

## Relevance and Significance of Lewy Bodies in Alpha-Synucleopathies Such as Parkinson's Disease

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Lewy bodies (LB) are the neuropathological hallmark for alpha-synucleopathies, such as Parkinson's disease (PD). These intracellular structures are a manifestation of the aberrant aggregation of the neuronal protein, alpha-synuclein. It is present in the healthy state, both in the brain and periphery, although its precise physiological role is unclear.

The relevance of these structures to the disease process has largely remained an enigma and not well understood. Nevertheless, their significance is highlighted by their occurrence in the asymptomatic form of PD or Incidental Lewy body disease [1]. Furthermore, more importantly, they appear to represent either a cause or consequence of detrimental neurocytotoxic process(es) associated with the illness.

Interestingly, recently, a growing body of evidence suggests the involvement of LB in the fabric of neurodegeneration, which is characteristic to the pathology of alpha-synucleopathies or synucleopathies. The other alpha-synucleopathies include disorders such as; multiple systems atrophy, diffuse Lewy body disease.

Genetic studies have proposed the involvement of alpha-synuclein in the development of familial PD, a rare form [2]. Additionally, it is principal component in the LB found in the more common sporadic form of PD. Therefore, that validates its importance in the pathology of the disease.

Perhaps the gene for this protein produces it in excess or an abnormal form? The latter appears to be the case, since mutations (duplication or triplication) in the alpha-synuclein gene (SNCA) have been reported (Singleton, *et al* 2003). The mutant form of SNCA may confer a predisposition to misfolding of alpha-synuclein to beta sheet-synuclein. This misfolding is of great significance as it yields to the formation of the cytotoxic culprit accountable for the polymerisation and production of oligomers and plaques, which subsequently form large intracellular pathological aggregates (such as, LB) and resulting in neuronal dysfunction and degeneration. Alarming, beta sheet-synuclein can propagate in a prion-like fashion [3], thus leading to a spread of LB pathology.

There appears to be some correlate between neuroinflammation and the production of these protein inclusions. In PD, microgliosis has been found in the brain [4]. The inflammatory processes have been suggested to play a pathological role. Furthermore, neuroinflammation has been implicated in the propagation of the misfolded alpha-synuclein [5]. This neuroinflammation is not restricted to the brain only. Indeed, acute and chronic inflammation of the intestinal wall corresponded with the expression of alpha-synuclein in the neurites of the gastrointestinal tract [6]. This offers host of possibilities as to the origin of the disease, such as, does PD begin in the peripheral nervous system and the spread prion like to the brain? More importantly, it furnishes new possibilities for neuroprotective strategies and treatment. Ideally, a combination of targets would be more effective, such as, dampening or halting the detrimental events prompted by microgliosis activation and enhancing the clearance of alpha-synuclein by microglia.

Finally, it appears that there is a clear involvement of Lewy body containing alpha-synuclein in the pathogenesis of the disease process itself. Also, it offers an ideal target for neuroprotective strategies aimed at halting or reducing the brunt of mechanism(s) and generation of neurotoxic species implicated in alpha-synucleopathies.

### Bibliography

1. Gibb WR and Lees AJ. "The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease". *Journal of Neurology, Neurosurgery, and Psychiatry* 51.6 (1988): 745-752.
2. Olanow CW and Brundin P. "Parkinson's disease and alpha synuclein: is Parkinson's disease a prion-like disorder?" *Movement Disorders* 28.1 (2013): 31-40.
3. Chu Y and Kordower JH. "The prion hypothesis of Parkinson's disease". *Current Neurology and Neuroscience Reports* 15.5 (2015): 28.
4. McGeer PL., *et al.* "Reactive microglia are positive for HLA-DR in the substantia nigra of Parkinson's and Alzheimer's disease brains". *Neurology* 38.8 (1988): 1285-1291.
5. Lema Tomé CM., *et al.* "Inflammation and  $\alpha$ -synuclein's prion-like behavior in Parkinson's disease--is there a link?" *Molecular Neurobiology* 47.2 (2013): 561-574.
6. Stolzenberg E., *et al.* "A Role for Neuronal Alpha-Synuclein in Gastrointestinal Immunity". *Journal of Innate Immunity* 9.5 (2017): 456-463.

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