Exploration of Schizophrenia: A neurological disorder using bioinformatics tools and techniques

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Abstract: Schizophrenia is one of the most confusing and disabling mental illness that makes it difficult to tell the difference between real and unreal experiences, to think logically, to have normal emotional responses, and to behave normally in social situations. Schizophrenia may occur due to environmental as well as the genetic factor. COMT is one of the genes responsible for Schizophrenia. We predicted the active site of COMT gene and its complementary ligand structures. This complementary ligand binds to the active site of the gene COMT. Binding ability of ligand to the COMT is important in drug design for curing Schizophrenia.
Keywords- Schizophrenia, genetic factor, ligand, COMT, Drug design.
Abbreviations: Catechol-O-methyl transferase **(**COMT).

I. Introduction

Schizophrenia is one of the most confusing and disabling mental illness that makes it difficult to tell the difference between real and unreal experiences, to think logically, to have normal emotional responses, and to behave normally in social situations [1, 2]. The COMT helps breakdown of nuerotransmitters such as epinephrine, norepinephrine and dopamine that causes Schizophrenia [3]. *1vid* is a transcript variant of COMT gene. We predicted the complementary ligands *1cma, 1cmc, 1adm* and *1eiz* using an approach of Homology modeling [4]. These predicted lignads are necessary for new paradigm of computational drug design.

II. Methodology

In this research work we predicted the motifs, domain, coiled region, transmembrane region, the primary and the secondary structure of the transcript variant [5-9]; then we predicted the complementary ligand to the transcript variant from Drugbank. Then we performed docking of all the predicted ligands one by one with transcript variant *1vid* using docking tool Hex 5.0 [10]. Here we observed that the ligand 1eiz exhibits maximum fit with 1vid and requires less energy involved in the binding of the 1eiz with 1vid than the remaining ligands. We visualized the structure of ligands and transcript variant using structure visualization tool SPDB Viewer [11].

III. Results and Interpretation

COMT is transmembrane gene (fig 1). The primary sequence of the protein is 271 residues long. The secondary structure comprises alpha helix, beta sheets and coiled region (fig 2). Atomic composition of COMT protein shows 1358 carbon, 2158 hydrogen, 354 nitrogen, 384 oxygen and 15 sulfur atoms. Amino acid composition contain 34 negatively charge amino acids and 24 positively charged amino acids. Secondary structure analysis shown 42.07 % (114) alpha helix, 15.87% (43) extended strands, and 42.07% (114) random coils. Finally we observed binding of *1vid* to a several predicted ligands using docking tool HEX 5.0 (fig 3).

IV. Conclusion

The ligand 1eiz exhibits maximum fit to the receptor 1vid, so it can be used to regulate the functioning of COMT gene. This approach is important in new paradigm of computer aided drug design.

V. References

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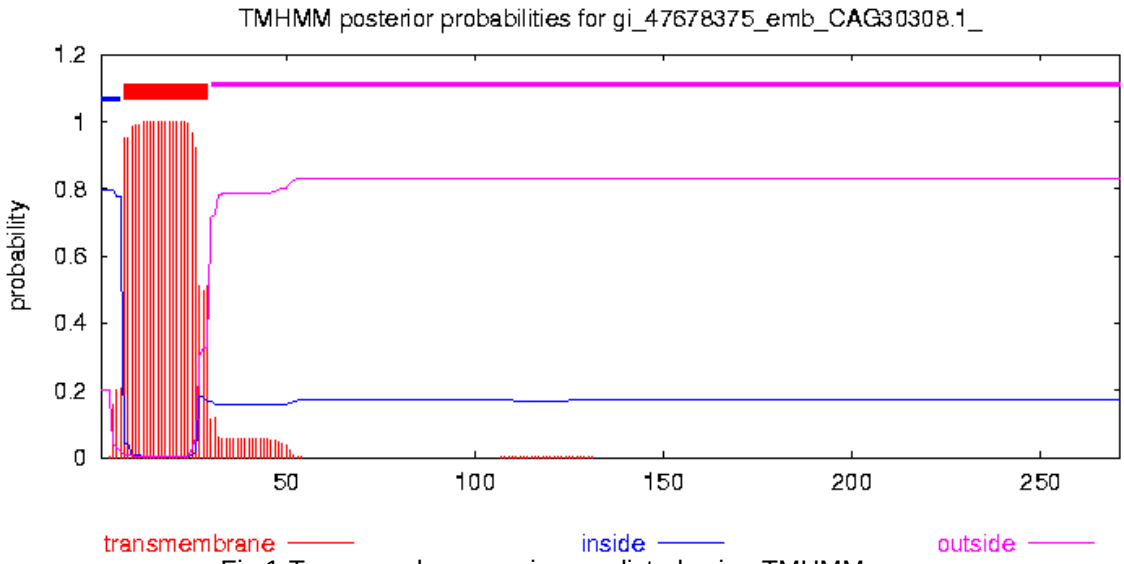

Fig.1-Transmembrane region predicted using TMHMM

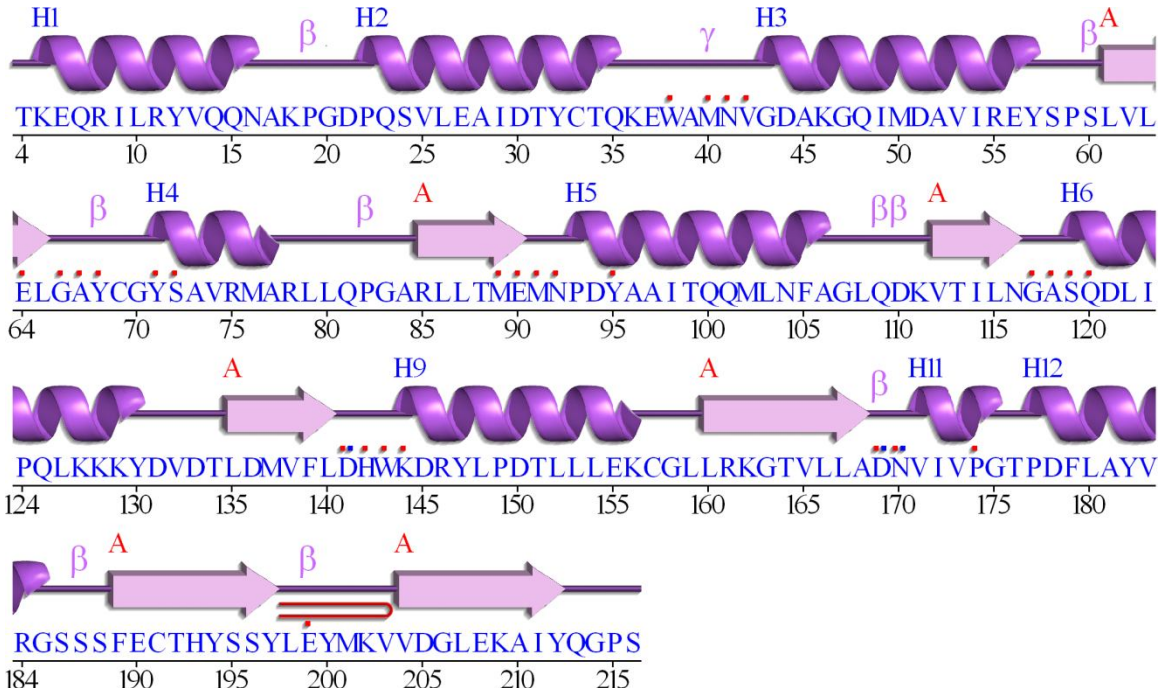

Fig.2-secondary structure of COMT protein having alpha helices, extended strands and coils

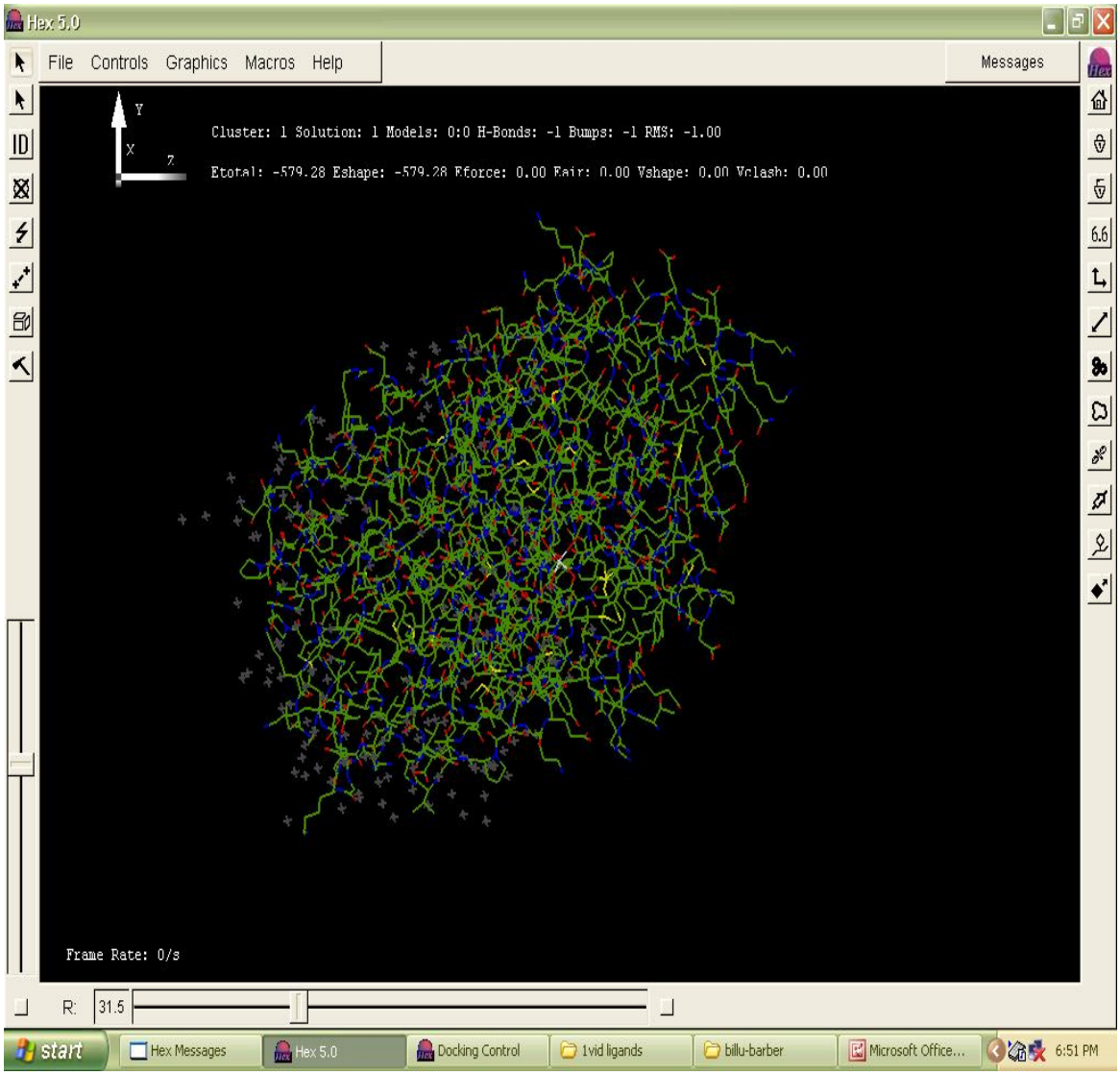

Fig.3-Superimposed structure of *1vid* with *1eiz* showing maximum fit