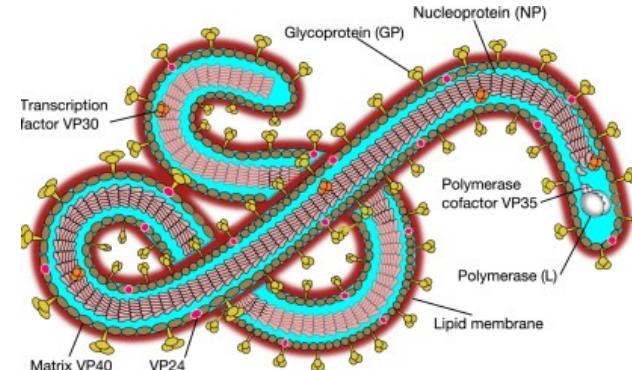


Phylogenetic analysis of Ebola virus secreted glycoprotein

Mahsa Askary Hemmat

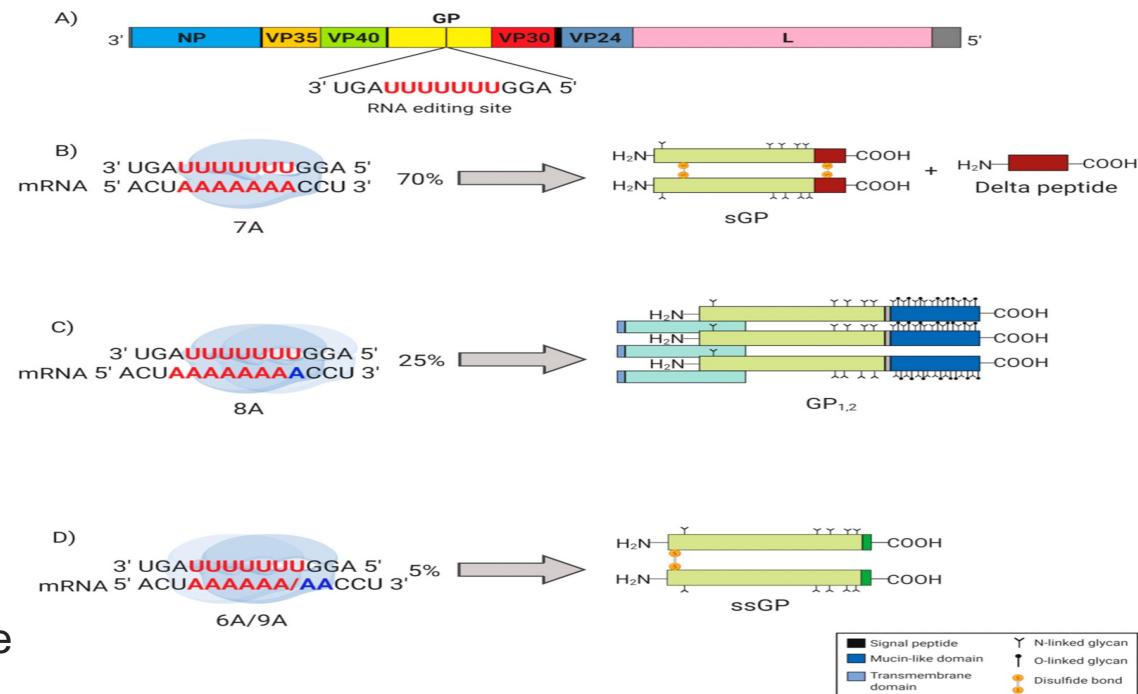
Ebola Virus Disease

- > Ebola virus disease (EVD) is a deadly disease with occasional outbreaks that occur mostly on the African continent.
- > Causes severe hemorrhagic fever in humans and nonhuman primates.
- > Its fatality rate can reach 90% and averages around 50%
- > Early detection is important, so infected individuals can be isolated and treated, which prevents the spread of the virus



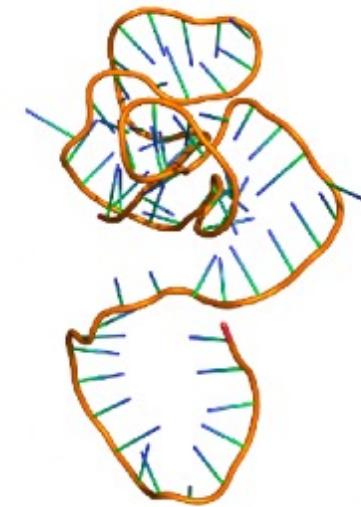
Soluble glycoprotein (sGP) is a diagnostic marker of Ebola virus infection

- > EBOV glycoprotein gene produces three protein products: surface glycoprotein (GP1,2) and two secreted proteins (sGP and ssGP)
- > sGP can be detected in significant amounts in the sera of acutely infected patients within 3 days of exposure to the virus



Aptamers as diagnostic tools

- > Aptamers are single-stranded oligonucleotides that bind to specific molecular targets, including proteins and small molecules with high affinity and specificity
- > The process of selecting an aptamer is called Systematic Evolution of Ligands by Exponential Enrichment (SELEX)
- > Because aptamers can be evolved to bind tightly and specifically to almost any protein, they have been regarded as potential diagnostic agents



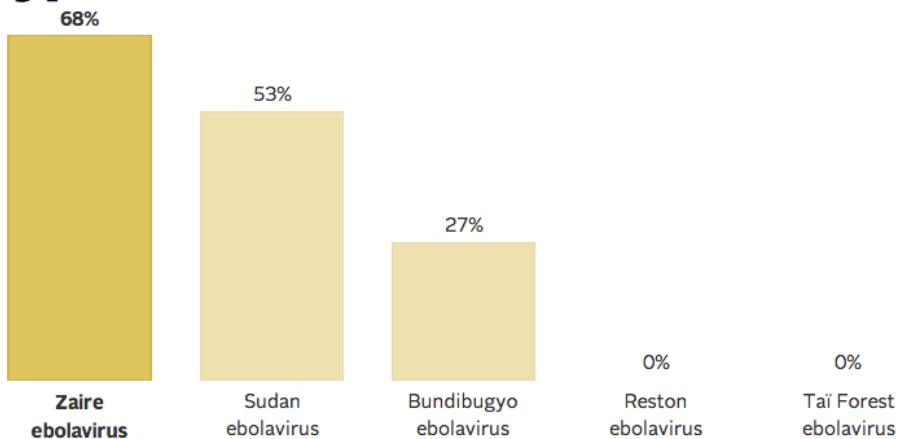
Aptamers have been selected to recognize Ebola virus sGP

Aptamer	Nucleic Acid Type	sGP, EBOV (K _d , nM)	sGP, SUDV (K _d , nM)	GP1,2, EBOV (K _d , nM)
6011	DNA	8.5 ± 3.2	165 ± 44	48 ± 32
6012	DNA	27 ± 12	151 ± 44	54 ± 23
39SGP1A	2'FY-RNA	* 13 ± 5	* 147 ± 59	104 ± 31
70SGP2A	DNA	27 ± 15	ND	58 ± 17

Soma Banerjee

Different strains of Ebola virus

Average death rates from the 5 types of Ebola viruses



New Ebola virus: Bombali (2018)

Source: CDC, WHO

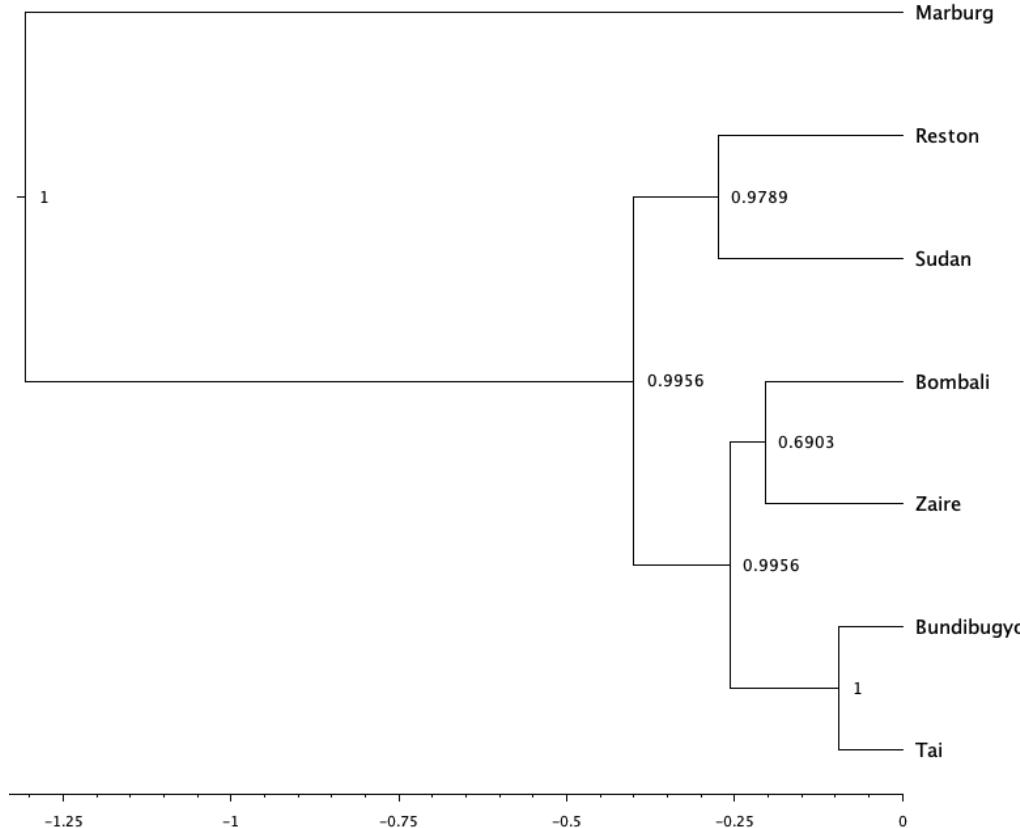


Using sGP sequence of different strains of EBOV to build a phylogenetic tree

Methods::

- > Downloaded sGP sequences of different strains of EBOV from NCBI (6 taxa, 364 amino acids)
- > Blast search > Marburg virus GP sequence (681 amino acids)
- > Aligned Sequences using clustalW
- > BEAST 2, Blossum62 substitution model, Yule model, 1000000 generations

Bayesian phylogenetic tree of EBOV sGP



Prediction of binding energies of sGP to the 70SGP2A aptamer

LETTER

doi:10.1038/nature23902

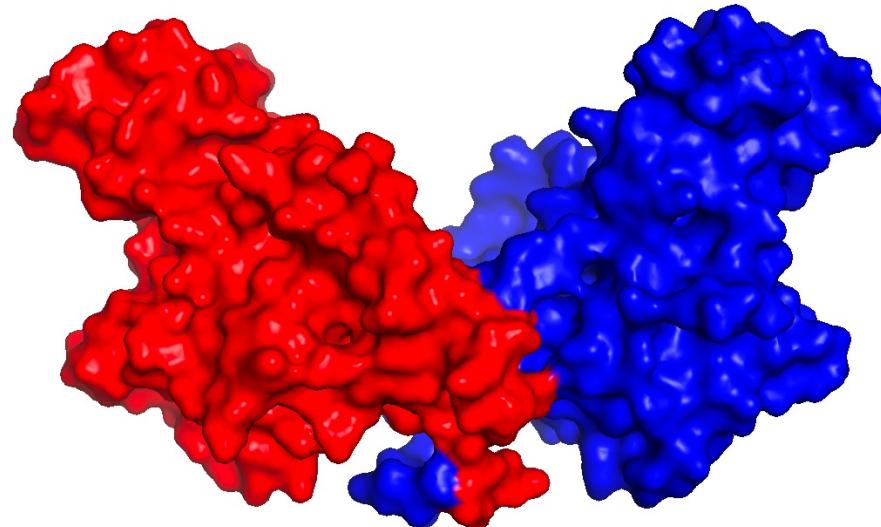
Alternative evolutionary histories in the sequence space of an ancient protein

Tyler N. Starr¹, Lora K. Picton² & Joseph W. Thornton^{2,3}

Structural modelling and predictions of RE-binding affinity. We used FoldX⁴⁹ to predict the affinity to SRE of all RH variants that were 11P-dependent (SRE-specific in the AncSR1+11P background and non-functional in AncSR1), or 11P-independent (SRE-specific in AncSR1; Extended Data Fig. 8a). For structure-based affinity prediction, we used the crystal structures of the AncSR1 DBD bound to ERE (Protein Data Bank (PDB) accession number 4OLN) and the AncSR2 DBD bound to SRE (PDB 4OOR) as starting points, with crystallographic waters and non-zinc ions removed. We removed chains E, F, K, and L from the 4OOR structure. We used the RepairPDB function to optimize both DBD structures according to the FoldX force field, and we used the BuildModel function to mutate the AncSR1/ERE structure to AncSR1:GSKV/SRE. The BuildModel function was

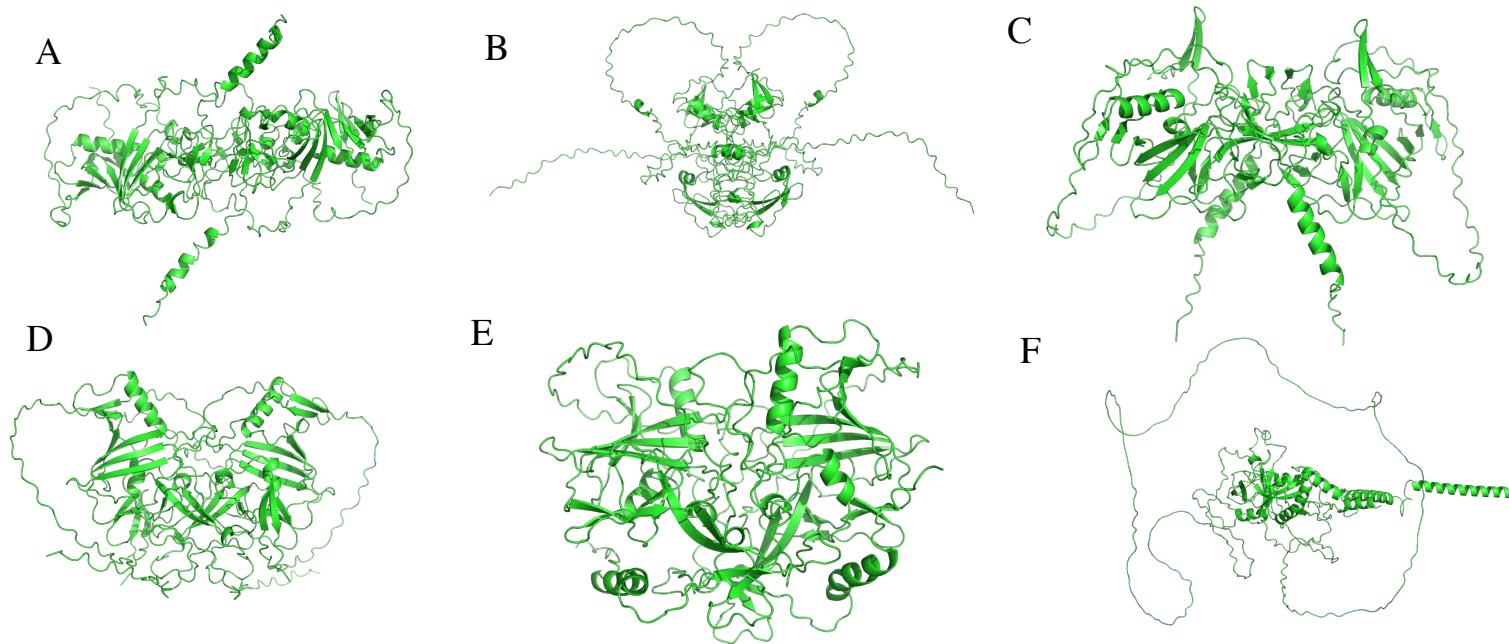
sGP structure

- > Downloaded from PDB database. (PDB ID: 5KEM)
- > Removed the antibodies



sGP

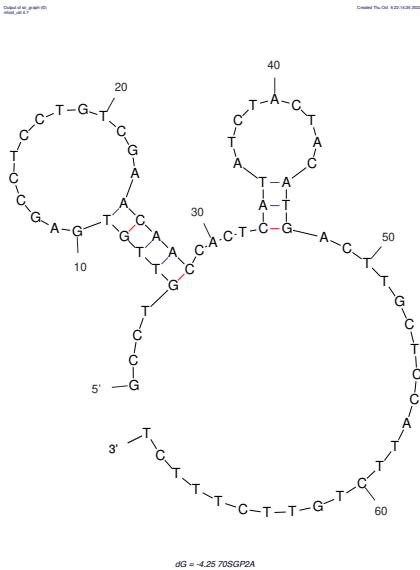
Prediction EBOV sGP and Marburg GP structure using Alphafold 2



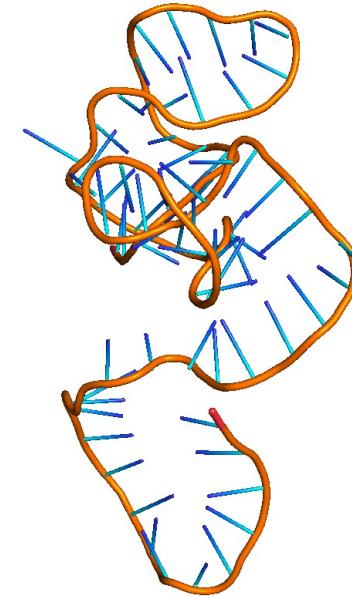
A. Sudan EBOV sGP, B. Tai Forest, C. Bundibugyo, D. Bombali, E. Reston, F. Marburg GP

Molecular modeling: Aptamer secondary and tertiary structure

70SGP2A

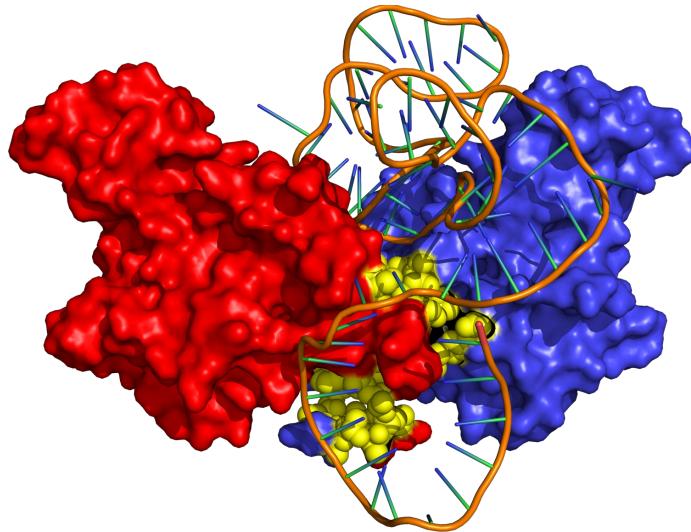


UNAfold- 23 °C



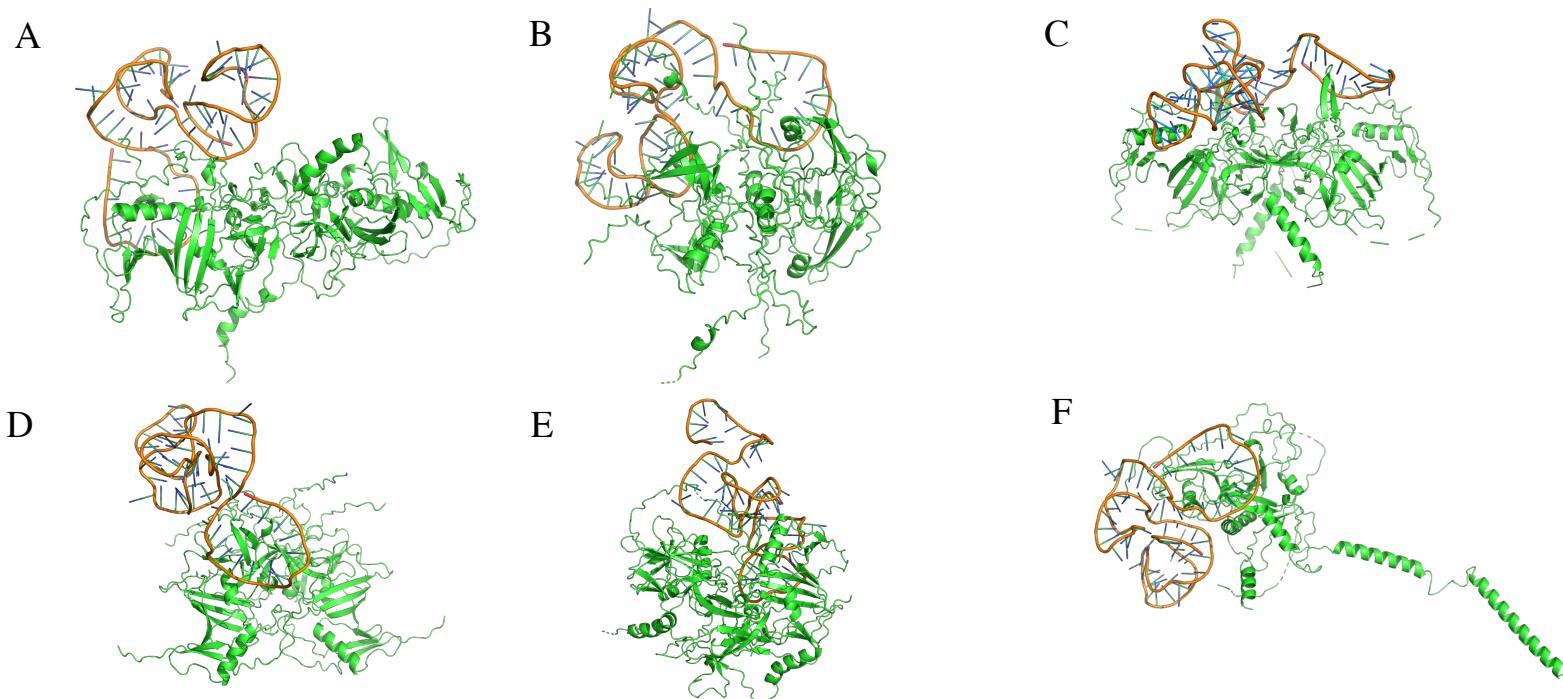
3dRNA/DNA web server

Molecular modeling-Docking



Zaire sGP docked to EBOV aptamer

Molecular docking of EBOV sGP and Marburg GP to 70SGP2A aptamer

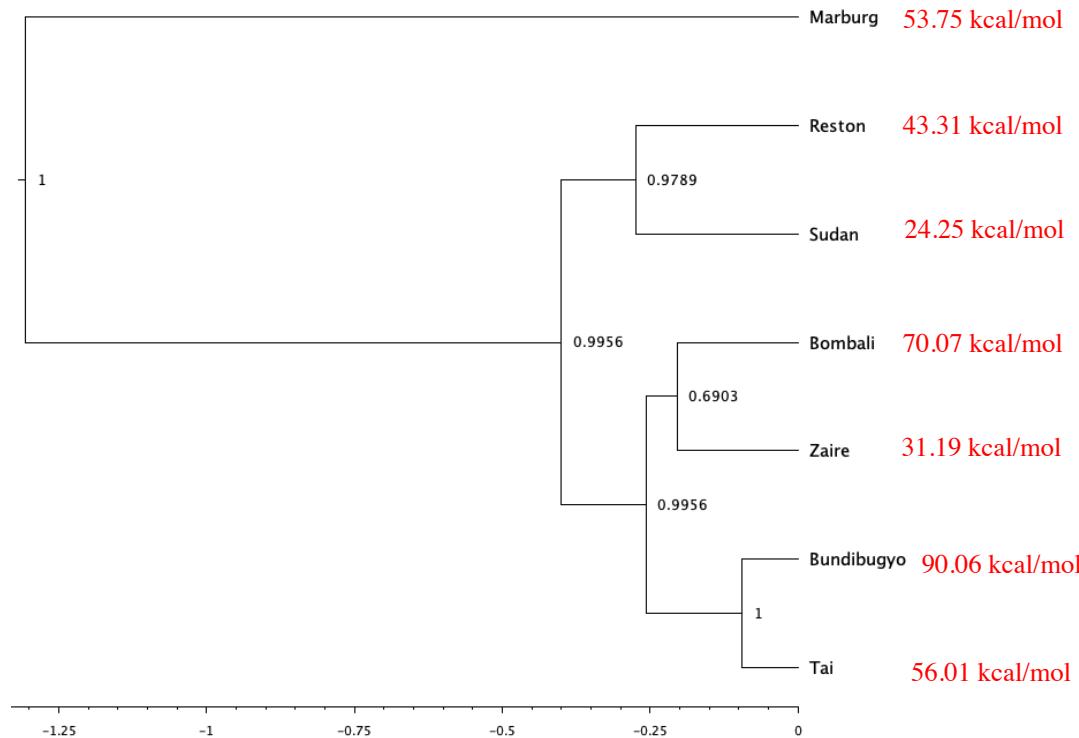


A. Sudan EBOV sGP, B. Tai Forest, C. Bundibugyo, D. Bombali, E. Reston, F. Marburg GP

Predicting binding energy using FoldX

Virus name and protein	Energy of binding (kcal/mol)
Bombali EBOV sGP	70.07
Bundibugyo EBOV sGP	90.6
Reston EOV sGP	43.31
Sudan EBOV sGP	24.25
Tai Forest EBOV sGP	56.1
Zaire EBOV sGP	31.19
Marburg virus GP	53.75

EBOV sGP phylogenetic tree with the predicted binding energies



Summary

- > Generated Bayesian Phylogenetic tree for EBOV sGP
- > Predicted binding energy of EBOV sGP to 70SGP2A aptamer
- > Compared the binding energy values with the evolutionary relationship of different strains of EBOV virus

Thank you