International Journal of Advance and Applied Research
www.ijaar.co.in
ISSN – 2347-7075 Impact Factor – 7.328
Peer Reviewed Bi-Monthly
Vol. 11 No. 4 March-April 2024

Immunomics: An Approach to Predict the Immunome

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DOI- 10.5281/zenodo.11059477

Abstract:

Omics approaches have emerged as efficient tools in identification and detailed study of pathways involved in pathogen invasion, host response during infection, and disease progression. Emergence of other omics approaches have expanded the existing catalogue of omic techniques and thus allowed unravelling of possible mechanism and factors responsible for pathogen entry and its consequences in host. Immunomics is a relatively new field of research which refers to effectively interpret linkage among molecular immunology, genomics, proteomics, transcriptomics and bioinformatics fields and establish an effective correlation between immunological research and its clinical implications. Since the pathogen and the immune system evolve simultaneously, immunomics is dependent on both the host and the pathogen. Immunomics address the determination of immunogenicity to identify virulence determinants. Now-a-days, immnomics tools such as T-cell and B-cell-epitope mapping algorithms are being incorporated. Advance technologies like system immunology can form their own diverse networks, and connecting with researchers from other disciplines.

Introduction:

Characterization of immunological components associated to natural infections is tend to provide a specific serological biomarkers applied in disease diagnostics, and selection of vaccine targets. To understand immunopathogenesis (response of immune system against pathogen) of infectious diseases, knowledge of antigens and epitopes recognized by immune system is mandatory. Awareness of this is also a prime need for development of vaccine and improvement in diagnostics (Sousa & Doolan, 2016).

During the last two decades, omic approaches have emerged as efficient tools in identification and detailed study of pathways involved in pathogen invasion, host response during infection, and disease progression. Proteomics, the study of the protein complement of biological systems, has a great role in driving discovery of vaccine candidate and to understand host–pathogen interactions (Lum & Cristea, 2016). Success in proteomics is directly related to advancement in proteomic technologies which enable sensitive detection of pathogens. Additionally, emergence of other omic approaches have expanded the existing catalogue of omic techniques and thus allowed unravelling of possible mechanism and factors responsible for pathogen entry and its consequences in host.

Immunomics is a relatively new field of research which integrates several disciplines together to solve the problems of immunology. The term ‘immunomics’ was coined in 2001 by Klysik (Klysik, 2001), who suggested that ongoing advances in technology should serve to address the correlations between genes and the functional properties of their protein products. Immunomics refers to effectively interpret linkage among molecular immunology, genomics, proteomics, transcriptomics and bioinformatics fields (Doolan, 2011) and establish an effective correlation between immunological research and its clinical implications. Immunomics focuses on the study of the immunome (the set of antigens or epitopes that interface with the host immune system) (Sette et al. 2005). However, the definition of immunomics might expand due to advancement in a particular domain and thus subjected to variation by embracing the investigating concepts into the consideration.

Three other correlated terms are reverse vaccinology, systems immunology and vaccinomics which are distinct from Immunomics with few aspects. Aim of reverse vaccinology is to identify the complete repertoire of secretory/surface antigens of an organism (Rinaudo et al. 2009). Systems immunology is a sub-discipline of systems biology (Six et al, 2012), which deals with understanding molecular mechanisms of various components of the immune system and their synergistic action (Narang et al. 2012).

Vaccinomics, aimed to create personalized vaccines by integrating immunogenetics/ immunogenomics with systems biology and immune responses (Poland et al. 2011). Since the pathogen and the immune system evolve simultaneously , immunomics is dependent on both the host and the pathogen (Tournier and Quesnel-Hellmann, 2006; Stilling et al. 2014). Furthermore, each component

of the immune response is extremely complex on its own, and consequently the interactions between them lead to complex network.

Immunomics for Discovery Of Virulence Determinants And Vaccine Candidates:

The experimental and informatic techniques involved in immunomics address the determination of immunogenicity to identify virulence determinants. Immunogenicity is one of the most widely used terms immunogenicity which can be defined as the property of a moiety (protein, lipid, carbohydrate, or some combination thereof) that allows it to induce a significant response of the immune system. Potential virulence factors can be determined by comparing immunoproteomes of (i) virulent and avirulent microbes (ii) microbes grown under different conditions (iii) changes apparently upon infection (iv) by identifying proteins that are co-regulated with known virulence genes.

Investigation and evaluation of the host-pathogen response are two essential aspects to vaccine development. Elicitation of cell mediated immune response either driven by Th1 in case of intracellular pathogen or Th2 in extracellular pathogen is strongly required for protection against any pathogen. These all consequences enhance antibody production and antibody-mediated cell killing. Additionally, in vitro knowledge of the interactions between pathogens and host cells is also crucial for investigation of bacterial components that attach to host cells.

Immunoproteomics is an extension of proteomics, which permits specific elucidation of antigens based on immunoreactivity. In process of immunoproteomics, 2-D blots are probed with serum collected from host post infection. This process has bypassed the lengthy process of testing of immunoreactivity and hence vastly boosted the vaccine discovery by directly allowing the identification of those novel proteins which evoke immune system.

The natural step up to, whereby 2-D blots are probed with host serum following infection or immunisation has greatly enhanced the identification of potential vaccine candidates, by enabling the discovery of novel proteins that stimulate the humoral host immune system. The main advantage of this approach is that bacterial proteins have already been processed and modified post-translationally in host system so finally expressed protein is obtained for analysis. Several groups have explored various potential vaccine candidates using this approach which is discussed below (Dennehy & McClean, 2012).

In Streptococcus pneumoniae immunoproteomics has been used to identify immunogenic proteins. 2-D blot of cell wall fractions from *S.* pneumoniae was probed with sera from healthy children or adults ravelled seventeen immunoreactive proteins. Of these, two proteins were further found to be protective in a mouse challenge model (Novic et al. 2017)

Furthermore, immunoproteomic analysis of the *S.* pneumoniae secretome also identified several novel antigens which were shown to be immunogenic. In another report, the use of immunoproteomics was to visualize and identify immunogenic Shigella flexneri soluble and membrane proteins, which were reactive to sera from *S.* flexneri infected patients (Jennison et al. 2006)

Another example of the immunoproteomic approach is, in identification of novel vaccine candidates from Neisseria meningitidis. In that study one immunoreactive protein was evaluated as vaccine component after getting protection data from mice (Hsu et al. 2008). In another study, numerous candidate proteins were elucidated from the immunome of Brucella abortus cell envelope for discovery of vaccines against Brucellosis in cattle and humans (Connolly et al. 2006). Furthermore, immunogenic proteins from soluble fraction of *Brucella* melitensis 16 M and M5 were identified using an immunoproteomic assay for developing subunit vaccine against Brucella infection.

In an immunoproteomics study of piscine Streptococcus agalactiae cellular proteins, four novel immunoreactive proteins were implicated as vaccine candidates and virulence factors (Liu et al. 2013). First immunoproteomic approach in Vibrio to identify immunogenic proteins of V. harveyi, provided a valuable tool for developing the protective antigens in future. There is an urgent need to develop polyvalent vaccine candidates that can protect from a broad spectrum of pathogen. For this, heterogeneous antiserum-based immunoproteomics approaches have been employed to explore outer membrane proteins with similar antigenicity that could be used as a cross-protective vaccine against several species of Vibrio (Li et al. 2010). More recently, a diverse set of antigenic proteins, were identified by analysing conidial and hyphal immunomes of the filamentous pathogenic fungus Lomentospora prolificans against healthy human serum which may be further used to discover potential therapeutic targets (Pellon et al. 2017).

Immunoproteomics approach has also been applied to combat viral diseases. To develop a universal flu vaccine, it has been implemented for the direct identification of HLA class I presented epitopes in the last decade, and recognized as a method for the identification of T cell epitopes. In one study, combination of T cell epitopes specifically occur on influenza A-infected cells and a cross-reactive epitope displayed by the ectodomain of influenza M2, was used to evaluate T cell immunity in influenza infection and uncover universal antigen against it (Testa et al. 2012).

Single-cell and multi-omics technologies is a way towards a better understanding of the complex cellular and molecular interactions of immune system for immunologists with an entry point. This provides the characterization of the dynamics of immune responses, and a good approach to understand the interaction of the immune system within organ systems (Bonaguro et al., 2022).

Conclusion And Future Prospects:

Characterization of antibody specifically associated to infections provides biomarkers which has further implications in molecular diagnosis and screening of targets for vaccine development. Immunomics deals with the inquiry pertaining to the interface between proteins derived from pathogens and the host immune system. The 'interface' involves investigation of the antigens and mapping the epitopes that stimulate an immune response. Earlier, to complete this task, antigen proteins were isolated from whole cell and epitopes were identified by checking stimulation of T-cell and B-cell. Now-a-days, immnomics tools such as T-cell and B-cell-epitope mapping algorithms are being incorporated.

Collectively, exposure of bacterial cell proteins to the host immune system provides a pool of the proteins having vaccine candidate potential. In future, immunology researchers must take advantage of advance technologies like system immunology to form their own diverse networks, and connecting with researchers from other disciplines.

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