OVEREXPRESSION OF ALPHA-SYNUCLEIN INDUCES PEROXISOME DYSFUNCTION IN A MOUSE MODEL OF PARKINSON'S DISEASE

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A progressive conversion of the soluble αS protein into insoluble, β-sheet rich filaments and their intraneuronal deposition into Lewy bodies (LB) and Lewy neurites underlie αS cytotoxicity in the synucleinopathies. Growing evidence suggests that brain lipids and specifically poly unsaturated fatty acids (PUFAs) play a role in αS pathogenesis.

Recently we have detected enhanced αS pathogenesis in brains of mice modeling peroxisome biogenesis disorder (Yakunin et al. J. Neuroscience Research, 2010) and suggested that peroxisomes may be involved in αS toxicity. The peroxisome is the cellular organelle involved in cell lipid metabolism including β-oxidation of long chain PUFA and pathogenic elevations in brain PUFA levels are found in patients with abnormal peroxisomes. We now show evidence for significantly altered peroxisomal gene expression; altered biochemical activity and lower levels of peroxisomes in vivo, in brains of A53T αS transgenic mice modeling the synucleinopathies.