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SARS-CoV-2: Tale of a Microscopic Murderer

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Independent Study

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I am delighted to introduce Josiah Garner's "SARS-CoV-2: Tale of a Microscopic Murderer." This independent study assignment explores the impact of a novel, deadly, and worldwide virus. The assignment also examines the fast development of vaccines to control the spread and reduce the symptoms of the virus.

Josiah's paper focuses on the early history of the emergence of COVID-19, the world response, and vaccine development. He demonstrates critical thinking skills and effectively utilizes various research methods to obtain and communicate his information. Josiah skillfully analyzed the information about the novel virus SARS-CoV-2 and current vaccines. After devoting substantial time to gathering scientific research about the virus, he shaped it into a story about the discovery of the virus, the spread of the pathogen, and the worldwide response to the emerging health crisis. Josiah worked diligently online, at the college's library, and via Zoom meetings to perfect his research paper. He has taken a difficult but timely subject and summarized its complexity through his research story.

SARS-CoV-2: Tale of a Microscopic Murderer

Josiah Garner

In December 2019, a new virus emerged in Wuhan, China. Authorities warned local hospitals and health institutions about a possible pneumonia outbreak in the area (Zhu et al., 2020). This virus is now identified as Severe Acute Respiratory Syndrome Coronavirus 2, or SARS-CoV-2.

SARS-CoV-2 has spread globally and was classified as a pandemic by the World Health Organization on March 11, 2020 (Alturki et al., 2020). On March 15, 2020, the United States government proclaimed SARS-CoV-2 a national emergency and issued a lockdown to impede the virus's spread. Immediately, an international effort was launched to discover the genetic properties of the virus, how it spread, and its point of origin (Ball, 2020). In addition, the coalition would work together to develop treatments and vaccines for the virus. Over two years later, much more is known about the virus and at least four vaccines have been approved around the world (Jalkanen et al., 2021; Lo et al., 2022; Novavax, 2022). Act 1 focuses on SARS-CoV-2's structure, onset, and origin.

Act 1: Outbreak

SARS-CoV-2 Genetic Code, Protein Subunits, & Family Line

SARS-CoV-2, the disease which causes COVID-19, is a member of the coronavirus family. Coronaviruses contain a positive-sense, single-stranded RNA

(Ribonucleic Acid) genome wrapped inside a protein casing with protein spikes (S) protruding the envelope (E) and membrane (M), giving the virus a corona-like appearance (Campbell & Reece, 2005; Koirala et al., 2020). RNA strands for coronaviruses contain over 30,000 nucleotides and are enclosed in a protein helical nucleocapsid, called N (Koirala et al., 2020). The strand encodes for a viral polymerase (enzyme that builds RNA molecules) (Alturki et al, 2020), which replicates the viral RNA strand in the infected cell. In the case of SARS-CoV-2, its genome is 29.8-29.9k nucleotides long (Khailany et al., 2020).

The S protein of SARS-CoV-2 enables it to infect human cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor, like SARS-CoV (Sharma et al., 2020). There are two subunits of the S protein, S1 and S2. The two S subunits are connected at an S1/S2 cleavage site with polybasic insertion; the S1/S2 site can be uniquely cleaved with Furin, a protease enzyme in humans (Andersen et al., 2020; Scudellari, 2021; Xia et al., 2020). This S protein is unlike the spike found on SARS-CoV, SARS-CoV-2's ancestor (Andersen et al., 2020). The S1 subunit contains the Receptor Binding Doman (RBD) and attaches to ACE 2 receptors on cells in respiratory, gastrointestinal, myocardial, renal, and hepatic tissue, and the S2 subunit fuses the viral membrane with the cellular membrane (Alturki et al., 2020); the virus's RNA strand interacts with ribosomes for the translation process to create proteins (Alturki et al., 2020; Scudellari, 2021). In genetic expression, translation occurs in the cytoplasm of the cell, outside the nucleus (Campbell & Reece, 2005). The ribosome then builds a viral polymerase, and that polymerase reconstructs the viral RNA by using the original strand

as a template (Alturki et al., 2020; Scudellari). The viral polymerase also creates subsections of the RNA genome that encode for the various protein structures. These subsections subsequently utilize other ribosomes to build the protein structures, and the components are fused together to create more SARS-CoV-2 viruses that exit the infected cell (Alturki et al., 2020; Scudellari, 2021).

SARS-CoV-2 Origin & Transmission to Humans

As stated, SARS-CoV-2 is a member of the coronavirus family, with closely related human pathogens SARS-CoV and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) (Andersen et al., 2020; Ball, 2020; Sharma et al., 2020). SARS-CoV-2 has an 86.9% genetic match to SARS-CoV, which also emerged from China (Naserghandi et al., 2020). SARS-CoV appeared in southern China, whereas Wuhan is in central China (Campbell & Reece, 2005). Another ancestor of SARS-CoV-2 is the bat coronavirus RaTG13, which has a 96% match and is kept in the Wuhan Institute of Virology (Callaway et al., 2020, para. 22; Fernández, 2021; Segreto & Deigin, 2021). RaTG13 was found in Yunnan, China, in 2013 and has the closest genetic match to SARS-CoV-2 that can be found in animals. Other animal matches come from Malayan bats (93%) and Malayan pangolins (92%) in Southeast Asia (Callaway et al., 2020).

SARS-CoV-2 Issue of Origin

Scientists still theorize about the exact origin of SARS-CoV-2. Since it uses the same binding technique as SARS-CoV (attaching to the ACE2 receptor), researchers hypothesized SARS-CoV-2 descended from SARS-CoV and explored the possibility SARS-CoV antibodies could recognize SARS-CoV-2; this approach was invalid

(Sharma et al., 2020). Not only is the RBD for SARS-CoV-2 different than SARS-CoV, but also the S1/S2 joining section in SARS-CoV-2 is not in SARS-CoV (Andersen et al., 2020; Segreto & Deigin, 2020).

Animal coronaviruses have a better possibility of a genetic match with SARS-CoV-2 than human coronaviruses. RaTG13, a bat coronavirus housed in the Wuhan Institute of Virology, is the closest genetic match to SARS-CoV-2 at 96%, but its RBD is different than SARS-CoV-2's RBD (Andersen et al., 2020; Callaway et al., 2020; Fernández, 2021; Segreto & Deigin, 2021). Moreover, SARS-CoV-2 mutates rapidly, a stark contrast to the coronavirus family (Ball, 2020). According to Callaway et al. (2020), a 4% genetic difference takes decades to occur in coronaviruses, and there must be a genetic match greater than 99% with SARS-CoV-2 for the original transmission to be considered animal-to-human transmission. In contrast, RaTG13 was found by the Wuhan Institute of Virology in 2013, more than seven years before SARS-CoV-2 erupted in Wuhan (Segreto & Deigin, 2020).

Mutations & Delta/Omicron Variant Issues

Another interesting fact of SARS-CoV-2 is its rate of mutation and the resulting increased transmissibility. A joint UT Austin/Houston Methodist study recognized multiple variants in the Houston area, greatly affecting the number of cases (University of Texas at Austin, 2020). Variants Delta and Omicron spread rapidly in 2021 and 2022, respectively, and contain mutations in the S protein (Katella, 2022; Scudellari, 2021). With a high growth in cases, scientists fear SARS-CoV-2 cases could quickly rise in areas with low vaccination numbers and/or incidence of previous infection (Katella,

2022). Additionally, both Delta and Omicron variants can be transmitted from protected and unprotected individuals, with the latter at higher risk of severe symptoms (Goldberg et al., 2022; Puhach et al., 2022).

Crisis in the World

What will happen in both the United States and the world? Will scientists find a cure, treatment, or vaccine to eradicate this powerful, invisible, microscopic enemy? Or will the murdering virus and army of mutant strains continue their rampage unimpeded? Stay tuned for the next act of SARS-CoV-2: Tale of a Microscopic Murderer.…

Act 2: Solution

In December 2019, a novel virus emerged in Wuhan, China (Zhu et al., 2020); this virus is a member of the coronavirus family and is labelled Severe Acute Respiratory Syndrome Coronavirus 2, or SARS-CoV-2 (Sharma et al., 2020). Within months, SARS-CoV-2 had spread around the world, with its point of origin shrouded in obscurity (Segetro & Deigin, 2021) and its variants rapidly mutating (Katella, 2022; Scudellari, 2021; University of Texas at Austin, 2020). Act 2 focuses on the vaccines designed to impede SARS-CoV-2.

SARS-CoV-2 Vaccine Development and Trials

In light of the development, rapid spread, and obscurity of SARS-CoV-2, vaccines and treatment have been created to aid in society's immunization from and combat of SARS-CoV-2. Currently, three vaccines are available in the United States, one more in the United Kingdom, and many more are in the final phases of research and development (Food & Drug Administration, 2022; Jalkanen et al., 2021; Novavax,

2022). The creation of these vaccines is due to a massive amount of funding unlike anything previously seen (including $10 billion from the U.S. alone), research on past coronaviruses such as SARS-CoV and MERS-CoV, and revolutionary vaccine techniques like mRNA technology and protein spike technology (Ball, 2020; U.S. Department of Health and Human Services, 2020). Even with this massive funding operation, there needed to be an infrastructure to coordinate, research, and share information with others (Ball, 2020). Operation Warp Speed poured funding into the Pfizer/BioNTech, Moderna/NIAID, Novavax, and AstraZeneca/Oxford University vaccines, and these are being used for vaccination worldwide (Jalkanen et al., 2021; Lo et al., 2022; Novavax, 2022; U.S. Department of Health and Human Services, 2020).

Pfizer/BioNTech BNT162b2 Vaccine

Pfizer/BioNTech used the revolutionary mRNA vaccine technology created over 25 years ago to build its BNT162b2 SARS-CoV-2 vaccine (Ball, 2020). Even though mRNA vaccines are made with genetic material, they cannot alter anyone's DNA (deoxyribonucleic acid) (Campbell & Reece, 2005). This premise is a result of genetic expression; in other words, it is how the body uses genetic information to perform necessary life functions. BNT162b2 has an mRNA strand that encodes for the S on SARS-CoV-2 (Alturki et al., 2020). Once the vaccine is administered into the body, the translation process begins, and the mRNA is decoded (Alturki et al., 2020; Sharma et al., 2020). The immune system then categorizes the built spike as a dangerous intruder and develops antibodies that target and paralyze the virus (Alturki et al., 2020; Sharma

et al., 2020). BNT162b2 has an immunogenicity (immune response) of 95% in preventing infection against SARS-CoV-2 Wild Type (Dolgin, 2020).

Moderna/NIAID mRNA-1273 Vaccine

Moderna and the U.S. National Institute of Allergy and Infectious Diseases (NIAID) developed their mRNA-1273 SARS-CoV-2 vaccine using RNA technology to replicate the spike on SARS-CoV-2 (Alturki et al., 2020; Ball, 2020). This vaccine encodes for the spike form prior to binding to the target cell; therefore, according to NIAID Vaccine Research Centre Deputy Director Barney Graham, "[i]t becomes a much better vaccine antigen" (as cited in Ball, 2020, p. 17). The mRNA-1273 vaccine holds an immunogenicity of 94% against SARS-CoV-2 Wild Type (Dolgin, 2020).

AstraZeneca/Oxford University AZD1222 Vaccine

AstraZeneca, a U.K. based company, and the Jenner Institute of University of Oxford paired up to build a SARS-CoV-2 vaccine with non-replicating viral vector technology (Sharma et al., 2020, paras. 29-34). Viral vector differs from RNA technology and uses a virus that either affects very few humans or none at all and combines the chosen virus with the spike protein (S) from SARS-CoV-2 (Alturki et al., 2020, para. 11). AZD1222 , or ChAdOx1, employs a modified chimpanzee adenovirus with the SARS-CoV-2 S that does not replicate and is ultra-safe (Alturki et al., 2020, para. 11; Sharma et al., 2020, paras. 29-34). In addition, vaccines with viral vector technology and boost strategy, such as AZD1222, have immunity lasting over a year and longer (Dolgin, 2020, para. 18). AZD1222 also has an immunogenicity ranging from 70% to 90% against SARS-CoV-2 Wild Type (Dolgin, 2020, para. 19). This discrepancy

is a result of different dosing regimens used in the Phase III trials (Van Beusekom, 2020, para 2-3, 9-12; Dolgin, 2020, para. 19).

Novavax NVX-CoV2373 Vaccine

Novavax, an American company, used another relatively new technology: recombinant protein spike technology and Matrix-M1 adjuvant (booster) (Alturki et al., 2020). Novavax's protein spike technology creates nanoparticles with the SARS-CoV-2 spike that are administered into the body, mimicking SARS-CoV-2's entry method and making the immune system act as though the particles are the virus (Alturki et al., 2020; Keech et al., 2020). The patients are then given Novavax's Matrix-M1 booster to increase the immunogenicity. Most of the participants in the trials lacked immunity to COVID-19. After the trials, immunity greatly increased (Keech et al., 2020). NVX-CoV2373 finished its Phase III trials with an 89.7% immunogenicity (Toback et al., 2022).

Vaccine Efficacy Levels & Updates

Although these vaccines have passed the safety trials, great concern still exists regarding both their short and long-term effects on people (Dolgin, 2020; Sharma et al., 2020). Since these vaccines took a far shorter time to be created and/or authorized, researchers are monitoring for possible adverse reactions and efficacy against variants (Alturki et al., 2020; Ball, 2020; Centers for Disease Control and Prevention [CDC], 2022; Klein et al., 2021). Currently, the two mRNA vaccines and boosters are generating high immune responses against new variants, including Delta and Omicron substrains (Andrews et al., 2022; Lauring et al., 2022; Wang et al., 2021). However,

AZD1222 does not appear to have significant efficacy against Omicron (Andrews et al., 2022).

One cause of worry is vaccinated persons are catching and spreading SARS-CoV-2, creating breakthrough cases (Goldberg et al., 2022). While the vaccines do not prevent transmission (Maragakis & Kelen, 2021; Sanderson, 2021), inoculating people has reduced morbidity and mortality by minimizing the severity of COVID-19 symptoms and the rate of hospitalization (Corey, 2021; Haas et al., 2021; Kustin et al., 2021; Lauring et al., 2022). Moreover, new studies demonstrate vaccination and infection combined produce a higher immunity against SARS-CoV-2 variants (Altarawneh et al., 2022; Callaway, 2022; Goldberg et al., 2022; Sidik, 2022).

Another concern pertaining to this pandemic is the safety and efficacy of the vaccine on children. This population group was not included in the initial Pfizer/BioNTech, Moderna/NIAID, AstraZeneca/Oxford University, or Novavax trials, nor were pregnant women, elderly individuals, and high-risk populations (Keech et al, 2020; Lo et al., 2022; Sharma et al., 2020). Nonetheless, the elderly and high-risk groups were slotted to receive the vaccine first after trials concluded that the vaccines are safe (Anderson et al., 2020; Sharma et al., 2020). Additionally, a SARS-CoV-2 vaccine, Pfizer/BioNTech's BNT162b2, has been authorized for emergency use for ages 6 months-15 years old in the United States (Food & Drug Administration, 2022).

There have been concerns among people in society regarding possible negative side effects on fertility and pregnancy as a result of the vaccine; so far these concerns seem to be unfounded (Cleveland Clinic: Infectious Disease, 2022). Shimabukuro et al.,

(2021) conducted a study examining the safety of mRNA vaccine technology in women ages 16-54 in all three trimesters and found no obvious safety signals among pregnant women who received the mRNA SARS-CoV-2 vaccine. Additionally, a safe vaccine for pregnant women has been authorized (Novavax, 2022). Novavax's NVX-CoV2373 uses nanoparticle and Matrix-M1 adjuvant technology, which have been demonstrated to be safe in tests with over 14,000 people, including "children, pregnant women, and older adults" that have used their nanoparticle and Matrix-M1 adjuvant technology (Keech et al., 2020, p. 2331). A different publication addressed fertility in men who received an mRNA SARS-CoV-2 vaccine, and the researchers found no substantive changes in sperm count of men who received both BNT162b2 and mRNA-1273 (Gonzalez et al., 2021; Cleveland Clinic: Infectious Diseases, 2022). Ultimately, fertility and pregnancy do not appear to be affected by authorized or potential SARS-CoV-2 vaccines (Gonzalez et al., 2021; Lo et al., 2022; Shimabukuro et al., 2021).

There have been other rare side effects reported in individuals who received mRNA vaccines (CDC, 2022; Diaz et al., 2021). Two reported side effects are increases in myocarditis and pericarditis, conditions characterized by an inflammation of heart tissue (CDC, 2022). The vast majority of myocarditis incidents are primarily in younger males (Diaz et al., 2021). In contrast, pericarditis is majorly affecting older vaccinated individuals. Another concern pertains to the effect of SARS-CoV-2 vaccines on the menstrual cycle (Cleveland Clinic: Women's Health, 2022). While changes in the menstrual cycle have been reported by some women, the overall consensus is that

these changes may not be permanent (Cleveland Clinic: Infectious Disease, 2022; Cleveland Clinic: Women's Health, 2022).

Vaccine Differences

There are many differences between the vaccine technologies. RNA technology has a simple manufacturing process. According to Rino Rappuoli, chief scientist at GlaxoSmithKline in Siena, Italy, people can use "the same facility to make RNA [vaccines] for different diseases" (as cited in Ball, 2020, p. 18). This is because RNA by itself cannot infect people in the same manner as live viruses, minimizing risk of infection during production. Furthermore, vaccines can be synthesized in days rather than months or years (Ball, 2020).

RNA technology is not the only vaccine process generating attention. Viral vector vaccine technology is another approach gaining headway, and it is classified as a conventional technique (Ball, 2020). Additionally, viral vector vaccines can be refrigerated instead of frozen, both increasing stability and decreasing cost (Van Beusekom, 2020; Dolgin, 2020). Moreover, viral vector technology has been tested more than RNA technology (Dolgin, 2020). Nanoparticle technology, another medical wonder achieving headlines, mimics the virus outer structure and fusion and has been tested on many at-risk populations not included in vaccine trials (Sharma et al., 2020; Keech et al., 2020).

Conclusion

Over two years have passed since SARS-CoV-2 emerged, and scientists now know a great deal about the virus. At least four vaccines are available for use, and more

options are coming (Food & Drug Administration, 2022; Jalkanen et al., 2021; Novavax, 2022). Human vaccination has leapt great bounds, especially as it relates to information availability and vaccine technology (Ball, 2020). The vaccines are a successful defense against SARS-Co-V-2 variants, including Delta and Omicron (Andrews et al., 2022; Chemaitelly et al., 2021; Jalkanen et al., 2021; Lauring et al., 2021; Wang et al., 2021). Moreover, immunity generated from SARS-CoV-2 vaccination and infection is extremely effective against new variants (Callaway, 2022; Sidik, 2022). In addition, scientists are establishing infrastructure to analyze virus families and share information in case another pandemic emerges (Ball, 2020). This approach was used to develop the SARS-CoV-2 vaccines, and many proponents are stating that the world could benefit from sharing and generating research about viral families.

Scientists are united about vaccine safety and optimistic about the future. According to Akiko Iwasaki, an immunologist at Yale School of Medicine, this extraordinary and stupendous breakthrough “is a good example of what science can do very quickly” (as cited in Ball, 2020, p. 18). Virologist Shane Crotty of La Jolla Institute for Immunity says that protective immunity, which lessens or negates symptoms, could last longer than sterilizing immunity (Callaway et al., 2020). Even though people with immunity to SARS-CoV-2 are becoming infected, the symptoms are significantly lessened (Altarawneh et al., 2022; Haas et al., 2021; Lauring et al., 2022). In the near future, the world can celebrate the global arrest of SARS-CoV-2 in person (Van Beusokom, 2020; Corey, 2021).

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