CVR
Coronavirus Vaccines R&D Roadmap

Research and Development (R&D) Roadmap for Broadly Protective Coronavirus Vaccines

EXECUTIVE SUMMARY

The historic, ongoing toll of COVID-19 on health and economic stability worldwide highlights the critical need to make R&D for broadly protective coronavirus vaccines a global priority. SARS-CoV-2, which emerged in 2019 to cause the COVID-19 pandemic, was the third coronavirus in just the past two decades to have emerged from an animal reservoir to cause human epidemics. Severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in 2003, followed by Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012.

Coronaviruses can be highly lethal. MERS-CoV has a 35% case-fatality ratio (CFR), meaning that about one third of infections result in death. For SARS-CoV, approximately 1 in 10 infections result in death (10% CFR). Fortunately, these two coronaviruses do not spread efficiently from person to person. Although SARS-CoV-2 has a much lower CFR, the virus is highly transmissible and has spread rapidly worldwide, resulting in far more deaths. By the end of 2022, SARS-CoV-2 infections had caused more than 650 million confirmed COVID-19 cases and more than 6.6 million deaths.

Beyond the global scourge of the current COVID-19 pandemic, even more concerning is the threat of a new coronavirus in the future that could be both highly transmissible *and* highly lethal. Thousands of different coronaviruses are circulating in animals worldwide, particularly in bats but also in other mammals and in birds. The trends of the past 20 years are intensifying, with increasing risk of coronaviruses spilling over from animal reservoirs to people, fueled by the rapid expansion of human populations into animal habitats and an increasingly interconnected world.

The limited durability and immunologic protection of currently available COVID-19 vaccines further highlight the crucial need for a new, proactive approach to develop coronavirus vaccines that provide better and longer protection against both circulating and future SARS-CoV-2 variants and other coronaviruses that have not yet emerged. Currently available COVID-19 vaccines have proven to be safe and effective for the prevention of severe disease and death, and form the backbone of the global public health pandemic response. However, these vaccines do not provide sufficient protection against infection, transmission, and the relentless emergence of new variants that evade the immune response.

Building a proactive response to coronavirus threats

The combination of three new coronavirus epidemics in just 20 years, coupled with our growing understanding of the breadth of animal reservoirs worldwide carrying coronaviruses and the limitations of currently available vaccines, is sending a clear signal. Coronaviruses represent a real and present threat to global health and stability that demands a response through a large, comprehensive, and coordinated R&D initiative to develop broadly protective and globally accessible coronavirus vaccines.

The goal of developing broadly protective coronavirus vaccines is therefore multi-faceted: (1) to create more efficacious and durable COVID-19 vaccines, (2) mitigate the potential threat of future coronaviruses that have not yet emerged, and, (3) ideally, prevent infections and transmission.

The ultimate objective of the CVR is to accelerate the development of durable, broadly protective coronavirus vaccines that:

1. Reduce severe illness and death (and potentially prevent infection) due to current and future human coronaviruses, both those known to infect humans and viruses at risk of spilling over from animals to humans in the future.
2. Mitigate the impact of future coronavirus epidemics worldwide.
3. Are suitable for use in all regions of the globe, including remote areas and low- and middle-income countries.

A structured, coordinated plan for broadly protective coronavirus vaccines

Development of broadly protective coronavirus vaccines is a large, complex, and costly endeavor. Advancing a global R&D vaccine initiative will require ongoing investment, communication, and coordination among researchers, governments, industry, multilateral and nongovernmental organizations, regulators, public health officials, and policymakers. The COVID-19 pandemic has resulted in millions of lives lost, trillions of dollars in economic damage, and social upheaval worldwide. The payoff from having the tools to avoid a repeat of this devastation is considerable. The scientific advances and partnerships that enabled the development of COVID-19 vaccines in record time demonstrate the potential to make rapid progress through a clear, structured, and coordinated coronavirus vaccine R&D initiative. Future advances must also ensure that global equity is a core principle of vaccine R&D, and that programs anticipate and resolve issues that may undermine this objective.

Over the past year, the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota, with funding from The Rockefeller Foundation and the Bill & Melinda Gates Foundation, and through the collaborative efforts of 50 experts from around the world, created a comprehensive Coronavirus Vaccines R&D Roadmap (CVR) for broadly protective coronavirus vaccines. The CVR provides a framework and timeline for essential research, leadership and investments, while offering a detailed assessment of specific scientific, regulatory, and logistical challenges. Many efforts are already under way that will contribute to advancement of broadly protective coronavirus vaccine R&D. The roadmap offers the structure and time-bound milestones to ensure this work is well-aligned and focused on building the coordination, leadership, and investment essential for achieving these ambitious objectives.

The CVR is organized into five topic areas. Each area includes a summary of key barriers and knowledge gaps along with a set of technical milestones for measuring success.

Virology applicable to vaccine R&D

Development of broadly protective coronavirus vaccines will require an improved understanding of the global distribution of coronaviruses through advancement of global surveillance, research, and information sharing. Coordinated and sustained efforts are needed to collect, characterize, and share viral information from the full range of wild and captive animal reservoirs worldwide, using standardized tools and methods. The knowledge gained from such work will guide a well-informed strategy for selecting diverse sets of coronaviruses that define the breadth of protection needed for future coronavirus vaccines.

Vaccinology

Achieving consensus on preferred product characteristics for broadly protective coronavirus vaccines will inform priorities and strategies for vaccine R&D. Key vaccine characteristics to consider include breadth of coverage, durability of protection, and feasibility of use worldwide, including in low-resource settings. Advancements in new technologies (such as new platforms and adjuvants and innovative delivery methods) will accelerate the development and distribution of broadly protective vaccines. In addition, identifying best strategies for conducting randomized controlled trials that compare new vaccine candidates to existing vaccines, particularly among people with preexisting exposure and immunity, will improve R&D efforts. A number of strategies and platforms hold potential for development of broadly protective vaccines; long-term commitment and investment will be essential to advance new candidate vaccines through the full pipeline from discovery to regulatory approvals.

Policy and financing

Broadly protective coronavirus vaccine candidates face high development costs, manufacturing complexities, and, once approved, uncertain demand and return on investment. Successful development and widespread availability of broadly protective coronavirus vaccines will require reinvigorating and sustaining a high level of political commitment and investment in vaccine R&D, surveillance, and global manufacturing and distribution. Detailed analyses that capture the wide range of potential social and economic benefits of broadly protective coronavirus vaccines, in the context of what is needed to develop and produce these vaccines, will serve as strong foundational documents to inform policymaking and essential global investment.

Immunology and immune correlates of protection

Developing broadly protective coronavirus vaccines will require advances in the science of human immunology. Key areas of research include identifying factors that expand the breadth and durability of immune protection, and characterizing the mechanisms involved in systemic and mucosal immunity that protect against coronavirus infection, disease, and transmission. Improved understanding of the role of immune imprinting from prior infection and vaccination will be critical to advance new vaccine R&D. Further identification of correlates of protection (immune responses that are markers of protection) will expedite the development of coronavirus vaccines using different antigens, platforms, and modes of administration. Standardization of assays, specimen collection and research methods, improved information sharing, and creation of virtual biorepositories will facilitate collaboration and accelerate scientific discovery.

Animal and human infection models for coronavirus vaccine research

The availability of a range suitable animal models is a key barrier to developing broadly protective coronavirus vaccines, and those models must be standardized, validated, and well-characterized. They must also be capable of mirroring a range of human immune responses and clinical disease related to coronavirus infection, including severe acute, chronic, and fatal outcomes. Maximizing the value of animal models also demands greater attention to supplying researchers with validated, reliable reagents; updated virus strains and stocks; and harmonized assays. A controlled human infection model (CHIM) has been developed for studying SARS-CoV-2 and could play an important role in assessing broadly protective coronavirus vaccine candidates. Additional efforts that optimize the CHIM will broaden its utility, including identification of best practices and expanded use of standardized ethical and safety guidelines.

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