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Medicinal chemistry advances in neurodegenerative disease therapy: part 2

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• neurodegeneration • neuroregeneration • prolyl oligopeptidase inhibitors

We are delighted to introduce the second installment of this special focus issue dedicated to medicinal chemistry advances in neurodegenerative disease therapy [1].

The WHO estimated that in April 2016 there were 47.5 million people suffering from dementia worldwide, and by 2050 this number could triple to a predicted 135.5 million [2]. Despite the efforts of a huge number of research groups around the globe, at present, all neurodegenerative diseases are incurable with only palliative treatments available.

Driven by this large and increasing need for new therapies, we have come together with renowned experts in the field to deliver the second half of our special focus issue of *Future Medicinal Chemistry*. The issue features a range of reviews and original research covering various aspects of medicinal chemistry in neurodegenerative disease therapy.

In our first article, Simoni *et al.* have investigated the design and biological evaluation of hybrid compounds that target both cholinergic transmission and amyloid- β aggregation in Alzheimer's disease, as a method to provide symptomatic relief of cholinergic potentiation and the neuroprotective prospects of antiaggregating agents [3]. This is an interesting approach and the authors present some promising compounds with activity against both of these features.

Continuing with the same aim of investigating multitarget compounds for Alzheimer's disease treatment, our second research article from Munoz-Torrero's group

focuses on brain-permeable rhein–huprine hybrids [4]. These second-generation compounds have potent acetylcholinesterase or BACE-1 inhibitory activities, as well as A β 42 and tau anti-aggregating and antioxidant activities. The identified compounds, which target several crucial pathogenic factors, could be extremely useful in Alzheimer's disease treatment.

Our final research article in this special focus issue reports the development of a new potential radiotracer to be used as a probe in Alzheimer's disease. Fernández *et al.* investigate how an indazole-based [18F]-PET-probe can be used to detect changing levels of acetylcholinesterase in the brain [5]. Animal models demonstrated that the probe had good blood–brain barrier penetration and reasonable half-lives.

As well as featuring original research, this special focus issue contains reviews focusing on potential Alzheimer's and Parkinson's disease therapies.

The first of the review articles in this issue, from our guest editor Bolognesi and co-workers investigates the interesting possibility of targeting neuroregeneration over neurodegeneration as a strategy for Alzheimer's disease drug discovery [6]. The authors highlight that targeting the endogenous brain regenerative process using small molecules or nanoparticles may be more beneficial for patient outcomes than therapies aimed at reverting neurodegeneration.

Babkova *et al.* have contributed an insightful review to this special issue based

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on naturally occurring prolyl oligopeptidase inhibitors and peptide-like inhibitors in relation to their biological effects in Alzheimer's and Parkinson's diseases [7]. Although to date, there is no prolyl oligopeptidase inhibitor available on the market, several clinical trials have been undertaken and some of them have shown promising results and interesting pharmacological profiles.

Our final article in this series focuses on the role of the α -synuclein protein in the pathogenesis of Parkinson's disease [8]. The review from Singh *et al.* also covers the development of small molecules as possible modulators of α -synuclein aggregation and their potential application in Parkinson's disease.

We hope that the articles featured in this issue of 'Future Medicinal Chemistry' provide useful insights

into the valuable contributions being made by medicinal chemists to the advancement of neurodegenerative disease drug discovery.

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