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Bioinorganic Implications and Strategies in Parkinson's Disease

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Brain metal compositions change with aging and with the progression of neurodegenerative diseases. Under oxidatively stressed conditions, redox metals can promote the generation of free radicals. Alpha-synuclein (αS), the structurally dynamic protein implicated in Parkinson's disease (PD) pathology, has shown variable changes in its native biophysical properties in the presence of redox metals. Such metal promoted αS misfolding and/or post-translational modifications can have detrimental effects on normal function. The presented research will highlight metal-induced changes in the folding pattern of αS and the distinguishable differences observed between various metal oxidation states. The aggregation propensity of αS has been examined by circular dichroism analysis, dynamic light scattering, FT-IR, and thioflavin T fluorescence assays, as well as through immunoblotting techniques. Another avenue of this research capitalizes on these innate bioinorganic characteristics to target the dissociation of aggregation prone αS. Macrocyclic metallospecies are being utilized to proteolytically cleave αS β-sheet fibrils. Thus, the same characteristics that can make aberrant metal-promoted chemistry detrimental, have also been utilized to affect αS aggregates, as are found in PD Lewy bodies. Through this work, new therapeutic strategies for the treatment of PD and related disorders may become apparent.

Biography

Heather R. Lucas obtained her Ph.D. in 2009 at the Johns Hopkins University and subsequently carried out research at Osaka University in Japan with the support of a fellowship through the Global Center of Excellence. She was additionally a Lenfant Biomedical Fellow at the National Heart, Lung and Blood Institute and an NIH postdoctoral fellow at the National Institute on Aging. Dr. Lucas then joined the faculty within the Virginia Commonwealth University Department of Chemistry and Chemical Biology Program as an Assistant Professor for the Spring of 2014, where her research group encompasses inorganic biochemistry, biophysics, as well as inorganic and organic syntheses.

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