

Editorial

Hydrogen Peroxide Signaling in Physiology and Pathology

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Reactive oxygen species (ROS) were originally described as toxic by-products of aerobic cellular energy metabolism associated with the development of several diseases, such as cancer, neurodegenerative diseases, and diabetes [1–3]. In these contexts, the accumulation of ROS in cells, referred to as oxidative stress, is a toxic event that damages a number of biomolecules. Over the last thirty years, research has focused on the development of strategies to reduce ROS in order to prevent tissue damage in normal aging tissues and in pathological situations. An industry related to “antioxidant” strategies expanded to the mainstream, and nowadays everybody seems aware of the toxicity of ROS.

However, recent findings have shown that ROS can also contribute to bona fide physiological processes, leading to a new paradigm in reversible post-translational modifications involved in signal transduction, defined as oxidative eustress [4,5]. Amongst ROS, hydrogen peroxide (H₂O₂) best fits the properties of a signaling molecule and is recognizable as the major ROS in the oxidative regulation of physiological activity [6]. H₂O₂ is mainly produced by NADPH oxidases and the mitochondrial electron transport chain [7,8]. This generation is controlled by growth factors, chemokines and physical stress, among other factors.

This Special Issue highlights the most recent advances in all the aspects of ROS signaling with examples of H₂O₂ signaling in *E. coli*, plants and animals. It has recently been shown that H₂O₂ can regulate Shh signaling during development and regeneration [9]. Thauvin et al. analyzed its molecular mechanism and discovered that Shh controlled H₂O₂ levels through a noncanonical Boc-Rac1 pathway [10]. In a positive loop, H₂O₂ regulates Shh trafficking. Thus, Shh directly impacts its own distribution and potentially the distribution of other morphogens via H₂O₂ level modulation. These founding results provide a molecular explanation for the robustness of morphogenesis and open a new path toward the integration of ROS regulation in morphogens signaling. It has been shown that ROS level oscillation is involved in cell cycle regulation in vertebrate early development [11]. Tokmakov et al. showed that ROS levels are also involved in fertilization via the control of calcium in *Xenopus laevis* oocytes [12]. This calcium and H₂O₂ signaling crosstalk is also at work in plants, as shown by Cheng et al. in this Issue [13]. In this article, the authors investigate the molecular targets of H₂O₂ and Ca²⁺ in melon and *Arabidopsis* seed germination. They show that H₂O₂ and Ca²⁺ form a reciprocal positive-regulatory loop to maintain a balance between abscisic acid (ABA) and gibberellic acid (GA₃) essential to promoting seed germination under ABA stress. Finally, Roth et al. performed a transcriptomic analysis of *E. coli* response to different concentrations of H₂O₂ [14]. This analysis reveals that different stress responses are activated by H₂O₂ exposure and emphasize the role of cysteine synthesis as an antioxidant response.

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References

1. Chaturvedi, R.K.; Flint Beal, M. Mitochondrial Diseases of the Brain. *Free Radic. Biol. Med.* **2013**, *63*, 1–29. [[CrossRef](#)]
2. Li, J.; O, W.; Li, W.; Jiang, Z.-G.; Ghanbari, H. Oxidative Stress and Neurodegenerative Disorders. *Int. J. Mol. Sci.* **2013**, *14*, 24438–24475. [[CrossRef](#)]
3. Liou, G.-Y.; Storz, P. Reactive oxygen species in cancer. *Free Radic. Res.* **2010**, *44*, 479–496. [[CrossRef](#)] [[PubMed](#)]
4. D’Autréaux, B.; Toledano, M.B. ROS as signalling molecules: Mechanisms that generate specificity in ROS homeostasis. *Nat. Rev. Mol. Cell Biol.* **2007**, *8*, 813–824. [[CrossRef](#)] [[PubMed](#)]
5. Sies, H.; Jones, D.P. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nat. Rev. Mol. Cell Biol.* **2020**, *21*, 363–383. [[CrossRef](#)] [[PubMed](#)]
6. Sies, H. Hydrogen peroxide as a central redox signaling molecule in physiological oxidative stress: Oxidative eustress. *Redox Biol.* **2017**, *11*, 613–619. [[CrossRef](#)] [[PubMed](#)]
7. Brandes, R.P.; Weissmann, N.; Schröder, K. Nox family NADPH oxidases: Molecular mechanisms of activation. *Free Radic. Biol. Med.* **2014**, *76*, 208–226. [[CrossRef](#)] [[PubMed](#)]
8. Bedard, K.; Krause, K.-H. The NOX Family of ROS-Generating NADPH Oxidases: Physiology and Pathophysiology. *Physiol. Rev.* **2007**, *87*, 245–313. [[CrossRef](#)] [[PubMed](#)]
9. Rampon, C.; Volovitch, M.; Joliot, A.; Vríz, S. Hydrogen peroxide and redox regulation of developments. *Antioxidants* **2018**, *7*, 159. [[CrossRef](#)] [[PubMed](#)]
10. Thauvin, M.; Amblard, I.; Rampon, C.; Mourton, A.; Queguiner, I.; Li, C.; Gautier, A.; Joliot, A.; Volovitch, M.; Vríz, S. Reciprocal Regulation of Shh Trafficking and H₂O₂ Levels via a Noncanonical BOC-Rac1 Pathway. *Antioxidants* **2022**, *11*, 718. [[CrossRef](#)] [[PubMed](#)]
11. Han, Y.; Ishibashi, S.; Iglesias-Gonzalez, J.; Chen, Y.; Love, N.R.; Amaya, E. Ca²⁺-Induced Mitochondrial ROS Regulate the Early Embryonic Cell Cycle. *Cell Rep.* **2018**, *22*, 218–231. [[CrossRef](#)] [[PubMed](#)]
12. Tokmakov, A.A.; Morichika, Y.; Teranishi, R.; Sato, K.-I. Oxidative Stress-Induced Overactivation of Frog Eggs Triggers Calcium-Dependent Non-Apoptotic Cell Death. *Antioxidants* **2022**, *11*, 2433. [[CrossRef](#)] [[PubMed](#)]
13. Cheng, M.; Guo, Y.; Liu, Q.; Nan, S.; Xue, Y.; Wei, C.; Zhang, Y.; Luan, F.; Zhang, X.; Li, H. H₂O₂ and Ca²⁺ Signaling Crosstalk Counteracts ABA to Induce Seed Germination. *Antioxidants* **2022**, *11*, 1594. [[CrossRef](#)] [[PubMed](#)]
14. Roth, M.; Jaquet, V.; Lemeille, S.; Bonetti, E.-J.; Cambet, Y.; François, P.; Krause, K.-H. Transcriptomic Analysis of *E. coli* after Exposure to a Sublethal Concentration of Hydrogen Peroxide Revealed a Coordinated Up-Regulation of the Cysteine Biosynthesis Pathway. *Antioxidants* **2022**, *11*, 655. [[CrossRef](#)] [[PubMed](#)]

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