MELATONIN AND FLUOXETINE INTERACTION WITH SHANK3 PROTEIN GENE FOR AUTISM SPECTRUM DISORDER

BIPIN NAIR B.J., ARUNJIT K., VIJESH BHASKARAN

Department of Computer Science, Amrita School of Arts and Sciences, Amrita Vishwa Vidyapeetham, Amrita University, Mysore Campus, Karnataka, India
E-mail: bipin.bj.nair@gmail.com, *anjukj13@gmail.com, jeeva10@zoho.com*

ABSTRACT

Autism spectrum disorder impairs the nervous system and affects the overall poignant, societal and substantial health of the affected human being. We here try to redesign the drug 2D structure through various predicting techniques and visualize drug-protein interaction through molecular dynamics and molecular docking techniques. We here collect the drug id of Fluoxetine, Melatonin and the protein SHANK3 form drug bank, then these two drugs are interacted with the protein SHANK3 through molecular docking technique and the 2D structure of their interaction is predicted.

Index Terms—Chemoinformatics, drug designing, ASD (Autism Spectrum Disorder)

I. INTRODUCTION

Autism spectrum disorder describes a wide range of conditions which can be classified as neurodevelopment disorder. In varying degrees are categorized by difficulty in social relations, verbal and nonverbal communiqué and monotonous behaviors. To prolong the symptoms of autism in a person the suppressants are administered as therapeutic treatment. A two-dimensional (2d) structure of a protein or a drug is an important source of information to better understand the function and its interaction with other compounds.

II. LITERATURE SURVEY

Molecular dynamics simulation approaches talk about how Structural constancy was well acquired for computation of region per lipid, tail order stricture, the wideness of lipid and secondary structural chattels. KPN00728 and SDH chain D in a membrane was subjected and performed molecular dynamics to comprehend its function has SDH [1]. The use of AMD 'Annealing Molecular Dynamics' to produce different type of stretched conformers. The structural properties of mutation sites are discriminated by AMD conformers which relate molecular volume and solvent-accessible surface per residue [2]. 'Human DAK gene' codes FMN cyclase of twodomain subunits. Integral homodimers are required by the kinase movement, and single domain subunit are required by cyclase to be curtailed. According to the authors study bifunctionality of FMN cyclase acknowledged and are recognized [3]. Talks about the computational study to sieve the utmost credible mutation potency related with OCA3 and according to the study it was also found that R356Q and R326H are diseases allied thru 'PolyPhen 2.0, SIFT, PANTHER, I-mutant 3.0, PhD-SNP, SNP&GO, Pmut' and Mutpred apparatuses. Which give more insight into the molecular association in 3D space, the intrinsic and altered (R326 H and R356Q) edifices are investigated using MDS (molecular dynamics simulation) methodology [4].

Arrangement of SG2NA protein and its isoforms and three-dimensional molecular modeling. According to the author the biologically applicable structural models were created using molecular dynamics. This paper provides direct meticulous evidence to comprehend the structural properties of SG2NA protein variant. It explains the acute fundamental structures of SG2NA proteins which convoluted numerous protein to protein collaborations and disclosed varying degree of malady at hand SG2NA structure fundamental interface and protein complex [5]. There are many tools used for a molecular simulation like GROMACS 4.5 and how its used and explained by the author [6]. The molecular mechanics Poisson Boltzmann, exterior region process assess the free energies values of binding. And used MSD (Molecular Dynamics Simulations) of protein-ligand from the molecular docking to expand the augmentation of molecular docking. In recent years computational modeling of polymeric nanoparticles as drug carriers have been broadly considered in line for their various functions, structures and the competency of meticulous drug [7].

Eight communal are exhibited and the copious properties have estimated. 'ADMET, QSAR', thermos-dynamic and electronic properties have anticipated and associated using 'SAR' through well-designed procedures of quantum mechanical density [8]. The distinctive emphasis on chronotherapeutics, several methodlogies in chronotherapeutic drug provision and solicitations [9]. Author reviewed critical commence-ments and unequivocal structures of small molecule protein docking procedures, highlight explicit applications and vigilant contemporary developments that aim to discourse the acknowledged precincts of traditional methodologies [10].

'Protein kinase-1' (PDK1) is Phosphoinositide-dependent, a dominant regulator of the AGC family of kinases and foremost factor of 'PI3K pathway'. The pathway is the most frequently liberalized in many cancers. There previous research have been recommended Myricetin as an anti-cancer agent. When 95% of equivalent Myricetin acuminated in 'PubChem' database was acknowledged for their structural understanding. To consider the bonding and pharmacokinetic properties of amalgams molecular docking and in Silico ADMET are performed on the amalgams [11]. It is said that about 1 % of the general population is affected by the ASD. In past decade alone multiple gens have been identified, we can also say that autism is a mutagenic disorder [12].

III. Flow Diagram

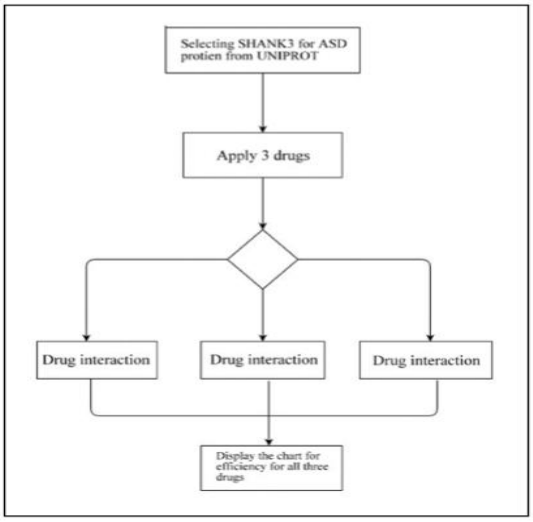

Figure 1: Flow chart

IV. Problem Definition

Autism spectrum disorder impairs the nervous system and affects the overall cognitive, emotional, social and physical health of the affected individual. Suppressants are used to prolong the effect of autism in a person. However, these drugs lack the accuracy and efficiency. Here the Two-dimensional (2D) structure helps in understanding the interaction between the drug and protein.

Our works aim at predicting Two-dimensional (2D) structure and analyze its interaction between the drug Fluoxetine and Melatonin and the protein SHANK3 using the various 2D modeling methods and molecular dynamic method.

V. Methodology

Step 1: Taking SHANK3 protein as a target.

Step 2: Identifying suppressor of ASD.

Step 3: Retrieving the SHANK3 ID from the drug bank.

Step 4: def __registerDrug(self,elmt):
"*elmt* is the ElementTree instance of drug"

Step 5: d = Drug(elmt)

Step 6: names = [d.name]; name_sets = []

Step 7: if getattr(d,'synonyms',None) is not None:
name_sets.append(d.synonyms)

Step 8: if getattr(d,'brands',None) is not None:
name_sets.append(d.brands)

Step 9: Retrieving the suppresser ID from the drug bank.

Step 10: def iterDrugs(self):

Step 11: for d in self.drugs.itervalues():

Step 12: yield d

Step 13: def iterProts(self):

Step 14: for p in self.prots.itervalues():

Step 15: yield p

Step 16: def __repr__(self):

Step 17: return "<DrugBank {0:g} drugs, {1:g} proteins,
{2:g} links>".format(

Step 18: self.info['no_drug'],self.info ['no_prot'],
self.info['no_intr'])

Step 19: Interact the suppresser with SHANK3 protein.

Step 20: Displaying the interaction in 2D format.

Step 21: Analyzing the drug-protein interaction.

VI. Experimental Result

Table 1. These are the following suppressor which we are using for the experiment result

Database	DrugBank
Compound Name	Fluoxetine
Compound ID	DB00472 (APRD00530)
Protein(SHANK3) UNIPROT ID	P04839

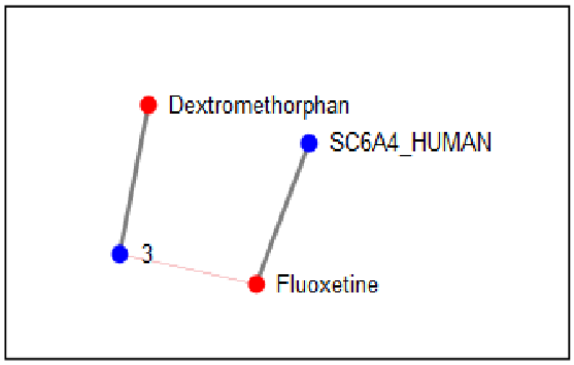

Figure 2: Interaction of Fluoxetine and SHANK3

The above figure elucidates how the Fluoxetine drug interacts with the SHANK3 protein. The protein SHANK3 is a human protein which is encoded by SHANK3 gene on chromosome

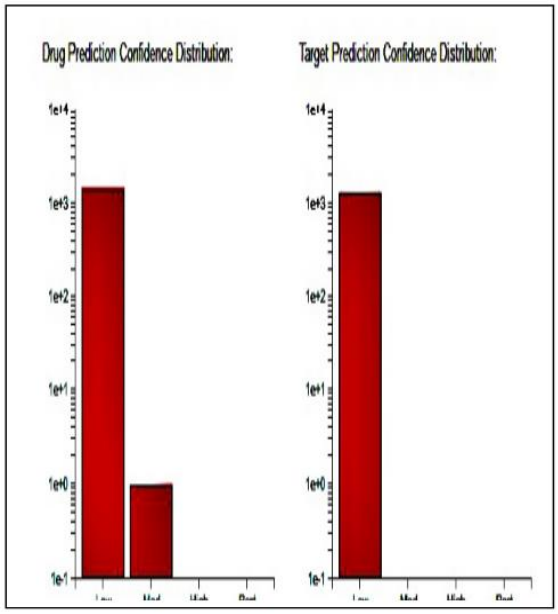

Figure 2: Mutation in this gene is associated with autism spectrum disorder. The Fluoxetine is an antidepressant of selective serotonin reuptake inhibitor class.

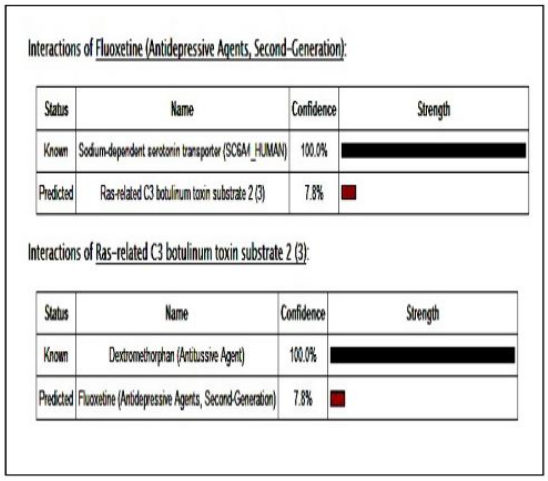

Figure 3: Drug prediction confidence distribution and Target prediction confidence distribution of Fluoxetine and SHANK3

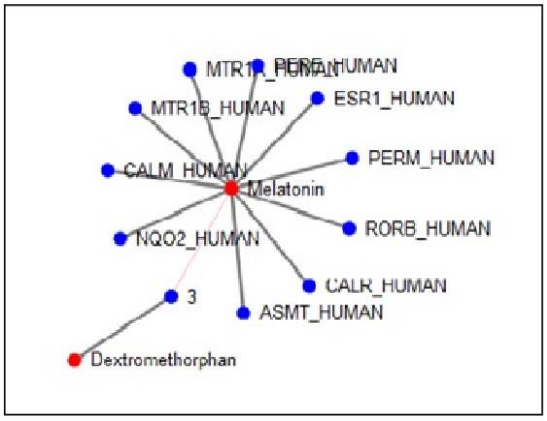

Figure 4: Drug-Target interaction of Melatonin.

The above figure depicts the drug target interaction of Melatonin drug with SHANK3 protein. Melatonin is a hormone produced by the pineal gland which regulates sleep and wakefulness. The Melatonin drug is administered to the patients with a history of depression or other psychiatric disorder. Here the Melatonin drug interacts with the different strains of SHANK3.

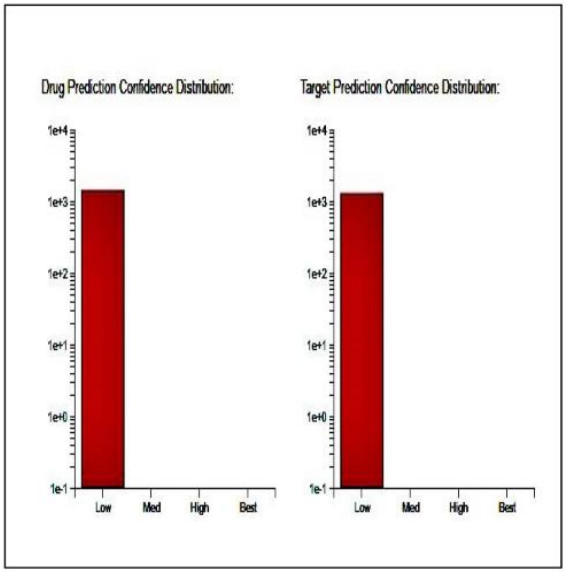

Figure 5: Drug prediction confidence distribution and Target prediction confidence distribution of Melatonin and SHANK3.

VII. Conclusion

In our work, we are designing the drug interaction for autism spectrum diseases and improving the efficiency of the drug. Using molecular dynamics concept and molecular docking methods.

With help of molecular docking techniques, we illustrate the drug and protein interaction. We can extend the work, for designing a proper drug for autism diseases using all the possible structural change with all permutations and combinations and reducing the side effects.

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