Chemical tools to elucidate the fate of S-Nitroso Homocysteine in proteins.
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Introduction
Homocysteine (Hcy) is a non-proteinogenic amino acid that has been associated for years as an independent risk factor for Alzheimer’s disease, cardiovascular disease, and renal failure among other ailments. Currently, it is unknown whether homocysteine acts as a causative agent for disease or is simply a biomarker. Hcy toxicity is attributed to the formation of the metabolites homocysteine thiolactone (HcyTL) and S-nitroso homocysteine (HcySNO). At present, the understanding of the physiological role of these metabolites is an area of interest. HcyTL is produced by the natural editing action of methionyl t-RNA synthetase and can react with lysine residues, thereby disrupting the secondary structure of proteins, leading to malfunction.

Much less is known regarding the physiological role of HcySNO in proteins. It is hypothesized that the metabolic pathway by which HcySNO is produced is a response designed to shear the damaging effects of high homocysteine levels, however neither free HcySNO nor protein HcySNO have been detected in vivo. The development of a selective detection method for capturing HcySNO is necessary to unravel the in vivo fate and biological role of homocysteine.

Research Strategy

Biotin based assay for HcySNO-N-protein:

Future Work

Future studies in this area should continue the preparation of homocysteine derivatives and also begin to screen the reaction conditions that are necessary for the peptide cleavage reaction.

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References