Universal Flu Vaccine - A Review

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Abstract :Influenza is a world health hazard. The only effective way against influenza disease is vaccination. But, the currently available vaccine for influenza only induces strain-specific immunity, they do have long-lasting serum antibody titers. Hence they are ineffective in the present pandemic situation. There is an emergency need for the production of new vaccines which could be more effective and have long-lasting immune protection against the flu virus. The innate immunity present in humans due to initial exposure to the influenza virus may affect the magnitude of immune responses by an influenza vaccine. Tempering is not needed every year. Even though there have been advances in vaccines since 2019 there is no approval for the usage of universal flu vaccine. Infectious diseases such as the human influenza virus are causing a drastic public health crisis resulting in economical strain worldwide. The presently available influenza virus vaccine is the most effective and reasonable countermeasure against both seasonal and influenza infections. Nevertheless, Hemagglutinin the main antigen of the influenza virus has very high pliability, due to viral polymerase that has high error rate and selections from immune pressure of circulating antibodies. Universal Vaccines can be defined and utilized when they show exquisite antigenic specificity, high efficiency, long-lasting, and can dramatically adapt to an incident and eliminate the pathogens. The presented review discusses current development, challenges faced obtaining proper potency of protection, precautions taken related to the use of universal flu vaccine

Keywords: Cross protection, Influenza virus, HA stalk, Live attenuated influenza vaccine, Universal flu vaccine .

1. INTRODUCTION

The only vaccine that is productive and functional against all influenza strains, inspired by the virus subtype and antigenic drift is known as the universal flu vaccine. (Nachbagauer and Krammer 2017) Tempering is not needed every year. Even though there have been advances in vaccines, since 2019 there is no approval for the usage of universal flu vaccine. (Khanna et al. 2014) Infectious diseases such as the human influenza virus are causing a drastic public health crisis resulting in economic strain worldwide.

The initial cause for the flu is due to the Influenza A virus, which is an enveloped RNA Virus that has numerous different strains.Hemagglutinin (HA) and Neuraminidase (NA) are the proteins present in the membrane which are crucial for the entry and release of the virus. (Willey, Sherwood, and Woolverton 2008) Ion channels, M2 proteins are other structural components of the virus, and can be identified by our immune system. (Hampson 2011) Based on the specific strain of influenza causing the infection, our immune system can build a specific response to influenza infection.

The presently available influenza virus vaccine is the most effective and reasonable countermeasure against both seasonal and influenza infections.never the less, Hemagglutinin the main antigen of the influenza virus has very high pliability, due to viral polymerase that has high error rate and selections from immune pressure of circulating antibody. (Gottlieb and Ben-Yedidia 2014) This procedure is called antigenic drift and it is essential to update the influenza virus vaccine on a yearly basis. (France et al. 2018) It is unwieldy strain selection based on monitoring and prognosis, it can happen that vaccine strains may not match the circulating strain leading to a sharp decline in vaccine effectiveness. (Koul and Bali 2016, Carragher et al. 2008). The evolution of universal vaccines is the main objective of global pandemic plans. At present, this process takes six months, a period during which the population can not protect the new pandemic virus which causes morbidity and mortality of the population. (Wrammert et al. 2011)

The evolution of a universal vaccine is one of the major objectives of the global pandemic plan. It is anticipated that a universal flu vaccine would have a lead over the currently available seasonal vaccine. (Abbasi 2020) The universal vaccine could require less requirement administration usually only once. (Mp, Brundha, and Nallaswamy 2019) This would reduce the subjection of the vaccinated individuals to adjuvants and abolishes the recurring cost of annual vaccination. These features would increase public acceptance of vaccination against the flu and thereby augment flu vaccine coverage. (Dance 2012) As influenza vaccination has different types of strains , causes pandemic leading to world crisis,Of all the viral respiratory diseases, influenza causes the most severe pathology and leads to the greatest damage to the population health and economy.

Structure of Influenza

The structure of the influenza virus is in a spherical shape. It has a genome of RNA which is an enveloped virus, the inner portion is the protein shell. It is composed of a lipid layer that has projections known as spikes containing glycoprotein called haemagglutinin and neuraminidase. (Han and Marasco 2011) The effectiveness of the binding of the virus is enabled by these proteins. (Brundha, Padma Shri, and Sundari 2019) Genetic information is present in the capsid. At the time of release, influenza contains eight strands of RNA that are tightly encapsulated, awaiting the time of release into a host cell. (Taubenberger and Kash 2010) The envelope of influenza A virus containing Hemagglutinin has its primary glycoprotein of influenza A virus, which is the target of all neutralizing antibodies.

HA0 is known as an immature polypeptide chain that becomes activated by host protease by yielding two subunits. A helical chain known as the stem is formed by HA 2 is attached to the viral lipid membrane. (Prashanthi and Brundha 2018, Kumar, Ashok Kumar, and Brundha 2016) The globular head which contains receptor binding sites and the majority of the virus antigenic sites is formed by HA1 Subunit. (Wiley, Wilson, and Skehel 1981) Since these HA

1 loops differ, vaccinations are limited to present circulating strains, because the antibodies in targeted are strain-specific.

Medical uses

The U.S Centers for Disease Control and Prevention (CDC) recommends the flu vaccine as the best way to protect people against the flu and prevent its spread. (Antrobus et al. 2012) The severity of the flu caused by the foreign strains can also be reduced by the flu vaccines. The flu vaccine can also reduce the severity of the flu if a person contracts a strain that the vaccine did not contain. (Osterholm et al. 2012)
It takes about two weeks for the following vaccination for protective antibodies to form.The efficacy of the vaccine is determined by which it reduces the risk of influenza at controlled conditions and its effectiveness is seen when there is reduction in risk after the vaccine is put into use.(Hannah et al. 2019) In the case of influenza, effectiveness is expected to be lower than the efficacy because it is measured using the rates of influenza-like illness, which is not always caused by influenza. (Subbarao and Joseph 2007, Preethikaa and Brundha 2018) Influenza vaccines generally show high efficacy, as measured by the antibody production in animal models or vaccinated people. (Yoon, Webby, and Webster 2014)(Dreyfus et al. 2012) However, in most years (16 of the 19 years before 2007), the flu vaccine strains have been a good match for the circulating strains, and even a mismatched vaccine can often provide cross-protection. (Baz et al. 2013) The virus rapidly changes due to antigenic drift, a slight mutation in the virus that causes a new strain to arise. (Kalaiselvi and Brundha 2016)

Potential role of WHO

According to a World Health Organization (WHO) estimate, annual epidemics cause 2–5 million severe cases and 250,000 to 500,000 deaths. (Huber 2014) The European Center for Disease Control (ECDC) estimates that seasonal influenza virus infections cause 38,500 annual excess deaths in Europe. (Lambert et al. 2012) In the United States seasonal influenza virus infections are responsible for 24,000 deaths per year on average (3,000–49,000 per season for seasons between 1976–2007) (Fiers et al. 2004) with annual attack rates that can reach high percentages (e.g. predicted 30.5% of the population in the 2012/2013 season.) The clinical trial options are given to the patients (Harsha and Brundha 2017)and the support surveillance of the model king's efforts to identify and predict emerging strains is more reliable. Economic losses caused by influenza and other acute respiratory viral infections account for approx 77% of the total damage from all infectious diseases. Significant losses are related both to the direct costs of patients' treatment and rehabilitation, as well as to the indirect losses caused by a decrease in productivity and a reduction in corporate profits. Influenza and acute respiratory viral infections account for 12-14% of the total number of temporary disability cases.

NIAID released its universal influenza vaccine strategic plan

The wide knowledge on the immunity and advanced knowledge in universal influenza vaccine is developed by three main specific research areas are Improving knowledge of transmission, natural history and pathogenesis of influenza infection to help understand factors that contribute to the spread, severity, and diversity of influenza, and to identify measures to improve disease control. (Nakaya et al. 2011) Over the past 60 years, many vaccines have been developed that have many advantages and outcomes. Moreover , the present vaccines are able to resolve the problems and help in controlling the harmfulness of

the influenza. Based on the high difference in pathogens (Brundha 2015) , vaccines can be described in two mechanisms, they are antigenic drift which is the change of antigenic structure due to accumulation of point mutations and Antigenic shift, genomic segments coding surface antigens. They might change after development of new subtypes during the outbreaks.

Characterizing influenza immunity and immune correlates of protection through the study of immune responses to natural influenza infection and vaccination over time can be used to identify measurable immune factors critical to vaccine design. (Lee et al. 2014)

Challenges and opportunities

Currently, the licensed influenza vaccines are effective in healthy young adults, several challenges remain. They include the dependence on embryonated eggs for vaccine production, the lengthy timeline for vaccine production, the need for annual vaccination, the emergence of antigenically novel viruses, the need for improved immunogenicity in the elderly, and the need for an improved correlate of protection. (Subbarao and Matsuoka 2013)

Furthermore, influenza infection can cause hidden damage, such as serious clinical complications associated with the nervous and cardiovascular systems, as well as the exacerbation of chronic diseases (diabetes, heart failure, chronic obstructive pneumonia, etc.) and lead to delayed death, especially in children under two years old, the elderly and people with poor health

Several approaches have been developed to overcome these challenges and improve the immunogenicity and efficacy of influenza vaccines. (Tripp and Tompkins 2014)

Prevention and Treatment

The seasonal vaccine has HA subunit which rosettes produced with baculoviruses and it has conventional TIV of 70% efficacy because of delivery of more NA and M2 Antigens, mucosal responses including IgA and potential for induction of Cd8T cell response. (Sridhar et al. 2013, Naveenaa, Rani, and Brundha 2020)

The pandemic vaccine has a small stockpile of MIV. The NA Inhibitors that are the antivirals have a short therapeutic window and are emerging drug resistance. Whereas the monoclonal antibodies are in development.(Fillette et al. 2008)

- Suitable for all age groups
- Protects the Influenza A of Group I and II
- Duration protection which will lasts at least 1year
- Monoclonal antibodies are in development
- Induction of CD8, T cell responses are the peptides which are gene-based approaches

Universal flu vaccine therapeutics

Recent studies have shown the benefit of boost schedules on the efficacy and strength of the immune response. Strategies mainly included in this study were the sequential use of different vaccine platforms. (Shreya and Brundha 2017) Current influenza vaccines need to be reformulated annually as the virus undergoes mutations, which means that influenza outbreaks are not covered by vaccines made for previous years. (Ravichandran and Brundha 2016) The choice of virus used in the vaccine is manufactured six months in advance of winter because the problem is even more substantial. The choice was actually erroneous and no protection is conferred from the current vaccine in the case of the 2015 strain. Clearly a better strategy is needed.

As mentioned in the article in Krammer and Palese,2013, stated the majority of antibodies produced during infections target the immunodominant HA head domain containing the receptor-binding site and several well-defined antigenic sites that accumulate mutations as the virus drifts under immense pressure. The HA stem domain is much more conserved, and more broadly reactive are the antibodies targeting this region. Based on a phylogenetic analysis, HA proteins fall into two groups; group 1 includes subtypes H1, H2,H5,H6,H8,H9,H11,H13,H16,H17 and H18, while group 2 includes subtypes H3,H4,H7,H10,H14 and H15.(Limberis et al. 2013, Balaji, Brundha, and Path 2016).Adjuvants for boosting and broadening the immune response are an additional approach to broadening vaccine immune response. Adjuvants can also spare the dose of antigenSeveral adjuvants are approved for use in human vaccines in other countries, but adjuvanted influenza vaccines are not yet approved in the U.S. (Giudice et al. 2006)

On expressing additional influenza antigens using viral vectors, vaccination has been alternatively introduced Viral vectors are replication-defective viruses capable of expressing high, sustained antigen levels. (Shenoy and Brundha 2016) Viral vectors can target specific types of cells, allow multiple routes of delivery, and the vectors themselves can act as adjuvants to improve the immune response. (Schmitz et al. 2012) An example of a viral vector influenza vaccine is the modified Ankara vaccine virus (MVA), which expresses an influenza NP fusion protein and a matrix 1 protein (M1) which induces T-cell responses but does not neutralize antibodies. (Timothy, Samyuktha, and Brundha 2019)

Future scope
Improving knowledge of transmission, natural history and pathogenesis of influenza

- Increases human challenges , study capacity and capability in the defined research area.
- Developing in Animal model is used for testing , advance knowledge in transmission pathogenesis

2. CONCLUSION

The ultimate goal of a universal influenza vaccine is to protect against all influenza A viruses, obviating the need for annual revaccination. Several promising approaches are under development to improve or overcome the drawbacks of the currently licensed vaccines and to induce broad immunity against other subtypes of influenza with pandemic potential.

Authors contribution
All authors have contributed equally to the study.

Conflict of interest
The authors declare no conflict of interest

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