

Genomics in Infectious Disease Drug and Vaccine Development

Posted on September 22, 2018

Abstract

The significant advancements in the genomic regime have shifted the focus of therapeutic developments and vaccination to sequence-based approaches from a microbiological orientation. It has been observed that the genome sequences offer the research to identify the mechanism of pathogenesis for the purpose of designing new vaccinations and drugs and their effect on the patient's health with the prescribed issues, immunomics, proteomics, structural genomics, metabolomics, transcriptomics, and genomics. With changing environmental lapses and conditions, numerous new diseases have taken over the major death toll in health statistics, and demands for developing new vaccines through advanced drug designs help patients resist the growing infections among human patients. Thus, for controlling emerging infectious diseases in the future, new genome-based approaches and genomic data will help in developing new vaccines, which are expected to be result-oriented within less time.

Keywords: Genome, Vaccination, Genome Sequences, Pathogenesis, Drug Design

Introduction

Infectious diseases have a history of taking over human health since the beginning. However, the introduction and usage of vaccination to [prevent and control the spread](#) of the disease has controlled these infectious diseases and saved many lives. The genomic era has been a blessing for human health, however, it shall be notified as well that all the newly designed vaccinations even though the advanced drug design is first attempted on animals and how they react towards this disease.

Though there have been numerous advancements in this field, even then, classic pathogens like measles and typhoid, which have been affecting human health around the world, have been studied and captivated through the identification of the actual viruses hepatitis C virus and *Helicobacter pylori*). It has also been observed that diseases in the past have re-emerged, such as Dengue and Group A streptococcus. These infections have developed immunity against the previous medications, and the genomics field has to conduct a detailed study to know the cause of the improvement of immunity of these bacterial cells against the vaccination and at what rapid rate they are growing and need to be countered (Moxon, 2002).

The World Health Organisation has reported fact that the changing environmental conditions have

increased the chances of the introduction of a new infection every year. Moreover, these pathogens break in the form of epidemics. Thus, to limit the spread and any major damage to the human population, the introduction of these vaccinations on time is the only effective solution with the guarantee of 100% effectiveness (Mutoloki, Cooper, Marjara, Koop & Evensen, 2010). The traditional empirical approaches for the development of vaccines, while screening a few candidates, are time-consuming and have not been proven to be result-oriented for every disease. Such as, the HIV virus cannot be contained in a laboratory, and the HCV virus cannot be experimented with through suitable animal models to identify the degree of infection and its treatment. These viruses are observed to be controlled by the T cell-dependent immune responses instead of humoral immune responses. Genomics is expected to be the first respondent in case of any pathogen attack and will help in immediate functional characterization, diagnostic development, and antigen identification (Ling, Ban, Wen, Wang & Ge, 2013).

The first ever genomic sequence was developed for 'Haemophilus influenza' in 1995. The finished bacterial genomic sequence has helped and assisted the sequencing technology in taking the lead and further improving on the set grounds. For each major human pathogen disease, at least one genomic sequence is available, which can be studied, and certain improvisations can help in the earlier control of the epidemic.

Genome-based approaches for Controlling EIDs (Izzo & Schneider, 2010)

The statistics of 2009 for the World Health Organization report that almost 1000 bacterial genomes have been completed in refined forms and are ready to be used, and over 3000 viral genomes are under observation and study to be launched for the development of a vaccine to control any future epidemic. Any bacterial pathogen has more than 4000 genes that need to be structured and evaluated for designing any vaccination. Once the entire sequence is identified, only when the potential candidates will be short-listed for experimentation. On the other hand, viral pathogens have as few as ten genes, which are not only convenient to be sequenced anytime soon but could be tested on any potential candidate for the restoration of the health issue.

Vectored Vaccines

DNA Vaccines

Construction of recombination of genes

Pathogen Genome Sequencing

Genes Identification

Cloning of Gene of interest

Subunit Vaccines

Vaccine Developmental Stages

Hence, the identification of host genomes and pathogens can help in the accurate targeting of drug targets and vaccinations. Thus, it has increased the chances of identifying possible pathogens in individuals compared to conventional methods. The genome-based projects have helped in a better understanding of protein functions, pathogenesis, epidemiology, and microbial physiology (Jeanguenin et al., 2011).

The Pili identification in terms of long filamentous structures extending from the bacterial surface and the basic streptococci pathogenic strains is a better example of understanding and conducting research on the right platform for discovering the genomic sequence for protein functions. The virulent factors and behaviors are best described in the pile of gram-negative bacteria. However, little information was available on the pili in gram-positive bacteria before the detailed analysis of *S. pneumoniae*, *S. agalactiae*, and *S. pyogenes* (Spier, 2014).

While analyzing the *S. agalactiae* genome sequences among them, three protective antigens were highlighted through pan-genomic reverse vaccinology (Niu & Liang, 2008). These antigens contain the LPXTG motifs, and these typical proteins with cell wall anchoring were observed to be combined with the pili. The bioinformatics analysis showed that the exposed antigen surfaces elicited protected immunity among mice when injected with these pathogens. Thus, due to the limited variability of *S. agalactiae* pili, it has been observed that the different combinations used for the three pilin subunits could lead to broader protective immunity among the suspected patients (Ogholikhan & Schwarz, 2016).

However, the complete genomic sequence of *S. pneumoniae* and the advanced information available for the pilus proteins in the pathogenic streptococci helped in discovering two pilus islands encoding proteins playing adherence to colonization in a murine model of infection and lung epithelial cells. These proteins are considered to be eliciting inflammatory responses among the host. The presence of the protective agent in the pili. Although there have been relative similarities between human infectious diseases and animal-based infectious diseases in pathogenesis, it shall definitely be explicitly acknowledged that the vaccination development for both types of health issues in different species is developed independently despite the similarities.

Thus, various factors have been identified for differentiating the vaccination even with the same symptoms, such as targeted outcomes after vaccination, types of animals to be vaccinated, economic benefits of vaccinations, and catering to the actual cost of the vaccination. Moreover, the vaccination developed for industrial animals is specially designed keeping in view the benefits like increasing the number of live stocks and their presence from any infectious disease that could be hazardous for consumption in humans. Another reason is that the animals cannot be exposed to chemotherapy as it will affect the quality of meat, and the toxins will affect the health of the consumers of their meat (Hogue & Ling, 1999).

There are different types of vaccinations developed for animals, such as increasing and protecting the meat of livestock meat, preventing the spread of disease to other animals, or preventing them from generating infectious viruses that are hazardous to human health. The non-therapeutic use of antibiotics may increase the risk of developing immunity against the pathogens in livestock and could be transferred as a residue to meat consumers, especially humans. Thus, the use of vaccines can help eliminate the development of such immunity (Sette & Rappuoli, 2010). However, for this purpose, the vaccines are to be improved over the course of time so that they are advanced and effective against pathogens. Due to these reasons, the use of antibiotics in animals has been strictly restricted in Australia and Europe. Recently, advanced measures have been taken to establish similar steps in the USA and other advanced countries' live stocks.

The vaccinations are produced by several different patterns, such as the production of a virus-like particle without specific genetic materials, insertion of a required gene into a carrier to be delivered or expressed, alteration of host-specificity for the pathogen, use of immunogenic components alone, and inactivation or attenuation of the pathogen. Moreover, apart from the benefits of developing vaccines for human-related diseases, it has been observed that numerous infections identified over the years have been passed on from animals to humans (Ogholikhan & Schwarz, 2016). Therefore, it was required that apart from designing the genomic sequence of drugs as per human needs, the vaccines shall be looking into treating the infections in animals first so that they are restricted to their hosts and are not transferred to humans through any type of contact.

The highlighted advantage of this process is that conducting the research is of lower cost in comparison to a human vaccine. In addition, the vaccines developed for animals require fewer clinical trials and complexities, which are mostly expected in human trials. Thus, the animal vaccine prepared is ready to be launched in less time than the human vaccine, and since many infections are transferred due to different species of animals, it is not hard to stay that such infections could be contained without reaching out to the human population and the expected damage to occur on a larger scale will be controlled within no time (Mutoloki, Cooper, Marjara, Koop & Evensen, 2010).

The demand for increasing the production of animal vaccines has grown over the past decade due to the emerging pathogens in the livestock industry (Sette & Rappuoli, 2010). However, it does not limit the effectiveness of the vaccine and demands that any vaccine developed comply with all the safety rules and be result-oriented rather than damaging animal health. There is indeed a novel concept for developing new vaccines due to the availability of a great deal of genomic information on various pathogens and advanced molecular techniques.

Viral Vaccines for Animals

The development and implementation of viral diseases are the most appropriate options for controlling any type of infectious disease. The reason that antibiotic drugs have been analyzed to be ineffective for controlling the virus rather than has turned out to be the source of transferring the

suspected virus to any person or animal coming in contact with the virus carrier. The majority of the vaccinations are produced by veterinary companies for secure livestock production and other industrial animals (Castiblanco & Anaya, 2015). Even the World Health Organization has been working on introducing vaccinations to protect wildlife from the outbreak of viruses in the wild due to pollution and sudden climatic changes. For this purpose, the vaccines for controlling the virus are produced by adding necessary proteins to the cell structure, chicken embryos, live animals, and tissues.

Effective Responders to Vaccination

Thus, it has been clarified from the above-stated research that the animal genome is different from the human genome, regardless of whether they are interrelated through similarities or their origin. Due to this, animal genomics specifically focuses on the individual response of each animal to any vaccination due to their different genetic traits ("Synthetic Genomics boosts RNA vaccines," 2017). Due to serious efforts and the recording of results, several disparities have been recorded in the clinical trials of animals regarding any new vaccination. The veterinarians involved in these clinical trials have been characterizing these changes in the response of animals as the animal challenges models. Thus, it has raised the need for robust regulatory standards like improved laboratory practices and sound biometric analyses (de Barse & Greub, 2013). It will help in avoiding any type of environmental and experimental biases in animal clinical trials. Thus, this attempt will help in the effective profiling of the vaccines and is expected to offer better improvisations in the vaccines for the eradication of the spread of infectious diseases among animals.

The recent issue of the OIE Scientific and Technical Review stated that the majority of the immunogenetics studies have focused on poultry species and livestock to resist the disease. It has been observed through few specific studies available that the immunological responses of an individual animal's genotype predetermine limited responses to vaccinations (Ling, Ban, Wen, Wang & Ge, 2013). A study by Newman et al. stated the differences in the large half-sibling families with the infused antibody responses of B. abortus Strain 19, which is known as a live attenuated bacterial vaccine with immediate effect when inoculated (Travis, 1999). The parametric statistical model was used for studying the incorporation of the effects of the bovine major histocompatibility complex and the parameters of related drugs (Kussell, 2005).

The study helped identify the individual animals' and families' responses toward the antibody production phenotypes, thus helping to identify the variation in the genetic structures of the experimental group of animals (Lee & Quan, 2016). While studying these traits, the traits were correlated with the bulls with individual responses suggesting individual BoLA types and the existence of side effects (Yuk & Jo, 2014). It was reported by Elizabeth Glass, teaching at the Roslin Institute in the United Kingdom, that the FMDV-specific T-cell and the BoLA haplotypes are closely interrelated. A cattle population that is fully genotyped has 186 microsatellite markers and is derived from the cross between two cattle with extreme variations in their genes (Ling, Pelosi & Walmsley, 2010). Thus, variations were observed in the responses, such as completely non-responding to a higher degree of

response. Among all the immune responses, significant responses or effects were seen for the IgG2 and IgG2 ratios, suggesting other types of genetic influences other than the MHC genes and the capacity of the host responses towards the FMDV peptide.

Another study conducted on the Holstein-Charolais crossbred study population was tested for the commercial bovine respiratory syncytial virus (BRSV) vaccine. The analysis didn't include the heritable factors, so their responses to the antibody contribution may not have differed greatly. Moreover, the study also didn't include any difference between the Charolais and Holstein calves. It has been understood and observed through these studies that the vaccine responses are a heritability of complex traits, therefore it is unlikely that it is controlled by a single gene. While catering to the host-pathogen interactions, the majority of the genes controlling the vaccine responses will show variations, and it is also expected that the individual genes will show polymorphism (Campbell & Heyer, 2007).

Discussion

The understanding of microbiology has been greatly influenced by the study of genomics. The study of microbial strains has been offering new information and insight into pathogen evolution. Most importantly, genotyping is influenced by gene variations and gene discovery, which leads to the design of vaccinations according to the latest needs (Moxon, 2002). It will ultimately help monitor the two-way communication between the pathogen and the host, and it will be recorded in the public database for the complete annotated genomic sequence.

However, there are still chances that the vaccination may not be completely able to eradicate the infection among the animals, but it is expected to reduce the severity of the result. There are chances that the vaccination may fail, and the reason identified for its failure is not due to the lesser effectiveness of the vaccine but due to the improper timings or circumstances for inoculating the vaccine (DUFFY, KRZYCH, FRANCIS & FRIED, 2005). On such occasions, it may result in poor health responses and adverse effects on the health of the animals. The vaccination costs, no matter how much it is, shall be lesser or more economical so that the majority of the animals are receiving quality health and, in return, are able to provide quality meat for the consumers (Sampson, Rengarajan & Rubin, 2003).

Moreover, to make the process more reliable, the vaccination shall be given due consideration and communication between the livestock handler, farmer, and the developers of the vaccinations. Only in this way are vaccinations considered to be more result-oriented. Other protocols like the cleanliness of the environment, level of stress, environmental control, and density will help achieve better vaccination results. Thus, the recent transference of diseases from animals to humans has proved that controlling the epidemic among humans and providing healthcare services is extremely expensive compared to controlling the expected epidemic among animals (Ali, Kroll & Langford, 2002). Animal vaccines and trials are not expensive and may not cause damage to any important loss

of a large population. In contrast to humans, where trials that are certainly expected to give positive results may fail in no time, it becomes hard for the researchers to contain a specific form of the virus in the lab and later eliminate it. There is always a chance that any individual coming in contact with the host is able to receive this virus. Vaccination is the only way that could help in the spread of any new epidemic, but for this purpose, researchers need to stay ahead and learn and research more about epidemic outbreaks so that they can control this issue within no time.

Conclusion

The concept of Vaccinogenomics, in which host genomics is used in vaccine research and integration of pathogens, is expected to revolutionize the approach through which scientists have been opting for the introduction and development of vaccination (Grandi & Zagursky, 2004). The stated research gives detailed profiling for increasing the effectiveness of animal vaccines. Future vaccine discovery research will be completely changed by identifying the genetic variances that control mechanisms of immune evasion, vaccine responsiveness, and disease resistance (Zhou & Xie, 2013).

The effectiveness of the vaccines shall be adequately commercialized so that every individual in need of the vaccines may understand and apprehend the message in detail. Since meat consumption has been increasing over time, the production of livestock has also increased. However, it has increased the chances of any new infection outbreak affecting major populations. Either the consumer needs are reduced for the consumption of animal meat, but in reality, it cannot be reduced. Therefore, effective measures are required to be taken to ensure that the livestock meat is safer and that no consumer of the animal meat is suspected of getting any type of virus.

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