Therapeutic Strategies for Neurological Disorders: From Natural Compounds to Innovative Molecular Designs

Neurological disorders (NDs) remain the second global cause of death, only behind cardiovascular diseases [1]. Among NDs, AD is one of the most prevalent pathologies together with epilepsy [1, 2], dramatically interfering with the quality of life of millions of people. Indeed, more than 55 million people live with dementia worldwide and is expected to increase to 75 million in 2030 and 132 million by 2050, with an estimated cost rising to US$ 2 trillion in 2030. This framework is preceded by the rise of global life expectancy together with the increased incidence of important risk factors (i.e., obesity, type 2 diabetes, cardiovascular diseases) and the lack of effective treatments to stop the AD progression, turning it into the most common form of dementia [4]. Although vast global efforts have been made in order to explain its onset and development (only 5% of AD cases have been attributed to genetic mutations), in most cases, its aetiology remains unknown, making it difficult to design therapeutic strategies [5].

Regarding epilepsy, it affects 50 million people, especially in low- and middle-income countries with the highest prevalence (80%) [6]. Although there is a better knowledge of causative mechanisms and the development of some effective treatments compared to AD, around 30% of the patients do not respond to the available treatments [7], evidencing the need to find new targets. Likewise, last year it was suggested that one of the possible therapeutic failures could be the late diagnosis, pointing out that the detection of early biomarkers could play a key role in the effectiveness of designed therapeutic strategies [8].

In this special issue, a multidisciplinary team of international experts in epilepsy and neurodegenerative diseases discusses some of the relevant topics on potential markers of AD and novel therapeutic strategies for NDs.

Although some drugs are currently used in treating neurodegenerative diseases, the measurements of drug concentration in plasma of epileptic drugs probably are not a suitable method to correlate with drug antiepileptic efficacy. Dr. Fagiolino and Dr. Vazquez review the drug concentrations in the aqueous spaces of the body in different tissues, which is important for pharmacodynamics responses and drug elimination from the body [9]. The concentrations of the drug are not homogeneous throughout the tissues, and they rarely reflect the free drug concentration in the blood. Tissue drug concentrations are heterogeneous because of the different blood flow fractions they receive and membrane transporters, efflux pumps, and metabolic enzymes. The article provides excellent experimental evidence of how physiological and pathophysiological changes in such driving forces can modify tissue drug concentration [9]. There is currently great interest in the development of markers for AD, both at the blood level and at the cerebrospinal fluid level. The research in this area would be to make a rapid and accurate diagnosis of the disease in addition to monitoring the therapeutic response of the drugs. Pomilio and colleagues aimed to review the recent progress made in the application of mass spectrometry and chip techniques in AD patients to discriminate between AD, mild cognitive impairment, and healthy controls [10]. The interest of this technique is that its application in blood samples from patients with AD has proven to be less invasive and fast enough to determine the diagnosis and stage of the disease. The same authors also report the development of non-invasive biomarkers at the level of urine, saliva, and ocular fluid that can provide an adequate strategy for initial diagnoses of AD, together with other strategies such as nanotechnologies and imaging techniques such as positron emission tomography (PET), single photon emission computed tomography (SPECT), and magnetic resonance imaging (MRI) [11]. In this line, Dr. Manzine and colleagues also describe blood protein biomarkers that may be useful for the diagnosis of AD and non-AD for the development of new drug targets as well as new therapeutic strategies. The interest is in protein-based markers of AD, Parkinson’s disease, Lewy body dementia, and frontotemporal dementia. Blood biomarkers may have a valid use in clinical practice as they show promise in diagnosing and differentiating diseases [12].

C-Phycocyanin is a biliprotein of the cyanobacteria Spirulina platensis. Dr. Marin-Prida and colleagues report the neuroprotective properties of this compound in models of ischemia. They proposed a molecular mechanism through the inhibition of the expression and activity of NAPDH oxidase, specifically the NOX2 isofrom, in addition to the modulation of genes related to neuroinflammatory processes [13].

Drug-resistant epilepsy is associated with an increased risk of seizure-related injuries, poor treatment outcomes, lower quality of life, and an increased likelihood of sudden and unexpected death (SUDEP). The risk of SUDEP spikes with the frequency and severity of uncontrolled seizures. Morales-Chacón and colleagues described the emission computed tomography methodology that allows the identification of cortical and subcortical brain regions that are not directly related to epileptogenicity, thus facilitating the understanding of the epileptogenicity network and SUDEP mechanism in drug-resistant epilepsy. Likewise, this methodology provides greater feasibility in clinical practice [14].

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REFERENCES


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