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PROTEOMIC ANALYSIS OF S-NITROSATED PROTEINS

Antonio Rodríguez-Ariza
Unidad de Investigación, Hospital Universitario Reina Sofía, Córdoba, Spain

One of the major tasks to be accomplished in the post-genomic era is the characterization of post-translational modifications in proteins. The S-nitrosation of protein thiols is a redox-based posttranslational modification that modulating enzymatic activity, sub-cellular localization, complex formation and degradation of proteins, largely contributes to the complexity of cellular proteomes. Although the detection of S-nitrosated proteins is problematical due to the lability of S-nitrosothiols (SNO), with the improvement of molecular tools an increasing range of proteins has been shown to undergo S-nitrosation.

The liver is one organ clearly influenced by nitric oxide, and acute and chronic exposure to this substance has been associated with distinct patterns of liver disease. Therefore, it is important to identify potential targets for protein S-nitrosation in human hepatocytes during alteration of SNO homeostasis. Treatment of human hepatocytes with L-nitrosocysteine increased cell death and augmented the levels of S-nitrosoproteins, detected both by chemiluminescence and the biotin-switch method. An increased S-nitrosoglutathione reductase (GSNOR) activity, related to augmented levels of ADH-5 mRNA, the gene encoding for GSNOR in humans, returned SNO content to basal levels. The identified S-nitrosoproteins in hepatocytes included proteins involved in metabolism, maintenance of cellular homeostasis and signalling. These results points to the relevance of this posttranslational modification to the physiology and pathophysiology of these cells.

Further proteomic approaches for the systematic assessment of potential targets for protein S-nitrosation have been recently developed. These strategies include methods for the identification of the modified cysteines, that will provide researchers with better tools for exploring this post-translational modification and for performing an in depth analysis of the cellular S-nitrosoproteome.