NEW CLUES TO METABOLIC REGULATION THROUGH CHANGES IN THE THIOL REDOX PROTEOME

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The natural reversibility of cys modifications allow them to play a role in modulation of protein function as redox switches involved in redox signalling. There is increasing evidence regarding the number of proteins whose function is regulated by the modification of a specific cys residue by H_2O_2 or by a simple thiol exchange from thiol to disulfide. The set of proteins that are susceptible to reversible sulphur oxidation has been named the “Redox Thiol Proteome”. The identification of these proteins and their fluctuations present a methodological challenge, the resolution of which is a mater of current interest.

In all cases due to the chemical reactivity and regulatory logic, the redox modifications of cysteines are not spontaneously reduced when redox homeostasis is restored but are regenerated with the help of the redoxins Grx, Trx and others. Much is known about the functions of these "redoxins", however their exact action and the metabolic processes they play physiologically important roles remains to be completely elucidated.

Here we used a shotgun proteomic approach consisting of searching within the redox proteome, for proteins that are differentially modified when the cells do not express a particular redoxin. The method selects for redox-sensitive cys-containing peptides thus allowing not only the identification of the protein but to map the exact cysteine involved, as well. When a protein is detected as redox modified in a mutant cell and not in the control, we conclude that the protein is modified as a consequence of the inflicted mutation. This strategy has allowed us to determine a kind of “redoxin functional interactome” without precluding subsequent confirmation of the existence of direct physical interaction or not. A parallel transcriptomic analysis has provided a coherent situation that correlates posttranslational redox modifications in key proteins with gene expression changes and metabolic remodelling.