

# Use of artificial intelligence in vaccine development against pathogens: Challenges and future directions

## Introduction

Owing to the high prevalence of viral diseases, and emerging drug resistance in microorganisms, particularly in parasites and bacteria have sparked the development of a novel vaccine candidate using artificial intelligence (AI – a term given by McCarthy in 1956)<sup>[1]</sup> and this provides an alternative to the traditional approaches because it takes years to generate an effective vaccine since conventional approaches are considerably costly and time-consuming. In an effort to target an important endemic infection, international health organizations are also speeding up their vaccine research program.<sup>[2]</sup> Substantial information, i.e., proteomic and genomic data have been developed in the research and medical fields by recent advances in high throughput experimental processes and such data allow AI to provide incredibly accurate forecasts and predictions. Adding to this, by 2025, it is predicted that the pharma industry will reach up to \$45.2 billion.<sup>[3]</sup> Nevertheless, population genetic diversity, new recombination with high mutation rates in viral replication, antigenic variations, species specificity of antigens (Ags), also development, affordability, acceptability, accessibility, and the 5C model of vaccine hesitancy cannot be disregarded. This cutting-edge, deep learning, and genetic algorithms technology, i.e., AI when paired with tried-and-true laboratory methods might hasten the creation of vaccinations against infectious diseases. AI methods such as deep neural networks, artificial neural networks, and gradient-boosting decision trees are leveraged to predict and detect the target epitopes-portions that activate the immune system thus, assisting in the preparation of a vaccine library key. AI is being effectively employed in the analysis of immunological data, immune response prediction for vaccine efficacy/disease progression, discovery of biomarkers, and large-scale immunological dataset analysis. This would lessen the time duration for target identification, streamline the development of future vaccine candidates, and expedite the creation of potential future vaccines.

More elaborately AI is the newest and most complex scientifically developed technique which is the broad discipline of computer science. Computational understanding of machines is made possible by

integrating biological and cognitive data sets to construct inventive machine learning (ML). Informatively and not to be overlooked there is the conceptual distinction between AI and ML, despite their close relationship as both are supervised learning. AI is meant to build devices or systems that are capable of carrying out activities that call for human intellect whereas ML is a subset of AI and is employed in the larger subject of AI to produce pronounced output.

In general, the vaccine candidate encompasses blueprints of the pathogens with other components to ensure efficacy and safety<sup>[4]</sup> and AI helps to identify the lead Ag that holds the potential to promptly trigger the immunity. Coalition for Epidemic Preparedness Innovations outlined to accelerate vaccine development employing AI and establishment of a vaccine library.<sup>[5]</sup> Throughout the years, AI has been firmly integrated with reverse vaccinology (RV) which is a genome-based vaccine design technology<sup>[6]</sup> and uses bioinformatics to examine the pathogen genome and identify a good candidate for vaccination.<sup>[7]</sup> For instance, VaxiJen is one of the earliest AI-driven prediction techniques for Ag identification, based on the characteristic feature of amino acid residues to exhibit antigenicity.<sup>[8]</sup> Using protein sequences' biological and physicochemical characteristics as input variables, Vaxign-ML trained five distinct machine learning models [Table 1]. The database Protegen which has been gathering and cataloguing protective Ags that have been empirically verified for the past 10 years, provided the input protein sequences.<sup>[9]</sup> Following are certain illustrations in different sections that how current AI technology improves the vaccine development pathway.

## Artificial Intelligence for Anti-viral Vaccines

As ascertained, the vaccine regulates the immune system by exposing the host to Ags without causing illness in the host. During the pandemic, there were certain challenges in selecting the Ag/s though the size of the SARS-CoV-2 virus was small as it has five proteins i.e., envelope glycoproteins (E), Membrane proteins; determine the shape of the virus (M), nucleocapsid proteins (N), spikeproteins (S1 and S2; binds to host membranes at the

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time of penetration), and hemagglutinin esterase; aids in adhesion. Therefore, the extensive literature survey, scrutinization of the epitopes, and data set to check for errors and other irregularities that occur naturally while gathering plenty of observations had been performed by AI. For instance, image analysis and graph-based knowledge were used to reveal new information about the disease and identify biomarkers 30% quicker than pathologists. AstraZeneca also employed ML approaches to expedite the evaluation of tissue samples in pathology during vaccine development. Furthermore, AI demonstrated how the monthly production of mRNA was increased from about 30 to over 1000 using robotic automation and AI algorithms. The experiences acquired from creating an Ebola vaccine were utilized along with the AI.<sup>[10]</sup> Fortunately, ERVEBO-an Ebola vaccine was prequalified by the WHO, which would impede the disease outbreaks. AI-driven RV techniques can find potential vaccine candidates for a number of diseases and viruses, such as dengue, HIV, respiratory syncytial, herpes simplex, and Zika. The application of modern AI methods along with developments in viral vectors and nucleic acid may completely transform efforts to generate vaccines.

### Artificial Intelligence for Anti-bacterial Vaccines

Explicitly and implicitly, AI has been used in the development of antibacterial vaccines also owing to the ready availability of microbial entire genome sequences for computational screening and analysis owing to rapid and affordable novel sequencing technology. For instance, the Bexsero/4CMenB; meningitis vaccine was eventually developed as a consequence of the first successful utilization of RV.<sup>[11]</sup> To illustrate further, utilizing AI techniques 22 membrane proteins of *Helicobacter pylori* were identified through *in silico* as putative Ags.<sup>[12]</sup> AI is also utilized in reports to identify and characterize the T-cell epitopes in *Mycobacterium* species computationally. With the aid of AI-based techniques, a FilF, an outer membrane protein of *Acinetobacter baumannii*, was investigated and validated through experimentation as a possible vaccine candidate. Using AI-powered RV systems, vaccine development against *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae* is underway.

### Artificial Intelligence in Parasitic Diseases

AI has enormous promise as a parasitology research tool but despite this, the pace is slow. The World Health Organization encourages the programmatic malaria vaccines, i.e., first RTS, S/AS01, and R21/Matrix-M, to prevent *Plasmodium falciparum* malaria in

children residing in malaria-endemic regions. Likewise, Ghana's Food and Drugs Authority has awarded full national authorization for the R21/Matrix-MTM malaria vaccine, which uses adjuvant technology from Novavax, since phase-II studies have shown the vaccine to be very efficacious and safe. It is noteworthy that these vaccine candidates are developed by recombinant technology rather than AI. AI is, nonetheless, gaining momentum in the creation of antiparasitic drugs, and its effectiveness must be utilized in the creation of parasite vaccines as well. In another domain, gastrointestinal nematodes (GINs) infect every human being of any age, and resistance against antinematode drugs is increasing at a rapid rate and the only long-term solution is a vaccine, i.e., anti-GINs vaccine. Given all abovementioned challenges that researchers are facing, AI can assist in many ways, however, there is relatively less data available on proteomics and genomics of nematodes. Hence, research on such disciplines should be sped up to aid AI for vaccine development.

### Challenges

With the intention to ensure precision and relevance while computing the Ag/clinical data, AI-using research organizations should have a comprehensive data-gathering procedure that takes into account the further mentioned aspects, i.e., lack of valid antigenic structure of all pathogens, computation should be based on learnable parameters, ethical infractions, incomplete understanding of immunopathology, genetic variability in population, societal skepticism, and intellectual property right violations. There is a dire need of developing a multifaceted strategy to secure sensitive data by developing data governance frameworks. It is essential to update the software along with ongoing research. In addition, the gaps should be filled by investigation and cooperation between AI scientists and immunologists.

### Future Directions

As a matter of fact, AI and ML are supervised learning and have proven a boon in the COVID-19 pandemic. We currently comprehend that using data to facilitate automation and improved predictions can be done, however, what AI method offers is the ability to handle ever-larger and more complex data sets and their interconnections with desirable inferences. AI is capable of reducing costs and improving effectiveness, as well as enhancing resource deployment, predictive maintenance, and quality assurance. To identify the significant patterns for making useful predictions by AI is totally relies on authentic data availability and correlation. This all further depends upon ML which demands the accurate and fast computed stand-alone/

**Table 1: An overview of cutting-edge AI-based methodologies/servers for screening possible vaccine targets**

Prediction Model	Types	Methodology Used	Mode of Function
<i>Antigenic</i>	Webserver	Random forest	Use the FASTA sequence; Less data and documentation.
<i>PunRV</i>	Standalone and computational automated pipeline	Logistic Regression, Random Forest and Support Vector Machine	Use the reverse vaccinology and microbial pangenome approach with antigenic data; Wide-spectrum; species-specific target selection.
<i>ReVacc</i>	Standalone	Logistic Regression, Neural Networks and Support Vector Machine	Use the pangenome approach; Redundancy-based method is used for the scoring approach.
<i>Vaxign ML</i>	Webserver	Extreme Gradient Boost, k-Nearest Neighbour, Logistic Regression, Random Forest, Support Vector Machine	A more user-friendly; Epitope prediction and analysis framework.

web server powered by high-tech software. Each AI deployment may need a practical grasp of the intended future use in real-world settings, and it should be carried out by people who have the capacity to understand the data and the underlying problem that each deployment is related to find a solution. While certain specialized software or tools with a narrow range of uses can be easily integrated into an organization, the majority of AI-based solutions can be specially designed to solve particular issues and may be trained on their own data.

To conclude, the use of AI in vaccine production is a revolutionary advancement that will improve precision, accelerate procedures, and expand our comprehension of infectious illnesses. We stress that while AI will greatly expedite the creation of vaccinations, these technologies are not a cure-all. When it comes to assuring vaccination safety and effectiveness, thorough “wet” laboratory, i.e., *in vitro* testing, as well as animal and human trials, are still necessary, and they should never be replaced by AI integration and must be followed by crucial receiving of regulatory clearance.

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Submitted: 06-Apr-2024  
Revised: 20-Apr-2024  
Accepted: 22-Apr-2024  
Published: 30-Apr-2024

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Quick Response Code:	Website: <a href="http://www.ijp-online.com">www.ijp-online.com</a>
	DOI: 10.4103/ijp.ijp_259_24

**How to cite this article:** Gorki V, Medhi B. Use of artificial intelligence in vaccine development against pathogens: Challenges and future directions. Indian J Pharmacol 2024;56:77-9.