Liliana Bernardino, J Neurol Clin Neurosci
ISSN:2752-809X | Volume 06

Received date: 28-02-2022 | Accepted date: 02-03-2022 | Published date: 26-07-2022

MicroRNA-based therapeutic approaches for Parkinson's disease

Liliana Bernardino
University of Beira Interior, Portugal

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder, and its incidence is rising, representing a substantial socioeconomic impact. The major neuropathological hallmarks are the degeneration of dopaminergic neurons in the nigrostriatal pathway and alpha-Synuclein inclusions known as Lewy bodies and Lewy neurites. Clinically, PD is defined by motor (e.g., rigidity, tremor, bradykinesia) and non-motor symptoms (e.g., depression, dementia). Although some treatments can reduce motor symptoms, no effective prevention and curative therapies have been developed yet. MicroRNAs (miR), small non-coding RNAs that post-transcriptionally regulate gene expression, are promising candidates for PD therapy, as they regulate several pathophysiological aspects of this multifactorial disease. miR have been used for stem cell-based therapies, inducing the differentiation into a specific cell phenotype, and as targets to modulate pathological mechanisms. However, effective clinical translation critically depends on developing efficient delivery systems. We first developed polymeric nanoparticles (NP) that release miR-124 to boost neurogenesis in the context of PD. miR-124 NP induced neurogenesis by targeting the stemness-related genes Sox9 and Jagged1 in vitro while increasing the number of new neurons in lesioned striatum and ameliorating motor symptoms in the 6-hydroxydopamine (6-OHDA) mouse model of PD in vivo. However, NP delivery has several challenges, such as degradation, bioaccumulation, retention in the basal lamina, and toxicity. Recently, we developed an innovative and novel delivery system based on small extracellular vesicles (sEV) as disease-targeted, biological delivery vectors for miR-124. In vitro, miR-124 sEV induced neurogenesis and protected N27 cells against 6-OHDA-induced toxicity. In vivo, although miR-124 sEV did not increase the number of new neurons in the lesioned striatum, our formulation protected dopaminergic neurons, which ameliorated motor symptoms. Thus, our findings support the therapeutic value of miR in the context of PD and the relevance of drug delivery systems to target distinct biological responses and enhance therapeutic effects.

Recent Publications:

1. Saraiva C, Talhada D, Rai A, Ferreira R, Ferreira L, Bernardino L, Ruscher K. MicroRNA-124-loaded nanoparticles increase survival and neuronal differentiation of neural stem cells in vitro but do not contribute to stroke outcome in vivo. PLoS One. 2018 Mar 1;13(3):e0193609. doi: 10.1371/journal.pone.0193609. PMID: 29494665; PMCID: PMC5832317.

2. Cláudia Saraiva, Marta Esteves, Liliana Bernardino, MicroRNA: Basic concepts and implications for regeneration and repair of neurodegenerative diseases, Biochemical Pharmacology, Volume 141, 2017, Pages 118-131, ISSN 0006-2952, https://doi.org/10.1016/j.bcp.2017.07.008.

3. Saraiva C, Ferreira L, Bernardino L. Traceable microRNA-124 loaded nanoparticles as a new promising therapeutic tool for Parkinson's disease. Neurogenesis (Austin). 2016 Nov 14;3(1):e1256855. doi: 10.1080/23262133.2016.1256855.

4. Saraiva C, Paiva J, Santos T, Ferreira L, Bernardino L. MicroRNA-124 loaded nanoparticles enhance brain repair in Parkinson's disease. J Control Release. 2016 Aug 10;235:291-305. doi: 10.1016/j.jconrel.2016.06.005. Epub 2016 Jun 3. PMID: 27269730.

5. Esteves M, Cristóvão AC, Saraiva T, Rocha SM, Baltazar G, Ferreira L, Bernardino L. Retinoic acid-loaded polymeric nanoparticles induce neuroprotection in a mouse model for Parkinson's disease. Front Aging Neurosci. 2015 Mar 6;7:20. doi: 10.3389/fnagi.2015.00020. PMID: 25798108; PMCID: PMC4351630

Biography

In 2003, Liliana Bernardino obtained her BSc in Biology and her PhD in Molecular Biology at the University of Coimbra, in collaboration with the Mario Negri Institute for Pharmacological Research, Milan, and the University of Southern Denmark, Denmark in 2008. During her career, she disclosed the effects of several molecules (e.g., histamine, retinoic acid, microRNA) on microglia activity and the impact on neuronal differentiation, function and survival. She also developed novel drug delivery systems, aiming to boost their therapeutic effects in the context of Parkinson's disease and ischemic stroke. Liliana Bernardino co-authored 58 publications, some in renowned journals (e.g., Nature Communications, Stem Cells, Journal of Neuroscience, Journal of Controlled Release, Journal of Neuroinflammation). Currently, she is an Assistant Professor with Habilitation at the University of Beira Interior. The main scientific interests of Liliana Bernardino's research group are to identify and develop novel brain repair therapies for Parkinson's disease.

libernardino@fcsaude.ubi.pt