Summary and Conclusions

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The comparative genome (nucleotide) analysis revealed that the Dengue Virus genome has 56.12 identity-similarities score with West Nile Virus whereas 52.59 score with Yellow Fever virus. Then the West Nile Virus has the 53.63 score with Yellow Fever Virus. The sequence alignment of three viruses revealed that all are belongs to the same family due of above fifty percent alignment score, indicates that remaining forty percent above sequence is in non-homology in nature. This non homology nature of sequence may be forms the specific characters in individual viruses.The sequence identity and similarity is equal from one virus to others means, they have historically close relation with each other.

In searching of non-human related proteins in viruses shown that the Dengue Virus has only one that type of non-human protein i.e. non-structural protein NS2A (NP_733808).Whereas the West Nile Virus have four non-human proteins including anchored core protein C (NP_776011.1), non-structural protein NS2A (NP_776016.1), non-structural protein NS5 (NP_776022.1) and core protein c (NP_776010.1). The Yellow Fever Virus not has any non-human proteins. The non-human proteins difference in number and protein names among three viruses may be due to the variation in genome itself. Although the three viruses shown fifty percent genome identity and similarity score, the dengue virus has only one protein non-homology with human, West Nile Virus have four protein non-homology proteins And Yellow Fever Virus not have non-homology proteins with the humans. These results revealed that the non-human proteins which are specific to the viruses are different from virus to virus although they are belongs to the same family.

Selected therapeutic drugs (Mycophenolic acid, Castanospermine, Triaryl pyrazoline, Ribavirin, and 6- Azauridine), are commonly act on the three viruses but their inhibitory concentrations are different to each virus was supports ourdocking results through the docking studies for non-human proteins. The results revealed that the drug Triaryl pyrazoline have differently binding affinity with the all non-human proteins of viruses (with Dengue Virus NS2A -7.5 kcal/mol, with anchored core protein c of West Nile Virus was -7.9 kcal/mol, with NS2A of westnile virus was -8.8 kcal/mol, with NS5 of West Nile Virus was -7.1 and with Core protein of west nile virus was -8.1 kcal/mol.). the other drugs also

not shown similar binding affinity with non-human proteins and also not shown the similar hydrogen bond interactions although it has common hydrogen bond donors and acceptors for all proteins. This difference in binding affinity and hydrogen bond interactions may be due to drug binding site amino acid composition in proteins and variation accessibility of drug into the active site of the proteins in viruses. This was due to direct link with genome sequence identity and translational effect on amino acid composition in viruses.

The non-structuralproteins of three viruses' homology relation clearly indicated that the same proteins in three viruses have the different amino acid sequence, accordingly their sequence identity and similarity score also differ from each other. Here three viruses came from common ancestor and belongs to the same family *Flaviviridae* and drugs which act on any one of the virus also shown their action on other two viruses (inhibitory concentration is vary) this is may be because of variation in their amino acid composition for each protein in viruses. Dengue Virus NS1 relationship score with the West Nile Virus is 42.05 and same protein relation with the Yellow Fever Virus was 51.42 whereas the West Nile Virus has 44.03 relational score value with the Yellow Fever virus.Dengue NS2A and NS2A of West Nile virus was 22.94, the score between Dengue and Yellow Fever Virus was 19.72 and 26.34 relationship score was showed between West Nile and Yellow Fever Virus. The Dengue virus NS2B protein has relation with West Nile virus was 29.23. The Dengue virus has 30.77 relational score with the Yellow Fever Virus. The West Nile Virus has the 27.69 relational score with the Yellow Fever Virus. The Dengue Virus NS3 showed 62.36 relational score with the NS3 protein of West Nile Virus and 51.86 relational score with the Yellow Fever virus. The West Nile Virus has showed 52.99 relation score with Yellow Fever Virus. The 36.15 relational score showed Dengue virus with the West Nile virus whereas 30.16 score with the Yellow Fever virus. The West Nile Virus showed 30.16 relational score with The Yellow Fever Virus. The evolutionary relationship among Dengue, West Nile and Yellow Fever Virus's NS4B protein was revealed that the Dengue Virus has 38.55 relational score with West Nile Virus and 34.94 score with Yellow Fever Virus. The West Nile Virus has the 30.4 relational score with the yellow fever virus.The evolutionary relationship for NS5 protein of Dengue virus with the West Nile Virus was 65.18 similarity-identity score whereas 60.29 similarity-identity score with Yellow Fever Virus. The West Nile Virus has the 60.44 similarity-identity score with the Yellow Fever Virus. It is clearly

explained that the proteins function and name is similar in there viruses the amino acid composition and their homology is difference.

The non-structural protein of the three viruses with therapeutic drugs revealed that the drug Triaryl pyrazoline only showed highest binding affinity with the all non-structural proteins of three viruses. In Dengue Virus the tri aryl pyrazoline showed highest binding affinity with NS3 protein where as in West Nile Virus highest binding affinity with NS1 protein and in Yellow Fever Virus highest binding affinity with the NS3. The same drug with different binding affinity with same proteins of same family may be due to the drug binding domain amino acid sequence composition from translation depending on genome sequence. Although amino acid sequence in drug binding domain of proteins have different, the function is same, it may due to not all the amino acids domain are not involved in the function of the protein few of them play key role.

In conclusion the three viruses (DENV, WNV and YFV) belongs to the same family *Flaviviridae* the genome sequence fifty percent different from each other, it produced the different protein products during translation that's why the non-human proteins also different for three viruses. Due to variation in sequence variation for single protein in three viruses the drug binding capacity is differs. These all are may be reasons for the drugs which are act on three viruses but their inhibitory concentration is differing.