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Potential Use of Banana Lectin to Detect or Cure Ebola Virus

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Abstract: To investigate protein, protein interactions between banana lectin and Ebola virus glycoprotein (Ebola GP). As snowdrop lectin was previously shown that it could bind to Ebola GP and removed Ebola virus from the patient's blood, thus, its interactions with Ebola GP were also investigated and used as a reference. Structures of Ebola virus glycoprotein and the two lectins were downloaded from PDB. Non-amino acid atoms were removed. The resulted structures were then energy minimized protein-protein dockings between Ebola GP and each of the lectins were subsequently studied. The correctness of the docking results from various methods was investigated using structure superposition method Interactions between Ebola GP and each of the lectins in the docked results were then investigated. Ebola glycoprotein bound preferably to banana lectin. Although, it is a dimeric protein, it could bind Ebola GP relatively well, compared to the binding of tetrameric snowdrop lectin to Ebola GP. Various amino acid residues were found to contribute to the interactions between Ebola GP and the two lectins. The results suggested the potential use of banana lectin in detecting Ebola virus or curing Ebola virus disease.

Key words: Ebola virus, glycoprotein, snowdrop lectin, banana lectin, protein-protein interactions, suggested

INTRODUCTION

Ebola virus disease is a hemorrhagic fever disease with high mortality rate of up to 90% (Cooper and Bavari, 2015; Lee and Saphire, 2009). Ebola virus is an enveloped RNA virus of Filoviridae family (Lee and Saphire, 2009). Although, there are five species of Ebola viruses, the latest Ebola virus disease outbreak in Africa was caused by Zaire Ebola virus (Cooper and Bavari, 2015). The surface glycoprotein of Ebola virus, Ebola GP, involves in the host cell entry of Ebola virus (Lee and Saphire, 2009). Thus, it is a good target for Ebola virus curing and detection development.

Lectins can specifically bind various glycoproteins (Akkouh *et al*., 2015). Diverse lectins are found in plants, animal and bacteria (Akkouh *et al*., 2015). They are involved in various biological processes such as cell targeting, host-pathogen interactions, apoptosis induction and cancer metastasis (Akkouh *et al*., 2015; Singh *et al*., 2014; Chau *et al*., 2015). The fruit of banana plant (*Musa acuminata*), banana, contains a mannose-specific lectin called banana lectin or BanLec (Akkouh *et al*., 2015; Singh *et al*., 2014). This lectin was shown to suppress HIV infection by binding to the glycosylated viral envelope (Akkouh *et al*., 2015; Singh *et al*., 2014). A plant lectin also possesses this ability is snowdrop lectin (Chau *et al*., 2015). Snowdrop (*Galanthus nivalis*) is a common herbaceous plant in Europe and parts of America Its mannose-specific lectin is called snowdrop lectin or *Galanthus nivalis* Agglutinin (GNA). Apart from inhibiting HIV infection, snowdrop lectin was also successfully used in lectin affinity plasmapheresis therapy to bind and eliminate Ebola virus from the infected patient's blood (Buttner *et al*., 2014). This resulted in the recovery of the patient.

Although, banana lectin could bind to HIV glycoprotein, its interactions with Ebola GP have never been studied. This study thus investigated protein-protein interactions of banana lectin to Ebola GP and the potential use of this lectin in detecting Ebola virus or curing Ebola virus disease. As snowdrop lectin was shown to successfully bind to Ebola virus (Buttner *et al*., 2014), protein-protein interactions between snowdrop lectin and Ebola GP were also investigated and used for referencing purpose.

MATERIALS AND METHODS

Structure of Zaire Ebola GP (Zhao *et al*., 2016), 5JQ3 was downloaded from Protein Data Bank (PDB) (Berman *et al*., 2000). Biological assembly of the structure as a trimeric protein was also downloaded from PDB Ebola GP in its trimeric form was then used in this study. Two plant lectins downloaded from PDB to investigate their

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interactions with Ebola GP were: banana lectin (2BMY) (Meagher *et al*., 2005) and mannose-specific snowdrop lectin (*Galanthus nivalis* agglutinin, 1MSA) (Hester *et al*., 1995).

Investigation of interactions between Ebola GP and the lectins: To prepare these structures for protein-protein docking step, non-amino acid atoms in these structures were removed using Jmol (Hanson, 2010). These structures were subsequently energy minimized using Yasara structure (Krieger *et al*., 2009). The resulted structures were then used for further investigation. Protein-protein interactions between Ebola glycoprotein and the lectins were investigated using two protein-protein docking servers: ClusPro 2.0 (Kozakov *et al*., 2013) and pyDockWeb (Cheng *et al*., 2007). Molecular visualization and analysis of all the structures including the protein-protein docking results were done using the following bioinformatics programs: Chimera (Pettersen *et al*., 2004) and Discovery Studio 4.5 Visualizer (Biovia, 2016).

RESULTS AND DISCUSSION

For ClusPro 2.0 server, the first and the highest rank model of the docking results between Ebola GP and snowdrop lectin obtained from using the balanced coefficient was used. This was because the server recommended using it when no prior knowledge of the forces dominate in the protein-protein complex was known. For the protein-protein docking results between Ebola GP and banana lectin, the first and the highest rank model from ClusPro 2.0 server employing the balanced coefficient was used.

pyDockWeb server yielded results of all possible docking poses between Ebola GP and each of the two lectins along with their ranking scores. Using these scores along with manual inspection, for each of the lectins only the highest rank model of the docking results was selected for further investigation.

To ensure the correctness of the selected docking models for each of the lectins, structure superposition method was used to compare the results obtained from using ClusPro 2.0 and pyDockWeb. The results are shown in Fig. 1 and 2. From Fig. 2, it is clear that the docking results were correct as the protein-protein complex poses from the two methods were almost identical. The docked structures were also further evaluated using Ramachandran plot (not shown). The results also suggested that the obtained docked structures were correct.

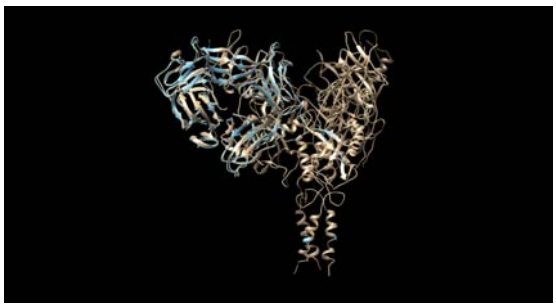

Fig. 1: Structure superposition of the highest rank docking models between Ebola GP and snowdrop lectin obtained from using ClusPro 2.0 (color in yellow) and pyDockWeb (color in blue). The resulted docking structure poses obtained from the two servers were almost identical

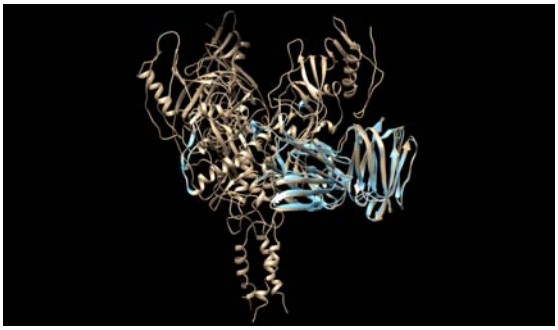

Fig. 2: Structure superposition of the highest rank docking models between Ebola GP and banana lectin obtained from using ClusPro 2.0 (color in blue) and pyDockWeb (color in yellow). The resulted docking structure poses obtained from the two servers were almost identical

In the protein-protein docking result between Ebola GP and tetrameric snowdrop lectin, the fusion loop and mucin domain of Ebola GP (Lee and Saphire, 2009) were involved in its interactions with snowdrop lectin as shown in Fig. 3. Although, banana lectin structure was smaller, it could still bind relatively well to Ebola GP (Fig. 4) and could cover substantial areas of Ebola GP to block its normal functioning (Fig. 2).

It should be noted that in each of the docking results only one lectin molecule was shown to bind to Ebola GP However, biological assembly of Ebola GP is a trimeric protein Thus in nature three molecules of the considered lectin should bind to Ebola GP in similar binding poses to those shown in Fig. 1 and 2.

The interactions in the complex structures between Ebola GP and each of the lectins were investigated. The amino acids contributed to the interactions between Ebola

Table 1: Residues participated in the interactions between Ebola GP and snowdrop lectin

Polypeptide chain of the participated residues from Ebola GP (Chain)	Participated residues from Ebola GP	Polypeptide chain of the participated residues from snowdrop lectin (Chain)	Participated residues from snowdrop lectin
A	Ala148	B	Phe53
A	Glu287	D	Ser11
A	Trp288	D	Pro67
B	Gly528	B	His107
B	Leu529	C	Asp91
B	Gly536	B	Thr58
B	Pro537	B	Asn81
B	Ala538	B	Thr58
B	Ala538	B	Asn81
B	Gly541	B	Asn81

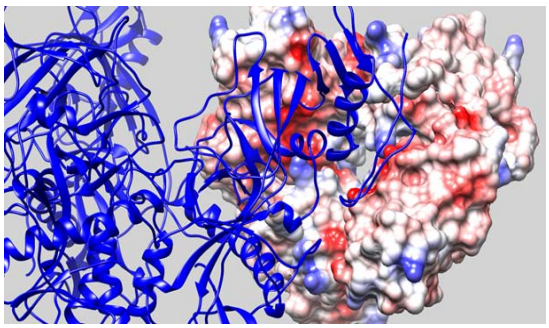

Fig. 3: Fusion loop and mucin domain of Ebola GP (shown in its ribbon form) were involved in its interactions with snowdrop lectin (shown in its surface form)

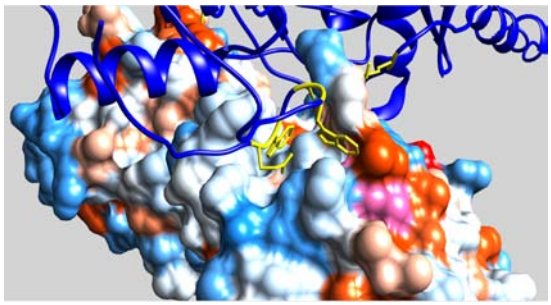

Fig. 4: Interactions between banana lectin (shown in its surface form) and Ebola GP (shown in its ribbon and stick form)

GP and snowdrop lectin are shown in Table 1. In Table 2, the amino acids contributed to the interactions between Ebola GP and banana lectin are shown. The distances of these amino acids from their interacting partners were <3 angstroms. Thus the results in this study show that banana lectin could favorably bind to Ebola GP. Ebola GP could thus potentially be further developed for Ebola virus detection or Ebola virus disease curing.

Table 2: Residues participated in the interactions between Ebola GP and banana lectin

Polypeptide chain of the participated residues from Ebola GP (Chain)	Participated residues from Ebola GP	Polypeptide chain of the participated residues from banana lectin (Chain)	Participated residues from banana lectin
A	Trp288	A	Leu139
A	Trp288	A	Ile5
A	Ala289	A	Asn2
A	Trp291	A	Pro22
A	Glu292	A	Glu140
B	Lys510	A	Met1
B	Lys510	A	Gly3
B	Ala525	B	Val7

CONCLUSION

From this study, banana lectin could favorably bind to Ebola GP. Thus, banana lectin could potentially be developed for Ebola virus detection. As Ebola GP is responsible for Ebola virus infection in host cell, its binding to banana lectin would block the normal functioning of Ebola GP. This would subsequently deter Ebola virus infection. Thus potentially banana lectin could also be developed for Ebola virus disease curing.

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