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EDITORIAL

How can we accelerate COVID-19 vaccine discovery?

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1. Introduction

The COVID-19 outbreak is an ongoing pandemic caused by
severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
[1] that is still severely impacting our lives, both as an indivi-
dual and as a community. But as always, each major event
means a source of progress. In fact, scientists created multiple
vaccines for SARS-CoV-2 within a year (while most vaccines
ordinarily take at least 15 years to be developed), along with
a never seen amount of funds employed for vaccine research
and development in the race to create a vaccine in response
to this pandemic emergency. Undoubtedly, vaccination is the
most important strategy to fight the pandemic [2].

The pipeline itself for SARS-CoV-2 vaccine development has
followed an accelerated timeline. Thanks to the existing
knowledge obtained by previous development platforms of
vaccines for SARS-CoV and MERS-CoV [3], the initial common
discovery phase was skipped and almost immediately phase I/
II trials were started.

Although this extraordinary speed in the rush for SARS-CoV
-2 vaccine development, many open issues remain. They
essentially relate to the difficulty of finding an immunogenic
formulation, selecting the optimal vaccine dosage, addressing
scaling-up manufacturing, and ensuring long-term storage
stability.

Actually, more than 180 vaccine candidates belonging to
different platforms are under development against SARS-CoV
-2. Globally, SARS-CoV-2 vaccines currently authorized for
emergence use are seven; other ones that have late-stage
clinical data available will be available in few months [4].

A faster vaccine development approach used to tackle
SARS-CoV-2, based on innovative strategies and resources,
could pilot enormous benefits to overcome this emergency
and open to positive changes for the future of vaccinology.

Several emerging technologies along with the existing
ones have been used to accelerate vaccines development
process and to control the COVID-19 pandemic.

2. Emerging technologies in fighting COVID-19

Emerging methodologies, such as artificial intelligence (AI),
precision medicine (including 'omic' sciences), novel mathe-
matical modeling, big data and internet of things (IoT), are
playing a fundamental role in accelerating vaccines develop-
ment and monitoring the spreading of COVID-19 disease
across the world.

In the last years, Machine Learning (ML) has contributed in
a determinant way to the improvement in many fields of both
science and engineering. ML finds its main application in
a variety of areas, especially in drug and vaccine discovery,
in terms of compound property prediction, activity prediction,
reaction prediction, and ligand–protein interaction [5].

Precision medicine, the use of comprehensive genomic,
transcriptomic, and proteomic or every 'omic' science to
guide medical decisions, also represents a helpful starting
point toward a truly personalized medicine in vaccinology.
This approach may be useful in understanding the genetic
status and variations to vaccine immune responses in different
individuals and contributing to the development of novel
vaccine candidates that could be targeted and predicted rela-
tively to the genetic history of an individual and/or popula-
tion [6].

Mathematical models are becoming increasingly important
as a key tool for the identification of candidate vaccines [7]. In
addition, the simulation trials that precede the implementa-
tion of a vaccine help to quantify the actual efficiency of
a candidate.

Big data tools represent an innovative technology which
can digitally store a large volume of data particularly useful in
this pandemic situation, collecting specific information for
personalized vaccine design and administration [8].

The Internet of Things (IoT) is a system of interconnected
computing devices that can transfer data over a network with
no human intervention. By using sensors incorporated in
mobile phones, drones, and robots, IoT can collect data that
can be sent to a central-cloud server for analysis and plays an

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essential role in preserving the COVID-19 vaccine during production, transport, and monitoring after vaccine administration [9].

In addition to the emerging technologies seen so far, one way for a fast-track vaccine is repurposing existing manufacturing platform for a new scope [10]. Other already existing vaccine platforms and trials based on past vaccine delivery efforts for non-SARS CoV-2 infections have been exploited to speed up the rush to a SARS-CoV-2 vaccine [11].

High content screening along with high throughput and comprehensive approach are also particularly useful to develop multiepitope vaccine against COVID-19 [12].

In Silico Trials (IST) is a new class of computational methods for the development and assessment of new medical products. A typical IST model involves four elements: a physiology model, a disease model, and a treatment model, which predicts how close to normality such behavior can protect/cure individuals from the disease, when they are treated with the preventive or therapeutic vaccine under investigation, as compared to the placebo (or the comparator treatment) [13].

In this context, the Universal Immune System Simulator (UISS) is an in silico trial platform to predict the outcome of specific vaccination strategy against SARS-CoV-2 and speed up the discovery pipeline of candidate vaccines [14]. UISS is based on Agent-Based methodology, belonging to the class of mechanistic models [15]. One of the key features of UISS is its capability to mimic the adaptive immune response and many of the immune systems mechanisms, which take part of the immune system machinery.

All of these emergent technologies described so far are summarized in Figure 1.

To make a long story short, an in silico approach example scenario in the process of vaccine development could include the following steps: an initial epitope prediction phase using sequence-based information, followed by modeling and simulation tools specific for immune system dynamics at cellular scale. Then, phase I trial is ready to be conducted along with dose-ranging studies supported by in silico dosage optimization predictions (previously confirmed by at least one in vivo targeted experiment).

3. Conclusions

The COVID-19 ongoing pandemic keeps needing great efforts that aimed to find potential solutions to prevent this infection properly, and all scientific community is answering this call proposing approaches based on both new and already existing technologies.

Several emerging technologies have been used to accelerate vaccines development process and to control the spreading of the disease. They aim to facilitate and speed up the vaccine development process, allowing researchers to create a general framework of the disease more accurate and comprehensive as possible upon which it is possible to simulate the vaccine effects and predict their risks.

Existing approaches, not specifically designed for COVID-19, have also been adapted and proposed in the fight against the pandemic. Already existing vaccine platforms that have been developed specifically against other infectious diseases
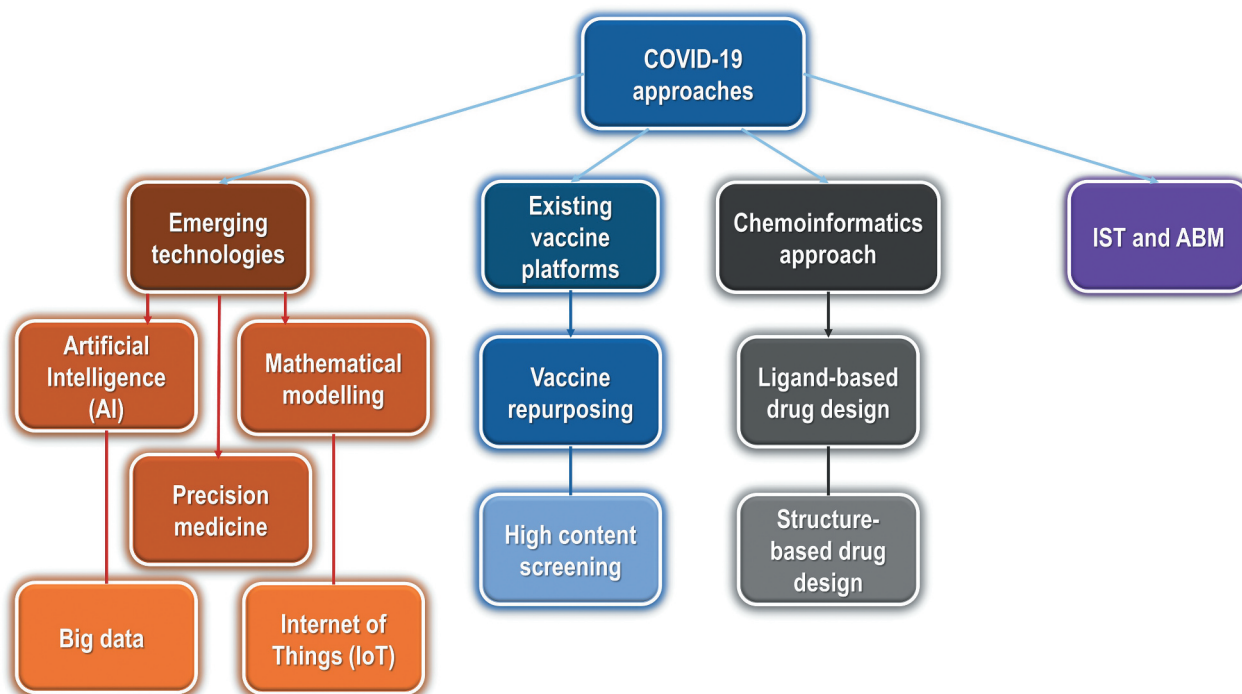

Figure 1. Schematic representation of some technologies and approaches that own the potentiality to accelerate SARS-CoV-2 vaccine development.

can be used in the process of COVID-19 vaccine development leading to vaccine manufacturing platform repositioning and boosting up the entire discovery process.

Another significant methodology involves the use of chemoinformatics approaches that predict molecular structures whose features may facilitate the interaction with the target molecule.

IST technologies aim to simulate the behavior of human body both in healthy conditions and subjected to a pathology over time, allowing to predict the effects of a specific vaccine, by using different modeling models, like biophysics models, machine learning models, statistical models, or mechanistic ones such as agent-based models.

These cutting-edge technologies will benefit the entire process of vaccine discovery and development, informing how to prioritize and focus on research and scientific efforts.

4. Expert opinion

In silico technologies represent today one of the most promising weapons against COVID-19 pandemic, since they can lead researchers to develop the best vaccine development strategies in the less time as possible.

Most of them certainly own a balanced equilibrium of advantages and disadvantages. To make some examples, artificial intelligence methodologies require a very high development cost, while omics technologies could present practical issues in the implementation of personalized medicine due to the availability and accuracy of the data used in their training phase.

Other risks emerge due to the weakness in the regulation of in silico technologies even though the increased use of modeling and simulation is going to motivate regulators in considering these digital tools capable of providing new scientific evidence to support vaccine product development.

In this perspective, in silico trials methodologies could represent one of the main interesting strategies to be employed for a more selected and faster vaccine development and evaluation. Indeed, in silico models enable rapid and safe design and testing of vaccines against infectious diseases, speeding up the development pipeline by predicting any therapeutic failure and minimizing the undesired effects. They can also readily target sensitive and under-represented populations and operate under conditions where ethics render trials on humans difficult, such as in this critical pandemic situation.

A combination of emerging technologies and the application of in silico trials is a practical solution to advantage COVID-19 pandemic and public health in general. However, this is a strategy which is yet to be effectively adopted: we expect in the few next years these powerful resources could integrate the ordinary vaccine discovery and development pipeline. Their growth in terms of usage is going to be exponential; its rate will be defined by how quickly we can lower a number of barriers, the first being the regulatory one. Indeed, the regulatory landscape for In Silico Trials to date is not quite outlined: for medical devices in the USA market, there is a clearly defined regulatory pathway with the Food and Drug Administration (FDA), here we can expect a rapid

adoption. In Europe, the lack of central authority for medical devices is making difficult to replicate this approach, but we believe it is only a matter of time. For medicinal products everything is moving more slowly; while the basis for the technical validation is most likely to be the ASME VV-40, initially intended for medical devices, we expect European Medicine Agency (EMA) and FDA to request also a clinical validation similar to that requested for the qualification of biomarkers.

Such a revolution in adopting the in silico technology in the conventional vaccine discovery pipeline could allow the inclusion of these new approaches to support clinical trials, in view of increasing the probability of success, reducing costs and timing, and accelerating time to patients.

Declaration of interest

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those discloses.

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