A proteomics approach to inventory protein thiol targets of peroxisome-derived hydrogen peroxide

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Keywords: hydrogen peroxide, redox signaling, redox proteomics, sulfenome.

Abstract

Ever since the first characterization of peroxisomes, a central theme has been their involvement in hydrogen peroxide (H_2O_2) metabolism. While the reputation of H_2O_2 drastically changed from an exclusively toxic molecule to a signaling messenger, the regulatory role of peroxisomes in these signaling events is still largely underappreciated. This is mainly because the number of known protein targets of peroxisome-derived H_2O_2 is rather limited and testing of specific targets is predominantly based on knowledge previously gathered in related fields of research. In order to gain a broader and more systematic insight into the role of peroxisomes in redox signaling, an unbiased approach is urgently needed.

To accomplish this goal, we have combined our previously developed cell system in which we can control peroxisomal H_2O_2 production[1] with a redox proteomics strategy established by the Van Breusegem group[2]. This strategy is based on the use of a modified yeast AP-1-like (YAP1) transcription factor to trap sulfenic acid-containing proteins *in cellulo* and affinity purify them for proteomics analysis. Sulfenic acid is a reversible cysteine thiol modification that is among the most relevant for redox signaling at physiological H_2O_2 concentrations. While the YAP1-based approach was originally used in *Arabidopsis thaliana*, we now optimized it for use in mammalian cells and targeted the probe to the cytosol, mitochondria, or peroxisomes. This enables us to inventory the primary protein thiol targets of peroxisome-derived H_2O_2 in these cellular compartments and to assess the contribution of peroxisomal H_2O_2 metabolism to cellular redox signaling. The most recent data will be presented and discussed.

References

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