

Lysosomal enhancement as a treatment for the multi-proteinopathy of Alzheimer's disease and other protein accumulation disorders

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Alzheimer's disease is an impending epidemic with a critical need for preventative approaches. Alzheimer-type pathogenesis is due to suspected imbalances between protein production and protein clearance, and we have identified a lysosomal regulation pathway that can be manipulated to prevent age-related deficits in proteolytic clearance linked to dementia. Deficits in the removal of misfolded or aggregating proteins constitute risk factors for Alzheimer's disease, and with age lysosomes become less effective at clearing the toxic accumulations. Reducing protein accumulations is essential for preventing the onset of Alzheimer's disease and to prevent the disorder's progression. Lysosomes and their degradative enzymes (cathepsins) are functionally enhanced by a new class of compounds. Development of the first-in-class lysosomal modulators has led to studies showing improved clearance of different proteins (including A β peptide, PHF-tau, and α -synuclein), recovered synaptic integrity, and corresponding cognitive improvement in two distinct transgenic mouse models. The amelioration of synaptic and behavioral deficits indicates that lysosomal enhancement prevents disease progression when induced during the initial or severe phase of protein accumulation pathology. This work provides a novel approach to prevent and/or manage the multi-proteinopathy of Alzheimer's disease and related neurodegenerative disorders including FTD and Parkinson's disease.

Biography

Ben A. Bahr received his Ph.D. in Chemistry from University of California-Santa Barbara. Dr. Bahr joined the Center for the Neurobiology of Learning and Memory at University of California-Irvine, then was a faculty member at the University of Connecticut. In 2009, he was appointed as the William C. Friday Chair at University of North Carolina-Pembroke. He has presented his research in 15 countries, has more than 130 publications, and has patents associated with first-in-class drugs for neurodegenerative diseases. He is a member of UNCP's Biotech Center, Northeastern University's Center for Drug Discovery, and the European Task Force on Brain and Lysosomal Storage Diseases.

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