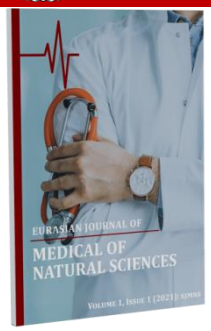
EURASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
Innovative Academy Research Support Center
IF = 7.921 www.in-academy.uz



THE IMPORTANCE AND RELEVANCE OF IMMUNOINFORMATICS IN MODERN MEDICAL PRACTICE OF DISEASE PREVENTION AND TREATMENT

Khumoyun Khozhiev Alisher o'g'li
Bioinformatician at Pharmaceutical Technical University,
E-mail; h.khojiev@pharmatechuni.uz, Phone number; +998906370672
https://doi.org/10.5281/zenodo.15663305

ARTICLE INFO

Received: 08th June 2025
Accepted: 13rd June 2025
Online: 14th June 2025

KEYWORDS

Immunogen design, illnesses, autoimmune disorders, tailored treatment, genomes, high-throughput techneologis.

ABSTRACT

For a number of illnesses, such as cancer, autoimmune disorders and infectious diseases, the immune system is crucial to the creation of tailored treatment. Computational immunology, often known as immunoinformatics, is a new field that offers basic approaches for studying immunomics, or immune-related proteomics and genomes. A deeper comprehension of immune-related disorders at different systems levels could result from the combination of immunoinformatics and systems biology methodologies. These techniques can support translational research that improves clinical practice by using scientific findings about the immune system. One new medical treatment for breast cancer is vaccination. Cancer vaccines can be developed to teach the immune system to identify tumor cells by focusing on the tumor antigen. As a result, in addition to technological advancements, the process of creating vaccinations is now beginning to employ more logical techniques, such as the use of immunoinformatics techniques to create peptide vaccines based on epitopes. Immunoinformatics techniques can help with the safety and antigenicity of vaccine design. Tumor antigen identification, protein structure analysis, T cell epitope prediction, epitope characterisation, and assessment of protein–epitope interactions are common procedures utilized in the development of epitope-based peptide vaccines. Measurements and catalogs of genes, proteins, interactions, and behavior are made possible by high-throughput techneologis. A better knowledge of the network of interactions between people, medications, and vaccinations may result from this view, opening up new avenues for studying illnesses and developing effective treatments. Lastly, despite prediction models' great accuracy, testing in vitro and in vivo can have the opposite effect. Therefore, more research is required to guarantee the efficacy of the vaccine that will be created. Adjuvants can improve the immunogenicity of epitope-based peptide vaccines, notwithstanding their modest immunogenicity.

Introduction. The development of tailored therapy for a number of illnesses, including as infectious diseases, autoimmune disorders, and cancer, depends heavily on the immune system. A new field called immunoinformatics, or computational immunology, offers basic approaches for studying immunomics or immune-related genomes and proteomics. Understanding immune-related disorders at different systems levels may improve with the combination of immunoinformatics and systems biology techniques. Translational research that improve clinical practice by incorporating scientific findings on the immune system can benefit from such approaches. Immune epitopes are among the immune system's most extensively researched components. Understanding disease, analyzing host-pathogen interactions, identifying antibiotic targets, and designing vaccines all depend on epitopes [1,2,3]. The immune system's genetic variety may be used to identify patient subgroups for customized medication or vaccine development. Disease pathogenesis and immunogen design are significantly influenced by cellular pathways and host immune-pathogen interactions. Understanding how environmental changes impact complicated immunological illnesses like allergies may be made easier with the aid of epigenetic research. In the field of global public health, vaccines play a significant role in the cost-effective interventions for major infectious illnesses. Having a successful candidate that can elicit an efficient humoral and cell-mediated immune response against a chosen pathogen is ultimately desirable in the crucial and complex work of vaccine design. Interestingly, over the past 200 years, the majority of vaccines have been developed using conventional methods, such as employing heat- or chemically-killed pathogens or attenuated pathogens; because of their high failure rate at advanced stages, these methods nearly took 15 to 20 years to develop into a successful vaccine against any given pathogen. Over the last few decades, a new field of vaccine design known as "Immunoinformatics" has advanced significantly and made significant contributions to the field [4-9]. Computational immunology, also known as immunoinformatics, combines computing power with the vast amounts of genomic and proteomic data gathered from pathogens to comprehend their immune response. This data is then used to build vaccines. The scientific community's attention has recently been drawn to the unusual need for rapid vaccine design as a result of previous epidemic outbreaks, including the COVID-19 pandemic, SARS, influenza virus and Zika virus. Human interaction with various infections has increased due to the growth of the human population and the exploitation of the natural habitats of various exotic species. Emerging infectious illnesses pose a serious hazard to humanity as a result. In this situation, vaccination has been shown to be the most successful method of halting the spread of illness and enables in-depth research on the host–pathogen interactome. As previously said, immunoinformatics-based candidates typically take two to three years to generate and enable us to screen numerous unique candidates at once, whereas the old approach takes fifteen to twenty years to produce a good candidate [10-14]. The two arms of the immune response—the humoral (B-cell) immune response, which neutralizes pathogens quickly, and the T-cell-mediated immune response, which produces immunological memory in the host by integrating dominant epitopes in the vaccine—can both provide protection against infection. Antigen identification and the selection of epitopes capable of eliciting an immune response are key components of the immunoinformatics approach to vaccine design. High-throughput genomics analysis, antigen search, molecular docking, and model simulations to predict immune

responses can all be completed more rapidly with the help of several efficient algorithms. Naturally, this will lessen the difficulty of laboratory testing. The immunoinformatics technique that can be used as a pilot study for developing breast cancer vaccines will be covered in more detail in this publication [15-19].

The main purpose of the presented field is to conduct a brief analysis based on reputable scientific research on the importance and relevance of immunoinformatics in modern medical practice of disease prevention and treatment.

Human homology, immunogenicity, antigenicity, and allergenicity are epitopes. The VexiJen v2.0 server was used to test the previously selected epitopes' capacity to function as an antigen. Epitopes with an antigenicity score of 0.5 or higher were chosen for the subsequent assessment of the "virus" model. The AllerTOP v.2.0 server was used to assess the allergenicity of epitopes. Using the default parameters, the IEDB's Class I Immunogenicity tool was also used to evaluate the immunogenicity of CTL epitopes. A BLASTp was conducted to evaluate the epitopes' resemblance to human proteins and reduce the likelihood of autoimmune. The particular epitope's amino acid sequence was submitted in opposition to the target organism, which was determined to be "Homo sapiens (NCBI Taxid:9606)." Epitopes exhibiting less than 70% similarity with human proteins (i.e., query coverage more than 70%) were deemed suitable for further examination [3-11].

Vaccine Design Strategy for Breast Cancer. Instead of employing cell- or virus-based immunizations, cancer vaccines now target subunit components. Due to HLA polymorphism's limits and the small size of antigen epitopes, peptide-based vaccines have a limited immunogenicity. Immune tolerance results from the inability to elicit a robust immunological response. Peptide-based immunizations are combined with adjuvants to enhance the immune response as a whole. Not every protein antigen location elicits the same level of B and T cell immunogenicity. To achieve a more focused immune response, peptide-based vaccinations target important neutralizing epitopes rather than inactivated tumor cells [4-9]. Both CD8+ and CD4+ T cell epitopes are frequently needed for peptide-based cancer vaccinations. While CD4+ T cells stimulate helper T cells to maintain CTL activity, CD8+ T cell epitopes use the antigen cross-presentation route to activate CTLs' tumor immunity. The effectiveness of the peptide vaccine is significantly influenced by the length of the peptide chain. Typically, CD8+ T cell epitopes are short peptides that have a brief half-life in vivo. There is no need for processing in specialized APCs because this peptide is administered directly to the HLA-I molecules of APCs or other nucleus cells. The absence of costimulatory molecules, which are necessary for CD8+ T cells to function properly, limits CTL activation [10-15]. The primary limitation of neoantigen-based cancer vaccines is their highly individualized nature, which requires a combination of high-throughput genomes, proteomics, and immunomics screening methods that are currently not widely available. Moreover, cancers' fast rate of mutation may make such a highly tailored approach less successful since it continuously produces new target mutated neoantigens, which in turn causes cancer immune evasion [17,18,19].

Immune Reaction to a Peptide Vaccine Based on Epitopes. The immune system is not able to identify every component of the antigen. Epitopes, also known as antigenic determinants, are the portion of antigens that can interact with free antibody molecules and B cell and T cell receptors. An epitope is between five and fifteen amino acids in size. Typically,

a single protein contains several epitopes with varying specificities. This is due to the fact that proteins typically have lengthy peptide chains and fold as a result of interactions between their residues. Proteins are more immunogenic than polysaccharides because of this protein complex. Epitope-based peptide vaccines must bind to the T cell receptor (TCR) and be presented by antigen-presenting cells (APC) through human leukocyte antigen (HLA) classes I and II in order to elicit a response from T cells. A surface molecule called HLA serves to display antigens that have been broken down by cell proteases into short peptides [2-6]. All nucleated cells express HLA class I, which interacts with CD8+ T cells' CD8 protein. HLA class II, on the other hand, only interacts with CD4 from CD4+ T cells and is exclusively expressed by APC. Since the genes encoding HLA are highly polymorphic, a population may contain a wide variety of alleles. Individuals may experience varying adaptive immune responses as a result of this. But because cancer is a complicated disease, immunosuppressive cells in the tumor microenvironment, like myeloid-derived suppressor cells (MDSCs) and regulatory T cells (Treg), assist cancer cells evade the immune system and modulate the immune response. The ultimate objective of a cancer vaccine is to eradicate cancer cells by vigorously activating the CD8+ T cell pathway, which is mediated by CD4+ T cells and overcomes immune suppression and self-tolerance [7-11].

The immunoinformatics method. The field that connects computer science and experimental immunology is called immunoinformatics, or computational immunology. It indicates the application of computational methods and tools to the understanding of immunological data. It not only helps manage enormous volumes of data, but it also contributes significantly to the creation of new hypotheses regarding immune responses. From identifying tumor antigens to assessing protein-epitope interactions, the immunoinformatics approach to cancer vaccine design will be covered in this section [8-12]. Global docking techniques, on the other hand, search for the peptide binding position and location at the same time. The simplest approach to global protein–peptide docking involves performing comprehensive rigid-body docking while taking into account the stiffness of the protein and peptide input conformations. More sophisticated algorithms employ a user-supplied sequence to predict the shape of peptides. Three steps are usually included in their pipelines: (i) generating input peptide conformations; (ii) rigid-body docking; and (iii) scoring and/or model refinement. The peptide conformation can be predicted using a variety of techniques, such as threading the sequence onto a predetermined set of template conformations, modeling peptide folding in solution, or employing structural fragments from monomeric protein structures [13-20].

The Following Action. Despite having a solid statistical foundation and using experimental data to train predictive models, many of the immunoinformatics techniques discussed above still have biases that should not be disregarded. Predictions may be inaccurate as a result of this bias. Thus, to measure the dependability of the predicted outcomes, predictive models always have values for accuracy, sensitivity, specificity, and so forth. Furthermore, immunoinformatics techniques do not adequately model many physiological processes. The prediction model may diverge from its actual value due to a variety of causes. Furthermore, the response of T cells following activation cannot be predicted by any predictive model. For instance, CD4+ T cells develop into Th1 or Th2 cells once they are activated. IFN-γ is the usual Th1 cytokine, while IL-4, IL-5, and IL-10 are the typical Th2 cytokines. However, costimulatory

signals, TLR, and PAMPS activation—rather than epitope—determine the shift in T cell response. Numerous studies have established that altering an amino acid in the epitope alters the sort of immunological response [1,5,7]. Consequently, additional in vitro and in vivo studies are required to validate the anticipated outcomes. As previously said, the design of the vaccine must satisfy three requirements at the very least: (1) have enough active components to immunize the recipient; (2) have a safety level that satisfies regulatory standards; and (3) have a low level of contamination that satisfies regulatory standards. The first and second points have been predicted by in silico investigations. Therefore, through in vitro and in vivo tests, future research should be able to confirm these three things in addition to the projected results produced [5-10]. Trastuzumab, an anti-HER-2 monoclonal antibody used to treat breast cancer, has been found to increase the susceptibility of HER-2-positive tumor cells to T cell-mediated and antibody-dependent cytotoxicity. Gall et al. found that trastuzumab enhanced HER-2-derived peptides (E75) cross-presentation and DC absorption, which led to anticancer immune priming and a rise in antigen-specific CTL production. Additionally, even after extended exposure, a phase IIb clinical research demonstrated that trastuzumab plus GM-CSF and E75 peptide was safe and did not cause any more harm than trastuzumab alone. Patients with triple-negative breast cancer (TNBC) had a significant clinical advantage, whereas those with HER-2 low-expressing breast cancer did not significantly differ in disease-free survival. These results support more research in phase III randomized trials and suggest that nelipepimut-S plus trastuzumab may be used as an adjuvant treatment for early TNBC [13-20].

Discussion. Inactivating a few pathogenic strains is not enough to create the perfect vaccines to fight diseases that might arise in the future. The goal of this research is to develop a multi-epitope vaccine based on peptides that is effective against several strains of the coronavirus 2 that cause severe acute respiratory syndrome. A library of peptides from the membrane, envelope, nucleocapsid, and spike structural proteins of different strains was created in order to build the vaccine. The fully protected epitopes and the fynomer scaffold were then used to optimize the final vaccine structure [1,4,7]. The vaccine candidate's secondary and three-dimensional structures, physicochemical characteristics, population coverage, toxicity, antigenicity, and allergenicity were assessed using bioinformatics methods. The vaccine's high quality was validated by the bioinformatic analysis. The physiochemical, hydrochemical, and antigenic properties of the protein are all included in protein structure analysis. Numerous T cell epitope prediction algorithms are accessible, including a range of prediction parameters and methods for filtering the prediction outcomes. Using predictors for allergenicity and toxicity, epitope characterisation, including toxicity and allergenicity, can also be carried out in silico. Molecular modeling can also be used to evaluate protein–epitope interactions *in silico*. Using an immunoinformatics approach, we will also talk about the latest and upcoming advancements in breast cancer vaccinations [2,3,5]. Lastly, despite prediction models' great accuracy, testing in vitro and in vivo can have the opposite effect. Therefore, more research is required to guarantee the efficacy of the vaccine that will be created. Last but not least, despite prediction models' great accuracy, testing both in vitro and in vivo can reveal the reverse. For the vaccine to be produced to be successful, more research is therefore required. The limited immunogenicity of epitope-based peptide vaccines is a drawback, however adjuvants may improve the situation. Making sure TAAs trigger the best possible

immune response is one of the most challenging problems. The immune system is carefully regulated to prevent damage to the body. However, the primary drawback of cancer vaccines based on modified neoantigens is that they are highly customized, and their discovery requires a combination of immunomics, proteomics, and high-throughput genomics screening tools that are currently not widely available. The ability of an epitope-based vaccine to appropriately elicit an immune response is one of its most crucial features. When the HLA-presented antigen concurrently binds with the TCR, T cells are activated. Tumor antigen identification, protein structure analysis, T cell epitope prediction, epitope characterisation, and protein–peptide interaction evaluation can all be aided by a variety of immunoinformatics tools and methods [6-11]. Numerous immunoinformatics tools that can support every stage of the development of cancer vaccines were covered. The main barrier to the development of peptide vaccines based on epitopes is their low immunogenicity. Adjuvants, however, may be able to help get around this problem. Combinatorial treatments that combine anti-cancer medications with cancer vaccinations also show promise. We can anticipate that future cancer vaccines will be increasingly individualized and focused as technology develops [12-16].

Conclusions. Genes, proteins, connections, and behavior may be measured and cataloged thanks to high-throughput technologies. This kind of perception could help us comprehend the network of interactions between people, medications, and vaccinations, which could lead to new understandings of illnesses and treatment options. Optimized vaccines and medications for individualized prevention and treatment may eventually result from the integration of immunomics data.

There is a lot of promise for expediting vaccine development with the immunoinformatics approach to epitope-based peptide vaccine design. Compared to traditional approaches, the immunoinformatics approach can offer more thorough data and information on vaccine candidates. When creating more specialized vaccinations, this data are quite beneficial. As a one-for-all approach, TAAs are helpful in creating a single vaccine that can be manufactured in large numbers and distributed to numerous individuals.

Additional research indicates that there is a robust and stable contact between the vaccination and receptors, and that this structure is comparable to that of natural protein. Structural compactness and stability in binding were also noted based on molecular dynamics modeling. Furthermore, the immunological simulation demonstrated that the vaccination can elicit immune responses that are comparable to those found in actual situations. Lastly, in silico cloning and codon optimization verified effective expression in more pathologies. To sum up, the fynomer-based vaccination is a novel approach to developing and modernizing vaccines that guard against coronavirus illness.

References:

1. Rawat SS, Keshri AK, Kaur R, Prasad A. Immunoinformatics Approaches for Vaccine Design: A Fast and Secure Strategy for Successful Vaccine Development. Vaccines (Basel). 2023 Jan 19;11(2):221. doi: 10.3390/vaccines11020221.
2. Hellysaz, A. & Hagbom, M. Understanding the central nervous system symptoms of rotavirus: A qualitative review. Viruses 13, 658 (2021).

3. Du, Y. et al. Global burden and trends of rotavirus infection-associated deaths from 1990 to 2019: an observational trend study. Virol. J. 19, 166 (2022).
4. mondiale de la Santé, O. & World Health Organization. Rotavirus vaccines: WHO position paper–July 2021–Vaccins antirotavirus: note de synthèse de l'OMS–Juillet 2021. Wkly. Epidemiol. Record = Relevé Épidémiologique Hebdomadaire. 96 28, 219–301 (2021).
5. Hasan, M. et al. Contriving a chimeric polyvalent vaccine to prevent infections caused by herpes simplex virus (type-1 and type-2): an exploratory immunoinformatic approach. J. Biomol. Struct. Dyn. 38, 2898–2915 (2020).
6. Joshi, A., Joshi, B. C., Mannan, M. A. & Kaushik, V. Epitope based vaccine prediction for SARS-COV-2 by deploying immuno-informatics approach. Inf. Med. Unlocked. 19, 100338 (2020).
7. Krishnan, G., Joshi, S., Akhtar, A., Kaushik, V. & N. & Immunoinformatics designed T cell multi epitope dengue peptide vaccine derived from Non structural proteome. Microb. Pathog. 150, 104728 (2021).
8. Devi, Y. D. et al. Exploring rotavirus proteome to identify potential B- and T-cell epitope using computational immunoinformatics. Heliyon 6, e05760 (2020).
9. Sharma, A. et al. T cell epitope based vaccine design while targeting outer capsid proteins of rotavirus strains infecting neonates: an immunoinformatics approach. J. Biomol. Struct. Dyn. 42, 4937–4955 (2024).
10. Thakur N, Bailey D. Advances in diagnostics, vaccines and therapeutics for Nipah virus. *Microbes Infection*. (2019) 21:278–86. doi: 10.1016/j.micinf.2019.02.002
11. Lo MK, Feldmann F, Gary JM, Jordan R, Bannister R, Cronin J, et al. Remdesivir (GS-5734) protects African green monkeys from Nipah virus challenge. *Sci Transl Med*. (2019) 11:eaau9242. doi: 10.1126/scitranslmed.aau9242
12. Zafar S, Ajab H, Baig S, Baig A, Habib Z, Jamil F, Ibrahim M, Kanwal S, Rasheed MA. Prediction and evaluation of multi epitope based sub-unit vaccine against *Salmonella* typhimurium. Saudi J Biol Sci. 2022;29(2):1092–9.
13. Priyadarsini S, Panda S, Pashupathi M, Kumar A, Singh R. Design of multiepitope vaccine construct against non-typhoidal Salmonellosis and its characterization using immunoinformatics approach. Int J Pept Res Ther. 2021;27(4):2333–48.
14. Seo H, Duan Q, Zhang W. Vaccines against gastroenteritis, current progress and challenges. Gut Microbes. 2020;11(6):1486–517.
15. Mancini F, Micoli F, Necchi F, Pizza M, Berlanda Scorza F, Rossi O. GMMA-based vaccines: the known and the unknown. Front Immunol. 2021. https://doi.org/10.3389/fimmu.2021.715393.
16. Negahdaripour M, Nezafat N, Eslami M, Ghoshoon MB, Shoolian E, Najafipour S, Morowvat MH, Dehshahri A, Erfani N, Ghasemi Y. Structural vaccinology considerations for in silico designing of a multi-epitope vaccine. Infect Genet Evol. 2018;58:96–109.
17. Goumari, M. M., Farhani, I., Nezafat, N. & Mahmoodi, S. Multi epitope vaccines (MEVs), as a novel strategy against infectious diseases. *Curr. Proteom.* **17**(5), 354–364 (2020).
18. Bayat, M., Asemani, Y. & Najafi, S. Essential considerations during vaccine design against COVID-19 and review of pioneering vaccine candidate platforms. *Int. Immunopharmacol.* **97**, 107679 (2021).

19. Kyriakidis, N. C., López-Cortés, A., González, E. V., Grimaldos, A. B. & Prado, E. O. SARS-CoV-2 vaccines strategies: A comprehensive review of phase 3 candidates. *NPJ Vaccines* **6**(1), 28 (2021).
20. Dixit, N. K. Design of monovalent and chimeric tetravalent dengue vaccine using an immunoinformatics approach. *Int. J. Pept. Res. Ther.* **27**(4), 2607–2624 (2021).