

Reactive cysteine persulfides, a novel regulator of oxidative stress and redox signaling.

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Professor Takaaki Akaike at Tohoku University Graduated School of Medicine and co-workers revealed the novel cellular system to produce reactive cysteine persulfide that have superior antioxidant activity and unique signaling function. Current common knowledge suggests that the enzymes metabolizing sulfur-containing amino acids, cystathionine β -synthase (CBS) and cystathionine γ -lyase (CSE), produce hydrogen sulfide (H₂S) and that H₂S acts as a signaling molecule in mammalian cells. Prof. Akaike's team developed a method for detecting persulfides and polysulfides by LC-MS/MS and explored the enzymatic production, cellular levels, and its reactivity. CBS and CSE metabolized cystine (Cys-SS-Cys) to cysteine hydropersulfide (Cys-SSH). Cys-SSH in the cells reacted with both oxidized and reduced glutathione (GSSG and GSH, respectively) to produce GSSH as well as other glutathione-derived per- and polysulfides. In mouse and human tissues, these persulfide species were found at various levels, and also protein-bound polysulfide species were identified in cells. The reactivity of persulfides to electrophilic signaling molecules, such as 8-nitro-cGMP, was much higher than that of H₂S. These suggest that H₂S may simply be a biomarker of persulfides formation and that reactive cysteine persulfide itself may have a primary role in cellular signaling and regulation of the pathogenesis of oxidative stress-related diseases. The results of this study were published in Proceedings of National Academy of Sciences of USA. The present finding is also comprehensively highlighted by a recent review article (cf. Figure shown below).



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<http://www.med.tohoku.ac.jp/english/org/medical/55/index.html>

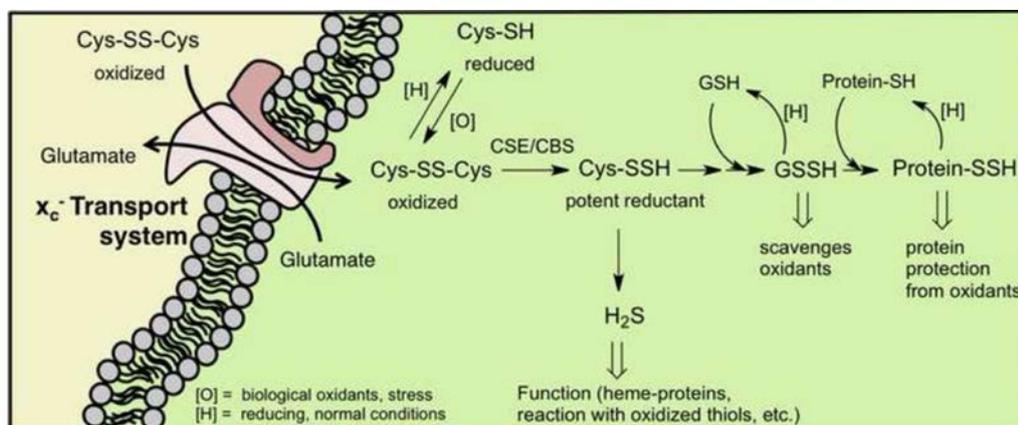


Figure. The overview of redox chemistry and chemical biology of H₂S, hydropersulfides and derived species (adapted from Ono et al, Free Radic Biol Med, in press, 2014).

Reactive cysteine persulfides and S-polythiolation regulate oxidative stress and redox signaling.

Ida T, Sawa T, Ihara H, Tsuchiya Y, Watanabe Y, Kumagai Y, Suematsu M, Motohashi H, Fujii S, Matsunaga T, Yamamoto M, Ono K, Devarie-Baez NO, Xian M, Fukuto JM, Akaike T.

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