EDITORIAL

In Silico Studies in Drug Research Against Neurodegenerative DiseasesLuciana Scotti^{1,2,*} and Marcus T. Scotti^{1,*}¹Federal University of Paraíba, Health Sci. Center, 50670-910, João Pessoa, PB, Brazil; ²Teaching and Research Management - University Hospital, Federal University of Paraíba, João Pessoa, PB, Brazil

Along with the steady advancement of *in silico* methods, such as predicting pharmacokinetics and/or pharmacodynamics in different stages, and in qualitative and quantitative approaches; researchers continue to use computational tools to filter and select new drug candidate compounds. Theoretical studies using *in silico* methods have aided in the process of drug discovery, and retain the advantages of selecting potential compound leads in less time, and of saving money that would have been spent through traditional experimental testing [1, 2].

In no way do bioinformatic tools replace *in vitro* and *in vivo* assays. Experimental results are of fundamental importance in the planning of new drugs [3]. These studies should be meticulous and accurate in order to ensure maximum effect with minimal adverse effects. The process that leads to the conception of a new drug is long and expensive, a fact that emphasizes the participation of *in silico* studies at the base of the pyramid.

Neurodegenerative diseases (NDs) include Parkinson's disease, Huntington's disease, Alzheimer's disease, Spinal-cerebellar Degeneration, Amyotrophic Lateral Sclerosis, Spongiform Encephalopathy and Epilepsy. These diseases often arise as a result of the natural aging process of the brain, and neuron death [4]. We often observe motor and cognitive impairment; occurring in differing degrees, depending on the area and severity of the central nervous system lesion.

Neurodegenerative diseases have a multifactor patho-etiological origin, and scientists have become persuaded that a multi-target therapeutic strategy is recommended; the simultaneous targeting of multiple proteins (and therefore etiologies) involved in disease development.

This issue will bring together theoretical studies from different methodologies, such as QSAR, docking, chemometric tools, artificial intelligence and its various applications in order to optimize the search for new drugs to cure and treat neurodegenerative diseases. A review by Dr Sehgal and colleagues; "Current therapeutic molecules and targets in neurodegenerative diseases based on *in silico* drug designing"; reported on *in silico* tools and drug targeting techniques, active molecules, molecular docking studies and future prospects for Alzheimer's disease, Parkinson's disease, Amyotrophic Lateral Sclerosis, and Huntington's disease. Drs. Makhouri & Ghasemi's review entitled "*In silico* studies in drug research against neurodegenerative diseases"; provides a basic background concerning neurodegenerative diseases and *in silico* techniques including: homology modeling, molecular docking, virtual high-throughput screening, quantitative structure activity relationship (QSAR), hologram quantitative structure activity relationship (HQSAR), 3D pharmacophore mapping, proteochemometric modeling (PCM), protein ligand interaction fingerprints (PLIF), fragment-based drug discovery, Monte Carlo simulation, molecular dynamic (MD) simulation, quantum-mechanical methods for drug design, support vector machines, and machine learning approaches. Dr. Baig's manuscript entitled "Computer aided drug design and its application to the development of potential drugs for neurodegenerative disorders"; discusses the CADD approach and its use in the development of the therapeutic drug candidates against NDs, successful application of CADD against NDs, and its limitations and future prospects. We believe that this review will be helpful in understanding CADD in the discovery of new ND drug candidates.

In the manuscript "3D-QSAR and *in-silico* studies of natural products and related derivatives for the treatment of inflammatory and neurological disorders"; Dr. Dhiman and co-workers critically discuss and outline recent advances in our knowledge of novel natural MAO inhibitors using *in-silico* methods. Along with molecular docking and quantitative structure-activity relationship studies, several natural heterocyclic compounds such as coumarins, β -carboline, piperine, naphthoquinone, morpholine, caffeine, amphetamine, and moreover flavonoids, chalcones, xanthenes, and curcumin are discussed concerning their MAO inhibitory profile.

The histamine H3 receptor (H3R) is an important target involved in several CNS disorders such as: narcolepsy, attention deficit hyperactivity disorder, and schizophrenia. H3R antagonists/inverse agonists have also demonstrated pro-cognitive effects in both animal and human models. Thus several reports have been published focusing on applications in the treatment of neurodegenerative diseases, such as Alzheimer's (AD) and Parkinson's (PD) diseases. Since QSAR modeling is a feasible approach to explain the role of molecular substituents in biological activity, it can help to improve the design of better H3R ligands. Correa & Fernandes, in their study "QSAR modeling of histamine H3R antagonists/inverse agonists as future drugs for neurodegenerative diseases"; review the current status of contributions from QSAR modeling in developing H3R antagonists/inverse agonists.

The past decade is characterized by a growing awareness of dementia's severity in the field of age-related and non-age-related diseases and the importance of investing resources into research for new and effective treatments. Alzheimer's stands out because of its, extremely high incidence and fatality. Many pharmacological strategies have been tried yet Alzheimer's remains incurable. The number of reported QSAR-related Alzheimer's drug design attempts is huge, but only a few results can be considered noteworthy. Providing a detailed analysis of the actual situation and reporting the most notable results in the field of drug design and discovery, Dr. Zanni and co-workers, in their review "Alzheimer: A decade of drug design. Why molecular topology can be an extra edge"; focus on the potential of molecular topology as a reliable tool in finding new anti-Alzheimer lead compounds.

In the paper, "Changing paradigm from one target one ligand towards multi target directed ligand design for key drug targets of Alzheimer disease: An important role of *In silico* methods in multi target directed ligands design"; Dr. Kumar *et al.* summarize some of the most prominent and computationally explored single targets against AD and further discuss successful examples of dual or multiple inhibitors for these same targets. While focused on ligand and structure-based computational approaches to design MTDLs against AD, However, to balance dual activities in a single molecule is not an easy task, yet computational approaches such as virtual screening docking, QSAR, simulation and free energy remain useful for future MTDL drug discovery; both alone or in combination with fragment based methods. Rational and logical implementations of computational drug design methods are capable of assisting AD drug discovery, and play an important role in optimizing multi-target drug discovery.

On one hand, there are multifactor origins and targets to be attacked in AD, revisited by Dr. Li *et al.* in "Combining in vitro and in silico approaches to find new candidate drugs targeting the pathological proteins related to the Alzheimer's disease"; On the other hand, researchers look to develop a drug with a good hydrophilic-lipophilic balance. This is addressed by Dr. Toropova and co-workers in "Blood brain barrier and Alzheimer's disease: Similarity and dissimilarity of molecular alerts".

Currently available pharmacological therapies for the treatment of Parkinson's disease are mostly inadequate, and new therapeutic agents are much needed. In our review, "Computer-aided drug design applied to Parkinson targets"; recent advances in computer-aided drug design for the rational design of new compounds against Parkinson's disease; using methods such as Quantitative Structure-Activity Relationships (QSAR), molecular docking, molecular dynamics and pharmacophore modeling are discussed. Four targets were selected: the enzyme monoamine oxidase, dopamine agonists, acetylcholine receptors, and adenosine receptors. The manuscript, "*In silico* studies targeting G-protein coupled receptors for drug research against Parkinson's disease"; by Dr. Lemos and co-workers, focuses on the impact of specific GPCR subclasses; including dopamine receptors, adenosine receptors, muscarinic acetylcholine receptors, metabotropic glutamate receptors, and 5-hydroxytryptamine receptors; and on the pathophysiology of PD and the importance of structure- and ligand-based *in silico* methods to explain small molecules to target these receptors.

We, the Guest-Editors, would like to express our gratitude to the many authors who contributed to this special issue, reporting investigations in various aspects of "*In silico* studies in drug research against the neurodegenerative diseases".

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