Editorial

New Avenues and Therapeutic Strategies for the Treatment of Neurodegenerative Diseases

Keywords: Neurodegenerative diseases, microRNAs, neuroinflammantion, mitochondria, proteolytic cleavage, cell-based therapy, nanotherapy, microtubule-focused therapies, neurotrophic factors, epigenetic alterations.

Neurodegenerative disorders represent a colossal disease burden not only in terms of human suffering but also in terms of economic cost. Worldwide population is rapidly ageing which is a risk factor for most neurodegenerative disorders. The current treatments available for neurodegenerative disorders, namely Alzheimer's disease and Parkinson's disease are very limited and only delay clinical symptoms rather than addressing the cause and preventing the disease progression.

Despite the therapeutic strategies and advances for the treatment of neurodegenerative disorders, affected patients eventually experience intolerable and untreatable debilitating conditions. A neuroprotective therapy that slows, halts or reverses the underlying progression of neuronal loss preventing the development of cumulative disabled symptoms remains the uppermost priority in the search for new therapeutic strategies.

In this thematic issue it will be reviewed some recent advances that underlie putative therapies for neuroprotection, as well as, potential targets that might be further exploited in the future. Recent scientific advances have identified new pathways involved in several neurodegenerative diseases that suggest new targets for the development of neuroprotective drugs. It will be summarized some of the most promising candidate targets for neuroprotection. These targets include agents that might improve mitochondrial function, microtubule dynamics or the degradation of defective mitochondria and protein aggregates; neurotrophic factors therapy; microRNAs; modulation of neuroinflammation; epigenetic alterations and cell replacement therapies. The diseases covered in this issue are Dementia, Alzheimer's disease, Parkinson's disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis and Polyglutamine diseases.

The first chapter will discuss microRNAs role in dementia. MicroRNAs are a family of small, non-coding RNAs that provide broad silencing activity of mRNA targets and post-transcriptional regulation of gene expression. Some reports suggest that microRNAs may be a contributing factor in neurodegeneration. Indeed, changes in the expression of several microRNAs have been associated with neurodegenerative disorders including Alzheimer's disease. Hence Cardoso and colleagues will shed light on the use of these small molecules as disease markers and new therapeutic targets for the treatment of dementia [1].

Neuroinflammation is characterized by the appearance of reactive astrocytes and microglia and seems to be highly involved in the disease pathogenesis of neurodegenerative disorders. In chapter 2 Lavrnja *et al*. will elucidate the recent advances in this field, as well as, limitations that need to be overcome in order to pursue neuroinflammation as a potential therapeutic approach. Specifically this chapter will focus on potential therapies that modulate neuroinflammation and are neuroprotective in a disease of unknown etiology, Multiple Sclerosis [2].

Several studies set mitochondrial dysfunction at the center of several neurodegenerative disorders. Taking this into account Morris and Wilkins will present the current therapeutic initiatives of how mitochondria might be effectively targeted as a therapeutic opportunity for neurodegenerative disorders such as Amyotrophic Lateral Sclerosis, Alzheimer's disease and Parkinson's disease [3].

Nóbrega and colleagues chapter will be focused in the involvement of proteolytic cleavage in Polyglutamine diseases. Failure in proteolytic cleavage leads to toxic polyglutamine-expanded proteins. These authors will discuss the mechanisms of fragment toxicity that are responsible for neurodegeneration in six types of spinocerebellar ataxia caused by polyglutamine expansion of proteins [4].

In chapter 5, cell replacement therapies will be discussed by Metcalfe, Bickerton and Fahmy as promising strategies to slow down or replace neuronal loss observed in neurodegenerative disorders. Cell-based therapy for neurodegenerative diseases and nanotherapy will be elucidated and their potential in cellular neuroprotection to repair degenerative brains will be clarified [5].

An effective axonal transport is extremely crucial within the neuron in order to move organelles, vesicles and proteins from the cell body to the axon (Anterograde) and to move proteins and organelles destined for degradation from the axon back to the cell body (Retrograde). In diseases where the progressive death of neurons occur, long axons degenerate and put at risk both retrograde and anterograde axonal transport leading to energy failure and the accumulation of proteins aggregates and dysfunctional organelles. Therefore Cappelletti and co-workers will discuss several evidences that suggest that targeting microtubules and microtubule-focused therapies envisaging an improvement of axonal transport may be effective in the treatment of neurodegenerative diseases [6].

Neurotropic factors are a family of proteins that are responsible for the growth, differentiation, survival of developing neurons and the maintenance of mature neurons, such as Brain-derived neurotrophic factor (BDNF) and Glial cell-derived neurotrophic factor (GDNF). Baltazar et al. will clarify the role of neurotrophic factors in Parkinson's disease [7]. Moreover these authors will discuss the current knowledge on neurothropic factors and the potentially benefic outcome of modulating neurotrophic factors.

Epigenetic is a regulator of gene expression by modifying histone tails or changing DNA methylation. Interestingly, several studies now suggest a relationship between epigenetic alterations and neurodegenerative diseases. Thus understanding epigenetic alterations hold great promises for the development of novel diagnosis methods and therapeutic approaches. In the final chapter, the emerging science of epigenetics will be reviewed by Maes and co-workers [8]. The authors will review the recent discoveries of new targeted therapies and biomarkers for neurodegenerative diseases, namely Parkinson's disease and Alzheimer's disease.

Overall we hope to contribute with a thorough and detailed issue with excellent reviews aiming to advance research in the field of neurodegenerative disorders and possible therapies whose major goal is to stop disease progression and resultant symptomatology.

1873-4286/17 $58.00+.00

Finally, I would like to express my gratitude for the effort of all authors to provide interesting and far-reaching chapters that expectantly will improve the scientific knowledge in the area of neurodegenerative diseases therapies, targets for treatment and biomarkers.

REFERENCES

[1] Viegas AT, Guedes J, Oliveira AR, Cardoso AM, Cardoso AL. miRNAs: new biomarkers and therapeutic targets in dementia. Curr Pharm Des 2017; 23(5): 669-92.
[2] Bjelobaba I, Savic D, Lavrnja I. Multiple sclerosis and neuroinflammation: The overview of current and prospective therapies. Curr Pharm Des 2017; 23(5): 693-730.
[3] Wilkins HM, Morris JK. New Therapeutics to modulate mitochondrial function in neurodegenerative disorders. Curr Pharm Des 2017; 23(5): 731-52.
[4] Matos CA, de Almeida LP, Nóbrega C. Proteolytic cleavage of polyglutamine disease-causing proteins: revisiting the toxic fragment hypothesis. Curr Pharm Des 2017; 23(5): 753-75.
[5] Metcalfe SM, Bickerton S, Fahmy T. Neurodegenerative disease: a perspective on cell-based therapy in the new Era of cell-free nano-therapy. Curr Pharm Des 2017; 23(5): 776-83.
[6] Cappelletti G, Cartelli D, Christodoulou MS, Passarella D. Microtubule-directed therapeutic strategy for neurodegenerative disorders: starting from the basis and looking on the emergences. Curr Pharm Des 2017; 23(5): 784-808.
[7] Tomé D, Fonseca CP, Campos FL, Baltazar G. Role of neurotrophic factors in Parkinson´s disease. Curr Pharm Des 2017; 23(5): 809-38.
[8] Ciceri F, Rotllant D, Maes T. Understanding epigenetic alterations in Alzheimer's and Parkinson's disease: towards targeted biomarkers and therapies. Curr Pharm Des 2017; 23(5): 839-57.

Ana Raquel Esteves

Center for Neuroscience & Cell Biology
Faculty of Medicine, 1st Floor
University of Coimbra
Coimbra, Portugal
Tel: (+351) 239 820 190
Fax: (+351) 239 822 776
E-mail: esteves.raquel@gmail.com