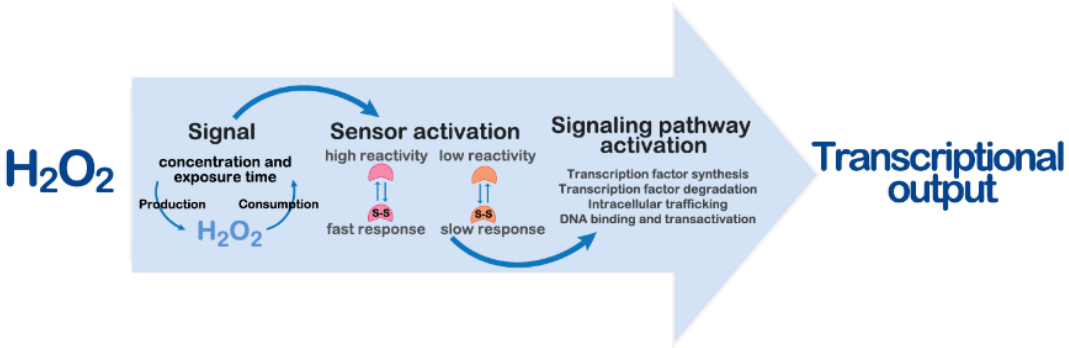
From oxidative stress to redox biology: understanding the cellular mechanisms of redox regulation by hydrogen peroxide



Hydrogen peroxide sensing, signaling and regulation of transcription factors

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Highly Cited Paper

Hydrogen peroxide (H_2O_2), a reactive oxygen species (ROS), is a ubiquitous oxidant present in all aerobic organisms. Since its first identification in a living cell, H_2O_2 was considered a toxic by-product of aerobic metabolism, something that cells had to remove. If H_2O_2 detoxification catalyzed by catalases and peroxidases was not adequate, H_2O_2 would diffuse and oxidize biological targets causing cellular malfunctions, i.e. oxidative stress, responsible for several pathologies and aging.

Starting in the 90s this paradigm of hydrogen peroxide as toxic started to change to a paradigm where hydrogen peroxide acts in cellular regulation and is involved in cellular signalling – redox signalling – through the oxidation of thiols in proteins that act as redox sensors. Nowadays, redox biology is an established field and the essential regulating role played by H_2O_2 *in vivo* with important implications in health and disease is unquestionable. In this work it was shown that the complexity of redox regulation increases along the phylogenetic tree and that H_2O_2 modulates gene expression at all steps from transcription to protein synthesis. Also, some of the unanswered questions regarding our understanding of redox-dependent regulation of gene expression were addressed:

What makes a good H_2O_2 sensor?

What are the common chemical and kinetic principles that govern H_2O_2 signaling?

Is it possible to obtain an integrative view of H_2O_2 regulation of transcription factors?