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Patent Landscape Report

COVID-19 vaccines and therapeutics

Insights into related patenting activity throughout the pandemic

WIPO

Contents

Acknowledgements

This Patent Landscape Report on COVID-19 vaccines and therapeutics is part of the WIPO COVID-19 response package launched by Director General Daren Tang to assist member states in addressing the COVID-19 pandemic and building back better as part of their sustainable post-COVID economic recovery efforts and is an update of the report published in 2022.

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The report benefited greatly from reviews by Amina Larbi (Medicines Patent Pool) and WIPO colleagues Carsten Fink (Department for Economics and Data Analytics) and Peter Bassam Khazin (Global Challenges Division). Thanks also go to Charlotte Beauchamp (Head, Publications and Design Section) for her invaluable support and advice, Vanessa Harwood for her editorial oversight and the WIPO Design Team for the report design.

Key findings

Since the start of the COVID-19 pandemic a remarkable research and innovation effort has gone into combating the SARS-CoV-2 virus and COVID-19 disease. This Patent Landscape Report provides observations on the field of COVID-19 vaccines and therapeutics, based on a comprehensive review of patenting activity and building on insights from the first WIPO COVID-19 Patent Landscape Report published in March 2022.

Pandemic-related filing activity has been extraordinarily active

The patent search undertaken for this report looked at related patent filings from January 2020 through September 2022. It found 7,758 patent filings on technologies related to COVID-19 in general, including 1,298 patent filings related to vaccine development and 4,787 to therapeutics. Patenting activity related to COVID-19 outpaced that of other recent viruses and illnesses, such as influenza and SARS, both in volume and speed of filing.

Patenting filing activity has been concentrated at four patent offices

Because COVID-19 vaccines and therapeutics have a global market, it should come as no surprise that related applications were filed and published by patent offices all over the world. Specifically, vaccine patents were published across 30 patent offices and therapeutic patents across 44 patent offices. The World Intellectual Property Organization (WIPO), administering the Patent Cooperation Treaty (PCT) system, received the most COVID-19-related vaccine and therapeutic patent applications, followed by the China National Intellectual Property Administration (CNIPA), the United States Patent and Trademark Office (USPTO) and the European Patent Office (EPO), all receiving a significant number of applications of either type. WIPO's current top ranking is a likely indication that patent applicants are leveraging the WIPO-administered PCT system in order to protect inventions across multiple jurisdictions.

Both business and the research community have contributed significantly to the patent landscape

Patent applicants are distributed almost equally between companies (52 percent of the vaccines and 49 percent of the therapeutics dataset) and universities and research organizations (42 percent of the vaccines and 38 percent of the therapeutics dataset), but with companies accounting for a larger proportion of the two datasets.

China is the leading origin of patent filings related to vaccines and therapeutics

A patent applicant's location can provide information about the profile and origin of the key players in terms of patenting activity. The top five patent applicant locations in the field of vaccines are China, the United States of America (US), Germany, the Republic of Korea and the Russian Federation. In the field of therapeutics, China, the United States, the Republic of Korea, India and Germany are the top applicant locations.

The relative frequency of discussions around mRNA and other types of vaccines for COVID-19 is at variance with patenting activity in the dataset

Although global discussion around vaccines was primarily focused on mRNA vaccines, a comparison of doses administered worldwide of the different categories of vaccine tells another story. Two apparent discrepancies are that COVID-19 mRNA vaccines accounted for the majority of vaccinations in the western world, but patents related to this type of vaccine accounted for just 11 percent of the dataset; but conversely, protein subunit vaccines accounted for less than 1 percent of vaccine doses administered in that same region, but represented the largest portion (47 percent) of the vaccine patent dataset. China has almost exclusively administered inactivated vaccines, whereas Africa has primarily administered viral vector vaccines.

Small molecule and biologic drugs are the two main types of therapeutics

Within the dataset, therapeutics for COVID-19 mostly fall into three main types: small molecules that include synthetic compounds but may also be natural products extracted and purified from plants; biologic drugs that include antibodies, non-antibody peptides/proteins, cell-based therapies and nucleic acid-based therapies; and traditional medicine. The largest proportion of COVID-19 therapeutics patent filings relates to small molecules and biologics (50 percent and 43 percent of the therapeutics patent dataset, respectively). However, traditional medicine also has a role to play in the fight against COVID-19. Within the therapeutics dataset, 10 percent of filings disclosed the use of traditional medicine in treating COVID-19.

Antibodies accounted for one-third of biologics, and in their newly developed virus-neutralizing form introduce a new class of antiviral

The fastest growing class of biologics, antibodies made up about one-third (34 percent) of the biologics disclosed in patent documents. COVID-19 therapeutic antibodies include newly developed neutralizing antibodies directed against the SARS-CoV-2 spike (S) protein, as well as previously developed antibodies that modulate the host's immune/inflammatory response to the virus. Virus-neutralizing antibodies represent a new class of antivirals. When given in combination, they are capable of binding to various regions of a crucial segment in the SARS-CoV-2 S protein and in so doing effectively block the viral S protein from interacting with its receptor on human cells. Other antibodies that target human host factors may be used to reduce inflammation and counter adverse effects from the cytokine storms seen in some severe cases of COVID-19.

The patent dataset discloses some innovative treatment approaches

The dataset includes information on other potential methods for COVID-19 treatment. Novel approaches include the use of CRISPR-Cas technology to target viral genes so as to disrupt the virus's ability to infect host cells; nucleic acid-based drugs (e.g., small interfering RNA, short hairpin RNA, microRNA, antisense oligonucleotides, aptamers) designed to attack SARS-CoV-2 at distinct stages of its lifecycle and/or to modulate host dependency factors; and, lastly, novel delivery vehicles, such as engineered exosomes (i.e., the membrane-bound extracellular vesicles of human cells). The advent of biotechnology related to exosomes enriched with the desired molecules, including drugs, has enabled the commercial production of novel delivery vehicles. Drug or cargo-loaded exosomes containing immune-modulating substances in combination with antiviral substances can provide rapid and targeted delivery for disease treatment. The potential application of these innovative strategies in the treatment of COVID-19 in clinical settings is yet to be determined.

Collaborations comprised pharmaceutical companies, biotech startups and universities

Cooperation between big pharmaceutical companies and relatively small biotech companies, and between universities and both these types of commercial organizations was evident across different regions of the world. For example, development of the oral antiviral therapeutic molnupiravir involved Emory University, Merck, and Ridgeback Biotherapeutics. Merck and the Medicines Patent Pool also had a licensing agreement to provide molnupiravir as a COVID-19 treatment to low- and middle-income countries. Developers of vaccines and therapeutics also collaborated with different manufacturers at the manufacturing stage (Global Healthcare Innovation Alliance Accelerator. (n.d.-a).

Patents related to booster vaccines are only a small part of the vaccine patent dataset

About 5 percent of vaccine patents in the dataset emphasized booster use. This is at variance with extensive media discussion, government recommendations and policy debates around the availability and use of boosters. Data on booster usage by country and income level show that high-income economies have higher levels of booster vaccination, whereas low-income regions have very low booster usage and middle-income countries range between the two.

Roughly a tenth of COVID-19 therapeutics patents related to traditional medicine

From January 2020 through September 2022, 523 patent applications related to traditional medicine were published. Most were filed by applicants located in Asia. Over 60 percent were filed at the China National International Property Administration (CNIPA). The intellectual property offices of India and Republic of Korea were the next biggest recipients of traditional medicine patents.

Patents related to long COVID made up less than 2 percent of the dataset

Therapeutics for the treatment of long COVID – defined by the World Health Organization as the continuation or development of new symptoms three months after an initial SARS-CoV-2 infection, with symptoms lasting for at least two months without another explanation – were disclosed in 22 patents (WHO, 2022b). The majority (13) disclosed small molecule therapeutics to treat long COVID. The remainder comprised biologics, traditional medicine and other types of therapeutics for long COVID treatment.

Corporate applicants filed the most patents related to pharmaceutical formulations for COVID-19 therapeutics

Over 90 percent of patent applications relating specifically to pharmaceutical formulations were submitted by corporate applicants, either alone or in combination with a university or research organization or an independent inventor. Within this subset of patents, the majority relate to formulations of small molecule therapeutics (64 percent), followed by biologics (34 percent).

Nearly one-quarter of patent applications were the result of collaboration between multiple applicants

Patent applications with more than one assignee made up 24 percent of the dataset. In the vaccine dataset, collaboration was between all applicant types, including companies, universities and research organizations. In the therapeutics dataset, the majority of collaborations were between universities and research organizations.

Introduction

In late 2019, a mysterious pneumonia-like illness emerged in China that caught the attention of the world's health experts and scientists. The illness quickly spread around the globe. Research into its cause revealed it to be the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In January 2020, the World Health Organization (WHO) declared a global public health emergency and named the illness COVID-19, in February 2020 (WHO, 2020). Soon afterwards, in March 2020, the WHO officially declared COVID-19 a global pandemic. As of November 28, 2022, there had been more than 637 million cases confirmed worldwide, resulting in over 6.6 million deaths (WHO, n.d.-g), making it one of the deadliest pandemics in modern history, second only to the 1918 flu pandemic (Adam, 2022). Its severity and the complexity in battling COVID-19 pandemic has been compounded by the ongoing emergence of SARS-CoV-2 variants, with sublineages of the Omicron variant currently of most concern (WHO, n.d.-f).

In response to the pandemic, scientists around the world have made great strides in understanding the SARS-CoV-2 virus. This in turn has led to the development of preventive vaccines and therapeutic agents. By leveraging decades of vaccine technology research and development (R&D), scientists have been able to quickly first develop and then deploy a variety of COVID-19 vaccines. As of December, 2022, more than 13.04 billion vaccine doses had been administered globally (WHO, n.d.-c). In parallel, existing drugs have been repurposed and new therapeutics developed to combat the disease.

This report is a follow-up to WIPO's first *COVID-19-related Vaccines and Therapeutics* Patent Landscape Report published in early 2022 (WIPO, 2022). It presents an updated overview of global patenting activity related to COVID-19 vaccines and therapeutics from January 2020 through September 2022, based on information publicly available as of September 30, 2022. Because of the lag in time between patent filing and publication of the related application (on average 18 months), this report does not give a complete picture but rather a perspective on publicly available COVID-19-related patent information up until September 2022.

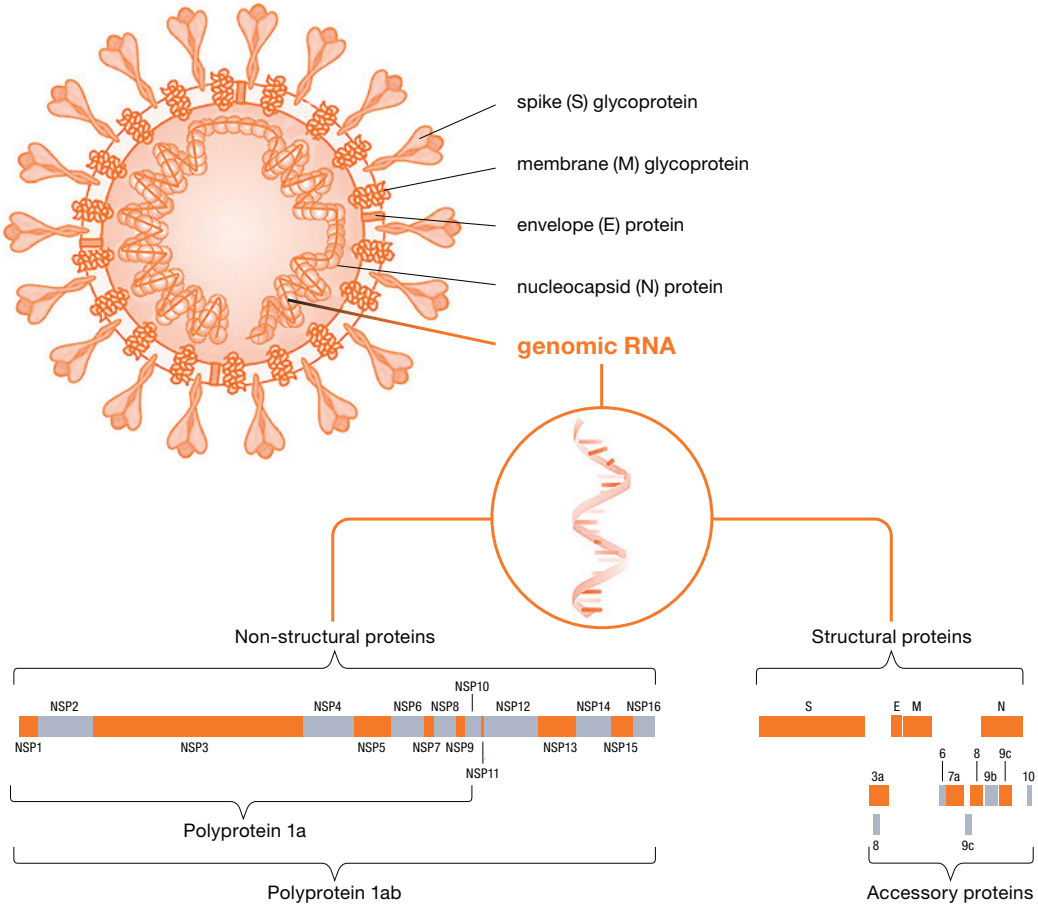
Since the pandemic began, various patent analytics and scientific publications have sought to shed light on patent activities and technologies related to COVID-19. A list of these publications can be found in the Further reading section.

Background – biology of COVID-19

The coronavirus that causes COVID-19 – SARS-CoV-2 – was unknown to the scientific community until discovered in late 2019. Since then, its structure and mechanism of action have been extensively studied. The full genetic sequence of the SARS-CoV-2 virus was first published on January 10, 2020, by Yong-Zhen Zhang at Fudan University, China (Zhang, 2020). Upon the sequence's release, it became possible to define the structure of the virus (shown in Figure 1). Since then, focus has been on identifying, understanding and tracking variants in order to predict whether existing vaccines and therapeutics are likely to prove effective in preventing and treating the associated disease.

Figure 1. The genomic landscape of SARS-CoV-2

The structure of the SARS-CoV-2 virus revealed the presence of the spike (S) glycoprotein that is key in causing infection.



Source: WIPO, based on Gordon *et al.*, 2020.

The SARS-CoV-2 virus's mechanism of action has been discussed in detail in the previous WIPO Patent Landscape Report on COVID-19 (WIPO, 2022). In short, the virus's outer lipid envelope is covered with spike glycoprotein (S protein). It is this S protein that interacts with human cells to cause infection. In the initial stage of infection, the coronavirus S protein binds to specific host cellular entry receptors. This opens the door for the virus to enter a cell. Once inside, the virus repurposes the host cell's system in order to replicate and invade further host cells. Vaccines and therapeutics are typically designed to disrupt this and associated subprocesses.

As viruses spread within a population, their genetic material mutates. Most mutations have little or no impact on the properties of a virus (Grubaugh *et al.*, 2020). Those mutations that do are typically called variants. Such variants can increase transmissibility or disease severity and decrease diagnostic effectiveness, as well as vaccine or therapeutic efficacy; all challenges impacting public health and the social measures needed to combat the virus (WHO, n.d.-f). Several variants of the original SARS-CoV-2 virus now exist, including the Alpha, Beta, Gamma, Delta and Omicron variants. Every one of these variants has subvariants or sublineages, commonly recognized by their Phylogenetic Assignment of Named Global Outbreak (Pango) identifier. Table 1 provides a high-level summary of SARS-CoV-2 variants. More information about variants can be obtained from the WHO's SARS-CoV-2 variant tracking website (WHO, n.d.-f).

Table 1. Summary of SARS-CoV-2 variants

Several SARS-CoV-2 variants have emerged since the pandemic began in early 2020. Omicron is the most recently sequenced variant of the SARS-CoV-2 virus. Unlike its predecessors, no one country of origin has been identified for this variant.

WHO label	Pango lineage	Date of 1st sequence documentation	Country of origin
Alpha	B.1.1.7	September 2020	UK
Beta	B.1.351	May 2020	South Africa
Gamma	P.1	November 2020	Brazil
Delta	B.1.617.2	October 2020	India
Omicron	B.1.1.529	November 2021	Multiple countries

Source: WIPO, based on data obtained from the World Health Organization, December 2022.

Omicron variant B.1.1.529 and its sublineages are currently of most concern. First classified as a *variant under monitoring* by the WHO on November 24, 2021, the Omicron variant was upgraded only two days later to a *variant of concern* on November 26, 2021 (WHO, 2021a). This variant has many sublineages, each of which has a variety of mutations that generally increase the risk of infection and reinfection through greater transmissibility and virulence (Fan *et al.*, 2022). The WHO has recommended that public health authorities monitor sublineages as distinct lineages, so as to track the virus's evolution and make informed public health decisions. A further concern is the ability of the Omicron variant and sublineages to evade not only natural but also vaccine-mediated immune responses. The only relief offered by this variant is its reduced pathogenicity, meaning less severe disease, fewer hospitalizations and not so many deaths (Fan *et al.*, 2022).

Substantial efforts have been made to develop safe and effective vaccines and therapeutics with which to combat COVID-19 and the many SARS-CoV-2 virus variants. Multiple vaccine platforms have been studied, including conventional (e.g., protein subunit and live attenuated and inactivated virus) and novel platforms (e.g., DNA and RNA-based). With the rise of SARS-CoV-2 variants, bivalent and multivalent vaccines to combat the virus more effectively are also being investigated. Additionally, the repurposing of many existing therapeutics to treat COVID-19 (e.g., remdesivir and fluvoxamine) has been considered and new therapeutics developed, including a diverse set of small molecule drugs and biologics.