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GENOME: WIDE APPROCHES FOR DEVELOPMENT OF VACCINES

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ABSTRACT

The outcome of drug therapy is often unpredictable, ranging from beneficial effect to lack of efficacy to serious adverse effects. The improved understanding of the human immune system and the genetic make-up of pathogens, have provided the new insights into variation of immune response within population. Vaccination has always played a significant role in controlling and eliminating life-threatening diseases. However, arrival of genome era has revolutionized vaccine development and catalyzed a shift from conventional-culture based approaches to genome-based vaccinology. There are many challenges which need to be overcome which holds the promise for development of new drug and ultimately selection of appropriate drug and dosage form. This ever-growing body of genomic data and new genome-based approaches will play a critical role in the future to enable timely development of vaccines and therapeutics to control emerging diseases.

Key words: Human Immune System, Vaccination, Genome Era.

INTRODUCTION

The development of the field of pharmacogenomics (associations of whole genomes and drug or vaccine response) and pharmacogenetics (associations of individual genes and drug or vaccine response) has provided both the science base and clinical outcomes that together increasingly allow for the practice of individualized drug therapy. The application of this same science when applied to vaccines is labeled as vaccinomics.[1]

The terms pharmacogenetics and pharma cogenomics are often used interchangeably, which causes some confusion. However, the term pharmacogenomics is preferred when referring to clinical practice. This is because the field of pharmacogenetics deals with the genetic determinants of a single gene that affects drug therapy, whereas pharmacogenomics focuses on candidate genes, often more than one, and may include transcriptome and proteome information that affect drug metabolism, pharmacokinetics and pharmacodynamics.

The Genome Era, initiated with the completion of first bacterial genome, that of heamophilus influenza in 1995 [2], catalyzed a long overdue revolution in vaccines development. The application of genome analysis to vaccine development, a concept termed "reverse vaccinology," initiated a positive feedback loop in terms of the development and application of novel approaches to the field of vaccinology [3].

Vaccinomics and vaccine development

It is clear that the ability to respond to the threat of disease depends on the ability of the host to mount an effective defense against an invading pathogen. The goal of pharmacogenomics and vaccinomics is to identify genetic variants that predict adverse responses to vaccines, predict aberrant immune responses, contribute to personalized therapy and that predict susceptibility to diseases and response to vaccines [4].

Vaccinomics may also be useful in the development and use of existing and novel vaccine adjuvants and stimulants. For example, specific polymorphisms of the TLR3 gene are associated with significantly diminished humoral and cell-mediated immune responses to the measles vaccine [5].

Understanding the mechanism by which such polymorphisms diminish innate and other immune responses may offer a critical insight into designing work around the limitations imposed by such polymorphisms either by developing new adjuvants that utilize other receptors, or by the addition of stimulant molecules that can potentiate or augment the immune response. Another area of importance is genetically determined vaccine-associated adverse events, which referred as adversomics.

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More recently, Vestergaard et al demonstrated an association between receipt of the MMR vaccine and subsequent febrile reactions and febrile seizures [6], providing a logical genetic basis for increased susceptibility to adverse events to live viral vaccines. Concerns over more severe vaccine-related side effects, such as neurotropic and viseotropic reactions to yellow fever vaccine, encephalitis-related reactions to smallpox vaccine, temporally occurring with vaccination and others, warrant further investigation for the potential of identifying genetic predictors of risk [7-10].

Challenges associated

Application of proper method for discovery of genetic variance and their future in pharmaceutical industry for providing better patients care as economic incentive will be a break through [11]. However, a lot of hurdles are yet to be overcome. Various issues like ethical, social and legal issues need to be addressed. What next?

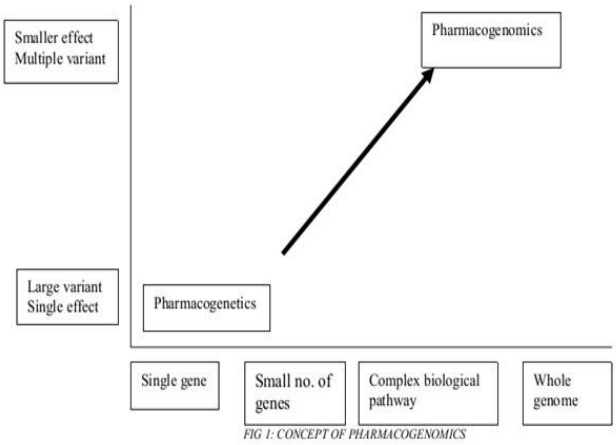

FIG 1: CONCEPT OF PHARMACOGENOMICS

In many ways the era of personalized vaccines has already begun [12].

For example, the rationale behind and utilization of personalized vaccinology in cancer vaccines is increasingly clear and a benchmark in this regard [13, 14]. At a minimum, we predict that the role of genomics in the field of vaccinology will serve to elucidate new mechanisms and biologic pathways in understanding vaccine-induced immune responses and adverse responses, as well as provide new insights into vaccine development [15]. As sophistication increases, the ability to detect meaningful associations through the contributions of multiple genes will be discernible and potentially clinically useful. Finally, the ability to understand and predict the effect of the presence/absence and interactions of the entire genome or heritable non-DNA encoded differences (epigenetics, complementation and so on) may prove the most useful in understanding an individualpatients benefit or risk in receiving a specific vaccine [16,17].

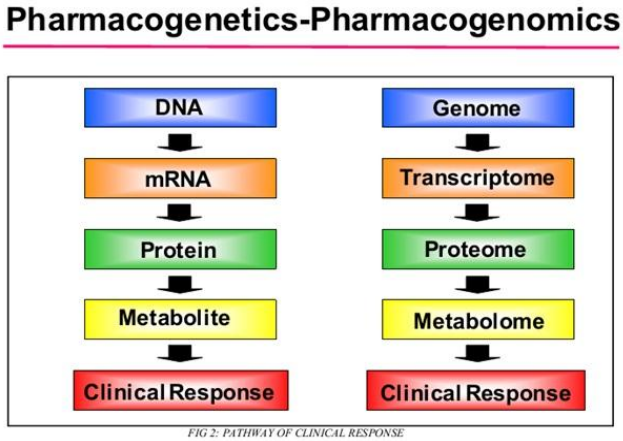

FIG 2: PATHWAY OF CLINICAL RESPONSE

DISCUSSION

The field of vaccinomics, adversomics and personalized vaccinology represents the evolution of new fields of study with new scientific possibilities informed by new paradigms and discoveries in immunology, genetics and bioinformatics. Growth in this field will be driven not only by scientific reasons, but also by consumer demands for increasingly safe and risk-free medical treatment, prevention and the desire to understand and prevent serious and severe vaccine adverse events. In general, while substantial difficulties need to be solved, it is believed that the vaccinomics era of personalized predictive vaccinology is coming and that this will eventually allow clinicians to predict the likelihood of a significant adverse event to a specific vaccine [18].

CONCLUSION

At the current time, a major barrier to vaccinomics and personalized vaccinology remains the cost. For the widespread application of personalized vaccinology, much d ata remains to be developed, genetic sequencing costs must be inexpensive and rapidly obtained with high-throughput sequencers, and increasingly more sophisticated and less labor-intensive bioinformatic approaches will need to be developed and validated. All these issues continue to experience substantial scientific and public interest, with regular new discoveries. Hence we believe that the future of vaccinology is bright indeed, and the era of empiric vaccine development, and a strict one-size-fits-all public health approach to vaccine delivery will diminish, with adoption instead of a philosophy of the best vaccine solution for each individual or subgroup of individuals.

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