Assessment of Subcellular ROS and NO Metabolism in Higher Plants: Multifunctional Signaling Molecules

Sukhmeen Kaur Kohli 1, Kanika Khanna 1, Renu Bhardwaj 1,*, Elsayed Fathi Abd_Allah 2,*, Parvaiz Ahmad 3,4,*, and Francisco J. Corpas 5,*

1 Department of Botanical and Environmental Sciences, Guru Nanak Dev University, Amritsar, Punjab 143005, India; sukhmeenkohli@gmail.com (S.K.K.); kanika.27590@gmail.com (K.K.)
2 Department of Plant Production, College of Food & Agricultural Sciences, King Saud University, Riyadh 11451, Saudi Arabia; eabdallah@ksu.edu.sa
3 Botany and Microbiology Department, College of Science, King Saud University, Riyadh 11451, Saudi Arabia
4 Department of Botany, S.P. College, Srinagar 190001, India
5 Department of Biochemistry, Cell and Molecular Biology, Estación Experimental del Zaidín, Consejo Superior de Investigaciones Científicas (CSIC), C/Profesor Albareda, 118008 Granada, Spain
* Correspondence: renubahardwaj82@gmail.com (R.B.); parvaizbot@yahoo.com (P.A.); javier.corpas@eez.csic.es (F.J.C.); Tel.: +91-9876215176 (R.B.)

Received: 5 November 2019; Accepted: 6 December 2019; Published: 12 December 2019

Abstract: Reactive oxygen species (ROS) and nitric oxide (NO) are produced in all aerobic life forms under both physiological and adverse conditions. Unregulated ROS/NO generation causes nitro-oxidative damage, which has a detrimental impact on the function of essential macromolecules. ROS/NO production is also involved in signaling processes as secondary messengers in plant cells under physiological conditions. ROS/NO generation takes place in different subcellular compartments including chloroplasts, mitochondria, peroxisomes, vacuoles, and a diverse range of plant membranes. This compartmentalization has been identified as an additional cellular strategy for regulating these molecules. This assessment of subcellular ROS/NO metabolisms includes the following processes: ROS/NO generation in different plant cell sites; ROS interactions with other signaling molecules, such as mitogen-activated protein kinases (MAPKs), phosphatase, calcium (Ca^{2+}), and activator proteins; redox-sensitive genes regulated by the iron-responsive element/iron regulatory protein (IRE-IRP) system and iron regulatory transporter 1(IRT1); and ROS/NO crosstalk during signal transduction. All these processes highlight the complex relationship between ROS and NO metabolism which needs to be evaluated from a broad perspective.

Keywords: antioxidants; reactive oxygen species; nitric oxide; organelles; signaling; stress

1. Introduction

Molecular oxygen (O_{2}), which is essential for life, is formed naturally by various aerobic metabolic processes. Reactive oxygen species (ROS) are redox molecules mainly produced in aerobic organisms, with some of the most important being photosynthetic cells, in which ROS production needs to be continually regulated to prevent undesirable functional collateral damage. ROS, which are involved in signaling processes in subcellular compartments and cells, as well as in mechanisms of defense against biotic and abiotic stresses, are also essential for cell survival [1,2].

In higher plants, the principal subcellular ROS production sites include chloroplasts, mitochondria, cytosols, vacuoles, peroxisomes, plasma membranes, apoplasts, and cell walls [3]. ROS, such as hydrogen peroxide (H_{2}O_{2}), superoxide anion (O_{2}^{•−}), hydroxyl radical (•OH), and singlet oxygen
(\(O_2\)) are metabolically closely associated with another family of molecules, called reactive nitrogen species (RNS), including peroxynitrite (ONOO\(^-\)) and S-nitrosogluthathione (GSNO), derived from the nitric oxide (\(^{*}\)NO) radical. Though generated under normal physiological conditions, these two molecular families are prone to uncontrolled overproduction under stressful circumstances, causing cellular nitro-oxidative damage which can hamper cell survival [4,5]. Figure 1 shows a simple model of ROS/RNS interplay in response to biotic and abiotic stresses, including nitro-oxidative stress, in plant cells. Usually associated with cytotoxicity, ROS/RNS also act as signal molecules involved in cellular interactions and mechanisms [6,7].

**Figure 1.** Simple model of the interplay between reactive oxygen species (ROS) and reactive nitrogen species (RNS) in response to biotic and abiotic stresses in plant cells which could have associated a nitro-oxidative stress. Reproduced with permission from Corpas and Barroso (2013) New Phytologist 11: 535-542. John Wiley and Sons and Copyright Clearance Center. Abbreviations: GR—glutathione reductase. GSNO—S-nitrosogluthathione. GSH—glutathione. GSSG—glutathione disulfide. O2•\(^-\)—superoxide anion. NH\(_3\)—ammonia. NO—nitric oxide. ONOO\(^-\)—peroxynitrite. ROS—reactive oxygen species. RNS—reactive nitrogen species.

ROS interact with many other signaling molecules which influence a broad spectrum of responses. More advanced transcriptomic techniques have identified important stress-responsive signaling molecules, such as mitogen-activated protein kinase (MAPK) and phosphatase, involved in ROS metabolism [8]. Plant MAPK signaling networks, which differentiate between stresses through receptors and sensors present on the cell surface, are subjected to transduction [9]. Calcium (Ca\(^{2+}\)) is also actively involved in intra- and extra-cellular signaling networks [10]. Ca\(^{2+}\) and ROS signaling interactions are considered to be bidirectional, as Ca\(^{2+}\) is necessary for ROS production, while ROS is primarily required for the regulation of cellular Ca\(^{2+}\) [11,12]. Stressed plant cells transduce signals via redox sensitive proteins and reversible redox reactions [13]. The iron-responsive element-iron-regulatory protein (IRE-IRP) system and iron-regulated transporter 1 (IRT1) are involved in the acclimation responses of stressed plant cells [14]. Furthermore, NO is considered to be a simple signal molecule with targets including thiols and the iron and sulfur group containing compounds and proteins [15]. The presence of NO in higher plants is well documented. However, how NO is enzymatically generated remains a matter of debate [16–18]. Up to now, two possible pathways have been recognized using as substrate either L-arginine (oxidative pathway) or nitrate/nitrite (reductive pathway) involving the contribution of a L-Arg-dependent NO synthase-like activity [19] and a nitrate reductase (NR) activity [20], respectively.
2. Overview of Principal Subcellular Compartments Involved in ROS/NO Production

Living organisms survive in an oxidizing environment where aerobic metabolism is supported by O$_2$. ROS are produced from oxygen under physiological conditions in response to abiotic and biotic factors, which eventually reduces O$_2$ to water containing physiologically important intermediates such as H$_2$O$_2$, O$_2$$^•$ and O$_2$$^•$− [21]. Attenuated or transient alterations in the cellular redox state occur in response to ROS accumulation in stressed cells. Oxidative stress is initiated by the generation of O$_2$$^•$−, which is dismutated either chemically or enzymatically to H$_2$O$_2$ and then converted to *OH via a Haber-Weiss reaction triggered by iron ions (Fe$^{2+}$/Fe$^{3+}$) [22] (Figure 2). Despite containing an O$_2$$^•$− pool of less than 0.5%, the protonated superoxide radical HO$_2$$^•$, also called a hydroperoxyl or perhydroxyl radical, is comparatively more toxic [23]. 1O$_2$, another toxic ROS species, is an electronically excited O$_2$ generated in chloroplasts [21], which is regulated by an antioxidant located close to each ROS production site. This system has two main functions: to avoid potential oxidative damage and to perform signaling processes, especially in the case of H$_2$O$_2$ and NO. For example, H$_2$O$_2$ acts as a retrograde signal from chloroplasts and mitochondria to the nucleus and triggers an appropriate response [6]. Although more is known about ROS in higher plants, our knowledge of RNS, which perform a similar function, is growing. The principal sites and pathways involved in ROS/RNS production in plant cells, as well as key reactions, are summarized in Table 1 and Figure 2, respectively.

Despite excellent reviews focusing on plant ROS and NO metabolism, this assessment aims to provide mainly researchers without specialist knowledge in the field with an up-to-date, multifaceted, and comprehensive overall view of the literature.

| Site of Production | ROS/RNS Produced | Pathways Involved |
|--------------------|------------------|-------------------|
| Chloroplasts       | O$_2$$^•$−, H$_2$O$_2$ | Light dependent photosynthetic reaction (PS I and PS II), Fenton reaction. SOD isozymes. NO synthase-like activity |
|                     | *OH, 1O$_2$, NO, ONOO$^•$ | |
| Mitochondria       | O$_2$$^•$−, H$_2$O$_2$, *OH NO, ONOO$^•$ | Respiratory ETC (mitochondrial complexes I and III). Nitrate reduction |
| Peroxisomes        | O$_2$$^•$−, H$_2$O$_2$, *OH, NO, ONOO$^•$ | β-oxidation. Photorespiration. Sulfite detoxification pathway. Purine metabolism. Polyamine catabolism. NO synthase-like activity |
| Vacuoles           | H$_2$O$_2$ | ROS metabolism (enzymatic and non-enzymatic antioxidants). |
| Plasma membrane    | O$_2$$^•$−, H$_2$O$_2$ | RBOHs |
| Apoplast           | H$_2$O$_2$, NO | ROS metabolism (SOD, GSH and NO interaction), thiol-disulfide network, cysteine rich kinases and polyamine catabolism (enhanced catabolism of spermine and spermidine). Nitrate reduction |
| Cell wall          | O$_2$$^•$−, H$_2$O$_2$, *OH, *NO | Peroxidases, Oxidized NADH and diamino oxidases. |

Abbreviations: O$_2$$^•$−—superoxide anion. H$_2$O$_2$—hydrogen peroxide. *OH—hydroxyl ion. 1O$_2$—singlet oxygen. *NO—nitric oxide. ONOO$^−$—peroxynitrite. PS I—photosystem I. PS II—photosystem II. SOD—superoxide dismutase. ETC—electron transport chain. ROS—reactive oxygen species. RBOH—respiratory burst oxidase homolog. GSH—reduced glutathione. NADH—nicotinamide adenine dinucleotide. The upper dot indicate in which atom is located the unpaired electron.
2.1. Chloroplasts

Chloroplasts, the most common organelles found in plants, are equipped with all the biochemical machinery necessary to transform light energy into chemical energy through photosynthesis, one of the primary sources of ROS generation.

2.1.1. ROS ($O_2^{•−}$, $H_2O_2$, and $¹O_2$) and NO production sites

ROS production in chloroplasts is directly related to photosynthetic light reactions in the thylakoid membrane. $O_2^{•−}$ is fundamentally produced by autooxidation of reduced ferredoxin at photosystem I (PSI) and plastoquinone (PQ) level in photosystem PSII and then dismutated to $H_2O_2$ (Figure 3).
Figure 3. Simple model of ROS and NO generation in chloroplasts. \( \text{O}_2^\cdot \) is produced by the autoxidation of reduced ferredoxin at the photosystem I (PSI) and the plastoquinone (PQ) level in photosystem PSI, and then dismutated into \( \text{H}_2\text{O}_2 \) by superoxide dismutase (SOD). Abbreviation: Chl/ Chl^*/—chlorophyll. Cyt b6/7—Cytochrome b6/f contains seven prosthetic groups. e^-—electron. Fe/S—Iron/Sulfur. FNR—ferredoxin-NADP reductase. \( \text{H}_2\text{O}_2 \)—hydrogen peroxide. MDA—monodehydroascorbate. \( \text{O}_2 \)—molecular oxygen. \( ^1\text{O}_2 \)—singlet oxygen. \( \text{H}_2\text{O} \)—water. \( \text{O}_2^\cdot \)—superoxide anion. \( \text{ONOO}^- \)—peroxynitrite. PC—plastocyanin. PS I—photosystem I. PSI—photosystem II. PQH_2/p700—photosystem II primary donors. PQ—plastoquinone. PQH_2/plastoquinol. Q—quinol. NADPH/\text{NADP}^+—nicotinamide adenine dinucleotide phosphate. NO—nitric oxide. PRX II—peroxiredoxin II. AsA—ascorbate. MDAR—monodehydroascorbate reductase. SOD—superoxide dismutase. tAPX—thylakoid-bound ascorbate peroxidases.

Under physiological conditions, the electron transport chain (ETC) from excited photosystem centers of the thylakoidal membrane is directed to \( \text{NADP}^+ \) to enable ferredoxin-NADP reductase (FNR) to produce NADPH at PSI. Under stress conditions, the electron transfer chain (ETC) is overloaded, with part of the electron directed to \( \text{O}_2 \), causing \( \text{O}_2\cdot^\cdot \) to be generated at PSI (Mehler reaction). \( \text{O}_2\cdot^\cdot \) is dismutated to \( \text{H}_2\text{O}_2 \) either spontaneously or by superoxide dismutase (SOD) in the thylakoid membrane. It is worth pointing out that the highly efficient SOD-catalyzed dismutation reaction occurs at a diffusion-limited rate of \( \sim 2 \times 10^9 \text{ M}^{-1}\text{s}^{-1} \), or \( \sim 10^4 \times \) times the rate constant for spontaneous dismutation, and \( \text{H}_2\text{O}_2 \) is then rapidly detoxified by ascorbate peroxidase (APX). The electron flow from \( \text{H}_2\text{O} \) at PSII to \( \text{H}_2\text{O} \) at PSI is called the water-water cycle [24]. This efficient cycle mechanism shortens the lifetime of photoproduced \( \text{O}_2\cdot^\cdot \) and \( \text{H}_2\text{O}_2 \) to suppress the production of \( \cdot\text{OH} \) radicals, whose interaction with target molecules is thus prevented, leading to photoinhibition. This outcome is particularly important under stress conditions, such as high temperatures, drought and salinity. Depending on the plant species, several chloroplastic SOD isoforms, including Fe-SODs and Cu/Zn-SODs, bind to the thylakoid membrane located close to PSI [24,25]. Similarly, various APX isoforms are located either in the stroma (sAPX) or bind to the thylakoid membrane (tAPX) [26].

\(^1\text{O}_2 \), whose formation is unique to the chloroplast, is generated in the thylakoid membrane, specifically through the transfer of energy from P680, the primary electron donor at PSII, to ground \( \text{O}_2 \) [24].
NO, which has been detected in chloroplasts, is generated by L-arginine- and NADPH-dependent NO synthase activity [27]. It stimulates chlorophyll biosynthesis and chloroplast differentiation [28,29] and mediates the PTMs, tyrosine nitration, and S-nitrosation, which affect chloroplast function [30]. The nitrated proteins identified in chloroplasts include FNR, β-carbonic anhydrase, glyceraldehyde-3-phosphate dehydrogenase, PSII light-harvesting complex II, methionine synthase, and Fe-SOD3 (SFD3), as well as subunits PsbO and PsbP of PSII lumen-exposed extrinsic proteins [31]. The S-nitrosated proteins identified include Rubisco, glyceraldehyde-3-phosphate dehydrogenase, dehydroascorbate reductase (DHAR), peroxiredoxin II E, fructose-1,6-bisphosphatase, phosphoribulokinase, and FNR [16,32,33]. All these data indicate that NO performs a regulatory function with respect to the chloroplast.

2.1.2. Enzymatic and Non-Enzymatic Antioxidants

As mentioned above, O$_2$•− overproduction, which is regulated by stromal and thylakoid-bound SODs, is dismutated to H$_2$O$_2$ and then regulated by the APX cycle as part of the water-water cycle. When H$_2$O$_2$ content, estimated at roughly 0.5µM under normal conditions, is exposed to differential stress, it increases to 1–15 µM. Thus, regulation of H$_2$O$_2$, which triggers retrograde signaling from chloroplasts to the nucleus, especially under stress conditions, is of great importance in preventing oxidative damage [34]. The chloroplast contains other antioxidant systems to regulate H$_2$O$_2$, mainly the ascorbate-glutathione (ASC-GSH) cycle, peroxiredoxins (Prxs), and thioredoxins (Trxs).

The ASC-GSH cycle is comprised of four enzymes: ascorbate peroxidase (APX), dehydroascorbate reductase (DHAR), monodehydroascorbate reductase (MDAR), and glutathione reductase (GR). These enzymes require the presence of non-enzymatic antioxidants ascorbate (ASC) and glutathione (GSH) (Figure 4), which scavenge virtually all types of ROS, while the chloroplast contains the main cellular ascorbate pool in the micromolar range [35]. In this cycle, NADPH acts as an electron donor provided by the fumarate and nitrate reduction (FNR) protein during photosynthesis. NADPH is also supplied by a group of NADP-dehydrogenases (NADP-DHs), including NADP-isocitrate dehydrogenase (NADP-ICDH), NADP-malic enzyme (NADP-ME), glucose-6-phosphate dehydrogenase (G6PDH), and 6-phosphogluconate dehydrogenase (6PGDH), with the latter two belonging to the oxidative pentose phosphate pathway. These NADP-DHs function under dark phase and stress conditions.

Prx and Trx systems are involved in a complex redox homeostasis network aimed at protecting the chloroplast against oxidative damage [36,37]. Prxs are thiol-based peroxidase enzymes, such as H$_2$O$_2$, alkyl hydroperoxide (ROOH), and ONOO•, present on various peroxide substrates. With a catalytic efficiency in the range of 10$^5$–10$^8$ M$^{-1}$ s$^{-1}$ greatly depending on thiol regeneration, Prxs contain one or two essential cysteines in conserved sequences and can be classified into four main groups in higher plants: 1-Cys Prxs, containing one conserved cysteine; 2-Cys Prxs; Prx Q; and Prx type II, containing two catalytic cysteines [38]. Arabidopsis has been observed to contain Prxs and cysteines (2-CysPrxA, 2-CysPrxB, PrxQ, and PrxIIIE) located in chloroplasts [39].

Trxs which are small thiol-disulphide proteins with 14 kDa, catalyze reversible disulphide bond formation, which facilitates the functional regulation of many proteins. Arabidopsis encloses twenty Trx isoforms, six of which (Trxs f1-2, m1-4, x, y1-2, z, and h) are present in chloroplasts [40]. Chloroplastic Trxs, which use a ferredoxin or NADPH reductant system, are designed as ferredoxin (Fd)-dependent Trx reductase (FTR) or NADPH-dependent Trx reductase (NTR) [37]. Both types of Trx regulate chloroplast redox homeostasis and interact with Prxs to establish a redox signal cascade and to modulate thiol groups [36]. A Trx combined with nitroreductase (NTR) at the C terminus is called NTRC, which, when involved in redox regulation, appears to affect starch and chlorophyll biosynthesis [41].

$^{1}$O$_2$ scavenging chiefly occurs through reactions with biomolecules such as tocopherols [42], carotenoids [43], and membrane lipids [44]. β-carotenes are involved in $^{1}$O$_2$-mediated chloroplast retrograde signaling [45]. $^{1}$O$_2$ and O$_2$•− have a short life-time and perform signaling functions due to
their involvement in other signaling components such as proteins EXECUTER 1 and 2 [46], which points to the involvement of \( ^1 \text{O}_2 \) in nuclear gene modulation. The \( ^1 \text{O}_2 \)-producing Arabidopsis flu mutant is totally defenseless against pararquet stress and enhanced chloroplast APX expression, suggesting an interaction between \( ^1 \text{O}_2 \) and \( \text{H}_2 \text{O}_2 \) signals [47]. Xanthophylls, such as violaxanthin, zeaxanthin and antheraxanthin, components of the xanthophyll cycle, provide protection against excessive ROS production [48]. Vitamin E (\( \alpha \)-tocopherol) scavenges \( ^1 \text{O}_2 \) to form \( \alpha \)-tocopheryl quinine [50], while tocopherols play a major role in inhibiting lipid peroxidation in thylakoid membranes by quenching lipid radicals [51].

Figure 4. Model of the functional interaction between \( \text{H}_2 \text{O}_2 \) and NO metabolism in plant cells. \( \text{H}_2 \text{O}_2 \) is formed by either the one-electron reduction of \( \text{O}_2^- \) chemically or by SOD isozymes. \( \text{H}_2 \text{O}_2 \) can be decomposed by different antioxidant systems depending on the subcellular compartments such as the peroxisomal catalase or a group of four enzymes which constitute the ascorbate glutathione cycle present in chloroplasts, cytosol, peroxisomes and mitochondria. NO can be generated either by NADPH and l-arginine-dependent NO synthase (NOS)-like activity or by nitrate reductase (NR). Dashed arrows indicate the NO effect on enzymatic activities; red: inhibition, black: enhancement. Blue line with a straight line at the end indicates peroxynitrate reduction by PRX II E. Abbreviations: APX—ascorbate peroxidase. AsA—ascorbic acid. CAT—catalase. NO—nitric oxide. ONOO\(^-\)—peroxynitrite. PRX II E—peroxiredoxin II type E. 6PGDH—6-phosphogluconate dehydrogenase. DHA—dehydroascorbate. DHAR—DHA reductase. GSH—reduced glutathione. FNR—ferredoxin-NADP reductase. NADP-DHs—nicotinamide adenine dinucleotide phosphate dehydrogenases. G6PDH—glucose-6-phosphate dehydrogenase. GR—glutathione reductase. GSNO—S-nitrosoglutathione. GSNOR—GSNO reductase. GSSG—oxidized glutathione. \( \text{H}_2 \text{O}_2 \)—water. \( \text{H}_2 \text{O}_2 \)—hydrogen peroxide. MDA—monodehydroascorbate. MDAR—monodehydroascorbate reductase. NADH—nicotinamide adenine dinucleotide. NAPD/NIADP\(^+\)—nicotinamide adenine dinucleotide phosphate. NADP-ICDH—NADP-isocitrate dehydrogenase. NADP-ME—NADP malic enzyme. NH\(_3\)—ammonia. NR—nitrate reductase. \( \text{O}_2^- \)—superoxide anion. RBOHD—respiratory burst oxidase homolog type D. SOD—superoxide dismutase.

2.1.3. Stromules and ROS

Stromules are tubular plastid extensions [52] whose synthesis is rapidly induced by ROS, sugar, hormones and pathogen effector proteins. The formation of stromules is directly dependent on photosynthetic reactions and chloroplast redox status [53]. They deliver ROS directly to the nucleus and signaling activity through chloroplast metabolite sequestration which regulates the number of nuclei and plastids in cells [54]. However, \( \text{H}_2 \text{O}_2 \) synthesized in the chloroplast in response to
light reactions is transferred to nuclei without stromule formation when the chloroplast is adjacent to the nucleus [54]. An in situ increase in H$_2$O$_2$ synthesis when the chloroplast near the nucleus is exposed to 405 nm laser light has been found to lead to a transfer of H$_2$O$_2$ to the nucleus [55]. Furthermore, the generation of chloroplastic ROS indirectly affects nuclear gene expression due to oxidative post-translation modifications (PTMs) of the 3'-phosphoadenosine 5'-phosphate (PAP) phosphatase SAL1 enzyme, which is inhibited by H$_2$O$_2$-dependent oxidative PTMs. Inactivated PAP acts as a secondary messenger and assists in the transfer of information from the chloroplast to the nucleus [56].

2.2. Mitochondrial ROS/NO Generation and Scavenging System

Mitochondria contain a respiratory electron transport chain (ETC) comprised of four key complexes: NADH dehydrogenase (complex I), succinate dehydrogenase (complex II), cytochrome c reductase (complex III), and cytochrome c oxidase (complex IV), in addition to two mobile electron transporters, cytochrome c, and ubiquinone [57]. The respiratory ETC generates an electrochemical potential which leads to ATP synthesis by ATP synthase. As with the chloroplast, the electron is transferred from complexes I and III to O$_2$ under abiotic stress conditions with a concomitant production of O$_2$•−, which is dismutated to H$_2$O$_2$ by MnSOD and quenched by APXs or Prxs. Unlike chloroplasts, mitochondria have only one Prx called Prx II F, while mitochondria have two Trxs (Trxo1 and Trxo2) which can activate alternative oxidase (AOX) [58]. To function effectively, Trxs require NADPH which is supplied by the flavoenzyme NTR. Likewise, H$_2$O$_2$ reacts with reduced Fe$^{2+}$ and Cu$^{+}$ to produce highly toxic •OH through a Fenton reaction. It is worth noting that the alternative oxidase (AOX) enzyme provides another route to the cytochrome pathway which facilitates its transfer to O$_2$ to form H$_2$O and dissipates energy in the form of heat to prevent the formation of ROS [59] especially under stress conditions [60]. Approximately 2–4% of O$_2$ absorbed by the mitochondrial membrane is reduced to O$_2$•−.

Under stress conditions, the active form of the AOX homodimer can be reduced to the oxidized inactive form of the AOX monomer, which disrupts the mitochondrial ETC, resulting in enhanced gene-encoding AOX expression and other target such as mitochondrial dysfunctional stimulon (MDS) gene. Enhancement of AOX activity directs free electrons to O$_2$ and reduces ROS production and counters changes in redox homeostasis. This reaction mixture is transduced to two endoplasmic reticulum (ER) transcription factors (TFs), Arabidopsis NAC domain-containing protein 13 (ANAC013) and ANAC017. These TFs are then translocated to the nucleus in response to stress signals [61]. However, mitochondrial DNA can be damaged by ROS over-production which eventually alters repair and replication processes [62]. Meanwhile, carbon monoxide and cyanide can also cause complex IV to be suppressed, leading to an increase in ROS production [63]. In maize plants, an increased mitochondrial ROS generation under water deficit conditions facilitates rapid acclimation due to positive interactions between ROS and abscisic acid [64]. The integration of ROS and phytohormones has been reported to mediate mitochondrial H$_2$O$_2$ production under heat and oxidative stress conditions [65]. In plants, the final stage of ascorbate synthesis is catalyzed by the inner membrane-bound enzyme L-galactono-1,4-lactone dehydrogenase (GalLDH) which oxidizes L-galactono-lactone to ascorbic acid [66] and supplies an electron to complex IV (terminal oxidase) in the mitochondrial matrix [67].

Mitochondria generate NO, which is produced by chemical reduction from nitrate and not by enzymatic activity [68]. NO counters mitochondrial ROS overproduction [62], while its production is currently thought to involve complexes III and IV, while its removal by AOX can occur under normoxia conditions [69]. It also impacts the functioning of certain mitochondrial enzymes, as enrichment of pepper fruits with NO has been found to increase GalLDH gene expression and enzyme activity, with a concomitant increase of 40% in ascorbate content [70].

Mitochondria also generate extensions called matrixules which appear to play an, as of yet, little understood role in the ROS signaling mechanism [1].
2.3. Peroxisomes

Plant peroxisomes are single membrane-bound organelles characterized by an adaptable and active nitro-oxidative metabolism [15,71–73]. ROS/RNS are produced in many peroxisomal metabolic pathways such as β-oxidation, photorespiration, purine, and polyamine metabolism, as well as auxin and jasmonic acid biosynthesis. Table 2 summarizes how peroxisome organelles, with their complex battery of enzymes, are involved in a diverse range of biochemical pathways which are shared with other subcellular compartments. To regulate ROS production, peroxisomes contain a set of antioxidant systems including catalase, SOD isozymes, four ASC-GSH cycle components, and a Prx-like protein. Peroxisomes are produced in a matrix, containing catalase, SOD, GR, DHAR, and Prx-like proteins, or a membrane-bound APX, with the exception of MDAR, which is present in both these peroxisomal locations. To support the ASC-GSH cycle, peroxisomes contain GSH, ascorbate, and several NADPH-generating enzymes including NADP-ICDH, G6PDH, and 6PGDH [71,74,75].

| Peroxisomal Enzyme                    | ROS/RNS |
|--------------------------------------|---------|
| Acyl-CoA oxidase                     | H₂O₂    |
| Glycolate oxidase                    | H₂O₂    |
| Urate oxidase (UO)                   | H₂O₂    |
| Xanthine oxidoreductase (XOR)        | O₂⁻     |
| O₂•⁻ -generating membrane polypeptides| O₂•⁻    |
| Polyamine oxidase (PAO)              | H₂O₂    |
| Copper-containing amine oxidase (CuAO)| H₂O₂   |
| Sulfite oxidase (SO)                 | H₂O₂    |
| Sarcosine oxidase (SOX)              | H₂O₂    |
| L-arginine-dependent NO synthase (NOS) | •NO     |

NO was first identified in plant peroxisome organelles, in which a NOS like activity oxidizes L-arginine to NO using NADPH as a donor requiring Ca²⁺ and calmodulin. Peroxisomal NO is necessary for various physiological functions such as pollen tube growth, leaf senescence, auxin-induced root organogenesis, and abiotic stress responses such as salinity, cadmium, and lead. Peroxisomes contain ONOO⁻ and GSNO, while peroxisomal proteins, such as catalase, MDAR, GOX, hydroxypyruvate reductase, and malate dehydrogenase, prone to tyrosine nitration and S-nitrosation, have also been identified. Like chloroplasts and mitochondria, peroxisomes appear to generate peroxules under ROS stress conditions [76].

2.4. Vacuoles

Vacuoles, which contain abundant antioxidants and play a multifunctional role in plant metabolism, are among the largest redox homeostasis maintenance sites in response to elevated levels of ROS under abiotic stress conditions [77]. Vacuolar sequestration of ROS is supported by class III peroxidases localized at the inner tonoplast membrane. Peroxidase attacks H₂O₂ generating •OH via the hydroxylic cycle, while proteomic analysis has revealed that RBOH is localized in the tonoplast region [78]. Cellular H₂O₂ is diffused through the tonoplast either directly or via aquaporins in vacuoles [79], which are mainly composed of flavonoids, ascorbate, and peroxidases present on the inner surface of the tonoplast [80]. Enhanced vacuolar ascorbate content is involved in ROS detoxification under high light [81] and drought stress [82] conditions. Despite its low content, GSH is accumulated in vacuoles in oxidized form (GSSG) in response to oxidative stress [83]. Soluble sugars (sucrose) and sugar alcohols (fructans) are sequestered in vacuoles in response to oxidative stress [77]. Fructans protect...
membranes against freezing and drought stress by scavenging •OH, a reaction which is triggered by enhanced phenolics, GSH and ascorbate present in vacuoles, suggesting that phenolics and fructans are synergistically active [84]. Finally, a recent study found that ROS overproduction causes photodamage to chloroplasts, which can induce chlorophagy, leading to vacuolar digestion of entirely photodamaged chloroplasts [85].

2.5. ROS and NO in Cell Membranes

The plasma membrane is an important center of ROS production due to the presence of membrane-bound NADPH oxidase, also known as the respiratory burst oxidase homolog (RBOH). RBOH can transfer free electrons from its intracellular region to molecular oxygen via the apoplast through the plasma membrane [86]. The complex RBOH protein is comprised of a membrane-bound RBOH (molecular weight of 105 to 112 kDa) and its cytosolic regulator Rop (Rho-like protein); as well as an integral plasma membrane protein consisting of six transmembrane domains (TMD1-6) connected by five loops (A to E). The TMD-3 and TMD-5 domains contain a pair of His residues required to bind to the heme group, FAD and NADPH hydrophilic domains, and two N-terminal Ca\(^{2+}\)-binding EF-hand motifs, indicating that RBOH activity is regulated by Ca\(^{2+}\) [87,88]. In addition to this complex structure, regulatory elements, including Ca\(^{2+}\)-dependent and Ca\(^{2+}\)-CaM-dependent protein kinases, as well as a S-nitrosation mechanism [87].

Although their number varies according to the plant species, RBOH genes belong to a multigene family composed often members in Arabidopsis thaliana, nine in rice (Oryza sativa), eight in tomato (Solanum lycopersicum) and sweet orange (Citrus sinensis) and seven in common grapevine (Vitis vinifera). RBOH activity is involved in many plant processes including cell growth, plant development, stomatal closure, pollen tube growth, abiotic stress, symbiotic interactions, and pathogen responses [89]. It is also involved in fruit ripening [90] and stone cell lignification in fruit-producing trees [91]. RBOH’s functional diversity suggests that each isozyme is characterized by a particular specialization.

2.5.1. Apoplasts

The apoplast, linking the environment and cells, is the plant cell region outside the plasma membrane. Apoplastic spaces are more complex than one would expect due to the presence of various components involved in ROS metabolism. These components, which have been found in the apoplast of different plant species, include APX, GR, guaiacol-dependent peroxidase, SOD isozymes, GSH, diamine oxidase (DAO), and polyamine oxidase [92], in addition to NO [93] which can undergo S-nitrosation [94].

In many cases, apoplastic ROS metabolism is crucial for processes, such as axillary bud outgrowth [95], signal and nutrient transfer [96], abiotic stress defenses [97], and microbial pathogens, in which the RBOH plasma membrane is involved [89]. Under water deficit and salinity stress conditions, apoplastic ROS are enhanced, leading to cell wall strengthening and elongation, as well as cell growth [98]. Apoplastic ROS production is also affected by chloroplastic ROS generation which, in turn, modulates nuclear gene expression [99], a fine example of retrograde signaling. An increase in NO has also been observed to boost Fe immobilization in Fe-deficient root apoplasts by decreasing cell wall pectin methylation [100].

ROS signaling in apoplastic spaces involves local signals including: (i) sensing mechanisms directly via oxidative PTMs and (ii) sensing mechanisms indirectly via oxidation of metabolites present in apoplastic regions [101]. Apoplastic spaces also contain a few cysteine-rich peptides (CRPs) namely cysteine-rich receptor-like kinases (CRKs) [102]. These findings that corroborate the role of CRKs in ROS sensing show that: (i) membrane proteins contain conserved cysteines; (ii) apoplastic ROS accumulation controls transcriptional regulation [96]; and (iii) that they also play a role in crk mutant plants [102]. A set of CRKs, which has been reported to interact with RBOHs, are also involved in ROS sensing and signaling [103]. Another cysteine-rich protein GRIM REAPER (GRI) and a receptor-like
kinase (RLK) POLLEN RECEPTOR LIKE KINASE 5 (PRK5) have been reported to combine to form an important ROS signaling unit [96,104]. GRI proteins are cleaved by the metacaspase 9 enzyme, resulting in the formation of a 12-amino acid GRI peptide which binds with its receptor PRK5 and initiates ROS-dependent programmed cell death [96].

Trxs, which are involved in regulating redox status under various environmental cues via thiol-disulfide interchange reactions, are also present in the apoplast [105]. Secretion of polyamines in the apoplast under abiotic stress conditions modulates its redox status [106], while apoplastic regions contain ROS-producing enzymes such as apoplastic peroxidases and polyamine oxidases (PAOs) [107]. Two peroxidases, PRX33 and PRX34, which play a key role in apoplastic ROS generation under biotic stress conditions, have been identified in the apoplastic region of Arabidopsis plants [108]. PAOs stimulate spermine and spermidine catabolism, while H$_2$O$_2$ is simultaneously produced. The H$_2$O$_2$ produced plays a pivotal role in plant biotic and abiotic stress [109] and development [110].

2.5.2. Cell Walls

Cell walls are another major location for the accumulation of ROS [111], whose production is boosted by enzymes such as class III peroxidase, amine oxidase, quinone reductase and oxalate oxidase [112]. For example, with their dual hydroxylic and peroxidative cycles, class III peroxidases can either generate ROS or oxidize cell wall aromatic compounds in proteins and phenolics which are free or linked to polysaccharides [113]. Cell wall peroxidase can oxidize NADH and stimulate O$_2^{•−}$ production, thus activating adaptive plant responses to abiotic stress conditions, particularly hyperthermia and drought [114]. Diamine oxidase is involved in cell wall ROS generation, while diamines, including spermine, spermidine, cadaverine, and putrescine, are used to reduce quinone to peroxide through autoxidation [111]. OH production in vivo and in vitro has been observed in various plant cell walls [115,116], while O$_2^{•−}$ and H$_2$O$_2$ generation in maize root cell walls has been confirmed by histochemical analysis. O$_2^{•−}$ and OH react with the methyl group of polysaturated fatty acids to form conjugated dienes, hydroperoxides, and peroxy radicals, which, in turn, react with metal ions such as Fe$^{2+}$, while the lipid radicals formed initiate a further chain reaction [117].

NO also affects cell wall metabolism [118] and induces Cd tolerance by increasing pectin and hemicellulose content in the root cell wall [119]. In the internal cell wall of rice, crosstalk between NO and ethylene has been found as well as phosphorus (P) remobilization, especially under P-deficient conditions [120]. In addition, S-nitrosoglutathione (GSNO) promotes cell wall remodeling and induces root hair formation in Arabidopsis [121].

Table 3 shows some representative examples of ROS/RNS metabolism in the different subcellular compartments mainly chloroplasts, mitochondria, peroxisomes, and cell wall under different stressful conditions including salinity.
Table 3. Representative examples of ROS/RNS metabolism in the different subcellular compartments under different stressful conditions.

| Sub-Cellular Compartment | Stress          | Plant                        | ROS/RNS Metabolism                                                                                                                                                                                                 | References          |
|--------------------------|-----------------|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Plastids                 | Osmotic stress  | Arabidopsis thaliana         | Increase of ROS along with ABA biosynthesis and activation of retrograde signaling proteins GUN1, and ABI4.                                                                                                        | Wilson et al. [122] |
| Chloroplast              | Salt and osmotic stress | Arabidopsis thaliana     | TOC apparatus (chloroplast membrane) regulated by the ubiquitin-proteasome system (E3ligase SUPPRESSOR OF PP1 LOCUS1 (SP1)) to limit the import of photosynthetic apparatus components, and decline ROS accumulation and photo-oxidative damage, to maintain organelle proteome. | Ling and Jarvis [123] |
| Chloroplast              | Salinity        | Nicotiana tabacca            | Plastid-targeted cyanobacterial flavodoxin, a flavoprotein that prevents ROS accumulation in chloroplasts.                                                                                                       | Lodeyro et al. [124] |
| Chloroplast              | Salinity        | Arabidopsis thaliana         | Distorted grana and thylakoid structures and chloroplastic NADP-MDH along with cytosolic and mitochondrial NAD-MDH mediated export of NADPH and metabolites among cellular compartments to maintain redox homeostasis via malate valve situated atchloroplast envelope membrane. | Kandoi et al. [125] |
| Chloroplast              | High light      | Arabidopsis thaliana         | Alternative oxidase led to enhanced reductants in chloroplast stroma, respiratory O₂ uptake, γ-aminobutyric acid (GABA) and N-rich amino acids while decline in photosystem II efficiency, intermediates of tricarboxylic acid (TCA) cycle and Calvin cyclesupported by dissipation of photosynthetic electron transport and primary metabolites. | Jiang et al. [126]  |
| Chloroplasts Mitochondria, Peroxisomes | Drought        | Triticum aestivum            | Rise in the levels of oxidized modified proteins and induced oxidative damage was prevalent with the lower content of ascorbic acid in the chloroplast stroma.                                                           | Bartoli [67]        |
| Mitochondria             | Salinity        | Nicotiana tabacca            | Disrupted shape from rounded to elongated, declined section area, branching of mitochondria, and emergence of triangular and rhomboid cristae, densification matrix, and contrasting membranes due to ROS effects.          | Baranova et al. [127]|
| Mitochondria             | High temperature| Triticum aestivum            | Exogenously supplied NO (SNP, sodium nitroprusside) reduced oxidative stress markers such as malondialdehyde, H₂O₂ and O₂•−                                                                                     | El-Beltagi et al. [128]|
| Mitochondria             | Low temperature | Capsicum annuum L.           | RNS and ROS mediated protein tyrosine nitration (NO₂-Tyr) and lipid peroxidation, inducing nitrosative and oxidative stress.                                                                                       | Airaki et al. [129] |
| Mitochondria             | Heat stress     | Laternula elliptica          | ROS induced loss of phosphorylation efficiency, enhanced mitochondrial oxygen demand and higher oxidative stress.                                                                                           | Heise [130]         |
| Sub-Cellular Compartment                  | Stress                        | Plant                        | ROS/RNS Metabolism                                                                 | References               |
|------------------------------------------|-------------------------------|------------------------------|----------------------------------------------------------------------------------|--------------------------|
| Mitochondria and Peroxisomes             | Salinity                      | Cakile martima               | Accumulation of ROS markers malondialdehyde and CO- proteins) in mitochondria and peroxisomes along with enhanced antioxidant enzymes and ascorbate-glutathione cycle. | Amor et al. [131]       |
| Peroxisomes                              | Heavy metal (Cr 200 µM)        | Zea mays L.                  | H$_2$O$_2$-mediated glycolateoxidase and NADPH-regenerating machinery signified generation of oxidative stress, while restoration of adverse effects of ROS through exogenous NO application. | Kharbech et al. [132]   |
| Peroxisomes                              | Heavy metal (Pb)              | Arabidopsis thaliana         | Overproduction of nitric oxide (NO), superoxide anion (O$_2$•−) and peroxynitrite (ONOO⁻) in organelles thereby decreasing the catalase activity | Corpas and Barroso [74]  |
| Cell wall, cytoplasm and organelles       | Heavy metal (Cd)              | Arabidopsis thaliana         | Increase in soluble sulfide in cell compartments and ROS mediated oxidative damage of cell wall and organelles. | Guan et al. [133]       |
| Cell wall, sub-cellular fractions and organelles | Fe deficiency stress          | Arachis hypogaea L.          | Exogenously applied NO (SNP) inhibited the malondialdehyde and ROS accumulation from different cell compartments. | Kong et al. [134]       |

Abbreviations: ABA—abscisic acid. Cd—cadmium. Cr—chromium. Fe—iron. GABA—γ-aminobutyric acid. H$_2$O$_2$—hydrogen peroxide. NAD-MDH—nicotinamide adenine dinucleotide-malate dehydrogenase. NADP—nicotinamide adenine dinucleotide phosphate. NADP-MDH—nicotinamide adenine dinucleotide phosphate-malate dehydrogenase. NO—nitric oxide. NO$_2$-Tyr—Tyrosine nitration. O$_2$—molecular oxygen. ONOO⁻—peroxynitrite. Pb—lead. ROS—reactive oxygen species. RNS—reactive nitrogen species. SPI—E3 ligase SUPPRESSOR OF PPI1 LOCUS1.TOC apparatus—total organic carbon apparatus. TCA—tricarboxylic acid. SNP—sodium nitroprusside. O$_2$•−—superoxide anion.
3. ROS and Signaling Molecules

Biological responses to ROS depend on the type of ROS, signal magnitude, formation site and crosstalk with other signaling molecules such as MAPK, NO, and Ca^{2+}.

3.1. Redox Modulation of MAPKs

The MAPK cascade is conserved in eukaryotes which initiate the signaling process when MAPK kinase kinase (MAPKKK) activates MAPK kinase (MAPKK) which, in turn, activates MAPKs. The relationship between the MAPK cascade and ROS has been described in various studies; exogenous H_{2}O_{2} mediates the activation of several components in the MAPK cascade by, for example, inactivating MAPK repressors, although, ROS have been observed to respond when this cascade is manipulated [135]. The cascade is involved in many physiological processes such as cell division, plant growth and development, stomatal movement, abiotic stress responses, and pathogen defenses.

MAPK cascades are considerably involved in retrograde signaling from chloroplast to the nucleus of the stressed plant cells [136]. This network is a fundamental signaling component in the conversion of ROS signals to protein phosphorylation. Adachi et al. [137] identified a W-box in the promoter region of the tobacco RBOH gene, as well as WRKY transcription factors, both of which, they suggest, are phosphorylated by MAPK, thus revealing further crosstalk between MAPK phosphorylation and RBOH.

3.2. Redox Stimulation of Ca^{2+} Mobilization

Cellular Ca^{2+} homeostasis is strictly regulated given the importance of Ca^{2+} as a second messenger which remains local or is transmitted throughout the whole cell in milliseconds to seconds. This regulation involves Ca^{2+} pumps, channels, cation exchangers, and Ca^{2+}-binding proteins, as the Ca^{2+} cation regulates multiple cellular activities. Moreover, crosstalk between Ca^{2+} and other signaling molecules, including ROS and NO, which affects gene expression and Ca^{2+}-dependent protein kinases, takes place under biotic and abiotic stress conditions [138].

Mutual crosstalk between ROS and Ca^{2+} signaling pathways can be both antagonistic and synergistic, depending on the ROS species, target protein type, duration, dosage, and tissue type. The formation and removal of ROS and their interaction with Ca^{2+} signaling are complex mechanisms which provide an excellent model to explore the molecular players involved in the interplay between ROS and other signaling cascades. An enhanced metabolic rate can lead to higher levels of O_{2}, which increases the leakage of respiratory ETC and ROS concentrations. ROS generation in mitochondria is directly associated with the metabolic rate, and Ca^{2+} accumulation reduces the level of ROS generated by complexes I and III under normal conditions, while increasing ROS formation when these complexes are suppressed by pharmacological agents. Ca^{2+} may stimulate three dimensional (3-D) conformational alterations in respiratory ETC complexes, which further induces ROS production in mitochondria [139]. When membrane potential is enormous in the absence of ATP synthesis, Ca^{2+} uptake reduces ROS formation. When membrane potential is in a depolarized range in the presence of ATP synthesis, ROS production is triggered which may be dependent on Ca^{2+} load. With a high Ca^{2+} load in mitochondria, ROS generation independently enhances the mitochondrial metabolic rate [140]. The overall effect of Ca^{2+} on ROS production and eradication depends on subcellular compartments and cell tissue. CaM, a Ca^{2+}-binding protein with approximately 16 kDa, modulates antioxidative enzyme activity and is associated with ROS homeostasis. The suppressed or activated status of redox regulation may alter the activity, transcript level, open channel and trafficking [141]. Receptor-triggered Ca^{2+} signals are important for fully functioning cells involved in the discharge of Ca^{2+} from its storage site and the entry of Ca^{2+} through plasma membrane channels. The two main categories of channel proteins associated with receptor-triggered Ca^{2+} entry signals are transient receptor potential and store-operated Ca^{2+} channels [142].
With regard to free-radical NO generation, Ca\(^{2+}\) needs to be present in crosstalk with H\(_2\)O\(_2\) for development purposes and in response to a diverse range of abiotic stresses [143]. At the subcellular level, peroxisomes are a good example of NO production, for which Ca\(^{2+}\) together with CaM and NADPH redox power are strictly required [75].

4. Redox-Sensitive Genes

Redox balance in stressed cells is maintained by the ASC-GSH cycle which plays important role in regulating H\(_2\)O\(_2\) concentrations. Oxidant-dependent sulfhydryl GSH-GSSG cysteine conversion plays a key role in stress management by regulating redox homeostasis and also controls the function of various transcription factors [144]. In addition, redox-sensitive gene expression needs to be regulated by ROS for detoxification purposes. Oxidative stress stimulates cell signaling [145], while H\(_2\)O\(_2\) signaling and receptor-like kinase activation play a significant role in regulating redox-sensitive gene expression [146]. H\(_2\)O\(_2\) signaling and accumulation also play an important role in activating enzymatic antioxidant-encoding gene expression and can be effectively used to regulate stress-responsive gene activity to withstand harsh environmental conditions. Furthermore, O\(_2^{*−}\) has specific targets including WRKY46, WRKY28, and WRKY22. Redox-sensitive genes include glutathione peroxidase (GPX), catalase (CAT), SOD2, quinone reductase, heme oxygenase-1, ferritin, GR, thioredoxin reductase, thioredoxin, metallothionin, cyclooxygenase-2, and γ-glutamylcysteine synthase which is required for GSH synthesis [147].

4.1. Role of ROS and NO in the Regulation of Transcription Factors (TFs)

In eukaryotic cells, TFs are regulated by complex redox-sensitive systems, consisting of many systematically ordered elements, including GTPase, phosphatase, and lipase, as well as phospholipid-dependent and MAP kinases. ROS-regulated TFs contain reactive cysteine thiol groups whose redox status is affected such as Ca\(^{2+}\)-ATPase, collagenase, and SRC tyrosine kinases. However, ROS not only regulate pre-existing protein activity but also induce the expression of certain genes that control the gene expression patterns of other signal transduction networks. Interest in how ROS and NO regulate gene expression under stress conditions and in identifying the TFs involved has been increasing. Available information indicates that highly complex signaling networks involving H\(_2\)O\(_2\) and NO, as well as phytohormones such as ABA, JA, and SA, are implicated in signaling cascades. Recently, up to sixty H\(_2\)O\(_2\)-responsive TFs involved in stresses such as cold, drought, heat, high light, and pathogens, were identified [148]. On the other hand, GSH enhances tolerance to Cd stress in tomato by increasing the antioxidant system, NO and S-nitrosothiols via a redox-dependent upregulation of TFs such as the ethylene-responsive TFs ERF1, ERF2 and myeloblast 1 (MYB1), as well as other stress response genes [149]. In the case of Arabidopsis thaliana exposed to GSNO, RNAseq analysis reveals overexpression of TF groups including five members of the WRKY gene family involved in pathogen and abiotic stress responses, four members of the MYBTF family, heat stress TFs, and the transcription factor-binding TF GT-1 which binds to the cis-acting element BoxII [32]. Recently, Hartman et al. [150] identified a mechanism of response to hypoxia in Arabidopsis in which ethylene boosts ERF VII TF stability by increasing NO-scavenger phytoglobin 1 in order to facilitate plant survival.

4.2. Regulation of Iron-Responsive Element-Iron Regulatory Protein (IRE-IRP) System

In eukaryotic cells, the IRE-IRP system consists of iron responsive elements (IREs) and iron regulatory proteins (IRPs). Iron (Fe) is an important nutrient which plays a significant role in cellular metabolism and morphogenesis. It acts as a co-factor in major enzymes such as ribonucleotide reductase, cytochrome P450, and leghemoglobin, as well as those involved in ROS metabolism including cytochrome c oxidase (COX), xanthine oxido-reductase, catalase, APX, Fe-SOD, and peroxidase [151]. However, through the Fenton reaction, the presence of higher concentrations of Fe leads to ROS synthesis. Nevertheless, cellular Fe homeostasis, which regulates gene expression at the post-transcriptional level, is critical for Fe transportation and accumulation inside the cell.
IRP1 and IRP2, which interact with IRE mRNA in the 3’ and 5’ untranslated regions (UTRs), are necessary for Fe homeostasis. Transferrin receptor-1 (TFR1) regulates Fe movements in cells and ferritin, as well as cellular Fe storage [152]. The fate of mRNA is decided by binding IRP1 and IRP2 to IRE which has a stem-loop structure consisting of roughly 30 nucleotides with a mandatory core 5’-CAGUG-3’ sequence for IRP binding. IRP binding to IRE TFR1 in the untranslated region enhances mRNA stability and the protein expression, while IRP binding to ferritin blocks mRNA translation and decreases protein expression.

It is crucial to monitor soil mineral absorption by root cells for plant growth and development purposes [153]. Any defect in iron-regulated transporter 1 (IRT1), a major regulator of plant iron homeostasis, can cause severe chlorosis [154]. The IRT1 gene is highly expressed in iron-deficient root cells, resulting in elevated levels of iron absorption which improves growth and development under iron-starved conditions. IRT1 is involved in the absorption of other minerals, including Zn, Mn, Ca, Co, and Ni [155], and in the main toxic metal entry pathway in iron-deficient plant cells. Various transcriptional factors bind directly to the IRT1 promoter in root epidermal cells and are induced by low concentrations of iron [156].

Plant root secretion of Fe-mobilizing phenolic compounds facilitates Fe detoxification phenomena [157]. Fe$^{3+}$ ions are reduced to Fe$^{2+}$ ions by ferric chelate reductase enzyme FRO2 and then transported through the rhizodermal cell membrane by IRT1 [158]. On the other hand, iron deficiency activates transcriptional changes, which stimulate Fe uptake, leading to over-accumulation of Fe and other divalent metals, namely Zn, Cd, and Mn, due to the low specificity of IRT1, whose recycling is used as a posttranslational technique by plants [155]. In Arabidopsis plants, IRT1 is sequestered and gradually degraded by ubiquitination and phosphorylation, a process triggered by IRT1 binding to metal ions other than Fe [159]. IRT1 proteins have been observed in the initial stages of early endosome/trans-Golgi network (EE/TGN) compartmentalization in response to ubiquitin- and clathrin-dependent late endosomes [155]. Despite regulation by RING-typeE3 ligase IDF1 [160], IRT1 ubiquitination is unaffected by primary substrate iron availability [155]. Nitrate root uptake increases pH in the rice rhizosphere, which triggers Fe deficiency. This is due to an increase in H$_2$O$_2$ induced by RBOH1, with a concomitant boost in lignin biosynthesis and low phenolic secretion, which blocks apoplastic Fe mobilization efficiency [161].

NO also preserves Fe homeostasis through crosstalk with ethylene and auxin phytohormones, ferritin and frataxin and through its ability to form nitrosyl iron complexes [162]. New elements, such as GSH, GSNO, and GSNO reductase, have been found in the complex relationships with the Long distance iron signal which moves from shoots to roots through the phloem to regulate Fe homeostasis [163]. GSNOR activity, in particular, has been found necessary for Fe homeostasis, especially under Fe-toxicity conditions in roots [164].

5. ROS and NO Intermediates in Signal Transduction

As outlined above, ROS and NO play a crucial role in signaling mechanisms, which modulate plant growth and development, transpiration, hormonal regulation, germination, stomatal gaseous exchange, flowering, fruit ripening, defense responses, and programmed cell death (PCD) [41]. Although the endogenous sources of enzymatic NO in higher plants remain a subject of debate such as it was mentioned previously, its presence and function in plant cells are clear [17]. NO performs a signaling function mainly through the PTMs, S-nitrosation, nitration, and metal nitrosylation, in order to regulate gene expression and its interaction with phytohormones [165].

5.1. Regulatory Role of NO PTMs, S-Nitrosation and Nitration in ROS Metabolism

In higher plants, S-nitrosation and nitration are the most studied NO PTMs [166,167]. While S-nitrosation involves reversible covalent binding of a NO group to the thiol (–SH) side chain of a susceptible Cys, nitration adds a nitro group (–NO$_2$) to susceptible amino acids, with tyrosine
(Tyr) being the most studied. In both cases, the PTM positively or negatively affects protein function but could also have no functional impact.

Over the last ten years, significant advances have been made in the regulation by NO of ROS metabolism in plants. Figure 4 shows a simple model of the most important ROS metabolism enzymes modulated by NO PTMs. Catalase, exclusively present in peroxisomes, is negatively regulated by both nitration and S-nitrosation [168]. On the other hand, S-nitrosation, which inhibits \( \text{O}_2^\bullet^- \)-generating RBOHD in Arabidopsis [169], does not affect SOD isozymes. However, nitration triggers the inhibition of chloroplastic Fe-SOD3 (FSD3), mitochondrial Mn-SOD1 (MSD1), and peroxisomal Cu,Zn-SOD (CSD3) [170]. Different components of the ASC-GSH cycle present in subcellular cytosol, chloroplast, mitochondrial and peroxisomal compartments which regulate \( \text{H}_2\text{O}_2 \) are differentially affected by nitration and S-nitrosation. Nitration inhibits, while S-nitrosation triggers an increase in APX activity [167]. Although both nitration and S-nitrosation inhibit MDAR activity, GR function remains unaffected by either PTM [167]. As mentioned above, Prxs are a complex family of antioxidant enzymes involved in thiol peroxidase activity on multiple peroxide substrates including \( \text{H}_2\text{O}_2 \), alkyl hydroperoxide (ROOH), and peroxynitrite (ONOO⁻), which are present in almost all cellular compartments [171]. In Arabidopsis, chloroplastic peroxiredoxin II E is involved in peroxynitrite reductase activity which is inhibited by S-nitrosation [172]. NADPH-generating enzymes maintain redox state and support antioxidant enzymes, such as GR, as well as \( \text{O}_2^\bullet^- \) and NO generation by RBOH and NOS-like activity, respectively. These NADP-DHs are differentially modulated by nitration/S-nitrosation: chloroplast FNR is inhibited by nitration, NADP-ICDH and NADP-ME are inhibited by both nitration and S-nitrosation [173], while G6PDH and 6PGDH appear unaffected [174]. Remarkably, the key enzyme S-nitrosoglutathione reductase (GSNOR), involved in physiological and stress processes [175], which regulates GSNO content and consequently S-nitrosation cellular capacity, is inhibited by S-nitrosation [176].

5.2. NO-Responsive Genes

Although NO regulates the expression of specific genes [177], high-throughput sequencing methods, called short-read massively parallel sequencing or RNA-seq, have advanced our knowledge of NO as a key regulator of gene expression reprogramming. Using NO donors, such as GSNO and NO gas, as well as Arabidopsis plants exposed to GSNO through the root system, 1945 responsive genes differentially expressed in leaves and roots, 114 of which corresponded to only one of these organs, were identified [178]. Modulation during pepper fruit ripening of roughly 2987 genes, 498 of which were modulated by NO, has also been studied [41].

5.3. NO and Crosstalk with Other Plant Growth Regulators

NO, produced in plants to combat pathogen attacks, is directly involved in defense-related signaling pathways via secondary messenger protein kinases, cyclic AMP, signaling lipids, \( \text{Ca}^{2+} \), cyclic GMP, and various plant hormones [179]. It also contributes to processes such as hypersensitive response reactions and systemic resistance [180].

Functional molecular analysis of NO-responsive genes in defense pathways has been used to identify encoding proteins for secondary metabolism and pathogen-related proteins [181]. Skelly and Loake [86] have fully characterized proteins involved in S-nitrosation and tyrosine nitration, with non-expressor of pathogenesis-related gene 1 (\text{npr1}) and AtRBOHD providing new insights into the role of NO in plant defenses. Many distinctive functions have been studied with regard to ROS-NO interactions, leading to the generation of related molecules such as NOx, \( \text{ONOO}^- \), \( \text{N}_2\text{O}_5 \), and \( \text{NO}_2 \). They also act as oxidizing molecules on different proteins involved in NO-ROS signaling, resulting in structural and functional alterations in these proteins [182].

Yang et al. [183] have elucidated senescence-inducing ROS-NO crosstalk in litchi plants and have described the morphological, structural, PCD, and expression characteristics of senescence genes after treatment with ROS and NO. Their results show the distorted structure and morphology as
well as the upregulation of \textit{LcRBOH}, \textit{LcMC-1}-like and \textit{LcPirin} genes, which play a role in ROS- and NO-mediated senescence and leaf abscission in litchi plants \cite{183}. NO and ROS have also been reported to play a vital role in signaling cascades and defense mechanisms in legumes and rhizobia \cite{184}. Interaction between ROS and NO assisted by post-translational changes in nitrosated and sulfenylated proteins occurs during nitrogen-fixing symbiosis (NFS) \cite{185}. In addition, glutamine synthetase 1, mainly nitrated inodules, is a critical enzyme involved in nitrogen fixation \cite{186}; this post-translational initiation of glutamine synthetase 1 activity directly correlates NO signaling with N\textsubscript{2} metabolism in nodules. In a study of inoculated \textit{M. truncatula} plants treated with an RBOH oxidase activity inhibitor, the NO scavenger clearly showed overlapping signaling pathways mediated by these molecules \cite{187}. Gene expression analysis has revealed that genes encoding for defense and secondary metabolites are up-regulated and altered during programmed cell death \cite{188}. However, with the aid of transcriptomic analysis, \textit{MtNR1}, \textit{Mtns-Hb1}, and \textit{MtNiR} genes have been observed to be upregulated in \textit{M. truncatula} roots as a result of mediation by H\textsubscript{2}O\textsubscript{2} of enzymatic transcriptional regulation to maintain NO homeostasis \cite{184}. Similarly, ROS generation activates the NR pathway in \textit{Arabidopsis} during plant pathogenesis, which leads to higher levels of NO production and affects RBOHD activity via S-nitrosation \cite{169}. For instance, the connection between NO and ROS through overlapping signaling pathways results in negative NO feedback from ROS generation.

6. Conclusions

ROS/RNS, a fundamental feature of plant cell metabolism, increase nitro-oxidative damage when overproduced and prevent regulation by the corresponding antioxidant systems. Figure 1 shows a simple working model of ROS and RNS metabolism in plant cells under stress conditions. ROS/RNS generation is associated with virtually all cellular compartments, particularly chloroplasts, mitochondria, peroxisomes, and the plasma membrane, with inter-compartmental cooperation acting as a regulatory mechanism. Some compartments also interact with the nucleus through retrograde signaling which enables gene expression to be regulated. In the future, this relatively new area of research should provide new insights into the complex networks both inside and between cells, as well as a reappraisal of redox metabolism. Important new avenues of research are opening up in relation to ROS/RNS metabolism, particularly with respect to items such as hydrogen sulfide (H\textsubscript{2}S), serotonin and melatonin. Finally, the complex relationships involved in cellular ROS/RNS metabolism need to be looked at from a broad perspective and we particularly hope that this assessment provides non-specialist researchers and academics alike with a clear understanding of this field of research.

Author Contributions: Conceptualization, S.K.K., R.B. and P.A.; writing—original draft preparation, S.K.K. and K.K.; writing—review and editing, R.B., P.A., E.F.A.A. and F.J.C.; funding acquisition, E.F.A.A. and P.A.

Funding: This research was funded by Research group No: RG-1435-014.

Acknowledgments: The authors would like to extend their sincere appreciation to the Deanship of Scientific Research at King Saud University for funding this research group No (RG-1435-014). Research in F.J.C. laboratory is supported by the ERDF co-financed grant from the Ministry of Economy and Competitiveness (AGL2015-65104-P), Spain.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Noctor, G.; Foyer, C.H. Intracellular Redox Compartmentation and ROS-Related Communication in Regulation and Signaling. \textit{Plant Physiol}. \textbf{2016}, \textit{171}, 1581–1592. [CrossRef] [PubMed]
2. Suzuki, N.; Katano, K. Coordination Between ROS Regulatory Systems and Other Pathways Under Heat Stress and Pathogen Attack. \textit{Front. Plant Sci.} \textbf{2018}, \textit{9}. [CrossRef] [PubMed]
3. Bae, Y.S.; Oh, H.; Rhee, S.G.; Yoo, Y.D. Regulation of reactive oxygen species generation in cell signaling. \textit{Mol. Cells} \textbf{2011}, \textit{32}, 491–509. [CrossRef] [PubMed]
4. Del Río, L.A. ROS and RNS in plant physiology: An overview. \textit{J. Exp. Bot.} \textbf{2015}, \textit{66}, 2827–2837. [CrossRef]
28. Tewari, R.K.; Prommer, J.; Watanabe, M. Endogenous nitric oxide generation in protoplast chloroplasts. *Plant Cell Rep.* **2013**, *32*, 31–44. [CrossRef]

29. Galatro, A.; Punatarulo, S.; Guiamet, J.J.; Simontacchi, M. Chloroplast functionality has a positive effect on nitric oxide level in soybean cotyledons. *Plant Physiol. Biochem.* **2013**, *66*, 26–33. [CrossRef]

30. Leitimáki, N.; Koskela, M.M.; Mulo, P. Posttranslational Modifications of Chloroplast Proteins: An Emerging Field. *Plant Physiol.* **2015**, *168*, 768–775. [CrossRef]

31. Takahashi, M.; Shigeto, J.; Sakamoto, A.; Izumi, S.; Asada, K.; Morikawa, H. Dual selective nitration in chloroplasts. *Plant Physiol.* **2013**, *168*, 31–42. [CrossRef] [PubMed]

32. Begara-Morales, J.C.; López-Jaramillo, F.J.; Sánchez-Calvo, B.; Carreras, A.; Orteaga-Muñoz, M.; Santoyo-González, F.; Corpas, F.J.; Barroso, J.B. Vinyl sulfone silica: Application of an open preactivated support to the study of transnitrosylation of plant proteins by S-nitrosogluthatione. *BMC Plant Biol.* **2013**, *13*, 61. [CrossRef]

33. Serrato, A.J.; Romero-Puertas, M.C.; Lázaro-Payo, A.; Sahrawy, M. Regulation by S-nitrosoylation of the Calvin-Benson cycle fructose-1,6-bisphosphatase in *Pisum sativum*. *Redox Biol.* **2018**, *14*, 409–416. [CrossRef]

34. Maruta, T.; Noshi, M.; Tanouchi, A.; Tamoi, M.; Yabuta, Y.; Yoshimura, K.; Ishikawa, T.; Shigeoka, S. H2O2-sensitive thioredoxin-like1 regulates the redox state of chloroplast thylakoids. *Electrophoresis* **2015**, *36*, 2569–2578. [CrossRef]

35. Foyer, C.H.; Noctor, G. Ascorbate and glutathione: The heart of the redox hub. *Redox Rep.* **2011**, *15*, 2–18. [CrossRef] [PubMed]

36. Yoshida, K.; Hara, A.; Sugiabori, T. Thioredoxin-like2/Cys peroxiredoxin redox cascade supports oxidative thiol modulation in chloroplasts. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, E8296–E8304. [CrossRef] [PubMed]

37. Kang, Z.; Qin, T.; Zhao, Z. Thioredoxins and thioredoxin reductase in chloroplasts: A review. *Gene* **2019**, *706*, 32–42. [CrossRef] [PubMed]

38. Dietz, K.-J.; Turkan, I.; Krieger-Liszkay, A. Redox- and Reactive Oxygen Species-Dependent Signaling into and out of the Photosynthesizing Chloroplast. *Plant Physiol.* **2016**, *171*, 1541–1550. [CrossRef] [PubMed]

39. Liebthál, M.; Maynard, D.; Dietz, K.-J. Peroxiredoxins and Redox Signaling in Plants. *Antioxid. Redox Signal.* **2018**, *28*, 609–624. [CrossRef] [PubMed]

40. Geigenberger, P.; Thomählen, I.; Daloso, D.M.; Fernie, A.R. The Unprecedented Versatility of the Plant Thioredoxin System. *Trends Plant Sci.* **2017**, *22*, 249–262. [CrossRef] [PubMed]

41. González-Gordo, S.; Bautista, R.; Claros, M.G.; Cañas, A.; Palma, J.M.; Corpas, F.J. Nitric oxide-dependent regulation of sweet pepper fruit ripening. *J. Exp. Bot.* **2019**, *70*, 4557–4570. [CrossRef]

42. Krieger-Liszkay, A.; Trebst, A. Tocopherol is the scavenger of singlet oxygen produced by the triplet states of chlorophyll in the PSII reaction centre. *J. Exp. Bot.* **2006**, *57*, 1677–1684. [CrossRef]

43. Ramel, F.; Birtic, S.; Cuniné, S.; Triantaphylidès, C.; Ravanat, J.-L.; Havaux, M. Chemical Quenching of Singlet Oxygen by Carotenoids in Plants. *Plant Physiol.* **2012**, *158*, 1267–1278. [CrossRef]

44. Farmer, E.E.; Mueller, M.J. ROS-Mediated Lipid Peroxidation and RES-Activated Signaling. *Annu. Rev. Plant Biol.* **2013**, *64*, 429–450. [CrossRef] [PubMed]

45. Ramel, F.; Birtic, S.; Ginies, C.; Soubigou-Taconnat, L.; Triantaphylides, C.; Havaux, M. Carotenoid oxidation products are stress signals that mediate gene responses to singlet oxygen in plants. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 5535–5540. [CrossRef] [PubMed]

46. Lee, K.P.; Kim, C.; Landgraf, F.; Apel, K. EXECUTER1- and EXECUTER2-dependent transfer of stress-related signals from the plastid to the nucleus of Arabidopsis thaliana. *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 10270–10275. [CrossRef] [PubMed]

47. Lalloi, C.; Stachowiak, M.; Pers-Kamczyc, E.; Warzych, E.; Murgia, I.; Apel, K. Cross-talk between singlet oxygen- and hydrogen peroxide-dependent signaling of stress responses in Arabidopsis thaliana. *Proc. Natl. Acad. Sci. USA* **2006**, *104*, 672–677. [CrossRef]

48. Latowski, D.; Kuczyńska, P.; Strzałka, K. Xanthophyll cycle—A mechanism protecting plants against oxidative stress. *Redox Rep.* **2011**, *16*, 78–90. [CrossRef]

49. Gill, S.S.; Tuteja, N. Reactive oxygen species and antioxidant machinery in abiotic stress tolerance in crop plants. *Plant Physiol. Biochem.* **2010**, *48*, 909–930. [CrossRef]
50. Halliwell, B.; Gutteridge, J.M. Free Radicals in Biology and Medicine; Oxford University Press: New York, NY, USA, 2015.

51. Müller, M.; Hernández, I.; Alegre, L.; Munné-Bosch, S. Enhanced α-tocopherol quinone levels and xanthophyll cycle de-epoxidation in rosemary plants exposed to water deficit during a Mediterranean winter. J. Plant Physiol. 2006, 163, 601–606. [CrossRef]

52. Mathur, J.; Mammone, A.; Barton, K.A. Organelle Extensions in Plant Cells. J. Integr. Plant Biol. 2012. [CrossRef]

53. Brunkard, J.O.; Runkel, A.M.; Zambryski, P.C. Chloroplasts extend stromules independently and in response to internal redox signals. Proc. Natl. Acad. Sci. USA 2015, 112, 10044–10049. [CrossRef]

54. Erickson, J.L.; Kantek, M.; Schattat, M.H. Plastid-nucleus distance alters the behavior of stromules. Front. Plant Sci. 2017, 8, 1135. [CrossRef]

55. Caplan, J.L.; Kumar, A.S.; Park, E.; Padmanabhan, M.S.; Hoban, K.; Modla, S.; Czymmek, K.; Dinesh-Kumar, S.P. Chloroplast Stromules Function during Innate Immunity. Dev. Cell 2015, 34, 45–57. [CrossRef] [PubMed]

56. Chan, K.X.; Mabbitt, P.D.; Phua, S.Y.; Mueller, J.W.; Nisar, N.; Gigolashvili, T.; Stroeher, E.; Grassl, J.; Arlt, W.; Estavillo, G.M.; et al. Sensing and signaling of oxidative stress in chloroplasts by inactivation of the SAL1 phosphoadenosine phosphatase. Proc. Natl. Acad. Sci. USA 2016, 113, E4567–E4576. [CrossRef] [PubMed]

57. Schertl, P.; Braun, H.-P. Respiratory electron transfer pathways in plant mitochondria. Front. Plant Sci. 2014, 5. [CrossRef] [PubMed]

58. Millar, A.H.; Whelan, J.; Soole, K.L.; Day, D.A. Organization and regulation of mitochondrial respiration in plants. Annu. Rev. Plant Biol. 2011, 62, 79–104. [CrossRef] [PubMed]

59. Millar, A.H.; Whelan, J.; Soole, K.L.; Day, D.A. Organization and regulation of mitochondrial respiration in plants. Annu. Rev. Plant Biol. 2011, 62, 79–104. [CrossRef] [PubMed]

60. Dahal, K.; Martyn, G.D.; Alber, N.A.; Vanlerberghge, G.C. Coordinated regulation of photosynthetic and respiratory components is necessary to maintain chloroplast energy balance in varied growth conditions. J. Exp. Bot. 2017. [CrossRef]

61. De Clercq, I.; Vermeirssen, V.; Van Aken, O.; Vandepoele, K.; Whelan, J.; Lázaro, J.J.; Sevilla, F.; Jiménez, A. Mitochondrial and Nuclear Localization of a Novel Pea Thioredoxin: Identification of Its Mitochondrial Target Proteins. Plant Physiol. 2009, 150, 646–657. [CrossRef] [PubMed]

62. Millar, A.H.; Whelan, J.; Soole, K.L.; Day, D.A. Organization and regulation of mitochondrial respiration in plants. Annu. Rev. Plant Biol. 2011, 62, 79–104. [CrossRef] [PubMed]

63. Piantadosi, C.A. Carbon monoxide, reactive oxygen signaling, and oxidative stress. Free Radic. Biol. Med. 2008, 45, 562–569. [CrossRef]

64. Suzuki, N.; Koussevitzky, S.; Mittler, R.O.N.; Miller, G.A.D. ROS and redox signalling in the response of plants to abiotic stress. Plant Cell Environ. 2012, 35, 259–270. [CrossRef]

65. Sawelam, N.; Kazan, K.; Schenk, P.M. Global Plant Stress Signaling: Reactive Oxygen Species at the Cross-Road. Front. Plant Sci. 2016, 7. [CrossRef]

66. Valpuesta, V.; Botella, M.A. Biosynthesis of L-ascorbic acid in plants: New pathways for an old antioxidant. Trends Plant Sci. 2004, 9, 573–577. [CrossRef] [PubMed]

67. Bartoli, C.G. Mitochondria are the main target for oxidative damage in leaves of wheat (Triticum aestivum L.). J. Exp. Bot. 2004, 55, 1663–1669. [CrossRef] [PubMed]

68. Horchani, F.; Prévot, M.; Boscari, A.; Evangelisti, E.; Meilhoc, E.; Bruand, C.; Raymond, P.; Boncompagni, E.; Aschi-Smiti, S.; Puppo, A. Both plant and bacterial nitrate reductases contribute to nitric oxide production in Medicago truncatula nitrogen-fixing nodules. Plant Physiol. 2011, 155, 1023–1036. [CrossRef] [PubMed]

69. Igamberdiev, A.U.; Bykova, N.V. Metabolism and Interplay of Reactive Oxygen and Nitrogen Species in Plant Mitochondria. In Nitric Oxide and Hydrogen Peroxide Signaling in Higher Plants; Springer International Publishing: Cham, Switzerland, 2015; pp. 1–14. [CrossRef]

70. Rodriguez-Ruiz, M.; Mateos, R.M.; Codesido, V.; Corpas, F.J.; Palma, J.M. Characterization of the galactono-1,4-lactone dehydrogenase from pepper fruits and its modulation in the ascorbate biosynthesis. Role of nitric oxide. Redox Biol. 2017, 12, 171–181. [CrossRef] [PubMed]
Corpas, F.J.; Barroso, J.B.; Palma, J.M.; Rodríguez-Ruiz, M. Plant peroxisomes: A nitro-oxidative cocktail. *Redox Biol.* **2017**, *11*, 535–542. [CrossRef]

Corpas, F.J.; del Río, L.A.; Palma, J.M. A Role for RNS in the Communication of Plant Peroxisomes with Other Cell Organelles? In *Proteomics of Peroxisomes*; Springer: Singapore, 2018; pp. 473–493. [CrossRef]

Corpas, F.J.; Palma, J.M.; Sandalio, L.M.; Valderrama, R.; Barroso, J.B.; del Río, L.A. Peroxisomal xanthine oxidoreductase: Characterization of the enzyme from pea (*Pisum sativum* L.) leaves. *J. Plant Physiol.* **2008**, *165*, 1319–1330. [CrossRef]

Corpas, F.J.; Barroso, J.B. Lead-induced stress, which triggers the production of nitric oxide (NO) and superoxide anion (O$_2^-$) in Arabidopsis peroxisomes, affects catalase activity. *Nitric Oxide* **2017**, *68*, 103–110. [CrossRef]

Corpas, F.J.; Barroso, J.B. Peroxisomal plant metabolism—An update on nitric oxide, Ca$^{2+}$ and the NADPH recycling network. *J. Cell Sci.* **2017**, *131*. [CrossRef]

Rodríguez-Serrano, M.; Romero-Puertas, M.C.; Sanz-Fernánde, M.; Hu, J.; Sandalio, L.M. Peroxisomes Extend Peroxules in a Fast Response to Stress via a Reactive Oxygen Species-Mediated Induction of the Peroxin PEX11a. *Plant Physiol.* **2016**, *171*, 1665–1674. [CrossRef]

Andreev, D.E.; O’Connor, P.B.F.; Zhdanov, A.V.; Dmitriev, R.I.; Shatsky, I.N.; Papkovsky, D.B.; Baranov, P.V. Oxygen and glucose deprivation induces widespread alterations in mRNA translation within 20 minutes. *Genome Biol.* **2015**, *16*. [CrossRef]

Keunen, E.L.S.; Peshev, D.; Vangronsveld, J.; Van Den Ende, W.I.M.; Cuypers, A.N.N. Plant sugars are crucial players in the oxidative challenge during abiotic stress: Extending the traditional concept. *Plant Cell Environ.* **2013**, *36*, 1242–1255. [CrossRef] [PubMed]

Bienert, G.P.; Møller, A.L.B.; Kristiansen, K.A.; Schulz, A.; Møller, I.M.; Schjoerring, J.K.; Jahn, T.P. Specific Aquaporins Facilitate the Diffusion of Hydrogen Peroxide across Membranes. *J. Biol. Chem.* **2007**, *282*, 1183–1192. [CrossRef] [PubMed]

Zipor, G.; Oren-Shamir, M. Do vacuolar peroxidases act as plant caretakers? *Plant Sci.* **2013**, *199*, 41–47. [CrossRef] [PubMed]

Heyneke, E.; Luschin-Ebengreuth, N.; Krajer, I.; Wolkinge, V.; Müller, M.; Zeichmann, B. Dynamic compartment specific changes in glutathione and ascorbate levels in Arabidopsis plants exposed to different light intensities. *BMC Plant Biol.* **2017**, *13*, 104. [CrossRef]

Koffler, B.E.; Luschin-Ebengreuth, N.; Stabentheiner, E.; Müller, M.; Zeichmann, B. Compartment specific response of antioxidants to drought stress in Arabidopsis. *Plant Sci.* **2014**, *227*, 133–144. [CrossRef]

Queval, G.; Jaillard, D.; Zeichmann, B.; Noctor, G. Increased intracellular H$_2$O$_2$ availability preferentially drives glutathione accumulation in vacuoles and chloroplasts. *Plant Cell Environ.* **2010**, *34*, 21–32. [CrossRef]

Peshev, D.; Vergauwen, R.; Moglia, A.; Hidge, É.; Van den Ende, W. Towards understanding vacuolar antioxidant mechanisms: A role for fructans? *J. Exp. Bot.* **2013**, *64*, 1025–1038. [CrossRef]

Izumi, M.; Nakamura, S. Vacuolar digestion of entire damaged chloroplasts in *Arabidopsis thaliana* is accomplished by chlorophagy. *Autophagy* **2017**, *13*, 1239–1240. [CrossRef]

Skelly, M.J.; Loake, G.J. Synthesis of Redox-Active Molecules and Their Signaling Functions During the Expression of Plant Disease Resistance. *Antioxid. Redox Signal.* **2013**, *19*, 990–997. [CrossRef]

Shi, Y.C.; Fu, Y.P.; Liu, W.Q. NADPH oxidase in plasma membrane is involved in stomatal closure induced by dehydroascorbate. *Plant Physiol. Biochem.* **2012**, *51*, 26–30. [CrossRef]

Marino, D.; Dunand, C.; Puppo, A.; Pauly, N. A burst of plant NADPH oxidases. *Trends Plant Sci.* **2012**, *17*, 9–15. [CrossRef] [PubMed]

Kámán-Tóth, E.; Dankó, T.; Gullner, G.; Bozsó, Z.; Palkovics, L.; Pogány, M. Contribution of cell wall peroxidase- and NADPH oxidase-derived reactive oxygen species to *Alternaria brassicicola*-induced oxidative burst in Arabidopsis. *Mol. Plant Pathol.* **2019**, *20*, 485–499. [CrossRef] [PubMed]

Chu-Puaga, Á.; González-Gordo, S.; Rodriguez-Ruiz, M.; Palma, J.; Corpas, F. NADPH oxidase (Rboh) activity is up regulated during sweet pepper (*Capsicum annuum* L.) fruit ripening. *Antioxidants* **2019**, *8*, 9. [CrossRef] [PubMed]

Cheng, X.; Li, G.; Manzoor, M.A.; Wang, H.; Abdullah, M.; Su, X.; Zhang, J.; Jiang, T.; Jin, Q.; Cai, Y. In Silico Genome-Wide Analysis of Respiratory Burst Oxidase Homolog (RBOH) Family Genes in Five Fruit-Producing Trees, and Potential Functional Analysis on Lignification of Stone Cells in Chinese White Pear. *Cells* **2019**, *8*, 520. [CrossRef]
Higuchi, T. Look back over the studies of lignin biochemistry. *J. Wood Sci.* 2006, 52, 2–8. [CrossRef]

Kärkönen, A.; Kuchitsu, K. Reactive oxygen species in cell wall metabolism and development in plants. *Phytochemistry* 2015, 112, 22–32. [CrossRef]

Francoz, E.; Ranocha, P.; Nguyen-Kim, H.; Jamet, E.; Burlat, V.; Dunand, C. Roles of cell wall peroxidases in plant development. *Phytochemistry* 2015, 112, 15–21. [CrossRef]
114. Kolupaev, Y.E.; Karpets, Y.V. Participation of reactive oxygen species in formation of induced resistances of plants to abiotic stressors. In Handbook on Reactive Oxygen Species (ROS): Formation Mechanisms, Physiological Roles and Common Harmful Effects; Suzuki, M., Yamamoto, S., Eds.; Nova Science Publishers: New York, NY, USA, 2013; pp. 109–136.

115. Spiteller, G. Are lipid peroxidation processes induced by changes in the cell wall structure and how are these processes connected with diseases? Med Hypotheses 2003, 60, 69–83. [CrossRef]

116. Liszkay, A.; van der Zalm, E.; Schofer, P. Production of Reactive Oxygen Intermediates (O₂−, H₂O₂, and OH) by Maize Roots and Their Role in Wall Loosening and Elongation Growth. Plant Physiol. 2004, 136, 3114–3123. [CrossRef]

117. Kim, M.J.; Ciani, S.; Schachtman, D.P. A Peroxidase Contributes to ROS Production during Arabidopsis Root Response to Potassium Deficiency. Mol. Plant 2010, 3, 420–427. [CrossRef]

118. Zhang, Z.; Wang, H.; Wang, X.; Bi, Y. Nitric oxide enhances aluminum tolerance by affecting cell wall polysaccharides in rice roots. Plant Cell Rep. 2011, 30, 1701–1711. [CrossRef]

119. Xiong, J.; An, L.; Lu, H.; Zhu, C. Exogenous nitric oxide enhances cadmium tolerance of rice by increasing pectin and hemicellulose contents in root cell wall. Planta 2009, 230, 755–765. [CrossRef] [PubMed]

120. Zhu, X.F.; Zhu, C.Q.; Wang, C.; Dong, X.Y.; Shen, R.F. Nitric oxide acts upstream of ethylene in cell wall phosphoryl reutilization in phosphorus-deficient rice. J. Exp. Bot. 2017. [CrossRef] [PubMed]

121. Moro, C.F.; Gaspar, M.; Silva, F.R.; Pattathil, S.; Hahn, M.G.; Salgado, I.; Braga, M.R. S-nitrosoglutathione promotes cell wall remodelling, alters the transcriptional profile and induces root hair formation in the hairless root hair defective 6 (rhd6) mutant of Arabidopsis thaliana. New Phytol. 2017, 213, 1771–1786. [CrossRef] [PubMed]

122. Wilson, M.E.; Mixdorf, M.; Berg, R.H.; Haswell, E.S. Plastid osmotic stress influences cell differentiation at the plant shoot apex. Development 2016, 143, 3382–3393. [CrossRef]

123. Ling, Q.; Jarvis, P. Regulation of Chloroplast Protein Import by the Ubiquitin E3 Ligase SP1 Is Important for Stress Tolerance in Plants. Curr. Biol. 2015, 25, 2527–2534. [CrossRef]

124. Lodeyro, A.F.; Giró, M.; Pali, H.O.; Bettucci, G.; Cortadi, A.; Ferri, A.M.; Carrillo, N. Suppression of Reactive Oxygen Species Accumulation in Chloroplasts Prevents Leaf Damage but Not Growth Arrest in Salt-Stressed Tobacco Plants. PLoS ONE 2016, 11, e0159588. [CrossRef]

125. Kandić, D.; Mohanty, S.; Tripathy, B.C. Overexpression of plastidic maize NADP-malate dehydrogenase (ZmNADP-MDH) in Arabidopsis thaliana confers tolerance to salt stress. Protoplasma 2018, 255, 547–563. [CrossRef]

126. Jiang, Z.; Watanabe, C.K.A.; Miyagi, A.; Kawai-Yamada, M.; Terashima, I.; Noguchi, K. Mitochondrial AOX Supports Redox Balance of Photosynthetic Electron Transport, Primary Metabolite Balance, and Growth in Arabidopsis thaliana under Light High Light. Int. J. Mol. Sci. 2019, 20, 3067. [CrossRef]

127. Baranova, E.N.; Khaliluev, M.R.; Spivak, S.G.; Bogoutdinova, L.R.; Klykov, V.N.; Babak, O.G.; Shpakovskii, D.G.; Klichevsky, A.V.; Shematorova, E.K.; Shpakovskii, G.V. Targeted Protection of Mitochondria of Mesophyll Cells in Transgenic CYP11A1 CDNA Expressing Tobacco Plant Leaves After NaCl-Induced Stress Damage. Proc. Latv. Acad. Sci. Sect. B Nat. Exact Appl. Sci. 2018, 72, 334–340. [CrossRef]

128. El-Beltagi, O.S.; Ahmed, O.K.; Hegazy, A.E. Protective Effect of Nitric Oxide on High Temperature Induced Oxidative Stress in Wheat (Triticum aestivum) Callus Culture. Not. Sci. Biol. 2016, 8, 192–198. [CrossRef]

129. Airaki, M.; Leterrier, M.; Mateos, R.M.; Valderrama, R.; Chaki, M.; Barroso, J.B.; Del Río, L.A.; Palm, J.M.; Corpas, F.J. Metabolism of reactive oxygen species and reactive nitrogen species in pepper (Capsicum annuum L.) plants under low temperature stress. Plant Cell Environ. 2011, 35, 281–295. [CrossRef] [PubMed]

130. Heise, K. Production of reactive oxygen species by isolated mitochondria of the Antarctic bivalve Laternula elliptica (King and Broderip) under heat stress. Comp. Biochem. Physiol. Part C Toxicol. Pharmacol. 2003, 134, 79–90. [CrossRef]

131. Amor, N.; Jimenez, A.; Boudabbous, M.; Sevilla, F.; Abdelly, C. Implication of peroxisomes and mitochondria in the halophyte Cakile maritima tolerance to salinity stress. Biol. Plant. 2019, 63, 113–121. [CrossRef]

132. Kharbech, O.; Houmani, H.; Chaoui, A.; Corpas, F.J. Alleviation of Cr(VI)-induced oxidative stress in maize (Zea mays L.) seedlings by NO and H₂S donors through differential organ-dependent regulation of ROS and NADPH-recycling metabolisms. J. Plant Physiol. 2017, 219, 71–80. [CrossRef] [PubMed]
133. Guan, M.Y.; Zhang, H.H.; Pan, W.; Jin, C.W.; Lin, X.Y. Sulfide alleviates cadmium toxicity in Arabidopsis plants by altering the chemical form and the subcellular distribution of cadmium. *Sci. Total Environ.* **2018**, *627*, 663–670. [CrossRef]  
134. Kong, J.; Dong, Y.; Song, Y.; Bai, X.; Tian, X.; Xu, L.; Liu, S.; He, Z. Role of Exogenous Nitric Oxide in Alleviating Iron Deficiency Stress of Peanut Seedlings (*Arachis hypogaea* L.). *J. Plant Growth Regul.* **2015**, *35*, 31–43. [CrossRef]  
135. Liu, Y.; He, C. Regulation of plant reactive oxygen species (ROS) in stress responses: Learning from AtRBOHD. *Plant Cell Rep.* **2017**, *35*, 995–1007. [CrossRef]  
136. Guo, H.; Feng, P.; Chi, W.; Sun, X.; Xu, X.; Li, Y.; Ren, D.; Lu, C.; Roaix, J.D.; Leister, D.; et al. Plastid-nucleus communication involves calcium-modulated MAPK signalling. *Nat. Commun.* **2016**, *7*, 1217. [CrossRef]  
137. Adachi, H.; Nakano, T.; Miyagawa, N.; Ishihama, N.; Yoshioka, M.; Katou, Y.; Yaeno, T.; Shirasu, K.; Yoshioka, H. WRKY Transcription Factors Phosphorylated by MAPK Regulate a Plant Immune NADPH Oxidase in *Nicotiana benthamiana*. *Plant Cell* **2015**, *27*, 2645–2663. [CrossRef]  
138. Marcé, M.J.; Gilroy, S.; Poovalah, B.W.; Tanaka, K. Mutual interplay of Ca²⁺ and ROS signaling in plant immune response. *Plant Sci.* **2019**, *283*, 343–354. [CrossRef]  
139. Brookes, P.S.; Yoon, Y.; Robotham, J.L.; Anders, M.W.; Sheu, S.-S. Calcium, ATP, and ROS: A mitochondrial love-hate triangle. *Annu. J. Physiol. Cell Physiol.* **2004**, *287*, C817–C833. [CrossRef] [PubMed]  
140. Adam-Vizi, V.; Starkov, A.A. Calcium and mitochondrial reactive oxygen species generation: How to read the facts. *J. Alzheimer’s Dis.* **2010**, *20*, S413–S426. [CrossRef] [PubMed]  
141. Bogeski, I.; Kummerow, C.; Al-Ansary, D.; Schwarz, E.C.; Koehler, R.; Kozai, D.; Takahashi, N.; Peinelt, C.; Brookes, P.S.; Yoon, Y.; Robotham, J.L.; Anders, M.W.; Sheu, S.-S. Calcium, ATP, and ROS: A mitochondrial love-hate triangle. *Annu. J. Physiol. Cell Physiol.* **2004**, *287*, C817–C833. [CrossRef] [PubMed]  
142. Wang, Y.; Deng, X.; Hewavitharana, T.; Soboloff, J.; Gill, D.L. Stim, ORAI and TRPC channels in the control of calcium entry signals in smooth muscle. *Clin. Exp. Pharm. Physiol.* **2008**, *35*, 1127–1133. [CrossRef]  
143. Niu, L.; Liao, W. Hydrogen Peroxide Signaling in Plant Development and Abiotic Responses: Crosstalk with Nitric Oxide and Calcium. *Front. Plant Sci.* **2016**, *7*. [CrossRef]  
144. Apel, K.; Hirt, H. REACTIVE OXYGEN SPECIES: Metabolism, Oxidative Stress, and Signal Transduction. *Annu. Rev. Plant Biol.* **2004**, *55*, 373–399. [CrossRef]  
145. Mylona, P.; Polidoros, A. ROS Regulation of Antioxidant Genes. In *Reactive Oxygen Species and Antioxidants in Higher Plants*; Science Publishers: New York, NY, USA, 2010; pp. 101–127. [CrossRef]  
146. Miller, G.; Mittler, R. Could heat shock transcription factors function as hydrogen peroxide sensors in plants? *Plant Cell Rep.* **2006**, *25*, 279–288. [CrossRef]  
147. Turpaev, K.T. Reactive oxygen species and regulation of gene expression. *Biochemistry* **2002**, *41*, 281–292. [CrossRef]  
148. Hieno, A.; Naznin, H.A.; Inaba-Hasegawa, K.; Yokogawa, T.; Hayami, N.; Nomoto, M.; Tada, Y.; Yokogawa, T.; Higuchi-Takeuchi, M.; Hanada, K.; et al. Transcriptome Analysis and Identification of a Transcriptional Regulatory Network in the Response to H₂O₂. *Plant Physiol.* **2019**, *180*, 1629–1646. [CrossRef]  
149. Hasan, M.K.; Liu, C.; Wang, F.; Ahammed, G.J.; Zhou, J.; Xu, M.-X.; Yu, J.-Q.; Xia, X.-J. Glutathione-mediated regulation of nitric oxide, S-nitrosothiol and redox homeostasis confers cadmium tolerance by inducing transcription factors and stress response genes in tomato. *Chemosphere* **2016**, *161*, 536–545. [CrossRef]  
150. Hartman, S.; Liu, Z.; van Veen, H.; Vicente, J.; Reinen, E.; Martopawiro, S.; Zhang, H.; van Dongen, N.; Bosman, F.; Bassel, G.W.; et al. Ethylene-Mediated Nitric Oxide Depletion Pre-Adapts Plants to Hypoxia Stress; Cold Spring Harbor Laboratory: New York, NY, USA, 2019. [CrossRef]  
151. Przybyla-Toscano, J.; Roland, M.; Gaymard, F.; Couturier, J.; Rouhier, N. Roles and maturation of iron–sulfur proteins in plastids. *J. Biol. Inorg. Chem.* **2018**, *23*, 545–566. [CrossRef] [PubMed]  
152. Recalcati, S.; Minotti, G.; Cairo, G. Iron Regulatory Proteins: From Molecular Mechanisms to Drug Development. *Antioxid. Redox Signal.* **2010**, *13*, 1593–1616. [CrossRef] [PubMed]  
153. Connorton, J.M.; Balk, J.; Rodríguez-Celma, J. Iron homeostasis in plants – a brief overview. *Metallomics* **2017**, *9*, 813–823. [CrossRef] [PubMed]  
154. Vert, G.; Grotz, N.; Dédauxdréchamp, F.; Gaymard, F.; Guerinot, M.L.; Briat, J.-F.; Curie, C. IRT1, an Arabidopsis Transporter Essential for Iron Uptake from the Soil and for Plant Growth. *Plant Cell* **2002**, *14*, 1223–1233. [CrossRef] [PubMed]
Barberon, M.; Zelazny, E.; Robert, S.; Conéjero, G.; Curie, C.; Friml, J.; Vert, G. Monoubiquitin-dependent endocytosis of the IRON-REGULATED TRANSPORTER 1 (IRT1) transporter controls iron uptake in plants. Proc. Natl. Acad. Sci. USA 2011, 108, E450–E458. [CrossRef] [PubMed]

Wang, N.; Cui, Y.; Liu, Y.; Fan, H.; Du, J.; Huang, Z.; Yuan, Y.; Wu, H.; Ling, H.-Q. Requirement and Functional Redundancy of Ib Subgroup bHLH Proteins for Iron Deficiency Responses and Uptake in Arabidopsis thaliana. Mol. Plant 2013, 6, 503–513. [CrossRef] [PubMed]

Fourcroy, P.; Tissot, N.; Gaymard, F.; Briat, J.-F.; Dubos, C. Facilitated Fe Nutrition by Phenolic Compounds Excreted by the Arabidopsis ABCG37/PDR9 Transporter Requires the IRT1/FRO2 High-Affinity Root Fe²⁺ Transport System. Mol. Plant 2016, 9, 485–488. [CrossRef]

Brumbarova, T.; Bauer, P.; Ivanov, R. Molecular mechanisms governing Arabidopsis iron uptake. Trends Plant Sci. 2015, 20, 124–133. [CrossRef]

Dubeaux, G.; Neveu, J.; Zelazny, E.; Vert, G. Metal Sensing by the IRT1 Transporter-Receptor Orchestrates Its Own Degradation and Plant Metal Nutrition. Mol. Cell 2018, 69, 953–964.e5. [CrossRef]

Shin, L.-J.; Lo, J.-C.; Chen, G.-H.; Callis, J.; Fu, H.; Yeh, K.-C. IRT1 degradation factor 1, a ring E3 ubiquitin ligase, regulates the degradation of iron-regulated transporter 1 in Arabidopsis. Plant Cell 2013, 25, 3039–3051. [CrossRef]

Chen, H.; Zhang, Q.; Cai, H.; Zhou, W.; Xu, F. H₂O₂ mediates nitrate-induced iron chlorosis by regulating iron homeostasis in rice. Plant Cell Environ. 2018, 41, 767–781. [CrossRef] [PubMed]

Buet, A.; Galatro, A.; Ramos-Artuso, F.; Simontacchi, M. Nitric oxide and plant mineral nutrition: Current knowledge. J. Exp. Bot. 2019, 70, 4461–4476. [CrossRef] [PubMed]

García, M.J.; Corpas, F.J.; Lucena, C.; Alcántara, E.; Pérez-Vicente, R.; Zamarreño, Á.M.; Bacaicoa, E.; García-Mina, J.M.; Bauer, P.; Romero, F.J. A Shoot Fe Signaling Pathway Requiring the OPT3 Transporter Controls GSNO Reductase and Ethylene in Arabidopsis thaliana Roots. Front. Plant Sci. 2018, 9. [CrossRef] [PubMed]

Li, B.; Sun, L.; Huang, J.; Göschl, C.; Shi, W.; Chory, J.; Busch, W. GSNOR provides plant tolerance to iron toxicity via preventing iron-dependent nitrosative and oxidative cytotoxicity. Nat. Commun. 2019, 10. [CrossRef] [PubMed]

Asgher, M.; Per, T.S.; Masood, A.; Fatma, M.; Freschi, L.; Corpas, F.J.; Khan, N.A. Nitric oxide signaling and its crosstalk with other plant growth regulators in plant responses to abiotic stress. Environ. Sci. Pollut. Res. 2017, 24, 2273–2285. [CrossRef]

Corpas, F.J. Reactive Nitrogen Species (RNS) in Plants Under Physiological and Adverse Environmental Conditions: Current View. In Progress in Botany; Springer International Publishing: Cham, Switzerland, 2016; pp. 97–119. [CrossRef]

Begara-Morales, J.C.; Sánchez-Calvo, B.; Chaki, M.; Mata-Pérez, C.; Valderrama, R.; Padilla, M.N.; López-Jaramillo, J.; Luque, F.; Corpas, F.J.; Barroso, J.B. Differential molecular response of monodehydroascorbate reductase and glutathione reductase by nitration and S-nitrosylation. J. Exp. Bot. 2015, 66, 5983–5996. [CrossRef] [PubMed]

Rodríguez-Ruiz, M.; Gonzalez-Gordo, S.; Cañas, A.; Campos, M.J.; Paradela, A.; Corpas, F.J.; Palma, J.M. Sweet Pepper (Capsicum annuum L.) Fruits Contain an Atypical Peroxosomal Catalase That Is Modulated by Reactive Oxygen and Nitrogen Species. Antioxidants 2019, 8, 374. [CrossRef]

Yun, B.-W.; Feechan, A.; Yin, M.; Saidi, N.B.B.; Le Bihan, T.; Yu, M.; Moore, J.W.; Kang, J.-G.; Kwon, E.; Spoel, S.H.; et al. S-nitrosylation of NADPH oxidase regulates cell death in plant immunity. Nature 2011, 478, 264–268. [CrossRef]

Holzmeister, C.; Gaupels, F.; Geerlof, A.; Sarioglu, H.; Sattler, M.; Durner, J.; Lindermayr, C. Differential inhibition of Arabidopsis superoxide dismutases by peroxynitrite-mediated tyrosine nitration. J. Exp. Bot. 2015, 66, 989–999. [CrossRef]

Pedrajas, J.R.; BárCena, J.A. Peroxiredoxins: Types, Characteristics and Functions in Higher Plants. In Antioxidants and Antioxidant Enzymes in Higher Plants; Springer International Publishing: Cham, Switzerland, 2018; pp. 95–121. [CrossRef]

Romero-Puertas, M.C.; Laxa, M.; Matté, A.; Zaninotto, F.; Finkemeier, I.; Jones, A.M.E.; Perazzoli, M.; Vandelle, E.; Dietz, K.-J.; Delledonne, M. S-Nitrosylation of Peroxiredoxin II E Promotes Peroxynitrite-Mediated Tyrosine Nitration. Plant Cell 2007, 19, 4120–4130. [CrossRef]
173. Begara-Morales, J.C.; Sánchez-Calvo, B.; Gómez-Rodríguez, M.V.; Chaki, M.; Valderrama, R.; Mata-Pérez, C.; López-Jaramillo, J.; Corporas, F.J.; Barroso, J.B. Short-Term Low Temperature Induces Nitro-Oxidative Stress that Deregulates the NADP-Malic Enzyme Function by Tyrosine Nitration in Arabidopsis thaliana. Antioxidants 2019, 8, 448. [CrossRef] [PubMed]

174. Muñoz-Vargas, M.A.; González-Gordo, S.; Palma, J.M.; Corporas, F.J. Inhibition of NADP-malic enzyme activity by H2S and NO in sweet pepper (Capsicum annuum L.) fruits. Physiol. Plant. 2019. [CrossRef]

175. Leterrier, M.; Chaki, M.; Airaki, M.; Valderrama, R.; Palma, J.M.; Barroso, J.B.; Corporas, F.J. Function of S-nitrosoglutathione reductase (GSNOR) in plant development and under abiotic stress. Plant Signal. Behav. 2011, 6, 789–793. [CrossRef] [PubMed]

176. Tichá, T.; Lochman, J.; Činčalová, L.; Luhová, L.; Petřívalský, M. Redox regulation of plant S-nitrosoglutathione reductase activity through post-translational modifications of cysteine residues. Biochem. Biophys. Res. Commun. 2017, 494, 27–33. [CrossRef] [PubMed]

177. Kim, Y.-H.; Park, S.C.; Yun, B.-W.; Kwak, S.-S. Overexpressing sweetpotato peroxidase gene swpa4 affects nitric oxide production by activating the expression of reactive oxygen species- and nitric oxide-related genes in tobacco. Plant Physiol. Biochem. 2017, 120, 52–60. [CrossRef] [PubMed]

178. Imran, Q.M.; Hussain, A.; Lee, S.-U.; Mun, B.-G.; Falak, N.; Loake, G.J.; Yun, B.-W. Transcriptome profile of NO-induced Arabidopsis transcription factor genes suggests their putative regulatory role in multiple biological processes. Sci. Rep. 2018, 8. [CrossRef]

179. Yun, B.-W.; Spoel, S.H.; Loake, G.J. Synthesis of and signalling by small, redox active molecules in the plant immune response. Biochem. Biophys. Acta (Bba) Gen. Subj. 2012, 1820, 770–776. [CrossRef]

180. Piterková A., Petřívalský, M.; Luhová, L.; Činčalová, L.; Lebeda, A. Local and systemic production of nitric oxide in tomato responses to powdery mildew infection. Mol. Plant Pathol. 2009, 10, 501–513. [CrossRef]

181. Besson-Bard, A.; Gravot, A.; Richaud, P.; Auroy, P.; Duc, C.; Gaymard, F.; Taconnat, L.; Renou, J.-P.; Pugin, A.; Wendehenne, D. Nitric Oxide Contributes to Cadmium Toxicity in Arabidopsis by Promoting Cadmium Accumulation in Roots and by Up-Regulating Genes Related to Iron Uptake. Plant Physiol. 2009, 149, 1302–1315. [CrossRef]

182. Serrano, I.; Romero-Puertas, M.C.; Sandalio, L.M.; Olmedilla, A. The role of reactive oxygen species and nitric oxide in programmed cell death associated with self-incompatibility. J. Exp. Bot. 2015, 66, 2869–2876. [CrossRef]

183. Yang, H.; Kim, H.-J.; Chen, H.; Lu, Y.; Lu, X.; Wang, C.; Zhou, B. Reactive oxygen species and nitric oxide induce senescence of rudimentary leaves and the expression profiles of the related genes in Litchi chinensis. Hortic. Res. 2018, 5. [CrossRef] [PubMed]

184. Damiani, I.; Pauly, N.; Puppo, A.; Brouquisse, R.; Boscuri, A. Reactive Oxygen Species and Nitric Oxide Control Early Steps of the Legume—Rhizobium Symbiotic Interaction. Front. Plant Sci. 2016, 7. [CrossRef] [PubMed]

185. Puppo, A.; Pauly, N.; Boscuri, A.; Mandon, K.; Brouquisse, R. Hydrogen Peroxide and Nitric Oxide: Key Regulators of the Legume—Rhizobium and Mycorrhizal Symbioses. Antioxid. Redox Signal. 2013, 18, 2202–2219. [CrossRef] [PubMed]

186. Blanquet, P.; Silva, L.; Catrice, O.; Bruand, C.; Carvalho, H.; Meilhoc, E. Sinorhizobium meliloti Controls Nitric Oxide–Mediated Post-Translational Modification of a Medicago truncatula Nodule Protein. Mol. Plant-Microbe Interact. 2015, 28, 1353–1363. [CrossRef]

187. Andrio, E.; Marino, D.; Marmey, A.; de Segonzac, M.D.; Damiani, I.; Genre, A.; Huguet, S.; Frendo, P.; Puppo, A.; Pauly, N. Hydrogen peroxide-regulated genes in the Medicago truncatula-Sinorhizobium meliloti symbiosis. New Phytol. 2013, 198, 179–189. [CrossRef]

188. Zago, E.; Morsa, S.; Dat, J.F.; Alard, P.; Ferrarini, A.; Inzé, D.; Delledonne, M.; Van Breusegem, F. Nitric Oxide and Hydrogen Peroxide-Responsive Gene Regulation during Cell Death Induction in Tobacco. Plant Physiol. 2006, 141, 404–411. [CrossRef]