



# In Silico Studies of Molecular Interaction of Filoviral Matrix Protein with Alpha Tubulin

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## Abstract:

The matrix protein of negative stranded RNA virus plays an important role in assembly and budding. The matrix protein of Ebola virus VP40 is involved in formation and release of filamentous Ebola virus like particles (VLP). The interaction and evolution of VP40 of Ebola virus could play an important step in studying the virus. In present study, VP40 matrix protein was computationally analyzed for its domain, evolutionary relationship and interaction with host protein tubulin. Here we carried out docking process of VP40 matrix protein of Ebola virus with host alpha tubulin using HEX docking software. Depending upon the docking energy values, we have chosen the best interacting structure (-890.36).

## Keywords:

Ebola virus, HEX, tubulin, VP40 matrix protein, docking, VLP.

## Introduction:

Ebola virus is a RNA virus with non segmented negative sense genome. It belongs to the family Filoviridae of order Mononegavirales. The virus causes severe hemorrhagic fever accompanied by extremely high mortality rates in humans and non human primates. (Feldmann *et al.*, 2003, Sanchez *et al.*). The genome of this virus codes for seven structural proteins –nucleoprotein (NP), viral protein 35 (VP35), VP 30 and L- and viral RNA forms the nucleocapsid, which is responsible for transcription and replication of the viral genome (Muhlberger *et al.*, 1999). The three other proteins are VP40, glycoprotein (GP) and VP24, membrane associated protein. VP40 interact with host protein during the budding process and hence play important role in budding.

Because of the pathogenicity, high mortality rate and public health concern efforts are being made to identify potential targets and to develop therapeutic drug against Ebola virus. Computational techniques enable to uncover new targets and thus contributing towards understanding more about this virus and its mechanism.

In this study the VP40 matrix protein of Zaire was searched for similar sequences and domain analysis, evolution and interaction which are carried out In silico.

## Material and methods:

The sequence for VP40 matrix protein of Ebola virus Zaire was queried at NCBI and retrieved with its GI and Accession number. This sequence was





analyzed for its domain. Similar sequences were searched using BLASTp tool (Altschul *et al.*, 1990). All these sequences were aligned by T Coffee program a multiple sequence alignment tool. Protein protein interaction of VP40 and host alpha tubulin was studied by docking method using Hex algorithm.(G. Macindoe *et al.*, 2010).

## Result and discussion:

As VP40 plays major role in egress and interacts with several proteins of host, therefore an attempt was made to study in detail about this protein using computational tools. One of the important step is interaction of VP40 protein with alpha tubulin which has been studied in vitro and hence three dimensional molecular study of this interaction was studied using in silico approach.

When VP40 was analyzed for its domain, Smart server (Schultz *et al.*, 1998, Letunic *et al.*, 2014) predicted its domain The query sequence was searched for its Pfam entry (Finn R. D. *et al.*). Pfam is a database of protein families that include their annotation and multiple sequence alignments generated using Hidden Markov Model. Three unique results for the query VP40 were found as shown in table 1.

VP40 Pfam 07447matrix protein VP40; this family contains viral VP40 matrix proteins that seem to be restricted to the Filoviridae. These play an important role in the assembly process of virus particles by interacting with cellular factors, cellular membranes, and the ribonuclear protein particle complex.

The query sequence (NCBI entry AIG96624, GI: 667853346) when searched for similar sequences, BLASTp tool returned twenty three sequences with significant similarity. When these sequences were aligned, the Tcoffee program (DiTommaso P, 2011) showed conserved regions and variable region. Pink shaded residues are well conserved regions. Asterisks denote identities while colons show similarities (Fig. no 2). The phylogenetic tree shows (Fig. no. 2a and 2b) that protein Vp40 of Ravn Ebola virus Kenya, Marburg virus, Victoria Marburg virus are closely related while Sudan virus, Tai forest ebola virus and Bundibugyo virus forms another group while other members are Zaire Ebola virus VP40. *Gi no. and names of VP 40 matrix protein*, (Table2) of which phylogenetic tree constructed.

The results were obtained in the form of 10 output files with docking structures of different binding energies the best output result was selected showing good interaction having binding energy value -890.36. Protein-protein interaction was studied by Hex docking software. The interaction between the two protein VP40 (pdb-1es6) and tubulin (pdb-1tub) were studied showing the three dimensional structure of VP40 (fig. No. 3), three dimensional structure of





alpha tubulin(fig.4) and shows docked three dimensional structure where VP40 interacts with tubulin,(fig.5).

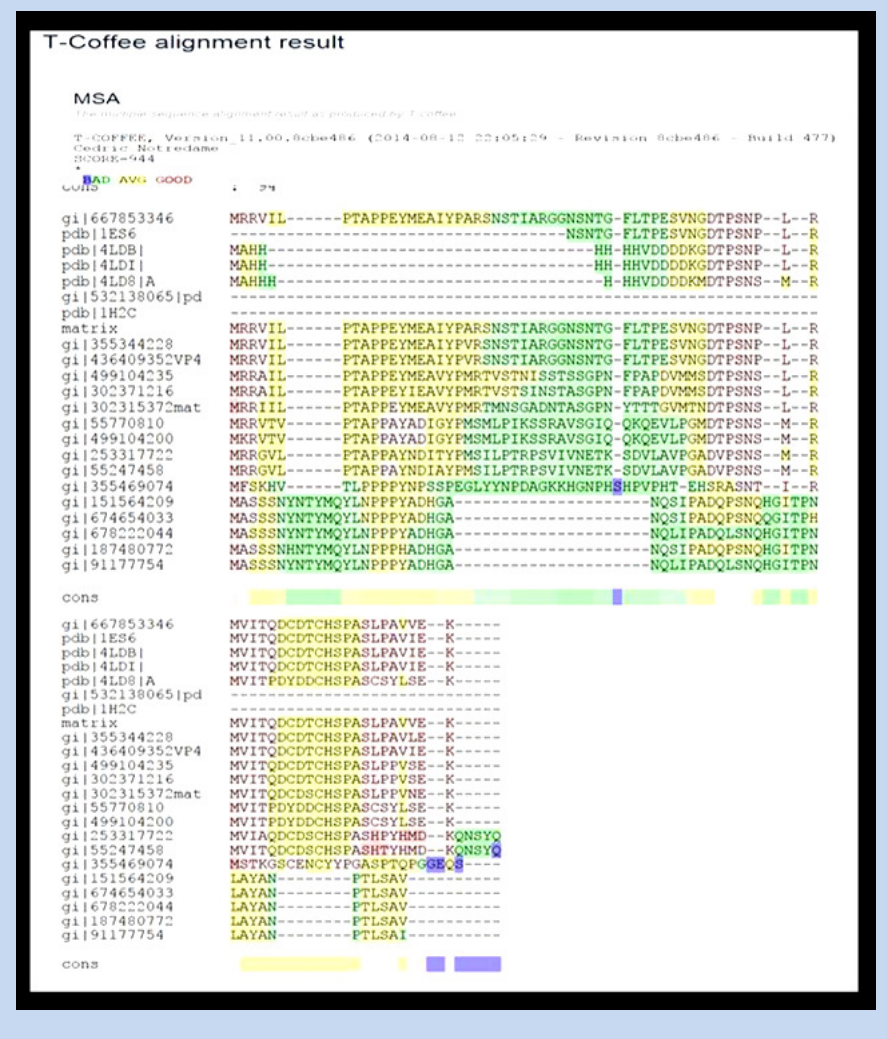
**Figure 1.** Domain architecture of V P 40 predicted using Smart server.

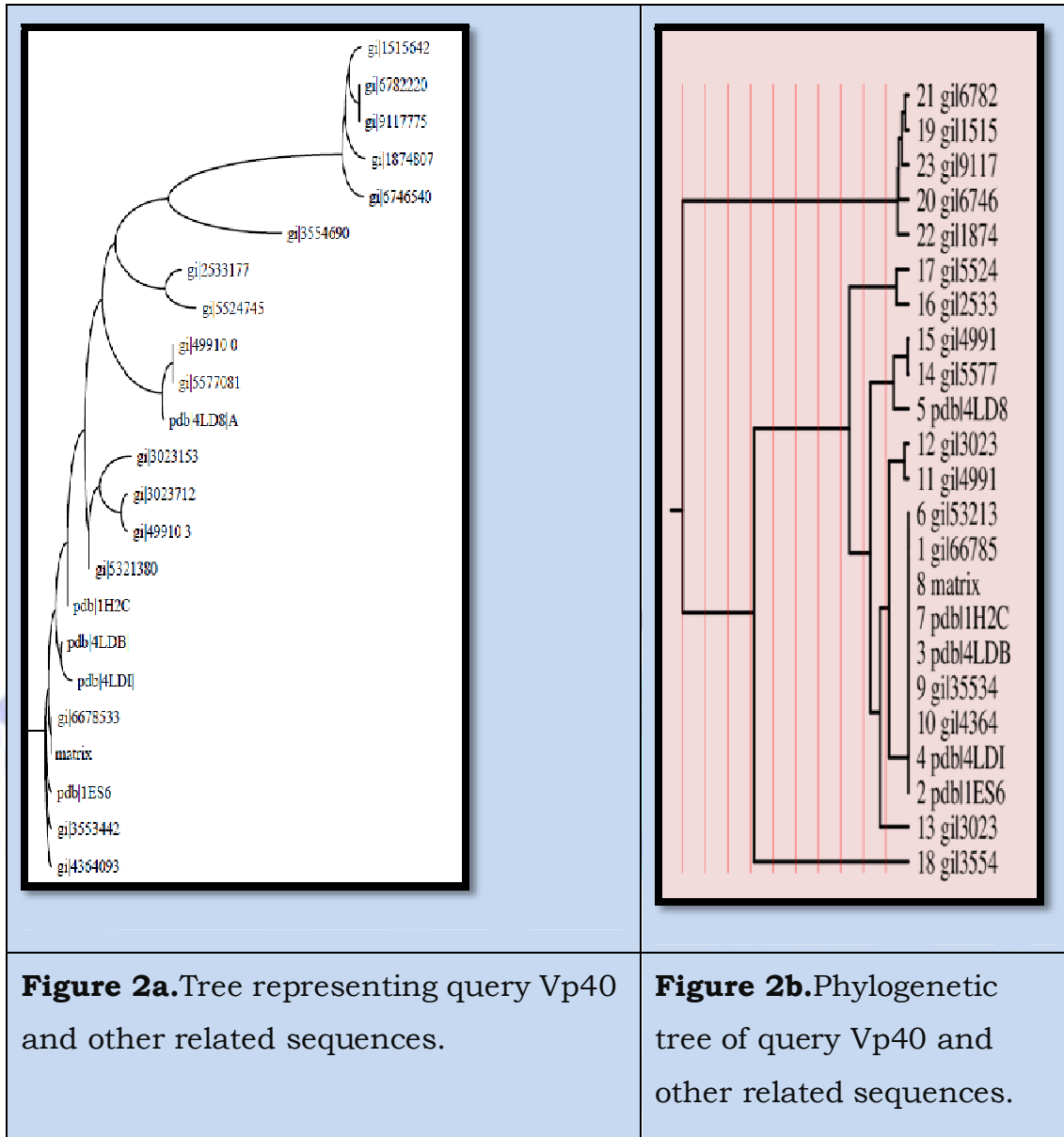


**Table 1:** Hits for VP40 sequence with their accession numbers.

Accession	ID	Description
<a href="#">PF07447</a>	<a href="#">VP40</a>	Matrix protein VP40
<a href="#">PF00397</a>	<a href="#">WW</a>	WW domain
<a href="#">PF04308</a>	<a href="#">DUF458</a>	Protein of unknown function (DUF458)

**Figure 2.** Multiple sequence alignments between queryVp40 and other related sequences.





**Figure 2a.** Tree representing query Vp40 and other related sequences.

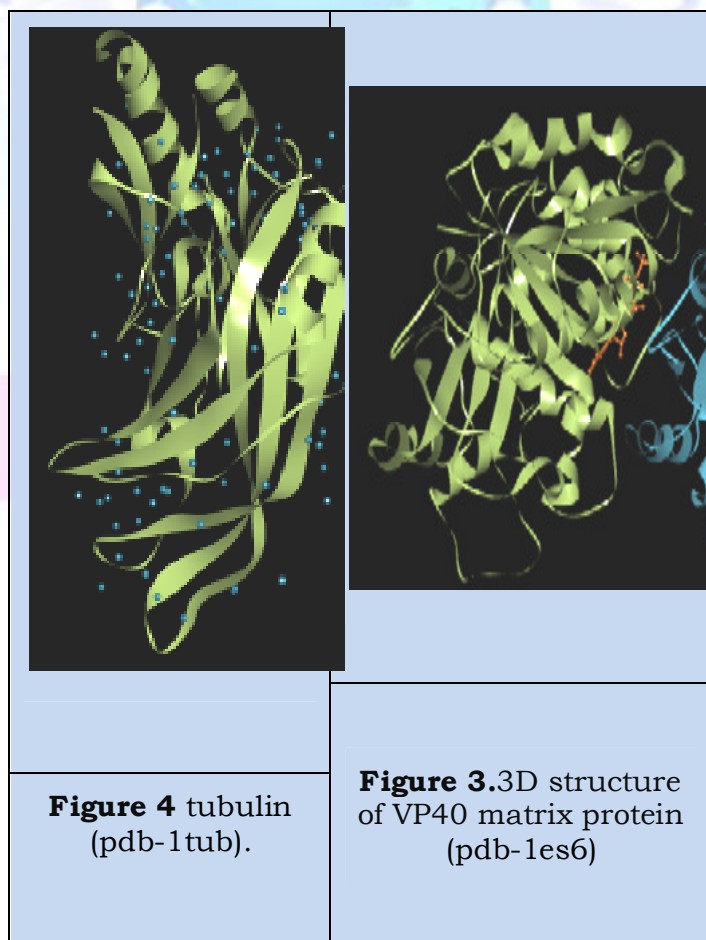
**Figure 2b.** Phylogenetic tree of query Vp40 and other related sequences.

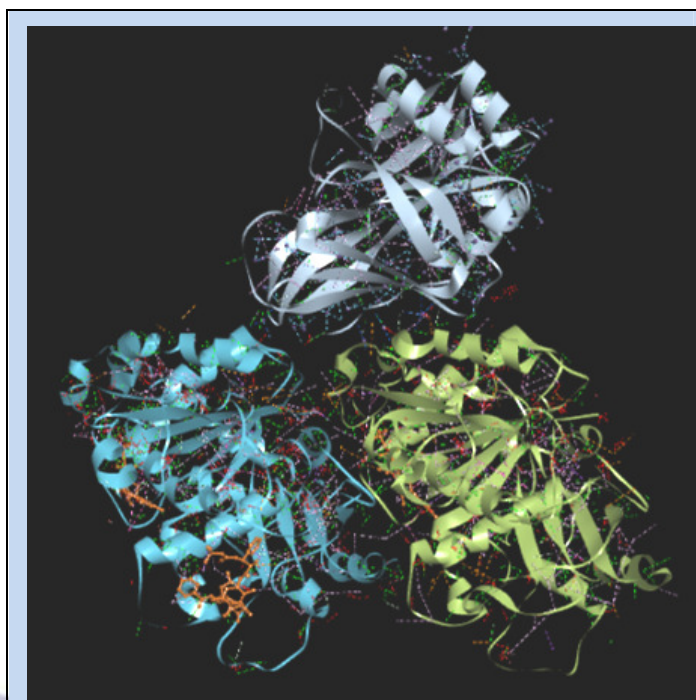
Table 2 : Taxon names of VP 40 association table	
Output Taxon Name	Original (Long) Taxon Name
gi_302315372	gi   302315372matrix protein Tai Forest ebola
gi_436409352	gi   436409352VP40 [Zaire ebolavirus]
gi_499104200	gi   499104200 viral protein 40 [Sudan ebolavirus]
gi_499104235	gi   499104235 VP40 [Bundibugyo virus]
gi_532138065	gi   532138065   pdb   4LDM
gi_55247458	gi   55247458 matrix protein [Reston ebolavirus]
gi_55770810	gi   55770810 matrix protein Sudan ebolavirus
gi_667853346	gi   667853346 matrix protein Zaire ebolav
gi_674654033	gi   674654033 VP40 Marburg marburgvirus



**Table 2 :** Taxon names of VP 40 association table

Output Taxon Name	Original (Long) Taxon Name
gi_678222044	gi 678222044 matrix protein Marburg virus
gi 151564209	gi 151564209 virion protein 40 Ravn virus Kenya
gi 187480772	gi 187480772 virion protein 40 Ravn virus Kenya
gi 253317722	gi 253317722 matrix protein VP40 Reston ebolav
gi 302371216	gi 302371216 matrix protein Bundibugyo virus
gi 355344228	gi 355344228 membrane-associated protein Zaire ebola
gi 355469074	gi 355469074 matrix protein Lloviucuevavirus
gi 91177754	VP40 Lake Victoria marburgvirus
Matrix protein_Zaireebola virus	matrix protein [Zaire ebolavirus]
pdb_1ES6	pdb 1ES6 Matrix Protein Ebola Virus
pdb_1H2C	pdb 1H2C
pdb_4LDB	pdb 4LDB  Ebola Virus Vp40
pdb_4LDI	Ebola Virus M24 1r
pdb 4LD8 A	Sudan Virus Vp40





**Figure 5.** Interaction of VP40 with tubulin

### Conclusion:

In this study VP40 matrix protein of Ebola virus was docked with host protein tubulin with the aim to understand interaction between these proteins which is important in viral egress, this study of VP40 could be further evaluated for drug designing.

### References:

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**Letunic et al. (2014)** *Nucleic Acids Res*doi: [10.1093/nar/gku949](https://doi.org/10.1093/nar/gku949). smart server

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