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Alpha-synuclein Amyloids Catalyze the Degradation of Atp and Other Nucleotides

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Intracellular accumulation of alpha-synuclein amyloids is a main pathological hallmark in a subgroup of human neurodegenerative diseases called synucleinopathies. Cell death of energy-deprived dopaminergic neurons causes decreased dopamine levels, which underly many of the neurological symptoms in the most prevalent synucleinopathy, Parkinson's disease. Amyloid-mediated toxicity can proceed via gain-of-function through diverse pathways. In this work, we report that alpha-synuclein amyloids can degrade adenosine triphosphate in a catalytic fashion, producing adenosine diphosphate and adenosine monophosphate. Upon prolonged incubation, all adenosine triphosphate is irreversibly consumed. Furthermore, these amyloids can also degrade all other ribonucleotides with different efficiencies, including guanosine, cytidine, and uridine triphosphates. Our findings uncover a previously unknown gain-of-function for alpha-synuclein amyloids, which may have far reaching implications for ATP and nucleotide metabolism during neurodegeneration in Parkinson's disease and other synucleinopathies.