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"FLAG" Tag Sequenced E-Protein Marker Demonstrating Tetravalent Dengue Virus Like Particles (DENV-Lps) As Potential Vaccine Candidate

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ABSTRACT

Dengue is a very deadly virus. It causes viral infections that are transmitted to humans through a small bite of specific mosquitoes. These mosquitoes are generally infected. The main primary vector of this deadly disease is *Aedes aegypti* mosquitoes. This virus is generally called the dengue virus or DENV. It is a single-stranded RNA virus. Due to this dengue virus causes deadly and hazardous infections. It mainly occurs in various tropical and subtropical regions. Dengue causes a very broad range of diseases, sometimes making the detection of symptoms quite hard. There are numerous causes that are directly and indirectly linked to the growth of the dengue virus in the environment. The symptoms may vary from simple flu to deadly fever. And till date, there is no specific treatment for dengue. In many countries especially the tropical regions, there has been a huge number of deaths from this DENV virus. The complicated pathogenesis of this deadly virus has been a constant barrier for scientists to discover a medicine or vaccine for this disease. Dengue virus falls under the family of Flaviviridae. It has four different types of serotypes present in it. Those are DENV-1, DENV-2, DENV-3, and DENV-4. The epidemiological patterns of these four serotypes are interlinked with each other. They can co-circulate among each other and can create severe to very severe infections. The most respectful nature of DENV is that it transmits from one person to another by various means. Though it is quite rare it is possible of creating local transmissions.

KEY WORDS: DENV, Dengue, Virus like particles, Vaccine

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INTRODUCTION

Dengue is a very deadly virus. It causes viral infections that are transmitted to humans through a small bite of specific mosquitoes. These mosquitoes are generally infected. The main primary vector of this deadly disease is *Aedes aegypti* mosquitoes. This virus is generally called the dengue virus or DENV. It is a single-stranded RNA virus. Due to this dengue virus causes deadly and hazardous infections. It mainly occurs in various tropical and subtropical regions. Dengue causes a very broad range of diseases, sometimes making the detection of symptoms quite hard. There are numerous causes that are directly and indirectly linked to the growth of the dengue virus in the environment. The symptoms may vary from simple flu to deadly fever. And till date, there is no specific treatment for dengue. In many countries especially the tropical regions, there has been a huge number of deaths from this DENV virus. The complicated pathogenesis of this deadly virus has been a constant barrier for scientists to discover a medicine or vaccine for this disease.

Dengue virus falls under the family of Flaviviridae. It has four different types of serotypes present in it. Those are DENV-1, DENV-2, DENV-3, and DENV-4. The epidemiological patterns of these four serotypes are interlinked with each other. They can co-circulate among each other and can create severe to very severe infections. The most depictful nature of DENV is that it transmits from one person to another by various means. Though it is quite rare it is possible of creating local transmissions.

The dengue virus has a very rough kind of structure. The microscopic structure clearly shows how the dengue virus can replicate inside a host organism. The structure consists of various viral genomes which are covered by an envelope and shelled by a couple of proteins. And the genome is made up

of singlestranded RNA that can easily get transformed into proteins. Certain studies have shown that the diameter of this dengue virus is approximately 500 Armstrong. And it has a very deep core covered by a lipid bilayer. It has a glycoprotein shell that is well structured and consists of almost 200 copies of each protein. And it is always said that DENV has a very unique structure with quite unique features as it changes to different conditions of the environment. And its replication occurs inside the cytoplasm of host or infected cells. The single-stranded RNA virus that is present in dengue virus has a length of approximately 11 kilobases. The envelope that is present in DENV is the major target protein. It is directly involved in receptor binding and helps in aiding a distinct structure of the dengue virus. And this E protein plays an important role in the designing of vaccines for this deadly virus.

Dengue is a very fatal and deadly disease. Although sometimes it is minor in nature, in most cases it can range from severe to very severe. The main disorder that the dengue virus causes is the plasma leaking. This part is much more dangerous than anything else as this affects each part of immune system internally. Fluid accumulation and respiratory discomforts are also associated with this deadly virus. Dengue virus eats off all the cells internally present in the body of the host organism. And in recent years, dengue has turned out to be an epidemic disease with a rapid increased of patients. The severe state of dengue decreases platelets count in the body. And we all know, platelets are one of the most important part of our body. A decrease in platelet count can result in various hazards like organ failure, mental shock, death, internal bleeding, etc. Dengue is indeed a life-threatening disease. Sadly, as of now, there are very few or no medications for the permanent eradication of dengue. Researches are working continuously to get a permanent vaccine for dengue virus but till now there has been no such successful results. Dengue is one of the most painful diseases in this whole world.

The incidence of Dengue has grown rapidly all over the world. And the need for permanent cure is indeed the need of hour. Due to no medications, this deadly virus is becoming more deadly day by day. It is required to get the treatment from the early stages of dengue. But due to rapid mutations, now-a-days people are becoming asymptomatic when gets affected with Dengue. Many diagnostics process has been developed to speed up the treatment but without medications, nothing is 100% successful. Besides this pandemic, dengue has given alarming pressure on researchers and scientists.

The challenge of creating a dengue vaccine has increased over the passing years. Despite the challenges and huge study of ADE (Antibody-dependent enhancement) protein has given rise to many cross-reactive antibodies that can bind to DENV virus and facilitate the certain receptors for the pathogenesis processes. The main challenge is to develop a tetravalent vaccine that can provide protection to all the four serotype of Dengue virus i.e. DENV-1, DENV-2, DENV-3, DENV-4. In recent times, certain virus like particles or VLPs are developed that has paved a new way for the development of dengue vaccine. As VLPs have certain structural properties that can induce immunization with DENV antibodies. These VLPs have certain structural and phenomenal features that help in the neutralization of all the serotypes of DENV as these are made through recombinant systems with high successful results.

Dengue vaccine is indeed a door of prevention and eradication of this deadly disease. Vaccines have always been considered as the most effective way of dealing with diseases. While developing vaccines, the study of ADE is quite important. And getting a strong vaccine for dengue requires the development of its own antigen. But one should study ADE to develop vaccines out of its mechanism. Nowadays, the dengue vaccine needs to be developed from activated T-cells and a combination of antibodies. This can lead to providing complete immunization against all the four serotypes of DENV. As this makes the next generation dengue vaccines more effective, safe, and sound to use.

DENGUE GEOTROPISM

Dengue has a deep global impact in the world. The cases of dengue have grown to the next level. In recent years, almost 200 to 300 million people has been affected with this deadly disease. The mosquitoes have increased their habitat and nutrition. As a result, mosquitoes have turned into a vector one due to the negative impacts of heavy pollution and global warming. The symptoms and nature strongly varies from slight illness to severe fever. This severe condition is very dangerous and difficult to tackle. And to date, there has been no specific treatment for this deadly virus.

DENV Response towards Vaccine

Dengue belongs to a very complicated family. The serotypes are cross linked with each other. Due to this, it is very difficult to get a permanent treatment or design a vaccine for this virus. The most typical and dangerous risk factor is the binding of certain neutralizing antibodies to the DENV virus. This process is known as antibody-dependent enhancement or ADE of the Dengue virus. As a result of this binding, the receptors get a defined pathway to enter the host cells. And this increases the viral load in the cells resulting in serious fatal disorder in the affected individuals.

The vaccine design mainly focuses on the E-protein, which serves as a target point. The main challenge in the process is to develop a tetravalent vaccine that simultaneously works for all the serotypes of DENV that is DENV-1, DENV-2, DENV-

3, and DENV-4. And due to extra complicated phenomena of ADE, the pathogenesis of dengue is very difficult to detect.

In around 2015, the first live attenuated vaccine was developed that is CYD-TDV, a yellow fever vaccine. In its process, it was shown in the testing of this vaccine that the potential highly increased in dengue negative children than in positive. Due to lots of controversies, this vaccine was stopped and to date, there has been no vaccine developed for Dengue.

In several studies, researchers have found VLPs or Virus-like particles to be the most suitable candidate for the development of vaccines. In various investigations, virus-like particles (VLP) have been produced as the new candidates for the dengue vaccine.
Because VLPs have structural and physicochemical properties similar to infectious particles, immunogenicity should be comparable to mature virion, and the vaccine's occurrence is unnecessary, strain derived Indeed, immunization with Dengue VLP resulted in the production of anti-DENV antibodies as well as cytotoxic T cell response whereas it appears that DENV infection did not cause the ADE VLP immunization has been shown to be effective in mouse models. Several protein expressions have resulted in the production of Dengue VLPs. Mammalian cells, for example, are used in systems. Pichia pastoris yeast, Escherichia coli, Silkworms were also transfected containing baculovirus genome recombinant Purified VLPs derived from recombinant expression systems progressively.

The occurrence of four closely related viruses poses a significant problem in the development of dengue vaccines. DENV serotypes that are related Individuals who are infected with one DENV serotype and then exposed to any of the other serotypes are more likely to acquire the disease.
Amore severe instances of the disease as a result of an antibody-dependent phenomena enhancement (ADE); nonneutralizing doses of anti-DENV have been found. By establishing a DENV-antibody complex, antibodies can improve viral penetration into host cells. There is concern that the first vaccine may result in an inadequate immune response that may produce ADE-mediated severe dengue illness between the first and second and the most recent immunizations As a result, safe and highly effective treatment is required. The dengue vaccine provides long-term protection to all the four serotypes.

VLPs: The New Generation Vaccine Candidate:
Many investigations have proved that in the absence of viral genomic RNA, prM and E can come together for the formation of VLPs. A finding was made a few years ago revealed that the DENV-2 E ectodomain (referred to hereafter as DENV-2) in P. pastoris, expressed in the absence of prM, possessed the innate potential to self-assemble into very complex structures. VLPs that is immunogenic. Subsequently, we discovered that this was true for P. pastoris-expressed E ectodomains to DENV-118, DENV-317, and DENV-419, also known as E1, E3, and E4, respectively. These VLPs were discovered based on probing; their E monomers preserve the majority of their antigenic integrity including a previously reported battery.

It should be noted that all of these VLPs are evoked primarily from homotypic responses, nAbs that are unique to their corresponding serotype. E2 VLPs protected AG129 mice against a fatal DENV-2 challenge16 and E3 VLPs were discovered to be devoid of considerable ADE potential17. Furthermore, nAbs evoked by these VLPs were detected to be directed almost entirely to the C-terminal EDIII, demonstrating that the VLPs indeed serve as effective transporters. Platforms for EDIII display. The receptor-binding22–24 and serotype-specific nAb-inducing epitopes25,26 are remarkable. The E protein is mapped to EDIII. When the intrinsic safety (lack of prM) and immunogenicity (the ability to elicit virus-neutralizing anti-EDIII antibodies) and inexpensive production costs (P. pastoris expression system) make the E-based VLPs ideal for the design of vaccines.

While physically mixing these four monovalent E VLPs into a single tetravalent formulation is doable, we did not do so. Many studies have wanted to see if it was possible to simultaneously express all four E VLPs to work effectively on the four serotypes of DENV. By avoiding the requirement to test the potential vaccine, such an approach would reduce its cost. In many researches, all four monovalent E VLPs are expressed and purified. At first, the feasibility of co-expressing two distinct Es, as well as their ability to co-assemble into bivalent mVLPs20 before co-expressing all four Es in a single P, need to be investigated.

Dengue viruses contain a positive-sense single-stranded RNA genome and are members of the Flavivirus genus, which is part of the Flaviviridae family. As per studies, four different viral serotypes have been identified: DENV-1, DENV-2, DENV-3, and DENV-4. During endemic cycles of transmission between humans and arthropod vectors, these serotypes appear separately. The dengue viral genome consists of a single open reading frame (ORF) that encodes a polyprotein that is cleaved co- and post-translationally by cellular and viral proteases into three structural proteins. This smooth enclosed virus has 180 copies of the E and proteins on its surface. On viral-induced modified endoplasmic reticulum, virus morphogenesis occurs membranes, allowing complete but immature particles to be assembled and budded into the ER system. During trafficking through the ER and trans-Golgi network (tGN), the spiky immature particles

undergo additional furin protease cleavage of prM, which contributes to the rearrangement of the E protein from trimer to dimer conformations and turns the virus into smooth mature particles before being released from infected cells. The surface E protein is the virus's key antigenic determinant and a major focus of the immune system. Immunity directed toward the E protein is predominantly mediated by neutralizing antibodies, which give protection against dengue when present. The study of E protein structure is quite important in neutralizing antibodies. To design a successful vaccine, a close study of all the proteins and membranes are highly required.

The Dengue virus is quite unpredictable in nature. Its main motive is to enter target cells during primary DENV infection after binding protein to cell surface receptors. Few Viral uptakes are accomplished through receptor-mediated endocytosis. Endosomal acidification causes a conformational shift in the E protein, culminating in membrane fusion and nucleocapsid release into the cytoplasm. Out of that, genome replication takes place in several areas of the endoplasmic reticulum (ER). the assembly of Viruses occurs in the ER, and virions are exocytosed by secretory vesicles generated from the Golgi. This pathway is very difficult and critical to predict.

Infection Pathway of Dengue Virus:

The pathway of this DENV cycle indicates the most severe type of DENV infection and reflects a complicated interaction between the host immune response and viral virulence factors. Certain Epidemiologic studies has given a relationship between immune system because there is an elevated risk of secondary DENV infection and in infants born are more prone to DENV-immune along than the mothers within the first year of life. The antibody-dependent immune enhancement (ADE) infection arose as a result of these data. In the line with the ADE pathogenesis hypothesis, antibody enhancement of DENV infection in monocytes in vitro was associated with an elevated risk of DHF, and peak viremia was higher in patients with severe secondary DENV infection. Differences in certain genetic factors between virus isolates may also exist. Because some DENV strains do not cause severe disease, they have an impact on virulence. Finally, the capillary leak syndrome associated with DHF may be exacerbated by a pathologic cytokine response that occurs after substantial T-cell activation. T cell activation and the growth of serotype-reactive low-affinity DENV-specific T cells that produce large quantities of vasoactive cytokines. This complete pathway gives high challenges to the scientists to prepare a permanent treatment against this deadly virus.

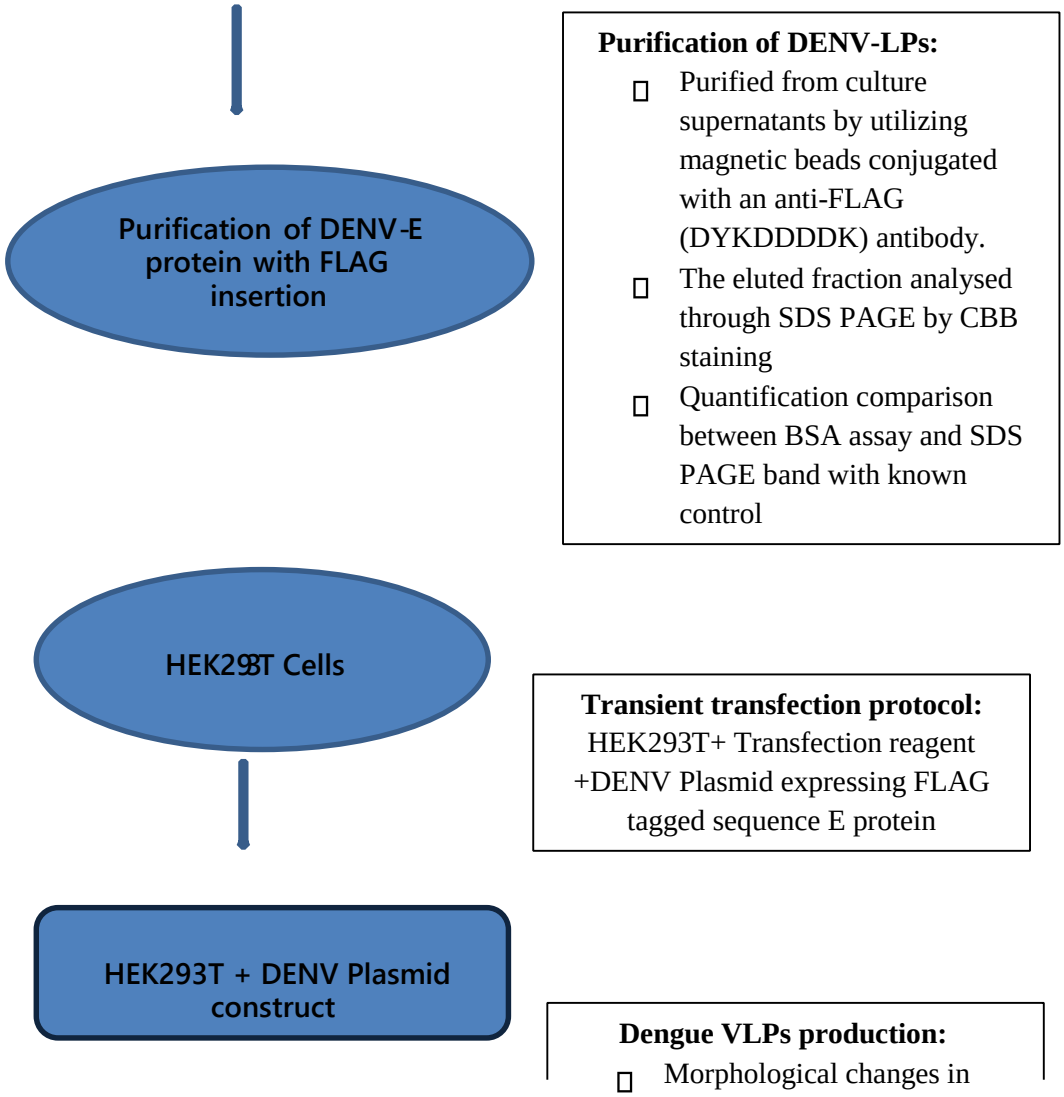
DENV is carefully injected into the bloodstream during mosquito feeding on humans, with bits of spillover done in the epidermis and dermis area, leading to infection of immature Langerhans cells (epidermal dendritic cells, and keratinocytes). The cells which are infected travel from the injection site to the site of lymph nodes, where they can be in contact with the monocytes and macrophages. And this becomes the main target for the budding infection. As a result, this doubles up the infection rate and the virus spreads via the lymphatic system. Many cells of the mononuclear lineage are infected as a result of thisnblood-derived monocytes, myeloid, and splenic and liver macrophages. DENV has been a constant of having a preference for circulating mononuclear cells in the blood as well as cells that reside in the body. In experimentally infected nonhuman primates, leukocytes were also found to be infected with DENV. It should be highlighted that high concentrations of DENV-specific immunoglobulin G (IgG) will complex freshly generated virus that clings to and is picked up by mononuclear cells during secondary infections with heterologous DENV. In this regard, factors that determine the number of infected target cells, and hence the levels of viremia, may influence the ratio of pro-inflammatory to anti-inflammatory cytokines, chemokines, and other mediators, as well as how the inflammatory response affects the hemostatic system. DENV infection has also been noticed to cause effects in bone marrow stromal cells.

The immune response that plays a vital role in DENV infection and in the timely return of infection is the adaptive immune response. It is also thought to play an important matter in the deterioration of disease in affected patients with DHF or DSS. As a result, DENV virus immunization should enhance the challenges of giving a good immunity from the antibody of this deadly virus. The appearance of neutralizing antibodies directed against the virus envelope (E) protein is clearly the principal mediator of protection against DENV infection, and inducing protective levels of neutralizing antibodies is thus the primary target of immunization. Vaccines that are both live attenuated and non-living, such as Virus vaccinations that have been inactivated, virus-like particles, or DNA vaccines all readily induce both neutralizing antibodies and protective immunity. After DENV infection, robust neutralizing antibody responses occur, which are thought to give lifelong protection against re-infection with the same DENV serotype and only a few months of protection against a heterologous DENV serotype. This brief period of cross-protection has been linked to the development of cross-reactive neutralizing antibodies, which fade quickly after infection; however, the particular mediator of this protection has yet to be established. The function of DENV-specific cellular immunity in re-infection resistance appears to be minor. However, similar to WNV, T-cell-mediated immunity to DENV is expected to contribute considerably to viral clearance, and more research is needed to characterize the role of T-cell-mediated immunity against DENV.

It is worth noting that one commonly cited argument in the literature is that when shock occurs, the virus is no more visible in the blood, and so the host reaction should play a crucial part in pathogenesis. The majority of autopsy data did not give an exact response about the occurrence of viral antigens or nucleic acid in blood and postmortem samples, but the minimal evidence implies that the replication of DENV shall appear in some organs although few replication actions are no more valid. In line with these studies, it was found that DENV can be extracted from findings of autopsy samples and not from blood in the rhesus macaque model.

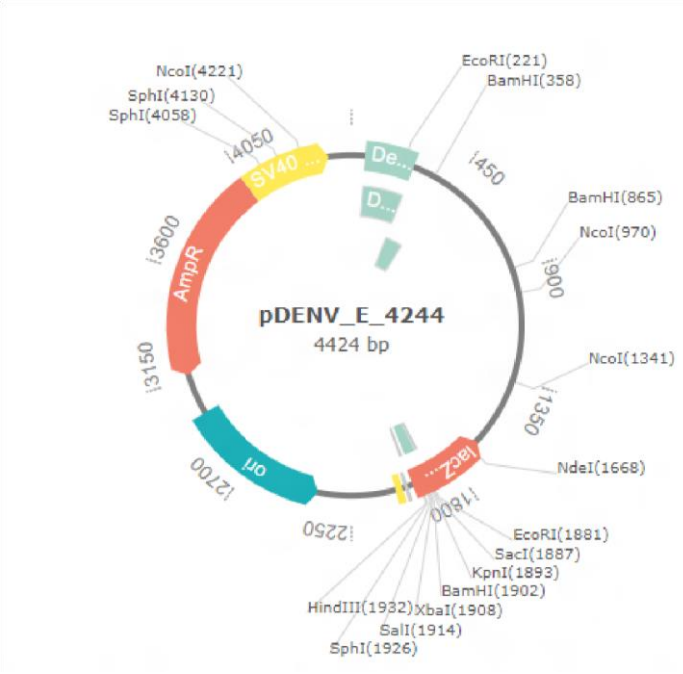
Protocol review and experimental design:

DENV-LPs propagation:



"FLAG" Tag Sequenced E-Protein Marker Demonstrating Tetravalent Dengue Virus Like Particles (DENV-Lps) As Potential Vaccine Candidate

Dengue Envelope protein plasmid construct:



1 ATGCGTTGTA TAGGAATATC AAATAGAGAC TTTGTGGAAG GGGTTTCAGG AGGAAGCTGG
61 GTTGACATAG TCTTAGAACA TGGAAGCTGT GTGACGACGA TGGCGAAAAA TAAACCAACA
121 TTGGATTTTG AACTGACAAA AACGGAAGCC AAACATCCAG CCACTTTAAG GAAGTATTGT
181 ATAGAGGCAA AGCTGACCAA CACAACAACA GCATCTCGCT GCCCAACACA AGGAGAACCC
241 AGCCTAAATG AAGAACAGGA CAAAAGGTTT GTCTGCAAAC ACTCCATGGT TGACAGAGGA
301 TGGGGAAATG GATGCGGATT ATTTGGAAAG GGAGGCATCG TGACCTGTGC AATGTTCACA
361 TGCAAAAAGA ACATGGAAGG AAAAGTCGTG CAACCAGAAA ACTTGGAGTA CACCATTGTG
421 ATAACACCTC ACTCAGGGGA AGAGAATGCA GTCGGAAATG ACACAGGAAA ACACGGCAAG
481 GAAATTAAGG TAACACCACA GAGTTCCATT ACAGAAGCAG AACTGACAGG TTATGGCACC
541 GTCACGATGG AATGCTCTCC GAGAACGGGC CTCGACTTTA ATGAGATGGT GTTGCTGCAA
601 ATGGAAGACA AGGCTTGGCT GGTGCACAGG CAATGGTTCT TAGACCTGCC GTTACCATGG
661 CTGCCCGGAG CAGACACACA AGGATCAAAT TGGATACAGA AGGAGACATT GGTCACTTTC
721 AAAAATCCCC ATGCGAAGAA ACAGGATGTT GTTGTTTTAG GATCCCAAGA AGGGGCTATG
781 CATACAGCAC TCACAGGGGC CACGGAAATC CAGATGTCAT CAGGAAACTT ACTGTTCACA
841 GGACATCTTA AGTGCAGGCT GAGAATGGAC AAACTACAGC TCAAAGGAAT GTCATATTCT
901 ATGTGTACAG GAAAGTTTAA AGTTGTGAAG GAAATAGCAG AAACACAACA TGGAACAATA 961 GTTATCAGAG
TACAATATGA AGGGGACGGT TCTCCGTGCA AGATCCCTTT TGAAATAATG
1021 GATTTGGAAA AAAGACATGT CTTAGGTCGC TTGATCACAG TCAACCCAAT TGTTACAGAA
1081 AAAGACAGCC CAGTCAACAT AGAAGCAGAA CCTCCATTCG GAGACAGTTA CATCATTATA
1141 GGAGTAGAAC CGGGACAACT GAAGCTCAGC TGGTTTAAGA AAGGAAGTTC TATTGGCCAA
1201 ATGTTTGAGA CAACAATGAG AGGAGCGAAG AGAATGGCCA TTTTAGGTGA CACAGCTTGG
1261 GATTTTGGAT CCCTGGGAGG AGTGTTCACA TCTATAGGAA AGGCCCTCCA CCAAGTCTTT
1321 GGAGCAATCT ATGGGGCTGC CTTTAGCGGG GTTTCATGGA CTATGAAAAT CCTCATAGGA
1381 GTTGTCATCA CATGGATAGG AATGAATTCA CGCAGCACCT CACTGTCTGT GTCACTAGTA
1441 TTAGTGGGGG TCGTGACACT GTATTTGGGA GTCATGGTGC AGGCC

DENV Envelope protein gene sequence_NCBI

CONCLUSION REMARKS

VLPs are the most self-centered particles; these particles have a defined structure that helps in making safe and effective vaccines for a deadly virus like Dengue. The morphology of these particles is highly immunogenetic in nature. As a result, the vaccines made from these particles are less infectious and do not have any kind of risk associated with their formation. These are likely to cut off all the risks involved in the ADE of the dengue variants. It's like a perfect meta balance between all the four serotypes of DENV. as using of VLPs ensures that there will be no replication amongst the serotypes of this deadly virus. According to a few recent studies, it has shown that VLPs are made from the expressions of flavivirus precursor membrane and envelop (E). This tetravalent vaccination using VLPs shows a robust antibody against all the four serotypes of DENV simultaneously. Thus, these particles prove to be the most advanced technology for the design of vaccines.

REFERENCES

I. Mr. Utkalendu Suvendusekhar Samantaray, & Ms. Piyanki Santra. (2021). Human Adenovirus Serotypes Efficiently Transducing HEK293 Cells: An In Vitro Propagation of HAdv. International Journal for Research in Applied Sciences and Biotechnology, 8(5), 17–21.

II. Swapnarani Sethi, & Mr. Utkalendu Suvendusekhar Samantaray. (2021). Isolation and Biochemical Characterization of Indole-3-Acetic Acid (IAA) Produced in Pseudomonas Sp. Isolated from Rhizospheric Soil. International Journal for Research in Applied Sciences and Biotechnology, 8(4), 1–14

III. Ms. Tanima Singh, & Mr. Utkalendu Suvendusekhar Samantaray. (2021). Optimization of Modified Murashige and Skoog (MS) Medium Promoting Efficient Callus Induction in Zinnia elegans. International Journal for Research in Applied Sciences and Biotechnology, 8(3), 202–211.

IV. Ms. Samuka Sahu, & Mr. Utkalendu Suvendusekhar Samantaray. (2021). Characterization and Cellulase Production Activity of different Aspergillus Sp. Isolated from "Puri, Odisha" Marine Fungal Strains. International Journal for Research in Applied Sciences and Biotechnology, 8(3), 71–87.

V. Utkalendu Suvendusekhar Samantaray, Ankita Mishra, & Yengkhom D. Singh. (2020). Biosynthesis and Antimicrobial activities of Silver Nanoparticles (AgNPs) by using Leaf Extracts of Tagetes erecta (Marigold) and Tridax procumbens (Tridax). International Journal for Research in Applied Sciences and Biotechnology, 7(6), 209–226.

VI. Samantaray US, Sahu S, PatroA, Tripathy S, Sethi S, Phytochemicals: A novel antiviral therapeutic approach for Prevention of lung injury and respiratory infection during COVID 19,SPR, Volume 2, issue 1, Page No.: 421-433. DOI: https://doi.org/10.52152/spr/2021.164 ISSN: 2635-0955

VII. Ms. Swagatika Tripathy, & Mr. Utkalendu Suvendusekhar Samantaray. (2021). Quantitative Analysis of Nutrients and Biochemical Evaluation in Pomfret Fish (Pampus argenteus) During Frozen Storage. International Journal for Research in Applied Sciences and Biotechnology, 8(3), 180–195.

VIII. Ms. Arpita Patro, & Mr. Utkalendu Suvendusekhar Samantaray. (2021). Comparative Study of Antioxidant Activity and ROS Production Profile among Clarias batrachus, Cirrhinus reba, Channa punctatus (Freshwater Species). International Journal for Research in Applied Sciences and Biotechnology, 8(3), 160–179.

IX. Cloning and cDNA Synthesis of PE & PPE Gene of Mycobacterium Strain H37rv5;Utkalendu Suvendusekhar Samantaray , Rudra Prasad Khuntia- International Journal of Medical, Pharmacy and Drug Research(IJMPD), Vol-6,Issue-2, March - April 2022, Pages 42-51 , 10.22161/ijmpd.6.2.6

X. mRNA vaccines against emerging infectious diseases; A challenging approach of novel vaccine discovery:Utkalendu Suvendusekhar Samantaray , Rudra Prasad Khuntia; International Journal of Medical, Pharmacy and Drug Research(IJMPD), Vol-6,Issue-2, March - April 2022, Pages 52-57 , 10.22161/ijmpd.6.2.7