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Docking studies on fungal lectin for inducing tumor necrosis factor related apoptosis inducing ligand-receptor 2 (TRAIL-R2): Using Hex

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ABSTRACT

Tumor necrosis factor Related Apoptosis Inducing Ligand (TRAIL) is member of cytokines which induce apoptosis only on cancer cells, by binding with their receptors called TRAIL-R1 and TRAIL-R2. But almost all cancerous cells are resistance to TRAIL mediated apoptosis. Here we described the docking of fungal derived lectins for induction of TRAIL-R2. Four fungal lectins Sclerotinia sclerotiorum (SSL), Flammulia velutipes (FVL), Psathyrella velutina (PVL), Xerocomus chrysenteron (XCL) and TRAIL-R2 structure were derived from Protein Data Bank. The binding energy of fungal derived Lectins with TRAIL-R2 were estimated by using Hex 6.0 docking software. All fungal derived Lectin peptides were showed good binding energy, among them XCL showed excellent binding energy (-539.72). Further in vitro and in vivo study is needed to confirm the up regulation of TRAIL-R2, decipher to TRAIL.

Key words: Anticancer, TRAIL, Docking

INTRODUCTION

Cancer is uncontrolled growth of cells, which may cause by physical, environmental metabolic, chemical and genetic factors [1]. Majority (90-95%) of cancer can be caused by factors such as tobacco, obesity, infections, radiation, and 5-10% of cancer causing due to the heredity. According to WHO's report in 2007, cancer cause human death about 7.9 million per year in worldwide and it will increase up to 12 million by 2030 [2]. So, all over the world development of new drug against cancer is vital at this moment.

Lectins, a group of highly diverse non- immune origin peptides found in plants, animals and fungi, and it is specifically bind to free sugars, glycans, glycoproteins and glycolipids without altering the structure of carbohydrate [3]. Lectins are capable of differentiate malignant tumors form normal cells [4], and it is used for diagnosis purpose [5]. Moreover lectins are having very good anticancer property, they killing the cancer cells via triggering the programmed cell death (PCD) [6]. TRAIL (Apo2L) is expressing on various immune cells include natural killer (NK) cells, T cells, natural killer T cells (NKT cells), dendritic cells and macrophages, they can also induce apoptosis via engage their cognate receptors on cancer cells, this process is known as extrinsic apoptosis. In the pathological condition, TRAIL-Rs are resistant to binding with its Ligand and apoptosis is not carried out properly. So the present investigation was aimed to come over this issue, it implicated analyze the binding efficiency of fungal lectins with TARIL-R2 by using Hex6.0 docking software.

MATERIALS AND METHODS

In the present investigation we used Protein Data Base and Hex 6.0 docking software.

The PDB (Protein Data Bank) was established in Brookhhaven National Laboratories (BNL) in 1971. It is an archive for biological macromolecular crystal structure, deposition of structural information of the macromolecules which determined by the X-ray crystallographic, NMR methods etc [7, 8].

Hex is an Interactive Molecular Graphics Program for calculating and displaying feasible docking modes of pairs of protein and DNA molecules. Hex can also calculate protein-Ligand Docking, assuming the ligand is rigid, and it can superpose pairs of molecules using only knowledge of their 3D shapes. It is still the only program using Spherical Polar Fourier (SPF) correlations to accelerate the calculations and its one of the few docking programs which has built in graphics to view the result. Also it using the modern graphics processor units to accelerate the calculation [9].

The structure of TRAIL-R2 and fungal lectin peptides, lectins SSL (2X2S), FVL (1OSY), PVL (2BWR), XCL (1XIO) were retrieved from PDB. The docking analysis was carried out in Hex 6.0 docking software. The fugal derived lectins binding with TRAIL-R2 were identified via docking and their binding energies were obtained.

Docking Parameters.

Correlation type – Shape only, Grid Dimension – 0.6,
Receptor range – 180, Ligand Range – 180,
Twist range – 360, Distance Range–40.

The fungal lectins were docked with the TRAIL-R2 using the above parameters.

RESULTS AND DISSUSION

The docking results were obtained, binding energy between TRAIL-R2 and fungal lectin were showed in Table.1. All fungal lectin showed good binding energy. Particularly XCL showed strong binding energy value (-539.72), and least was observed in PVL (-389.83).

Table 1.Binding Energy value of Fungal Lectins with TRAIL-R2

S.No	Name of Fungal Lectin	E- Value
1	SSL	-517.43
2	FVL	-533.24
3	PVL	-389.83
4	XCL	-539.72

Present investigation is suggesting that fungal derived lectins are capable to bind with the TRAIL-R2. By analyzing the binding energy values of Table.1, all lectin were decrease in energy values, it indicates lectin peptides are compatible with the TRAIL-R2. XCL was found to be most compatible peptide, it stimulate drastic changes in the actin cytoskeleton after binding at the cell surface and internalization, also having insecticidal activity. XCL contain 140 amino acid residues, ß- standard. This protein fold never reported with other lectins protein family and displays no sequence similarity in databases. The special feature of XCL is target specific components of membrane bilayers, and form cavity in proteins [10]. But reason for high affinity with TRAIL-R2 is not know. FVL having low binding energy next to XCL, it is reported for enhancing transcription of IL-2, IFN-g and TNF-a, and hemagglutinates red blood cells. FVL also in ß- standard structure, this structure may critical for their activity [11].

Several plant lectins are reported to activate the TRAIL-Rs. Ricin-B was reported to up regulated the expressions of caspase 8, caspase 7 and caspase 3 [12], Caspase 8 may induced via TRAIL-Rs. GNA- related lectin triggers both intrinsic and extrinsic pathways of apoptosis, GNA- lectins with mutation sites is binding with various receptors of cancerous cell and causing cell death by different signaling pathways [13]. PCL is lectin which isolated from Polygonatum cyrtonema, it induce the apoptosis with activation of caspase-9, caspase-8 and caspase-3 activation in L929 and A375 cells [14]. Mannose binding lectin POL was observed to induce the cell death via death receptors of FasL and Fas-Associated protein with Death Domain (FADD) proteins and results in caspase-8 [15]. FasL and

FADD proteins are associated with TRAIL-Rs, where they act as adaptor proteins. So far three different plant lectins (ConA, PHA-L, ML-I) are currently in clinical trials for different cancer therapy [16]. Among them anticancer property of ML-I hypothesized for inducing the tumour necrosis factor-alpha (TNFalpha) family receptors. But, there is no much study focused on fungal lectins for screening anticancer property as well as their binding capacity towards TRAIL-Rs. Our study has revealed the binding effeiceiency of fungal lectin with TRAIL-R2, this binding may activate the apoptosis.

Figure 1: Docking result of TRAIL-R2 with *Sclerotinia sclerotiorum* Lectin (SSA)

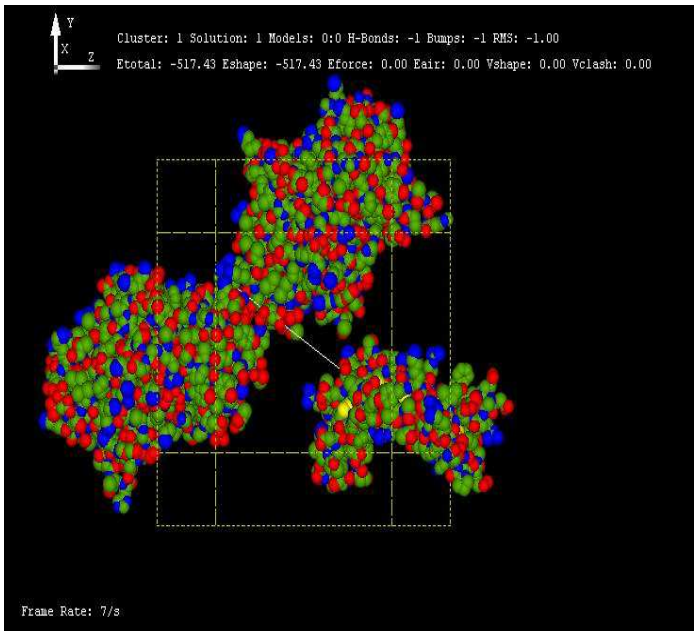


Figure 2. Docking result of TRAIL-R2 with *Flammulia velutipes* Lectin (FVL)

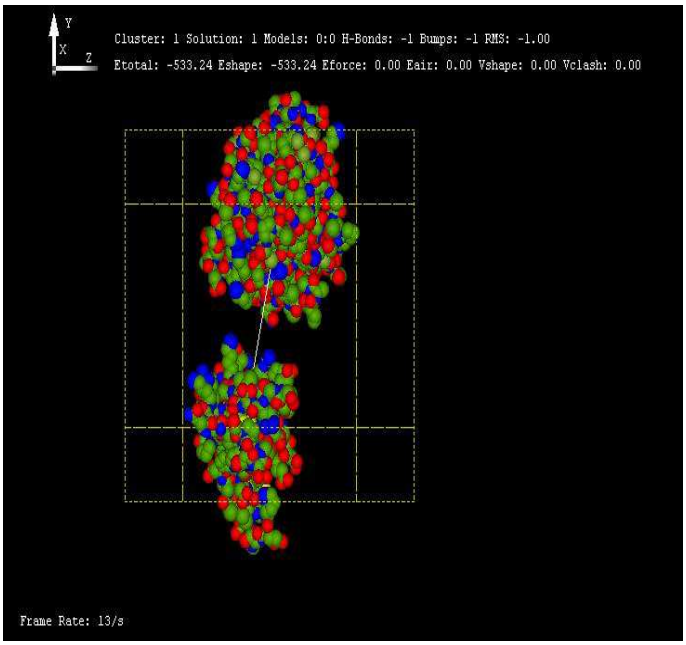


Figure 3. Docking result of TRAIL-R2 with with *Psathyrella velutina* Lectin (PVL)

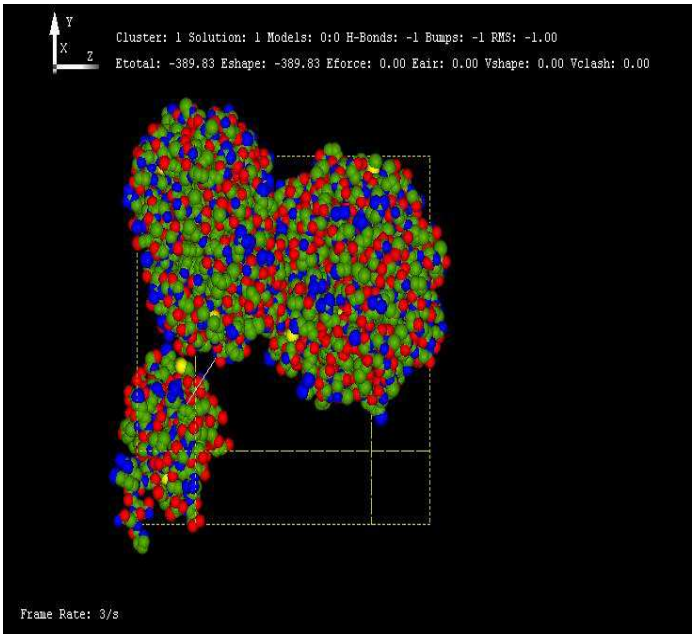
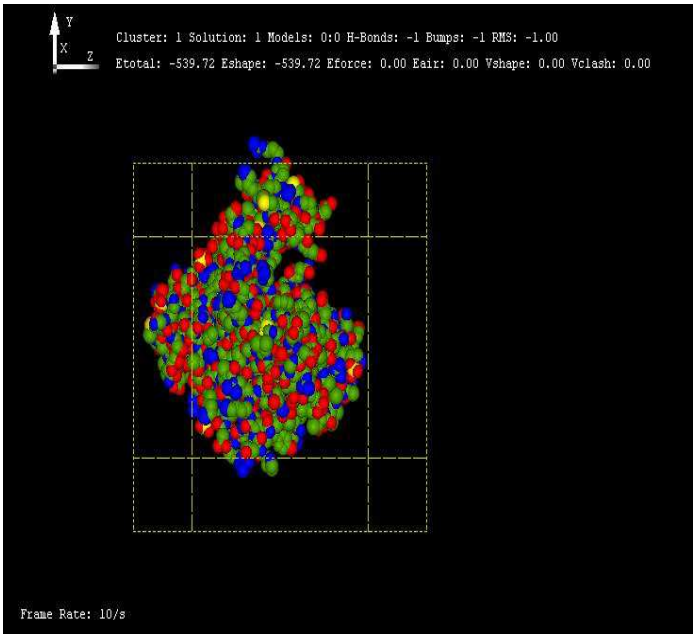


Figure 4. Docking result of TRAIL-R2 *Xerocomus chrysenteron* Lectin (XCL)



CONCLUSION

Fungal lectin might also posses very good anticancer property equal to plant lectin which need to be explore. Untapped fungal lectins having extreme affinity power towards the TRAIL-R2, so it can be potent anticancer agent. Further in vitro and in vivo study is needed to confirm the induction of extrinsic apoptosis pathway mediating by TRAIL-R2.

REFERENCES

[1] Anupama P, Rajesh S, Maheshwari I, *Der. Pharmacia. Sinica*, **2013,** 4 (3), 121-129.
[2] Hitesh D P, Saavani A S, *Der. Pharmacia. Sinic*, **2012,** 3(2), 199-210.
[3] Van Damme E J, Peumans W J, Barre A, Rouge P, *Crit. Rev. Plant. Sci*, **1998**, 17, 572-692.
[4] Mody R, Joshi S, Chaney W, Phar J. *Toxi. Med*, **1995,** 33, 1-10.
[5] Gupta G, Surolia A, Sumpathkumar S G, *OMICA*, 2010, 14, 419-436.
[6] Li C Y, Meng L, Liu B, Bao J K, *Curr. Chem. Bio*, **2009,** 3, 323-333.
[7] Helen M B, John W, Zukang F, Gary G, Bhat T N, Helge W, llya N S, Philip E B, *Nucl. Aci. Res*, **2000,** 28, 235-242.
[8] Daisy P, Suveena S, *Der Pharma Chemica*, **2010**, 2(6), 67-72
[9] Dave Ritchie, Hex 6.3 *User Manual, Laboratoire lorrain de recherché en informatique et ses application*, France, **2010**, pp 1.
[10] Catherine B, Luminita D, Marty-Detraves C, Andre L, Schulze-Briese C, Patrice K, Didier F, Paquereau L, Jean-Pierre S, *J.mol.Biol*, **2004**, 344, 1409- 1420.
[11] Palasingam P, Jeremiah S J, Seow S V, Shai V, Howard R, Kaw Y C, Prasanna R K, *J.Mol.Biol*, **2003,** 332,461-470.
[12] Polito L, Bortolotti M, Farini V, Battelli M G, Barbieri L, Bolognesi A, *Int. J. Biochem. Cell. Biol*, **2009,** 41, 1055-1061.
[13] Peng H, Lv H, Wang Y, Liu Y H, Li C Y, Meng L, *Pept*, **2009,** 30, 1805-1815.
[14] Zhang Z T, Peng H, Li C Y, Liu J J, Zhou T T, Yan Y F , *Phytomedi*, **2010**,18, 25–31.
[15] Y. Karasaki, S. Tsukamoto, K. Mizusaki, T. Sugiura, S. Gotoh, *Food Res Int.* **2001**, 34, 7–13.
[16] Lei-lei F, Cheng-cheng Z, Shun Y, Jia-ying Y, Liu B, Jin-ku B, *Int. J. Biochem. Cell. Biol*, **2011,** 43, 1422-1449.