EDITORIAL

Improving Neuropharmacology using Big Data, Machine Learning and Computational Algorithms

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1. INTRODUCTION

Drugs perform dynamic role in perturbing the functional phenotypes of organism; for example, a drug with the vasorelaxant role may have an impact on the nervous system however poses side effects of fatigue [1]. The principal aim of neuro-pharmacology is to explain the impact of therapeutic interventions on the nervous systems [2]. Integrating the continuum of biomedical and healthcare data types forms key factor in understanding therapeutics in neurology and its associated side effect [3-5]. Utilizing the biomedical and healthcare data and implementing precision medicine-aided clinical pathways are anticipated to improve patient outcomes suffering from neurological disorders [6, 7]. In the given context, our special issue of the ***Current Neuropharmacology*** emphasizes ***"Neuroinformatics, Bioinformatics, and Computational Chemistry, for Neuropharmacology"***. Our special issue brings an exciting volume of research and review articles that include representative results all the way from application of computational and statistical research to clinical research. Our special issue covers a broad range of topics including structure-based drug discovery, machine learning, molecular modeling, comparative pharmacological evaluations, dual-drug targeting methods and computational docking studies. The special issue covers research on diverse range of neuro-disorders *per se* Alzheimer's disease, schizophrenia, Parkinson's disease, depression, epilepsy, dementia, migraine and stroke, Niemann-Pick type C disease, rapid-eye-movement (REM) sleep behavior disorder (RBD), amyotrophic lateral sclerosis (ALS) and Huntington's disease. Multiple research articles in this special issue have used various translational bioinformatics and chemoinformatics approaches and thus provide the collective value of computational approaches in therapeutic discovery and development [8-12].

2. QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS (QSAR) OF ACETYLCHOLINE ESTERASE (AChE) INHIBITORS TO TREAT ALZHEIMER'S DISEASE

Alzheimer's disease is a major public health challenge that affects the cognitive ability of the patients [13]. In this study, Babita *et al.* present an example of the application of chemoinformatics tools to identify physicochemical properties of AChE inhibitors [14]. This research could inspire several follow-up studies to evaluate these compounds in preclinical models [15].

3. APPLICATION OF COMPOSITE MACHINE LEARNING ALGORITHMS TO EVALUATE CHEMICAL FEATURES OF HERBAL INHIBITORS FOR THE TREATMENT OF SCHIZOPHRENIA

The gamma-amino butyric acid (GABA) is a key inhibitory neurotransmitter. In this study, Sahila *et al.* combine machine learning, computational chemistry and phytochemistry to ascertain the chemical properties of natural inhibitors to treat Schizophrenia. Schizophrenia is a disease with high morbidity and mortality rate and developing natural compounds to alleviate and manage the symptoms would be an innovative approach to address the complex neurological condition [16].

4. COMPARATIVE EFFICACY OF ARIPIPRAZOLE AND RISPERIDONE IN SCHIZOPHRENIA

In this study, Sajeev*et al.* provide compelling insights into the efficacy of two prominent monotherapies for schizophrenia from a single-center in India. It is further interesting as the study is from the Southeast Asia region and thus adds to the global catalog of pharmacological evaluation of available therapeutic efficacies for available neuro-pharmacological therapies [16, 17]. Similarly, independent post-marketing comparative efficacy studies would further

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help to evaluate the frontline treatments would also contribute to establish personalized, precision therapies for neuro-psychiatric illness [17-20].

5. STRUCTURE BASED DISCOVERY AND EVALUATION OF DUAL TARGET LIGANDS FOR PARKINSON'S DISEASE

Perez-Castillo *et al.* present an innovative structural bioinformatics study that uses mathematical approaches to derive docking scores to understand protein-ligand interaction to target not one, but dual targets. Derivation and biophysical interpretation of docking scores is a relevant theme in structure-based drug discovery [21-23]. This innovative and challenging research will open new avenues for evaluating drug targets that could target pleiotropic protein targets and could also improve drug repositioning [24-26].

6. ANTIDEPRESSANT DRUG TARGETS OF URSOLIC ACID

Singla and Dubey's research leverage bioinformatics and chemoinformatics tools to determine neurological targets of ursolic acid. The antidepressant role of ursolic acid is known for a while, in this study authors provides complementary evidence using computational studies [27].

7. CHEMOINFORMATICS EVALUATION OF TARGETING MONOAMINE OXIDASE B ADENOSINE AND A(2A) RECEPTOR (MAO-B/A_{2A}AR) USING CHROMONE DERIVATIVES

Chromones (1-benzopyran-4-ones) are a natural product with therapeutic implications in cancer, diabetes, cancer and inflammatory diseases. In this study, Cruz-Monteagudo presents quantitative chemistry evaluations to assess the effect of chromone derivatives for dual targeting MAO-B/A_{2A}AR [28].

8. LEVERAGING STRUCTURE-BASED DRUG DESIGNING TO DEVELOP THERAPIES TO TARGET NEURO-LOGICAL DISORDERS

Combining a large amount of molecular class specific data has been useful to develop predictive models and algorithms to understand mechanisms like 3D domain swapping, a hallmark feature of neurological diseases including Alzheimer's and Parkinson's disease [29-32]. Recent efforts in integrating genetic variants and drug target data have revealed several novel therapeutic associations for neurological disorder [33-35]. Aarthy *et al*. provide an overview of several recent advances in neurological drug discovery. Authors here discuss the application of structural bioinformatics, chemo-informatics methods to neurological disorders. Authors further discuss different neurological disease modalities including Alzheimer's disease, Niemann-Pick type C disease, REM-RBD, ALS, epilepsy, dementia, migraine, and stroke. The review offers an excellent balance between the clinical, biochemical and bioinformatics methods and thus could help students, researchers and clinicians to understand various inter-disciplinary aspects of drug development [36].

9. STRUCTURAL MODELING OF VOLTAGE-GATED SODIUM ION CHANNEL FROM ANOPHELES GAMBIAE

Irrespective of global public health efforts to control malaria and other infectious diseases transmitted by mosquitoes, we are still in search for developing efficient vector controlling measures. The majority of diseases transmitted by mosquito including malaria, dengue, West Nile virus, encephalitis and Zika fever have complications that affect the neurological systems [37-39]. Understanding the molecular role of the vector proteins is critical to developing repellents, vector controlling agents and other chemical agents to control mosquitoes that spread viral diseases [40, 41]. In their research paper, Rithvik and Sowdhamini present results from a challenging task of modeling an ion channel from *Anopheles gambiae*. The findings surge in the development of novel anti-infectious agents that combat mosquito borne diseases including Zika virus pathogenicity [42].

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