

ANTI-AGING PROPERTIES OF PROTEIN PERSULFIDATION

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An oxidative-posttranslational modification of thiols called protein persulfidation (RSSH) represents the underlying mechanism of biological actions ascribed to new gasotransmitter hydrogen sulfide (H₂S). We developed a new dimedone based method for detection of protein persulfidation and its selectivity was tested and confirmed in various experimental models (*D. melanogaster*, *C. elegans*, *M. musculus*, human cell lines and samples). Obtained results demonstrated that persulfidation represents an evolutionary conserved modification that correlates to the H₂S production capacity and is accompanied with numerous physiological implications. One of such general observations is that persulfidation represents protective mechanism for the reduction of sulfenic acids under conditions of oxidative stress. When *C. elegans* mutants for CSE and MST were exposed to different oxidative stress inducers they showed enhanced sensitivity, while pretreatment with H₂S donors rescued them. Additionally, we observed a strong correlation between protein persulfidation levels and development and aging in different experimental models. Fluctuations in the level of persulfides were observed during development of *C. elegans* with prominent increase in L3 larval stage. Our data showed that after strong peak in L3, persulfide levels decreases during life in *C. elegans*. Decline of persulfide levels in the adult worms of different age was also observed. Similar effect was discovered in the brains of rats of different age. Immunohistological analysis of brain sections for H₂S producing enzymes revealed the decrease in intensity of immunopositivity during aging process. Our results strongly propose protein persulfidation represents a rescue loop from cysteine hyper-oxidation and subsequent loss of protein function. This general mechanism represents a promising tool in overcoming the consequences of increased oxidative stress during aging process.