Chapter 13
Alpha-Synucleinopathies: Parkinson's Disease, Dementia With Lewy Bodies, and Multiple System Atrophy

Carlos Henrique Ferreira Camargo
Hospital Universitário dos Campos Gerais – UEPG, Brazil

Marcus Vinicius Della-Coletta
State University of Amazonas, Brazil

Delson José da Silva
Federal University of Goias, Brazil

Hélio A. G. Teive
Federal University of Paraná, Brazil

ABSTRACT

Alpha-synuclein is a protein that forms a major component of abnormal neuronal aggregates known as Lewy bodies. A particular group of neurodegenerative disorders (NDs) is characterized by the abnormal accumulation of α-synuclein; termed the α-synucleinopathies, this group includes Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). Lysosomal storage diseases have also been linked to α-synuclein toxicity. Several therapeutic targets have been chosen among steps of metabolism of α-synuclein. Reducing α-synuclein synthesis or expression and increasing the clearance can be achieved in many ways. The development of immunotherapeutic approaches targeting α-synuclein has received considerable attention in recent years. The aim of this chapter is to present the α-synucleinopathies, as well as to present the most recent researches about treatment of synucleinopathies based on knowledge of the pathophysiology of α-synuclein pathways.

DOI: 10.4018/978-1-5225-5282-6.ch013

INTRODUCTION

A common feature among a number of neurological disorders is the abnormal aggregation of a protein as observed with amyloid beta in Alzheimer's disease (Selkoe et al., 1990) and huntingtin protein in Huntington's disease (Vonsattel et al., 2011). In 1912, Frederick Lewy first described the cytoplasmic inclusions now known as Lewy bodies in the substantia nigra in PD Cortical Lewy bodies were first reported in association with dementia in 1961 (Okazaki et al., 1961) but they were felt to be a relatively rare finding until the 1980s, when first ubiquitin and later α-synuclein immunostains made it easier to see them (Spillantini et al., 1997) and demonstrated that Lewy bodies were a common neuropathologic finding in dementia (Gomperts, 2016). α-Synucleinopathies is a particular group of NDs characterized by the abnormal accumulation of α-synuclein (Gomperts, 2016; Kahle, 2008) (Figure 1). Lysosomal storage diseases have also been linked to α-synuclein toxicity (Wong and Krainc, 2017). There are new treatments being researched based on the pathophysiology of alpha-synuclein, and immunology. The aim of this chapter is to present the α-synucleinopathies, as well as to present the most recent researches about treatment of synucleinopathies based on knowledge of the pathophysiology of α-synuclein pathways.

BACKGROUND

Despite the early knowledge of the involvement of α-synuclein in several neurodegenerative disorders, only recently has there been, as a Holy Grail, a search for the cause and cure of these diseases through α-synuclein cellular and extracellular mechanisms and pathways. A heated discussion on this topic was

Figure 1. Main common features among α-synucleinopathies