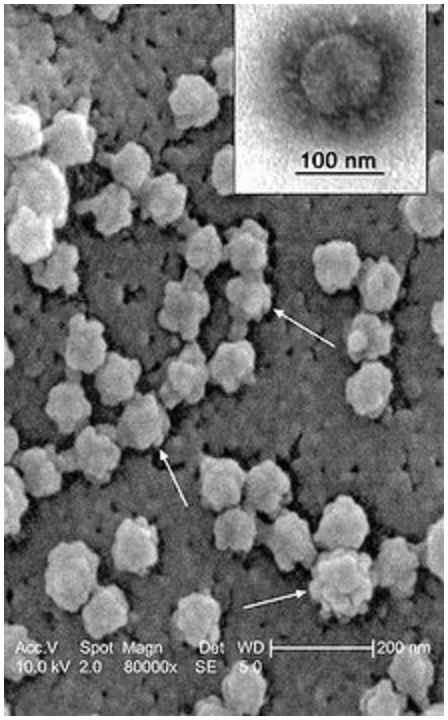
ON 12 APRIL 2003, SCIENTISTS working at the Michael Smith Genome Sciences Centre in Vancouver finished mapping the genetic sequence of a coronavirus believed to be linked to SARS. The team was led by Marco Marra and worked in collaboration with the British Columbia Centre for Disease Control and the National Microbiology Laboratory in Winnipeg, Manitoba, using samples from infected patients in Toronto. The map, hailed by the WHO as an important step forward in fighting SARS, is shared with scientists worldwide via the GSC website (see below). Donald Low of Mount Sinai Hospital in Toronto described the discovery as having been made with "unprecedented speed".The sequence of the SARS coronavirus has since been confirmed by other independent groups.

In late May 2003, studies from samples of wild animals sold as food in the local market in Guangdong, China, found a strain of SARS coronavirus could be isolated from masked palm civets (*Paguma* sp.), but the animals did not always show clinical signs. The preliminary conclusion was the SARS virus crossed the xenographic barrier from palm civet to humans, and more than 10,000 masked palm civets were killed in Guangdong Province. The virus was also later found in raccoon dogs (*Nyctereuteus* sp.), ferret badgers (*Melogale* spp.), and domestic cats. In 2005, two studies identified a number of SARS-like coronaviruses in Chinese bats.Phylogenetic analysis of these viruses indicated a high probability that SARS coronavirus

originated in bats and spread to humans either directly or through animals held in Chinese markets. The bats did not show any visible signs of disease, but are the likely natural reservoirs of SARS-like coronaviruses. In late 2006, scientists from the Chinese Centre for Disease Control and Prevention of Hong Kong University and the Guangzhou Centre for Disease Control and Prevention established a genetic link between the SARS coronavirus appearing in civets and humans, confirming claims that the virus had jumped across species.

# vIROLOGY

SARS-CORONAVIRUS FOLLOWS the replication strategy typical of the coronavirus subfamily. The primary human receptor of the virus is angiotensin-converting enzyme 2 (ACE2), first identified in 2003.




SCANNING ELECTRON MICROGRAPH of SARS virions

# Part TWO

## *Severe Acute Respiratory Syndrome Coronavirus 2*

**Severe acute respiratory syndrome coronavirus 2** (**SARS-CoV-2**),colloquially known as the **coronavirus** and previously known by the provisional name **2019 novel coronavirus** (**2019-nCoV**),is a positive-sense single-stranded RNA virus.It causes coronavirus disease 2019 (COVID-19), a respiratory illness. SARS-CoV-2 is contagious in humans, and the World Health Organization (WHO) has designated the ongoing pandemic of COVID-19 a Public Health Emergency of International Concern.The strain was first discovered in Wuhan, China, so it is sometimes referred to as the "Wuhan virus"or "Wuhan coronavirus".Because the WHO discourages the use of names based upon locationsand to avoid confusion with the disease SARS,it sometimes refers to SARS-CoV-2 as "the COVID-19 virus" in public health communications.The general public frequently calls both SARS-CoV-2 and the disease it causes "coronavirus", but scientists typically use more precise terminology.

# vIROLOGY

## Infection

HUMAN-TO-HUMAN TRANSMISSION OF SARS-CoV-2 has been confirmed during the 2019–20 coronavirus pandemic.Transmission occurs primarily via respiratory droplets from coughs and sneezes within a range of about 1.8 metres (6 ft). Indirect contact via contaminated surfaces is another possible cause of infection. Preliminary research indicates that the virus may remain viable on plastic and steel for up to three days, but does not survive on cardboard for more than one day or on copper for more than four hours; the virus is inactivated by soap, which destabilises its lipid bilayer.[32] Viral RNA has also been found in stool samples from infected people.

The degree to which the virus is infectious during the incubation period is uncertain, but research has indicated that the pharynx reaches peak viral load approximately four days after infection. On 1 February 2020, the World Health Organization (WHO) indicated that "transmission from asymptomatic cases is likely not a major driver of transmission". However, an epidemiological model of the beginning of the outbreak in China suggested that "pre-symptomatic shedding may be typical among documented infections" and that subclinical infections may have been the source of a majority of infections.

Taxonomically, SARS-CoV-2 is a strain of *Severe acute respiratory syndrome-related coronavirus* (SARSr-CoV). It is believed to have zoonotic origins and has close genetic similarity to bat coronaviruses, suggesting it emerged from a bat-borne virus.[An intermediate animal reservoir such as a pangolin is also thought to be involved in its introduction to humans. The virus shows little genetic diversity, indicating that the spillover event introducing SARS-CoV-2 to humans is likely to have occurred in late 2019.

Epidemiological studies estimate each infection results in 1.4 to 3.9 new ones when no members of the community are immune and no preventive measures taken. The virus is primarily spread between people through close contact and via respiratory droplets produced from coughs or sneezes. It mainly enters human cells by binding to the receptor angiotensin converting enzyme 2 (ACE2).

# Reservoir

THE FIRST KNOWN INFECTIONS from the SARS-CoV-2 strain were discovered in Wuhan, China.The original source of viral transmission to humans remains unclear, as does whether the strain became pathogenic before or after the spillover event.Because many of the first individuals found to be infected by the virus were workers at the Huanan Seafood Market,it has been suggested that the strain might have originated from the market.However, other research indicates that visitors may have introduced the virus to the market, which then facilitated rapid expansion of the infections.

Research into the natural reservoir of the virus strain that caused the 2002–2004 SARS outbreak has resulted in the discovery of many SARS-like bat coronaviruses, most originating in the *Rhinolophus* genus of horseshoe bats, and two viral nucleic acid sequences found in samples taken from *Rhinolophus sinicus* show a resemblance of 80% to SARS-CoV-2.A third viral nucleic acid sequence from *Rhinolophus affinis*, collected in Yunnan province and designated RaTG13, has a 96% resemblance to SARS-CoV-2.Bats are considered the most likely natural reservoir of SARS-CoV-2,but differences between the bat coronavirus and SARS-CoV-2 suggest that humans were infected via an intermediate host.

A metagenomic study published in 2019 previously revealed that SARS-CoV, the strain of the virus that causes SARS, was the most widely distributed coronavirus among a sample of Sunda pangolins.[50] On 7 February 2020, it was announced that researchers from Guangzhou had

discovered a pangolin sample with a viral nucleic acid sequence "99% identical" to SARS-CoV-2.[51] When released, the results clarified that "the receptor-binding domain of the S protein of the newly discovered Pangolin-CoV is virtually identical to that of 2019-nCoV, with one amino acid difference."[52] Pangolins are protected under Chinese law, but their poaching and trading for use in traditional Chinese medicine remains common.[53][54]

Microbiologists and geneticists in Texas have independently found evidence of reassortment in coronaviruses suggesting involvement of pangolins in the origin of SARS-CoV-2.[55] However, pangolin coronaviruses found to date only share at most 92% of their whole genomes with SARS-CoV-2, making them less similar than RaTG13 to SARS-CoV-2.[56] This is insufficient to prove pangolins to be the intermediate host; in comparison, the SARS virus responsible for the 2002–2004 outbreak shared 99.8% of its genome with a known civet coronavirus.

HORSESHOE BATS are among the most likely natural reservoirs of SARS-CoV-2

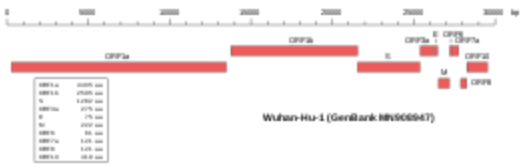
# Phylogenetics and Taxonomy

SARS-CoV-2 belongs to the broad family of viruses known as coronaviruses. It is a positive-sense single-stranded RNA (+ssRNA) virus. Other coronaviruses are capable of causing illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome (MERS). It is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HKU1, MERS-CoV, and the original SARS-CoV.[57]

Like the SARS-related coronavirus strain implicated in the 2003 SARS outbreak, SARS-CoV-2 is a member of the subgenus *Sarbecovirus* (beta-CoV lineage B).[58] [59] Its RNA sequence is approximately 30,000 bases in length.SARS-CoV-2 is unique among known betacoronaviruses in its incorporation of a polybasic cleavage site, a characteristic known to increase pathogenicity and transmissibility in other viruses.[60][61]

With a sufficient number of sequenced genomes, it is possible to reconstruct a phylogenetic tree of the mutation history of a family of viruses. By 12 January 2020, five genomes of SARS-CoV-2 had been isolated from Wuhan and reported by the Chinese Center for Disease Control and Prevention (CCDC) and other institutions;[62] the number of genomes increased to 42 by 30 January 2020.[63] A phylogenetic analysis of those samples showed they were "highly related with at most seven mutations relative to a common ancestor", implying that the first human infection occurred in November or December 2019.[63] As of 27 March 2020, 1,495 SARS-CoV-2 genomes sampled on six continents were publicly available.[64]

On 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) announced that according to existing rules that compute hierarchical relationships among coronaviruses on the basis of five conserved sequences of nucleic acids, the differences between what was then called 2019-nCoV and the virus strain from the 2003 SARS outbreak were insufficient to make them separate viral species. Therefore, they identified 2019-nCoV as a strain of *Severe acute respiratory syndrome-related coronavirus*.[2]

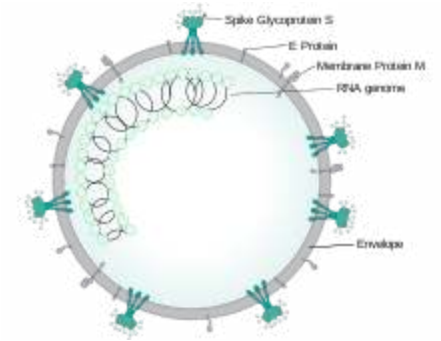



Genomic organisation of isolate Wuhan-Hu-1, the earliest sequenced sample of SARS-CoV-2

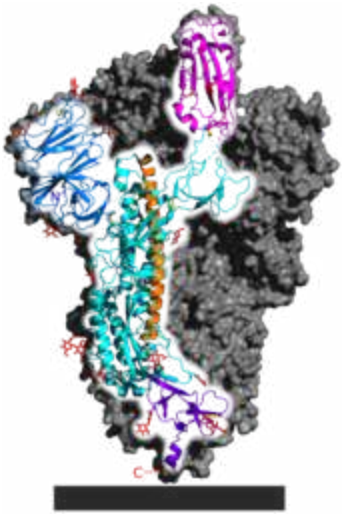
| | |
|---|---|
| **NCBI genome ID** | MN908947 |
| **Genome size** | 29,903 bases |
| **Year of completion** | 2020 |

# STRUCTURAL BIOLOGY

Each SARS-CoV-2 virion is approximately 50–200 nanometres in diameter.Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope.[65] The spike protein, which has been imaged at the atomic level using cryogenic electron microscopy,[66][67] is the protein responsible for allowing the virus to attach to and fuse with the membrane of a host cell.

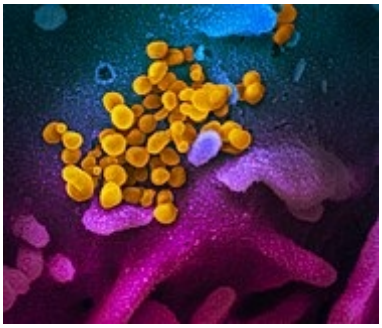


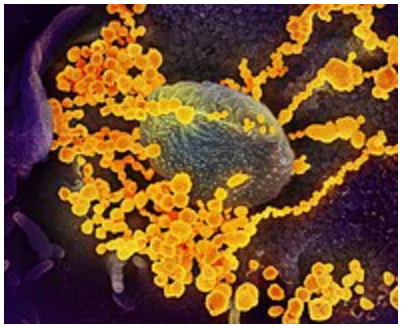

STRUCTURE OF A SARSR-CoV virion



SARS-COV-2 SPIKE HOMOTRIMER WITH one protein subunit highlighted; the ACE2 binding domain is in magenta

Protein modeling experiments on the spike protein of the virus soon suggested that SARS-CoV-2 has sufficient affinity to the receptor angiotensin converting enzyme 2 (ACE2) on human cells to use them as a mechanism of cell entry.[68] By 22 January 2020, a group in China working with the full virus genome and a group in the United States using reverse genetics methods independently and experimentally demonstrated that ACE2 could act as the receptor for SARS-CoV-2.[69][70][71] Studies have shown that SARS-CoV-2 has a higher affinity to human ACE2 than the original SARS virus strain.[66][72] SARS-CoV-2 may also use basigin to assist in cell entry.[73]





Digitally colourised electron micrographs of SARS-CoV-2 virions (yellow) emerging from human cells cultured in a laboratory

INITIAL SPIKE PROTEIN priming by transmembrane protease, serine 2 (TMPRSS2) is essential for entry of SARS-CoV-2. After a SARS-CoV-2 virion attaches to a target cell, the cell's protease TMPRSS2 cuts open the spike protein of the virus, exposing a fusion peptide. The virion then releases RNA into the cell, forcing the cell to produce copies of the virus that are disseminated to infect more cells.[74] [*bettersourceneeded*] SARS-CoV-2 produces at least three virulence factors that promote shedding of new virions from host cells and inhibit immune response.[65]