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Alzheimer's disease and Parkinson's disease overlap-A role for Oxysterols?

Othman Ghribi

University of North Dakota School of Medicine, USA

Alzheimer's disease (AD) and Parkinson's disease (PD) are the most two common neurodegenerative disorders. Both AD and PD are characterized by deposition in the brain of insoluble protein aggregates: β-amyloid (Aβ) in AD and α-synuclein-containing Lewy bodies in PD. The differences in protein aggregate types that accumulate either in AD or PD suggest that these diseases are two distinct entities. Intriguingly, a significant proportion of dementia brains showing features of AD also exhibit α-synuclein inclusions. On the other hand, a subset of PD patients shows Aβ aggregates in addition to the α-synuclein load. This indicates that AD and PD overlap, and that this overlap is caused by common factors that can trigger the overlapping features (i.e.Aβ and α-synuclein). Identification of such common factors is paramount for designing therapeutic strategies that can halt or stop the progression of Aβ- and α-synuclein-related.

We have identified the oxysterol product 27-hydroxy-cholesterol (27-OHC) as an agent that regulates Aβ and α-synuclein accumulation in human neuroblastoma SH-SY5Y cells. 27-OHC increases Aβ accumulation involving increased APP, BACE1 as well as ABCA1 levels and increases α-synuclein by inhibiting liver x receptors (LXR).

Several studies have shown increased levels of 27-OHC in both AD and PD brains. Our results suggest that 27-OHC might be the missing link between plasma cholesterol and neuropathological hallmarks of AD/PD.

Biography

Othman Ghribi has completed his Ph.D in 1994 at the University René Descartes, Partis France, and postdoctoral studies from The University of Quebec and the University of Virginia. He has published more than 50 papers in reputed journals and serving as a Senior Editor of The Journal of Alzheimer's Disease and is a member on the editorial board of the Journal of Alzheimer's Disease and Parkinsonism.

othman.ghribi@med.und.edu