ABBREVIATIONS

aa	amino acid
Ab	Antibody/antibodies
ADE	Antibody Dependent Enhancement
AOX1	Alcohol oxidase 1
AOX1	Alcohol oxidase 1 gene
AOX2	Alcohol oxidase 2
AOX2	Alcohol oxidase 2 gene
ATCC	American Type Culture Collection
P_{AOX1}	Alcohol oxidase 1 promoter
APS	Ammonium per sulfate
BHK-21	Baby Hamster Kidney cells
BMGY	Buffered complex medium containing glycerol
BMMY	Buffered complex medium containing methanol
bp	Base pairs
CHAPS	3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate
cm	centimetre
CVD	ChimeriVax-DENV
DC	Dendritic cell
DC-SIGN	Dendritic cell-specific intercellular adhesion molecule-3-Grabbing Non-integrin
DENV	Dengue Virus
DF	Dengue fever
DHF	Dengue Hemorrhagic Fever
DMEM	Dulbecco's Modified Eagle Medium
DSS	Dengue shock syndrome
E	Envelope protein
EDIII	Envelope domain III
EDIII-T	Protein containing EDIIIs of all four serotypes linked in tandem
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
FCS	Fetal Calf Serum
GuHCl	Guanidine-HCl
HBcAg	Hepatitis Bcore antigen
HBcAg	Hepatitis B core antigen gene
HBV	Hepatitis B virus
His	Histidine
hr	hour(s)
IFN	Interferon
IgG	Immunoglobulin G
IgM	Immunoglobulin M
kDa	Kilo Dalton
kb	Kilo base pairs
L	Litre
LAV	Live attenuated virus

LB	Luria-Bertani
M	Molar
mAb	Monoclonal Antibody
µF	micro-Farad
µg	micro-gram
µl	micro-litre
µm	micro-metre
min	minute(s)
mg	milli-gram
ml	milli-litre
mM	milli-molar
mRNA	messenger RNA
ms	milli-second
MIR	Major Immunodominant Region
MOI	Multiplicity of Infection
Mut^+	Methanol utilization plus
Mut^S	Methanol utilization slow
Mut^-	Methanol utilization minus
N	Normal
NCR	Non-coding region
ng	nano-gram
NGC	New Guinea C
Ni-NTA	Nickel-Nitriloacetic acid
nm	nanometre
NS	Non-structural
Ω	Ohm
OD/OD_{600}	Optical density/ Optical density at 600nm
PAGE	Polyacrylamide gel electrophoresis
PBS	Phosphate buffered saline
PBST	Phosphate buffered saline with Tween 20
pfu	Plaque forming units
PRNT	Plaque Reduction Neutralization Test
PVP	Polyvinylpyrrolidone
rpm	Revolutions per minute
SDS	Sodium dodecyl sulphate
STAT	Signal transducers and activation of transciption
TEMED	N, N, N', N' - Tetramethylethylenediamine
TMB	3,3',5,5'-Tetramethylbenzidine
TT	Transcription termination sequence
Tyk	Tyrosine kinase
VLP	Virus-like-particle
V	Volt
WHO	World Health Organization
YF17D	Yellow Fever virus vaccine
YPDS	Yeast extract-Peptone-Dextrose-Sorbitol plates
YPD	Yeast extract-Peptone-Dextrose medium

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Introduction

Dengue is a highly endemic disease of the tropics and is rapidly spreading to the other parts of the world. It is caused by any of the four dengue virus serotypes DENV-1, -2, -3 and -4. Dengue virus belongs to flavivirus genus of flaviviridae family. There is no approved dengue vaccine candidate till now, though there are few vaccine candidates in the clinical phase of development. It is pre-requisite for a vaccine candidate to be safe for human use. Hence, non-replicating subunit vaccine candidates, which are safer than live-attenuated virus, are drawing attention in the field of dengue vaccine development.

Dengue envelope domain III is one of the most critical domains of dengue envelope protein. It is highly accessible on the virion surface and is involved in binding of the virion to the receptor on the host cell surface. This domain also contains virus neutralizing epitopes.

Virus-like-particles (VLPs), as recombinant subunit vaccines, have come into focus with the success of the VLP-based vaccines for Human Papilloma Virus and Hepatitis B Virus. Several viral structural proteins possess an intrinsic ability to assemble into non-infectious, non-replicating structures known as VLPs. VLPs mimic the structure of a virion and thus combine the advantages of whole virus vaccines, with respect to immunogenicity, and recombinant subunit vaccines, with respect to their being non-infectious and safer. One such viral protein, capable of forming VLPs, is Hepatitis B virus core antigen (HBcAg). It has been fused with a variety of antigens, from bacterial, viral and protozoan pathogens, to form chimeric VLPs.

In the present study, dengue envelope domain III has been fused to Hepatitis B core antigen, to further enhance the immunogenicity of envelope domain III. This chimeric protein was expressed in eukaryotic host *P. pastoris* and purified. The chimeric protein was able to form VLPs. It was evaluated immunologically by immunization in mice. The antiserum, so raised, was found to neutralize dengue virus.