Protein-Protein interaction studies between TSHR Protein in Human and Photosystem II Protein D1 of *Ulva fasciata* using *Insilico* Protocols

Abstract

The most prevalent mutation in Hypothyroid Protein, TSHR impacts the course and prognosis of Hypothyroidism in human. We employ 3D *Insilico* drug docking techniques to make the possible mutant TSHR interact with Photosystem II Protein D1 of *Ulva fasciata*. To carry out drug docking techniques, the translated amino acid sequence and three-dimensional chemical compound were obtained from the NCBI database. The use of sophisticated 3D molecular visualization tools was employed in post-docking experiments. The use of sophisticated 3D molecular visualization tools was employed in post-docking experiments. The docking study results unequivocally show that Photosystem II Protein D1 directly suppresses amino acid mutational sites. TSHR and Photosystem II Protein D1's electrostatic force is depicted in a three-dimensional manner using notions from molecular dynamics techniques. In the end, we determined that Photosystem II Protein D1, a medicinal component of *Ulva fasciata*, helps in treating hypothyroidism. Hypothyroidism, being one of the major Endocrinological disorders, our research work helps to prove that the sea weed, *Ulva fasciata* can effectively act a novel therapeutic agent for treating this disorder.

Keywords: TSHR, *Ulva fasciata* and Protein Docking

Introduction

A diverse range of illnesses, including hypothyroidism, hyperthyroidism, subclinical hypothyroidism (SH), subclinical hyperthyroidism, structural abnormalities, and malignancy,

are referred to as thyroid disorders (TD) [1]. Globally, the incidence of TD and associated impact have increased dramatically due to rising life expectancy, particularly in older persons [3]. Different regions have different incidence and frequency of TD. But some TD, like hypothyroidism, are thought to impact 5% of the world's population [4], whereas hyperthyroidism affects 0.8% and 1.3% of people in Europe and the USA, respectively [2,5]. Additionally, the age-standardized thyroid carcinoma (TC) rates for women and men worldwide are 3.1 and 10.1 per 100,000, respectively [6].

There are reports that hypothyroidism is also common in the Arabian Gulf States [7], but treatment for it is frequently uneven and incorrect. In Saudi Arabia, no studies examining hypothyroidism at the population level have been carried out. However, primary hypothyroidism prevalence was reported to be 47.8% in a cross-sectional study that was carried out in outpatient clinics of a tertiary care hospital in Riyadh between December 2018 and December 2019. The study comprised 463 patients [8]. Additionally, 10% of patients visiting a primary care clinic had subclinical hypothyroidism, according to cross-sectional study conducted in Riyadh [9]. Comparably, another study carried out in Saudi Arabia estimated that the prevalence of hypothyroidism was 18.7%; 72.9% of individuals reported feeling lethargic and sluggish, and 69.4% reported experiencing mood swings [10]. Furthermore, a study done in the Al Bahah region revealed that subclinical hypothyroidism was common among a sample of 567 Saudis (15.9%) [11].

The anti-cancer properties of *U. fascicata* have been demonstrated by a number of earlier investigations. Ulvan's ability to fight cancer has been investigated in a number of ways. Ulvan is one such chemopreventive drug that can be utilized to treat liver cancer [12, 13, 14]. Sulfated polysaccharides found in ulvan inhibit the growth of hepatocellular cancer and cause apoptosis. Recently, it has been found that *U. lactuca, U. australis, U. compressa, U. rigida, and U. ohnoi* exhibit the anticancer effect of ulvan. We have demonstrated in our study how U. fasciata can be used to treat hypothyrodism.

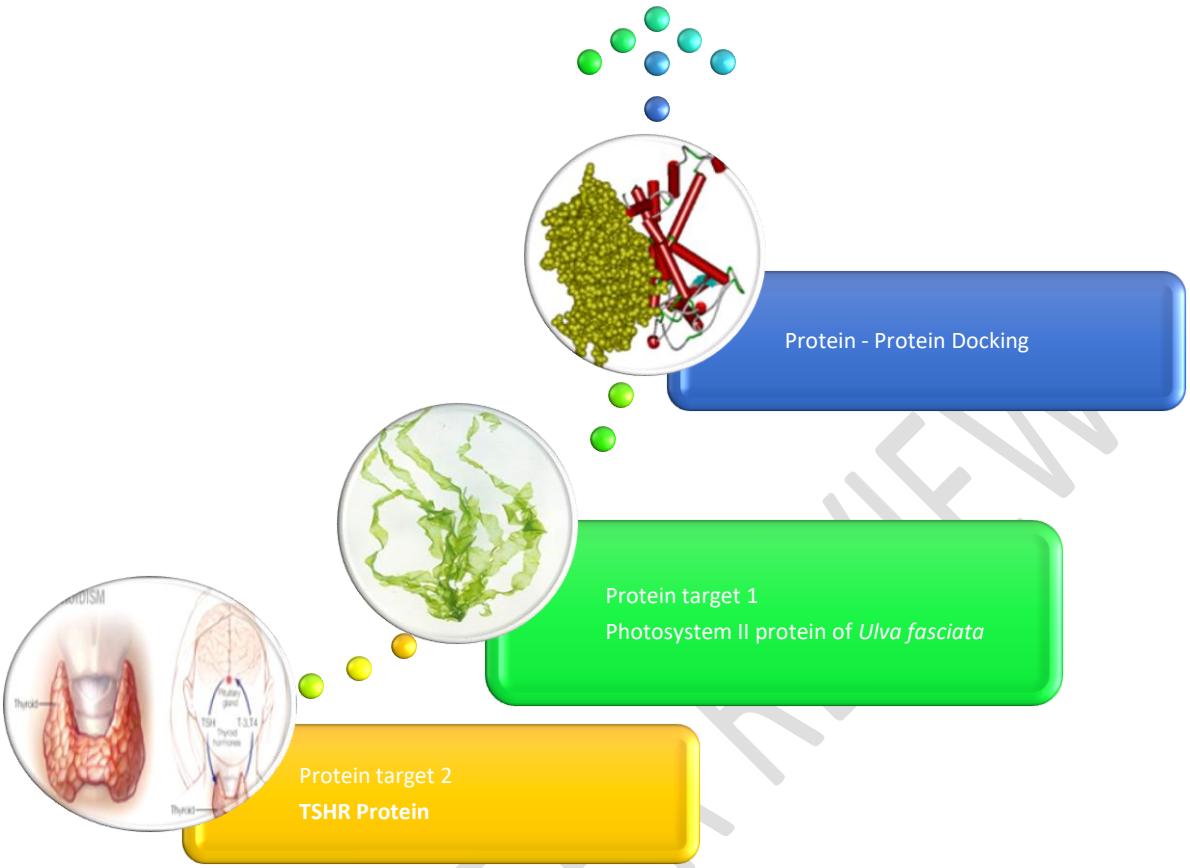
We conducted a detailed molecular analysis of the interactions between the human Thyroid Stimulating Hormone Receptor (TSHR) and *Ulva fasciata's* Photosystem II Protein D1. The final results unambiguously demonstrated how the thyroid stimulating hormone receptor inhibits Photosystem II Protein D1.

Methodology

Protein selection: For the purpose of conducting molecular drug docking study, the data was used from the NCBI Genpept database (YP_009220463.1 photosystem II protein D1 [15] (*Ulva fasciata*) and (AAI20973.1 TSHR protein (Human). Three-Dimensional structures were predicted using Discovery Studio, a potent molecular visualization program.

Protein Docking: Molecular drug docking research have made use of HDOCK, an automated molecular drug docking service (http://hdock.phys.hust.edu.cn/) [16]. The molecular affinities of TSHR protein and photosystem II protein D1 (Ulva fasciata) in human hypothyroidism were determined by means of a 3D molecular dynamics technique.

H Bond interactions: Post-docking experiments were carried out using the Discovery Studio program. A detailed analysis of the three-dimensional image based on the docking score (3D Electrostatic interactions) was conducted using the molecular dynamics concept.



Pic 1. Diagrammatic depictions of the *Insilico* research project overview

Result and Discussion

Ulva fasciata

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>YP_009220463.1 photosystem II protein D1 (chloroplast) [Ulva fasciata]
MTAILERREASSLWARFCEWVTSTENRLYVGWFGVIMIPTLLTAISVFIIAFVAAPPVDIDGIREPVSGS
LLYGNNIISGAVVPTSNAIGLHFYPIWEAASVDEWLYNGGPYQLIVCHFFLGVCAYMGREWELSFRLGMR
PWIAVAYSAPVAAASAVFIVYPIGQGSFSDGMPLGISGTFNFMIVFQAEHNILMHPFHMLGVAGVFGGSL
FSAMHGSLVTSSLIRETTENESANEGYKFGQEEETYNIVAAHGYFGRLIFQYASFNNSRSLHFFLAAWPV
VGIWFTALGISTMAFNLNGFNFNQSIVDSQGRVLNSWADIINRANLGMEVMHERNAHNFPLDLASVEAPS
ING
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Fig.1: Amino acid sequence of the sea weed, *Ulva fasciata*

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>AAI20973.1 TSHR protein [Homo sapiens]
MRPADLLQLVLLLDLPRDLGGMGCSSPPCECHQEEDFRVTCKDIQRIPSLPPSTQTLKLIETHLRTIPSH
AFSNLPNISRIYVSIDVTLQQLESHSFYNLSKVTHIEIRNTRNLTYIDPDALKELPLLKFLGIFNTGLKM
FPDLTKVYSTDIFFILEITDNPYMTSIPVNAFQGLCNETLTLKLYNNGFTSVQGYAFNGTKLDAVYLNKN
KYLTVIDKDAFGGVYSGPSLL
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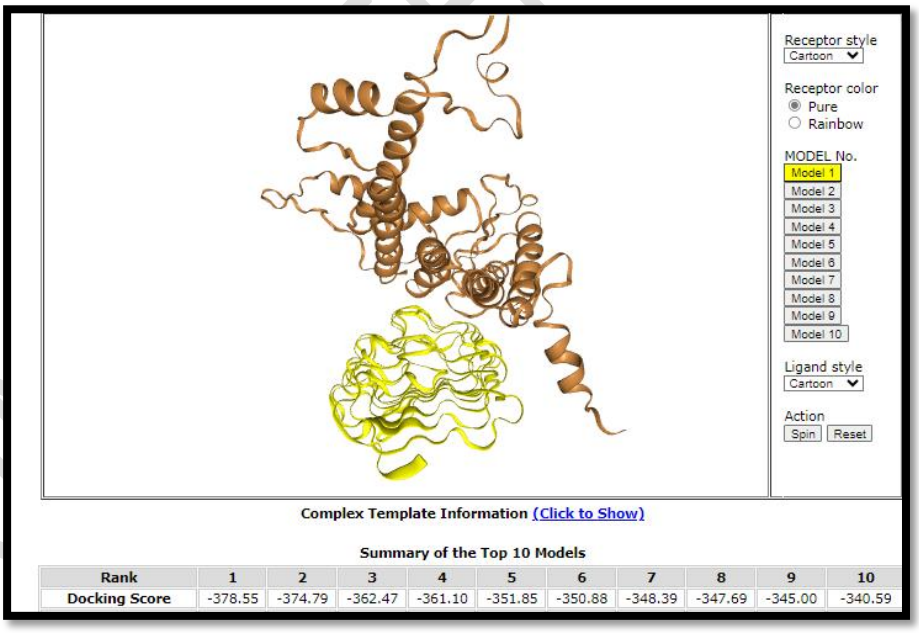
Fig.2: Amino acid sequence of human TSHR protein



Rank	1	2	3	4	5	6	7	8	9	10
Docking Score	-378.55	-374.79	-362.47	-361.10	-351.85	-350.88	-348.39	-347.69	-345.00	-340.59

Fig.3: Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using H-Dock server with respective binding scores.

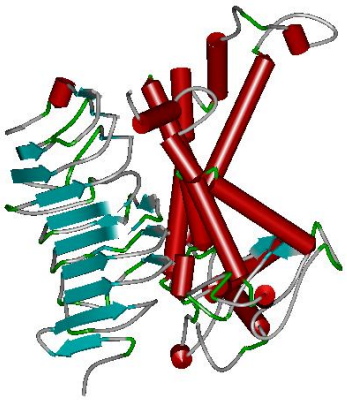


Fig.4: 3D Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using Discovery Studio Software.

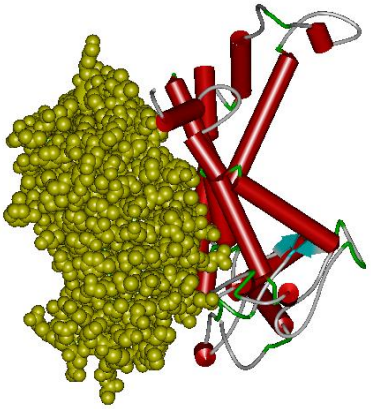


Fig.5: Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using Discovery Studio Software. Yellow coloured structure represents the TSHR protein.

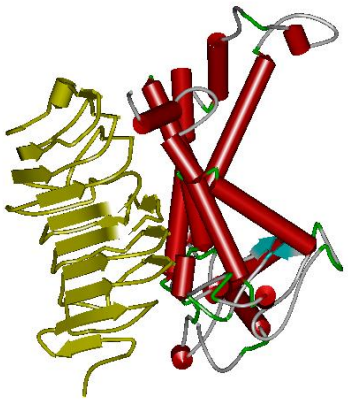


Fig.6: 3D Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using Discovery Studio software (Binding Interaction Mode).

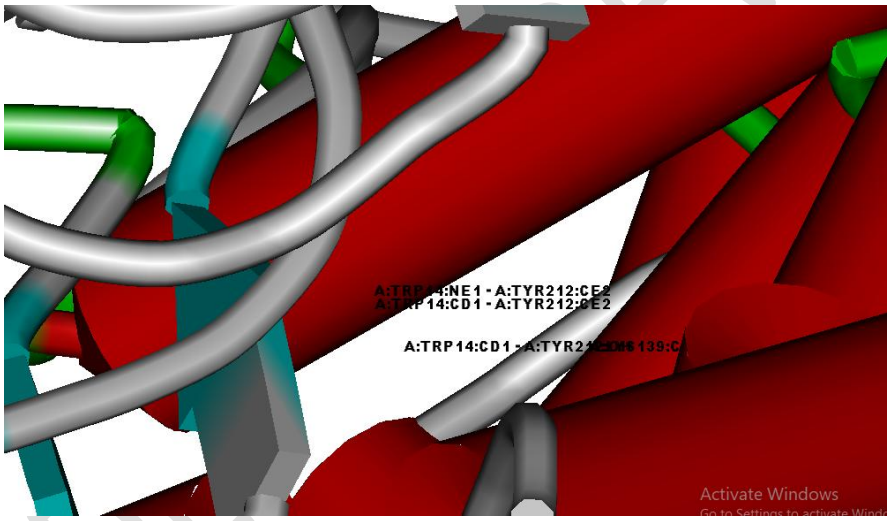


Fig.7: 3D Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using Discovery Studio software (Binding Interaction Mode with respective amino acid labels/positions).

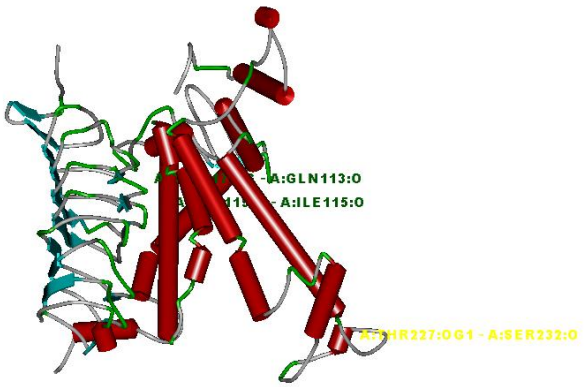


Fig.8: 3D Complex form of human TSHR protein and Photosystem II protein of *Ulva fasciata* viewed using Discovery Studio software (Amino acids interacting at Domain and Motif).

The amino acid sequences corresponding to the gene-coded proteins of photosystem II protein D1 (*Ulva fasciata*) and TSHR are 353aa and 231 aa, respectively (Fig: 1 and 2). In our research work, we use the potential inhibitor derived from algae (*Ulva fasciata*).

Macroscopic, multicellular, eukaryotic photosynthetic organisms that are part of the Plantae kingdom are referred to as marine macroalgae, or seaweed. These marine plants that live in salt can be found on the seabed or solid rock strata beneath it, as well as on rock surfaces, corals, shells, pebbles, and other plants. In areas of the water where light is most abundant, such as the tidal and subtidal zones, marine algae typically flourish. They can easily adjust to physiological changes by creating chemicals that can tolerate stress, which allows them to survive in extreme environments such as heat, cold, UV radiation, salinity, and desiccation [17]. They generate a wide range of primary and secondary metabolites as a result of their existence. Numerous physiologically active substances with a variety of medicinal uses can be found in marine algae [18].

The complex form of the TSHR protein retrieved via the H-Dock server and photosystem II protein D1 have a 3D docking score of -378.55 *kcal/mol*, (Fig :3) as illustrated in Fig. (1). Using Discovery Studio software, the H-bond interactions between photosystem II protein D1 and the TSHR protein are displayed in detail (Fig: 4, 5, 6, 7, 8). It is clear from this image that the TSHR protein and the photosystem II protein D1 protein

structure have interacted non-covalently. Therefore, it may be said that, as demonstrated by earlier research, the TSHR protein will be downregulated. Our docking studies are consistent with a number of prior investigations [19, 20, 21, 22, 23, and 24].

Our retrieved protein's functional domain area is the *Ulva fasciata* 213 ALA (208-213) N-myristoylation site (PS00008). Our research demonstrates that gentamicin, an antibiotic, interacts directly with the domain areas. Our study unequivocally demonstrated that the following amino acids are present at the drug-protein binding region: GLN: 113, HIS: 92, PHE: 119, ILE: 119, ALA: 213, THR: 227, SER: 232.

Conclusion

Our study unequivocally demonstrates the interaction between the seaweed protein and the human hypothyroidism protein, TSHR. The *Ulva fasciata* Photosystem II protein binds efficiently to the TSHR protein's functional domain area, as demonstrated by our clear docking data. The H-bond interaction is clearly defined by the binding relationship between Photosystem II protein and TSHR protein, as assessed by docking scores. Therefore, we conclude that *Ulva fasciata* seaweed protein functions as a possible Endocrinological medication that lessens the symptoms of hypothyroidism in humans. Our *Insilico* study clearly shows that the human TSHR protein may be pharmacologically affected by the Photosystem II protein.

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