

P002 Redox regulation of SUMO proteases
**Zheng XU, Levina Suk Mi LAM, Lok Hei LAM,
So Fun CHAU, Tzi Bun NG and
Shannon Wing Ngor AU**

*Department of Biochemistry, The Chinese University of
Hong Kong, Hong Kong*

Sumoylation is an indispensable post-translational modification modulating the functions of a broad spectrum of proteins. SUMO proteases catalysing SUMO maturation and deconjugation are crucial in maintaining a proper balance of sumoylation-desumoylation. Here, we show that H_2O_2 can induce formation of inter-molecular disulfide linkage of human SUMO protease SENP1, via the active-site Cys 603 and a unique residue Cys 613. Such reversible modification confers higher enzyme activity recovery which was also observed in yeast Ulp1, but not in human SENP2, suggesting its protective role against irreversible sulfhydryl oxidation. *In vivo* formation of disulfide-linked dimeric SENP1 was also detected by immunoprecipitation from cells stimulated with H_2O_2 . The modifications are further elucidated by the crystal structures of Ulp1 with catalytic cysteine oxidized to sulfenic, sulfinic and sulfonic acids. Our findings suggest that, in addition to SUMO conjugating enzymes, SUMO proteases may act as redox sensors and effectors modulating the desumoylation pathway and specific cellular responses to oxidative stress.