SARS-CoV-2 and COVID-19: An Evolving Review of Diagnostics and Therapeutics

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Authors

- **Halie M. Rando**
  0000-0001-7688-1770 · rando2 · tamefoxtime
  Department of Systems Pharmacology and Translational Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America · Funded by the Gordon and Betty Moore Foundation (GBMF 4552)

- **Casey S. Greene**
  0000-0001-8713-9213 · cgreene · GreeneScientist
  Department of Systems Pharmacology and Translational Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America; Childhood Cancer Data Lab, Alex's Lemonade Stand Foundation, Philadelphia, Pennsylvania, United States of America · Funded by the Gordon and Betty Moore Foundation (GBMF 4552)

- **Michael P. Robson**
  0000-0002-4859-0033 · mprobson
  Department of Computing Sciences, Villanova University, Villanova, Pennsylvania, United States of America

Abstract

Since late 2019, Coronavirus disease 2019 (COVID-19) has spread around the world, resulting in the declaration of a pandemic by the World Health Organization (WHO). This infectious disease is caused by the newly identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Research on the virus SARS-CoV-2 and the diease it causes is emerging rapidly through global scientific efforts. The development of diagnostics, treatments, and vaccines will be critical to mitigating the impact of the virus. Here we present a collaborative effort to organize and consolidate the rapidly emerging scientific literature related to SARS-CoV-2. We present information about the virus in the context of what is known about related viruses and synthesize studies emerging about the diagnosis and treatment of COVID-19 alongside literature about related illnesses. A broad scientific effort to understand this pandemic and related viruses and diseases will be foundational to efforts to predict possible interventions. This text is an evolving and collaborative document that seeks to incorporate the ever-expanding body of information related to SARS-CoV-2 and COVID-19.

Introduction

General Background

On January 21, 2020, the World Health Organization (WHO) released its first report concerning what is now known as the Coronavirus disease 2019 (COVID-19) [1]. This infectious disease came to international attention on December 31, 2019 following an announcement by national officials in China about 44 cases of a respiratory infection of unknown cause. The first known cases were located in Wuhan City within the Hubei province of China, but the disease subsequently began to spread rapidly beyond Wuhan within China and around the world. At the time of the first situation report [1], 282 confirmed cases had been identified, primarily in China, but also the first 1 to 2 cases had been found in each of Thailand, Japan, and the Republic of Korea. One week later, 4593 confirmed cases had been identified, spanning not only Asia, but also Australia, North America, and Europe [2]. On March 11, 2020, WHO formally classified the situation as a pandemic [3]. By WHO Situation Report 61, released on March 20, 2020, 266,073 confirmed cases had been reported worldwide, with cases on every continent except Antarctica [4]. At this time, over 11,000 deaths had been reported worldwide.

[Note: Maybe add a graph here, update as new reports come out.]

COVID-19 is caused by the newly identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a coronavirus, a type of RNA virus known to cause respitatory infections in humans and other species. Other well-known coronaviruses include those associated with previous infectious diseases of global concern, including Severe Accute Repiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS); however, some coronaviruses are associated with less virulent illnesses including the common cold. The SARS-CoV-2 virus was unknown until approximately January 12, 2020, when Chinese officials released its genetic sequence to aid in worldwide efforts to diagnose the disease [1]. As researchers worldwide work to characterize SARS-CoV-2 and COVID-19, information about the transmission and life cycle of the virus as well as the diagnosis and treatment of the disease is emerging rapidly. In this review, we seek to consolidate information about the virus in the context of related viruses and to synthesize what is known about the diagnosis and treatment of COVID-19 and related diseases. This is a real-time, collaborative effort that welcomes submissions from scientists worldwide.

Coronaviruses: What are they, and what do we know about SARS-CoV-19?

Coronaviruses are RNA viruses that... [Summarize relevant mechanisms for cell entry & address evidence for/against ACE2 being important]

Mechanisms of Coronavirus-driven Disease in Humans

Coronaviruses are known to cause respiratory illnesses in humans through the following possible mechanisms...

Presentation of COVID-19

Information is rapidly becoming available about the wide range of symptoms that can be associated with COVID-19 as well as the range of symptom severity, onset from exposure, and possible risk or protective factors...

Vaccines for Viruses: Strategies for and challenges to development

What information is needed to develop a vaccine? How have vaccines for other viruses such as H1N1 been developed?

Diagnostics and Therapeutics for Viruses

Two major concerns within diagnosis include the detection of current infections in individuals with and without symptoms, and the detection of past exposure without a live infection. In the latter category, identifying whether individuals can develop or have developed sustained immunity is also a major consideration.

Within therapeutics, some possible efforts include efforts to identify strategies for the management of symptoms as well as the development of antivirals...

In this review, we seek to consolidate information about efforts to develop strategies for diagnosis and therapeutics as new information is released by the scientific community.

Diagnostics

This section will include a review of the available information about diagnostics.

Therapeutics

This section will include a review of information available about therapeutics.

Additional Items

Competing Interests

Author	Competing Interests	Last Reviewed
Halie M. Rando	None	2020-03-22
Casey S. Greene	None	2020-03-22
Michael P. Robson	None	2020-03-23

Author Contributions

Author	Contributions
Halie M. Rando	Project Administration, Writing - Original Draft, Methodology
Casey S. Greene	Conceptualization
Michael P. Robson	Software

Formatting Examples

This manuscript is a template (aka “rootstock”) for Manubot, a tool for writing scholarly manuscripts. Use this template as a starting point for your manuscript.

The rest of this document is a full list of formatting elements/features supported by Manubot. Compare the input (`.md` files in the `/content` directory) to the output you see below.

Basic formatting

Bold text

Semi-bold text

Italic text

Combined *italics and* ***bold***

~~Strikethrough~~

1. Ordered list item
2. Ordered list item
    a. Sub-item
    b. Sub-item
        i. Sub-sub-item
3. Ordered list item
    a. Sub-item

- List item
- List item
- List item

subscript: H_2O is a liquid

superscript: 2^{10} is 1024.

unicode superscripts^{0123456789}

unicode subscripts$_{0123456789}$

A long paragraph of text. Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum.

Putting each sentence on its own line has numerous benefits with regard to editing and version control.

Line break without starting a new paragraph by putting
two spaces at end of line.

Document organization

Document section headings:

Heading 1

Heading 2

Heading 3

Heading 4

A heading centered on its own printed page

Horizontal rule:

`Heading 1`'s are recommended to be reserved for the title of the manuscript.

`Heading 2`'s are recommended for broad sections such as *Abstract*, *Methods*, *Conclusion*, etc.

`Heading 3`'s and `Heading 4`'s are recommended for sub-sections.

Links

Bare URL link: https://manubot.org

Long link with lots of words and stuff and junk and bleep and blah and stuff and other stuff and more stuff yeah

Link with text

Link with hover text

Link by reference

Citations

Citation by DOI [5].

Citation by PubMed Central ID [6].

Citation by PubMed ID [7].

Citation by Wikidata ID [8].

Citation by ISBN [9].

Citation by URL [10].

Citation by tag [11].

Multiple citations can be put inside the same set of brackets [5,9,11]. Manubot plugins provide easier, more convenient visualization of and navigation between citations [6,7,11,12].

Citation tags (i.e. aliases) can be defined in their own paragraphs using Markdown's reference link syntax:

Referencing figures, tables, equations

Figure 1

Figure 2

Figure 3

Figure 4

Table 1

Equation 1

Equation 2

Quotes and code

> Quoted text

> Quoted block of text
>
> Two roads diverged in a wood, and I—
> I took the one less traveled by,
> And that has made all the difference.

Code `in the middle` of normal text, aka `inline code`.

Code block with Python syntax highlighting:

```
from manubot.cite.doi import expand_short_doi

def test_expand_short_doi():
    doi = expand_short_doi("10/c3bp")
    # a string too long to fit within page:
    assert doi == "10.25313/2524-2695-2018-3-vliyanie-enhansera-copia-i-
        insulyatora-gypsy-na-sintez-ernk-modifikatsii-hromatina-i-
        svyazyvanie-insulyatornyh-belkov-vtransfetsirovannyh-geneticheskih-
        konstruktsiyah"
```

Code block with no syntax highlighting:

```
Exporting HTML manuscript
Exporting DOCX manuscript
Exporting PDF manuscript
```

Figures

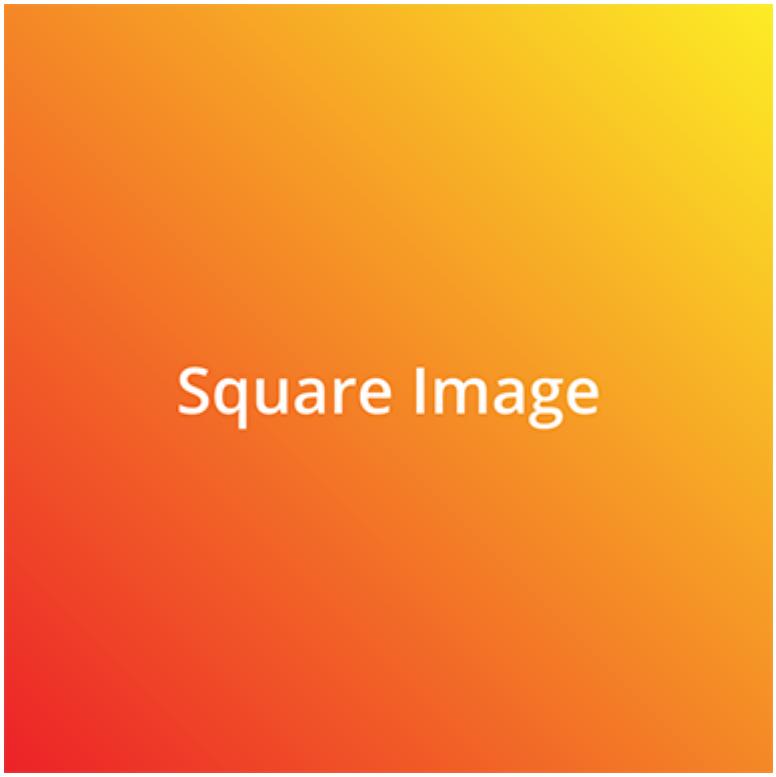

Figure 1: A square image at actual size and with a bottom caption. Loaded from the latest version of image on GitHub.

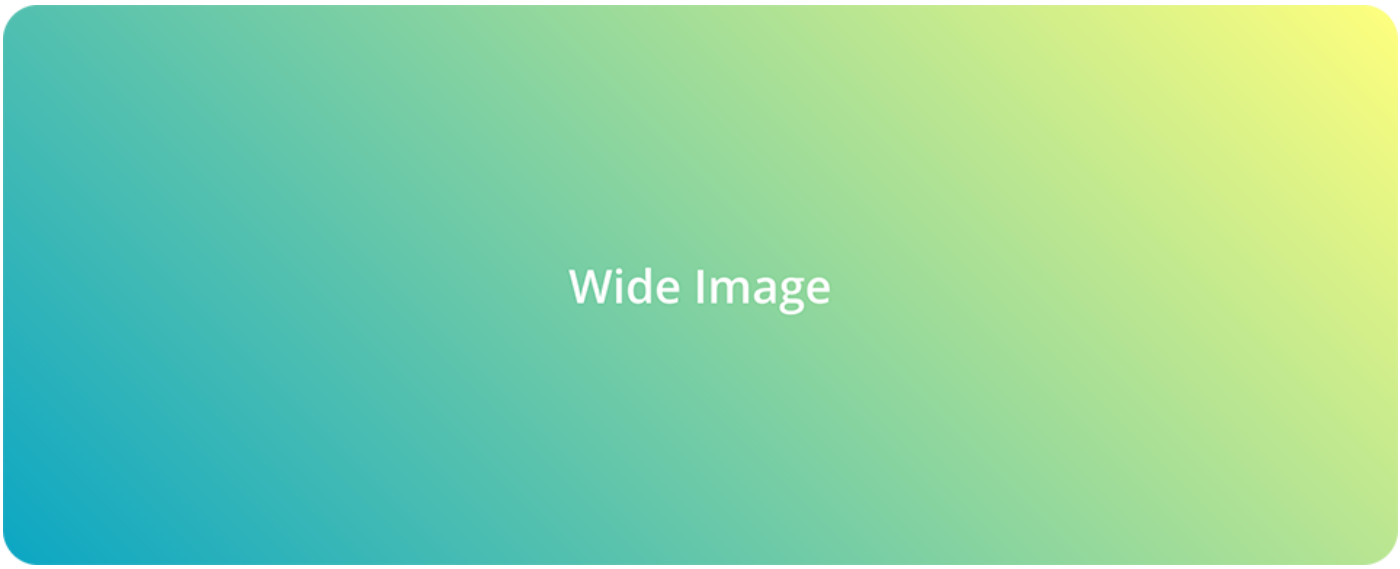

Figure 2: An image too wide to fit within page at full size. Loaded from a specific (hashed) version of the image on GitHub.

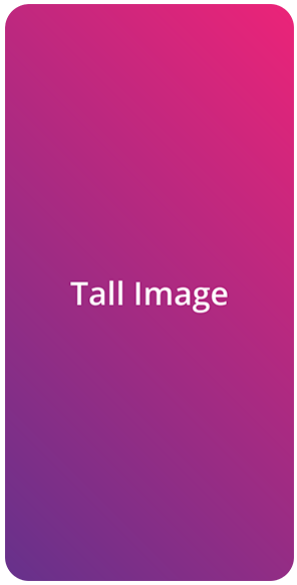

Figure 3: A tall image with a specified height. Loaded from a specific (hashed) version of the image on GitHub.

Figure 4: A vector `.svg` image loaded from GitHub. The parameter `sanitize=true` is necessary to properly load SVGs hosted via GitHub URLs. White background specified to serve as a backdrop for transparent sections of the image.

Tables

Table 1: A table with a top caption and specified relative column widths.

Bowling Scores	**Jane**	**John**	**Alice**	**Bob**
Game 1	150	187	210	105
Game 2	98	202	197	102
Game 3	123	180	238	134

Table 2: A table too wide to fit within page.

	Digits 1-33	**Digits 34-66**	**Digits 67-99**	**Ref.**
pi	3.14159265358979323 846264338327950	28841971693993751 0582097494459230	78164062862089986 2803482534211706	`piday.org`
e	2.71828182845904523 536028747135266	24977572470936999 5957496696762772	40766303535475945 7138217852516642	`nasa.gov`

Table 3: A table with merged cells using the `attributes` plugin.

	Colors	
Size	**Text Color**	**Background Color**
big	blue	orange
small	black	white

Equations

A LaTeX equation:

$$\int_0^\infty e^{-x^2} dx = \frac{\sqrt{\pi}}{2} \tag{1}$$

An equation too long to fit within page:

$$x = a + b + c + d + e + f + g + h + i + j + k + l + m + n + o + p + q + r + s + t + u + v + w + x + y + z + 1 + 2 + 3 + 4 + 5 + 6 + 7 + 8 + 9 \tag{2}$$

Special

⚠ **WARNING** *The following features are only supported and intended for* `.html` *and* `.pdf` *exports. Journals are not likely to support them, and they may not display correctly when converted to other formats such as* `.docx`*.*

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Adding arbitrary HTML attributes to an element using Pandoc's attribute syntax:

> Manubot Manubot Manubot Manubot Manubot. Manubot Manubot Manubot Manubot. Manubot Manubot Manubot. Manubot Manubot. Manubot.

Adding arbitrary HTML attributes to an element with the Manubot `attributes` plugin (more flexible than Pandoc's method in terms of which elements you can add attributes to):

> Manubot Manubot Manubot Manubot Manubot. Manubot Manubot Manubot Manubot. Manubot Manubot Manubot. Manubot Manubot. Manubot.

Available background colors for text, images, code, banners, etc:

`white` `lightgrey` `grey` `darkgrey` `black` `lightred` `lightyellow` `lightgreen` `lightblue` `lightpurple` `red` `orange` `yellow` `green` `blue` `purple`

Using the Font Awesome icon set:

✔ ? ★ 🔔 ⊗ •••

Light Grey Banner
useful for *general information* - manubot.org

Blue Banner
useful for *important information* - manubot.org

Light Red Banner
useful for *warnings* - manubot.org

References

1. Cramer
(2020-01-27) https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf

2. Ikejezie, Mr. Juniorcaius (WDC)
(2020-01-28) https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200128-sitrep-8-ncov-cleared.pdf

3. Ikejezie, Mr. Juniorcaius (WDC)
(2020-03-11) https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf

4. Ikejezie, Mr. Juniorcaius (WDC)
(2020-03-21) https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200321-sitrep-61-covid-19.pdf

5. **Sci-Hub provides access to nearly all scholarly literature**
Daniel S Himmelstein, Ariel Rodriguez Romero, Jacob G Levernier, Thomas Anthony Munro, Stephen Reid McLaughlin, Bastian Greshake Tzovaras, Casey S Greene
eLife (2018-03-01) https://doi.org/ckcj
DOI: 10.7554/elife.32822 · PMID: 29424689 · PMCID: PMC5832410

6. **Reproducibility of computational workflows is automated using continuous analysis**
Brett K Beaulieu-Jones, Casey S Greene
Nature biotechnology (2017-04) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6103790/
DOI: 10.1038/nbt.3780 · PMID: 28288103 · PMCID: PMC6103790

7. **Bitcoin for the biological literature.**
Douglas Heaven
Nature (2019-02) https://www.ncbi.nlm.nih.gov/pubmed/30718888
DOI: 10.1038/d41586-019-00447-9 · PMID: 30718888

8. **Plan S: Accelerating the transition to full and immediate Open Access to scientific publications**
cOAlition S
(2018-09-04) https://www.wikidata.org/wiki/Q56458321

9. **Open access**
Peter Suber
MIT Press (2012)
ISBN: 9780262517638

10. **Open collaborative writing with Manubot**
Daniel S. Himmelstein, Vincent Rubinetti, David R. Slochower, Dongbo Hu, Venkat S. Malladi, Casey S. Greene, Anthony Gitter
Manubot (2020-01-14) https://greenelab.github.io/meta-review/

11. **Opportunities and obstacles for deep learning in biology and medicine**
Travers Ching, Daniel S. Himmelstein, Brett K. Beaulieu-Jones, Alexandr A. Kalinin, Brian T. Do, Gregory P. Way, Enrico Ferrero, Paul-Michael Agapow, Michael Zietz, Michael M. Hoffman, … Casey S. Greene
Journal of The Royal Society Interface (2018-04-04) https://doi.org/gddkhn
DOI: 10.1098/rsif.2017.0387 · PMID: 29618526 · PMCID: PMC5938574

12. **Open collaborative writing with Manubot**
Daniel S. Himmelstein, Vincent Rubinetti, David R. Slochower, Dongbo Hu, Venkat S. Malladi, Casey S. Greene, Anthony Gitter
PLOS Computational Biology (2019-06-24) https://doi.org/c7np
DOI: 10.1371/journal.pcbi.1007128 · PMID: 31233491 · PMCID: PMC6611653