S-Nitrosylation Mediates Protein Misfolding and Mitochondrial Dysfunction in Neurological Diseases

ABSTRACT:
Neurodegenerative disorders including Alzheimer’s disease (AD) and Parkinson’s disease (PD), manifest deposits of misfolded proteins, and result from synaptic injury and neuronal death. Recent studies have suggested that nitrosative stress due to generation of excessive nitric oxide (NO) can mediate excitotoxicity in part by triggering protein misfolding and aggregation, and mitochondrial fragmentation in the absence of genetic predisposition. S-Nitrosylation, or covalent reaction of NO with specific protein thiol groups, represents a convergent signal pathway contributing to NO-induced protein misfolding and aggregation, compromised dynamics of mitochondrial fission-fusion process, thus leading to neurotoxicity. I will summarize our recent findings on the effect of S-nitrosylation on protein function under excitotoxic conditions, and present evidence suggesting that NO contributes to protein misfolding and aggregation via S-nitrosylating E3 ubiquitin ligase parkin, and mitochondrial fragmentation through beta-amyloid related S-nitrosylation of dynamin-related protein-1 with the relevance to disease pathogenesis.

BIOGRAPHICAL:
Dr. Zezong Gu has a MD from Tianjin Medical University in China and PhD from the University of Texas Medical Branch at Galveston. He was recruited to the School of Medicine Department of Pathology and Anatomical Sciences from the prestigious Sanford-Burnham Medical Research Institute at La Jolla, California where he still holds an adjunct faculty position. His research is currently funded by the grants from NIH/NIEHS, American Heart Association NSDG and BGIA programs, and the DANA Foundation Brain Imaging program.