Nanomedicine & Biotherapeutic Discovery

Bachurin, J Nanomedine Biotherapeutic Discov 2015, 5:2
http://dx.doi.org/10.4172/2155-983X.1000e137

Editorial Open Access

Contemporary Approaches for Pharmacological Intervention of Abundant Neurodegenerative Disorders

Sergey Bachurin

Institute of Physiologically Active Compounds, Severny pr.1, Chernogolovka, 142432, Russia

The development of CNS drugs from one side is one of most attractive and socially requested and from the other side one of the most risky area in the pharmaceutical business. So, the application-to approval time for CNS agents usually takes about 2 years in comparison with approximately 1 year for non-CNS drugs, chance of approval for CNS drugs estimated as 8% versus 15% for non-CNS agents, chance of success in Phase 3 trials for CNS and non CNS agents estimated as 46% versus 66% [1]. What is more, the last decade no new drugs for Alzheimer's or Parkinson's diseases were approved, though more than 20 new agents successfully passed Phase 2 clinical trial. From the other hand, the potential market for CNS agents exceeds the market for cardiovascular drugs (15.8% versus 14.5% of total pharma market in 2009) and estimate approximately about US $ 60 billion per year [2].

The analysis of contemporary approaches for the discovery of novel efficient agents for dementia and other widespread neurodegenerative diseases treatment permits to outline the following main trends:

1. The development of therapeutic agents acting on the main stages in pathogenesis of neurodegenerative process. These agents are called "Disease Modifying Drugs (DMD)" [3]. Such agents should slow the progression of structural damages and produce the improvement of neuronal functions in patients that persists even after abolishment of the agent. The main strategies in the development of DMD focused on blockade of pathogenic oligomers formation, such as amyloid, tau, FUS, TDP-43 etc., in particular, inhibition of enzymatic pathways, leading to the formation of such pathological aggregates. Number of promising drug-candidates had show promising results of phase 1 and 2 clinical trials, but unfortunately, none of them passes phase 3 clinical trials yet.

2. Search and study of novel potential biotargets related to the pathogeneses of neurological disorders. Recent years number of new promising mechanisms and molecular targets for treating of neurodegenerative process in nervous system has been proposed. In particular, stabilization of mitochondrial functioning, prevention of pathological protein aggregation in brain (proteinopathy) and activation of pathways leading to a clearance of such pathological aggregates from the brain, activation of endogenous mechanism of nervous cell protection, in particular, activation of autophagy and ubiquitine-proteosome system, stimulation of neurogenesis, modulation of ApoE pathway etc. Some original agents, which utilize such mechanisms as novel efficient neuroprotectors and pro-neurogenic compounds, have been reported.

3. The multifactorial nature of most neurodegenerative disorders such as Alzheimer's disease or Parkinson's disease predetermines strong interest to the developing novel of multi-targeted drugs, acting simultaneously on a group of principal biotargets in the disease pathogenesis [4]. Among them special attention is focused on the compounds acting on acetylcholinesterase and monoaminoxidase, different subtypes of glutamate receptors, pharmacophores which possess additionally NO-generating and antioxidant activities, multi-target biologically active compounds from plants.

4. The high risk and low approval rates of drugs targeting diseases such as Alzheimer's, Parkinson's, depression, anxiety, schizophrenia and stroke have sent billions of dollars down the drain in recent years. As a result of a very low outcome from clinical trials of innovative drugs the alternative strategy based on the repositioning of the already known drugs for neurologic diseases treatment (as its new application) has been actively developing last decade [5].

Of course, in many cases the proposed promising drug-candidate combine number or all of the above-mentioned trends. As an example, it is possible to mention quite promising agents Dimebon [6] and Bexarotene [7] proposed for Alzheimer's disease last years. Both compounds belong to a fast-growing group of "old" drugs that were suggested to be effective for therapy of pathological conditions different from their original targets. Both compounds have typical multitarget mechanism of action, and in both case the investigation of mechanism of their action on nervous system revealed number of novel potential biotargets for the disease treatment.

Finalizing this short report, it should be mentioned that despite the high risks, the rewards of developing next medication for neurodegenerative diseases treatment and it social effect appear to be much higher.

References

1. Tufts Center for the study and Drug Development, 2012.
2. Pharmaceutical Market Trends, 2010 – 2014.
3. Salomone S, Caraci F, Leggio GM, Fedotova J, Drago F (2012) New pharmacological strategies for treatment of Alzheimer's disease: focus on disease modifying drug. Br J Clin Pharmaco l73: 504-517.
4. Geldenhuys WJ, Van der Schyf CJ (2013) Rationally designed multi-targeted agents against neurodegenerative diseases. Curr Med Chem 20: 1662-1672.
5. Corbett A, Pickett J, Burn A, Corcoran J, et al (2012) Drug repositioning for Alzheimer's disease. Nat Rev Drug Discov 11: 833-846.
6. Bharadwaj P, Bates KA, Porter T, Teimouri W, Perry G, et al. (2013) Latrepirdine: molecular mechanisms underlying potential therapeutic roles in Alzheimer's and other neurodegenerative diseases. Transl Psychiatry e332.
7. Cramer PE, Cirrito JR, Wesson DW, et al. (2012) ApoE-Directed Therapeutics Rapidly Clear β-Amyloid and Reverse Deficits in AD Mouse Models. Science 335: 1503-1506.

***Corresponding author:** Institute of Physiologically Active Compounds, Severny pr.1, Chernogolovka, 142432, Russia; E-mail: bachurin@ipac.ac.ru

Received January 31, 2015; **Accepted** February 03, 2015; **Published** February 09, 2015

Citation: Bachurin S (2015) Contemporary Approaches for Pharmacological Intervention of Abundant Neurodegenerative Disorders. J Nanomedine Biotherapeutic Discov 5: e137. doi:10.4172/2155-983X.1000e137