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Review

Oxidative post-translational modifications controlling plant-pathogen interaction

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ABSTRACT

Pathogen recognition is linked to the perception of microbe/pathogen-associated molecular patterns triggering a specific and transient accumulation of reactive oxygen species (ROS) at the pathogen attack site. The apoplastic oxidative "burst" generated at the pathogen attack site depends on the ROS-generator systems including enzymes such as plasma membrane NADP (H) oxidases, cell wall peroxidases and lipoxygenase. ROS are cytotoxic molecules that inhibit invading pathogens or signalling molecules that control the local and systemic induction of defence genes. Post-translational modifications induced by ROS are considered as a potential signalling mechanism that can modify protein structure and/or function, localisation and cellular stability. Thus, this review focuses on how ROS are essential molecules regulating the function of proteins involved in the plant response to a pathogen attack through post-translational modifications.

1. Introduction

Reactive oxygen species (ROS) are continually produced in plant and animal cells under stressful and non-stressful conditions. These molecules are highly reactive with cellular components such as DNA, lipids and proteins, and they can cause serious cellular damage. Nevertheless, cells have adapted to survive through the highly reactive nature of ROS, and even utilize these small molecules as powerful cues to control cellular protein homeostasis, plant development, hormonal signalling and immune responses (Hakmaoui et al., 2012; Moreau et al., 2010; Torres, 2010).

One early reaction in the induction of plant defence response has been associated with the recognition of certain molecules derived by pathogens known as elicitors or microbe/pathogen-associated molecular patterns (MAMPs/PAMPs) (Segonzac and Zipfel, 2011; Camejo et al., 2016; Kadota et al., 2015). Upon elicitor recognition, several transduction signals are activated, leading to the development of several events, including ROS accumulation, at the pathogen attack site. Rapid and transient ROS accumulation at the infection site is known as oxidative "burst", a common feature of plant response. Superoxide anion ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2) and the hydroxyl radical ($^{\bullet}OH$) are the principal ROS accumulated during a pathogen attack, and can act as toxic molecules with strong oxidant power, promoting the oxidative destruction of cells (Floryszak-Wieczorek and Arasimowicz-Jelonek, 2016; Mittler et al., 2017).

Post-translational modifications (PTMs) are considered as chemical alterations of protein structure that can modify their activity, localisation, stability and protein-protein interactions. In plants, more than 300 types of PTMs have been identified, including the addition of simple chemical groups such as a phosphate, acetyl, methyl, nitrosyl, carbonyl or hydroxyl groups, more complex groups such as AMP, ADP-ribose, sugars, or lipids, and small polypeptides such as ubiquitin or ubiquitin-like proteins (Camejo et al., 2013, 2015a; López-Vidal et al., 2016; Ruiz-Mayet al., 2018). H_2O_2-dependent oxidative PTMs are chemical modifications on sulfur atoms in cysteine (Cys) and methionine (Met) residues, but only some of them are targets for oxidative PTMs in ROS-sensitive proteins (Withers and Dong, 2017; Waszczak et al., 2018). Accumulating evidence indicates that ROS largely signal through oxidation of Cys and Met residues (PTMs), providing strong spatial and temporal control of protein conformation, localization and function.

One of the recognised reversible redox-based PTMs is the oxidation of a Cys thiol group to a sulfenic acid (Cys-SOH) through the chemical reaction called sulfenylation (Roos and Messens, 2011). Sulfenylation has been intensively studied, and it acts as redox sensor involved in signal transduction pathways (Waszczak et al., 2014). ROS can also attack Met residue, leading to the formation of reversible Met sulfoxide

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(MetSO). In contrast with sulfenylation, methionylation has received little attention, and only a few examples of functional consequences of this modification have been described in plants (Drazic and Winter, 2014; Waszczak et al., 2018). Thus, a fine and specific regulation of both Cys and Met oxidation may be related to the biological role of some proteins to guarantee the survival, adaptation, tolerance or resistance of living beings.

A considerable number of PTMs, most notably phosphorylation, ubiquitination, sulfenylation and methionylation, have been reviewed (see Adachi and Yoshioka, 2015; Yoshioka et al., 2015; Zhou et al., 2014; Withers and Dong, 2017). However, an important issue is the search to highlight discoveries that have demonstrated how the ROS and their impact on target proteins trigger the plant immune response.

2. ROS accumulation defines plant-pathogen interaction

Particularly, H_2O_2 is considered as an oxidative stress-signalling molecule because of its relatively long half-life and its size, which enable it to oxidize biomolecules outside the generation site and even in neighboring cells. However, in plant cells, little is known about how exactly changes in ROS levels can lead to a final oxidative stress response or whether they are necessary for the progression of various response mechanisms including plant immune response.

Perception of PAMPs by plants via pattern recognition receptors (PRRS) triggers ROS production through activation of enzymes such as NADPH oxidases and peroxidases, leading to PAMP-triggered immunity (PTI)-dependent basal defences that stop invading pathogens. The apoplastic oxidative "burst" generated at an pathogen attack site may be sufficiently cytotoxic to kill pathogens or it can act as signalling molecules, triggering plant immune and cell death responses (Park et al., 2013; Torres, 2010; Jwa and Hwang, 2017). The accumulation of ROS during plant defence is biphasic, with a low-amplitude and transient first phase, followed by a second phase with a substantial and prolonged accumulation of ROS (Fig. 1). The first phase of ROS accumulation is associated with infection of plants by either virulent (*vr*) or avirulent (*avr*) pathogens, and is likely independent of de novo synthesis of ROS-generating enzymes (see Torres et al., 2006; Kadota et al., 2015). The second phase of ROS accumulation, however, is associated only with infection of *avr* pathogens and is an induced response dependent on the increased transcription of mRNA encoding ROS-generating enzymes. The ROS accumulation during the second phase precedes the HR and cell death that often accompanies successful pathogen recognition, leading to incompatible interaction.

Thus, transient and rapid ROS accumulation as well as the induction of specific cell death are biochemical events activated during the necrotrophic interaction between tomato-*Botrytis cinerea* pathogen (Pietrowska et al., 2015). The authors observed two different types of tomato cell death, depending on the susceptibility of the cells to the *vr B. cinerea* pathogen. Cells with necrotic nuclei dominated in susceptible tomato cells, whereas vacuolar death prevailed in less susceptible cells (Pietrowska et al., 2015). In Arabidopsis an early H_2O_2 accumulation accompanied by higher expression of AtRbohD and AtRbohF was observed in resistant ecotypes (Columbia-0, Col-0; and Rubezhnoe-1, Rbz-1) infected with necrotrophic fungus *Sclerotinia sclerotiorum*, although it was not detected in extremely susceptible ecotype (Shahdara, Sha) in the early stages of the infection (Perchepied et al., 2010). Expression of *AtRbohD* and *AtRbohF* genes were generally higher in the Rbz-1 resistant ecotype compared with the Sha susceptible ecotype.

New insights show how the steady-state levels of ROS are altered in potato leaves after infection with the hemibiotroph *Phytophthora infestans* (Floryszak-Wieczorek and Arasimowicz-Jelonek, 2016). Using an avirulent strain of *P. infestans* and potato (*P. infestans*-potato *avr*), ROS accumulation and NO generation together with the activation of a battery of SA-dependent defence genes, led to the establishment of the HR successfully arresting the pathogen invasion. In contrast, *vrP. infestans*-potato system induced a reduction in the production of ROS and also NO, which may be crucial in the delayed up-regulation of *PR-1* and *PR-3* genes and compromised resistance to the hemibiotrophic pathogen (Floryszak-Wieczorek and Arasimowicz-Jelonek, 2016). Recent studies have revealed that the S-(hydroxymethyl)- glutathione dehydrogenase gene in *Magnaporthe oryzae*, *MoSFA1* is involved in NO metabolism and the virulence of pathogen in the course of penetration or the biotrophic phase during plant-pathogen interaction (*Oryzae sativa* cv. CO-39-*M. oryzae*) (Zhang et al., 2015). Additionally, the authors demonstrated with barley leaf that *MoSFA1* deletion mutants exhibited a stronger accumulation of H_2O_2, a lower infection rate, a delay in the growth of the hyphae during the penetration phase and expansion from cell to cell. Similar studies carried out in rice plant demonstrated that during the *Oryza sativa- M. oryzae* interaction the oxidative "burst" generated in infection cell is an essential event for triggering the plant defences (Marroquin-Guzman et al., 2017). Inhibiting or quenching host ROS during infection suppressed innate immunity response and allowed the growth and development of fungus in infected rice cells. *M. oryzae NMO2* gene was identified as essential for maintaining redox balance and suppressing the first line of plant defences against microbial pathogens. The loss of *M. oryzae NMO2* restricted the invasive hyphal growth, increased the formation of granular deposits and caused a host oxidative "burst" that triggered innate immunity, resulting in multi-BIC (biotrophic interfacial complex) development and impaired biotrophic growth (Marroquin-Guzman et al., 2017). These results dissect the fine-tuned molecular and cellular interplay between host and pathogen and identify some key points which govern the plant immune response and fungal development in the context of the host cell environment.

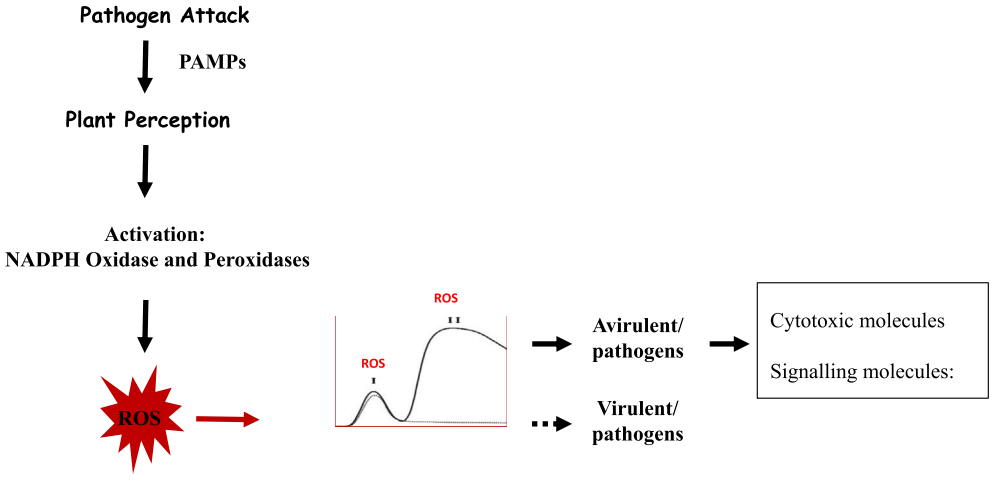

Fig. 1. Schematic representation of the generation of reactive oxygen species (ROS) induced by virulent or avirulent pathogens. Biphasic accumulation of ROS, with a low-amplitude and transient first phase, followed by a second phase with a substantial and prolonged accumulation is induced by avirulent pathogens. NADPH oxidase (RBOH) and peroxidases (class III POx) are enzymes responsible for the apoplastic ROS generation.

Given the importance of symbiotic interaction between legumes-*Rhizobium* bacteria promoting the ROS and NO accumulation in early stages of the interaction, we discuss here representative studies carried out by Damiani et al. (2016). ROS and NO accumulation during symbiotic interaction led to specific and essential events that modified and impaired the development of the symbiotic association. The authors observed that the decrease of ROS level prevented root hair curling and infection threads formation, while the NO led to delayed nodule formation. In root hairs, NADPH oxidase was identified as the main source of ROS generation and it may be strongly linked to hair tip growth (Damiani et al., 2016). Additionally, the early steps of the legumes-*Rhizobium* interaction were also characterized by: *a*) the production of bacterial Nod factors; *b*) the reorientation of root-hair tip growth; *c*) the formation of an infection thread in the root hair; *d*) the induction of cell division in inner cortical cells of the root, leading to a nodule primordium formation. The wealth of evidence has served to conclude that the participation of ROS and NO in the symbiotic interaction, the induction of the early nodulin gene expression, and the repression of plant defence are key events that favor symbiosis (Damiani et al., 2016).

2.1. Post-translational modifications (PTMs)

PTMs are known as chemical alterations that occur after protein synthesis and can change their conformation, activity, subcellular localization and interaction with other proteins (protein-protein interactions). PTMs are considered as transient and rapid alterations that plant cells use to adjust their immune response according to the type pathogen infection.

Most proteins present in animal and plant cells contain sulfur atoms in Cys and Met residues, but only some are primary targets for H_2O_2-dependent oxidative PTMs of ROS-sensitive proteins (Withers and Dong, 2017; Waszczak et al., 2018). This fine control and protein-specific regulation controlling their spatial localisation and protein structure and/or function may be related to the biological role of some proteins to guarantee the survival, adaptation, tolerance or resistance of living beings. Hydrogen peroxide is capable of directly oxidizing the two sulfur-containing amino acids, Cys and Met. Oxidation of Cys in particular has been intensively studied, and it is known that its different oxidation states can affect various proteins (Waszczak et al., 2014). Met oxidation, in contrast, has received little attention, and only a few examples of functional consequences of this modification have been described in plants (Drazic and Winter, 2014; Waszczak et al., 2018). The catalytic and structural role of Met residues is still not clear because any other hydrophobic residues, such as Ile, Leu, Phe, and Val can often replace Met residue (Rao et al., 2013; Rao et al., 2015). Thus, oxidation and subsequent reduction of Met residues may have a separate, distinct, and more specific regulatory potential.

2.2. Oxidative PTMs of Cys residues

One of the recognised reversible redox-based PTMs is the oxidation of a thiol group (Cys-SH) to a sulfenic acid (Cys-SOH) through the chemical reaction known as sulfenylation (Fig. 2). Sulfenylation promoted by ROS do not always occur in all Cys residues or at the same rates in an individual protein. The reactivity of Cys residues towards ROS is correlated with the pKa of a specific Cys and, therefore, with the balance between the thiol (SH) and the thiolate anion (S–) state of these residues (Roos and Messens, 2011; Roos et al., 2013). Sulfenic acids readily react with other thiols of the same protein to form intramolecular disulfide bonds, or with thiols from other proteins to form intermolecular disulphide bonds (Cys-S-S-Cys) (Fig. 2). Sulfenic acid can also react with small low-molecular-weight thiols (LMW thiols) to form mixed disulfide bonds. Alternatively, the sulfenic acid reacts with a backbone amide nitrogen of adjacent residues to form a sulfenamide, or condenses with another sulfenic acid to form a thiosulfinate (Akter et al., 2015). These oxidative thiol modifications are fully reversible, and their reduction is catalyzed by LMW thiols or by members of the glutaredoxin (Grx) or thioredoxin (Trx) system using NADPH as reducing power (Martí et al., 2009; Meyer et al., 2008). Grxs and Trxs are selective toward their target proteins and their reactivity depend the cell redox status determined by the availability of reducing equivalents, glutathione (GSH) and reduced ferredoxin or NADPH (Schürmann and Buchanan, 2008). However, in the presence of severe oxidative stress, overoxidation of the sulfenic acid to irreversible sulfinic or sulfonic acid can take place (Fig. 2). Exceptionally, a mitochondrial ATP-dependent sulfiredox is able to reduce back the sulfinic form of atypical mitochondrial peroxiredoxin (Prx) together with Trx (Iglesias-Baena et al., 2011 Lázaro et al., 2013).

2.2.1. Oxidative PTMs of Cys residues controlling cellular redox-state

Sulfenylation of proteins under oxidative stress has been demonstrated in animal, yeast, *E. coli* and in plant systems (Svoboda et al., 2012; Waszczak et al., 2014; Yuan et al., 2017). In Arabidopsis cell suspensions exposed to oxidative stress 66 proteins susceptible to sulfenylation were identified, of which 19 were identified as protein degradation, 13 as proteins involving the transduction and signal perception, 7 as RNA-binding translation proteins and 7 as redox proteins. Additionally, 6 proteins related with the primary metabolism were identified as well as 5 related with the amino acid metabolism, 5 proteins related with protein transport and 4 with hormone homeostasis (Waszczak et al., 2014). The authors demonstrated that the Dehydroascorbate Reductase 2 protein was regulated through a sulfenic acid-dependent switch, leading to S-glutathionylation, which could avoid the over oxidation of the protein and, in consequence, its functional inactivation.

Recent studies in Arabidopsis plants have demonstrated that biotrophic (*Pseudomonas syringae* pv. tomato DC3000)-pathogen-induced salicylic acid (SA) accumulation inhibited auxin and jasmonic acid (JA) biosynthesis by inhibiting CATALASE 2 (CAT 2) activity (Yuan et al., 2017). The authors proposed that the CAT 2 orchestrates the auxin biosynthesis controlling the sulfenylation of the tryptophan synthetase b subunit 1, a key protein in the auxin biosynthetic precursor tryptophan. Whereas, the absence of CAT 2 activity does not allow the direct interaction of the JA biosynthetic enzymes Acyl co-enzyme A oxidase 2 and Acyl co-enzyme A oxidase 3 (Yuan et al., 2017).

Fig. 3 shows a general scheme of the functional regulation of some proteins such as NADPH oxidase and peroxidases by PTMs involving in the oxidative “burst” and cellular redox balance generated during plant-pathogen interaction. NADPH oxidase together with class III peroxidases are the main enzymatic systems involved in the early ROS generation activated by pathogens, with plasma membrane and apoplastic space being actively involved in the oxidative “burst” (Camejo et al., 2016). Yun et al. (2011) demonstrated the regulation of oxidative “burst” by S-nitrosylation of NADPH oxidase and its impact on HR. The authors observed that the NADPH oxidase activity decreased in plants with high SNO concentration, suggesting that it is a target of S-nitrosylation and that this modification affects the protein function. To further our understanding, these authors demonstrated that AtRBOHD recombinant is S-nitrosylated at Cys 890 residue when treated with *S*-nitrosoglutathione (GSNO) or Cys-NO and, in consequence, its ability to synthesize reactive oxygen intermediates was eliminated. To explore the biological significance of the PTMs during plant-pathogen, the NADPH oxidase activity was tested in mutant *atrbohD* plants expressing either a wild-type AtRBOHD transgene or the Cys890Ala derivative after *P. syringae* pv. tomato DC300 avrB infection. The main results indicated that the ROS accumulation increased in the AtRBOHD Cys890Ala line in comparison with the wild type, so facilitating the plant cell death and development of HR (Yun et al., 2011). In this case, S-nitrosylation of the AtRBOHD directly controls the cellular ROS homeostasis and indirectly modulates plant cell death induced by HR. However, specific phosphorylation of NADPH oxidase (RBOHD) by the

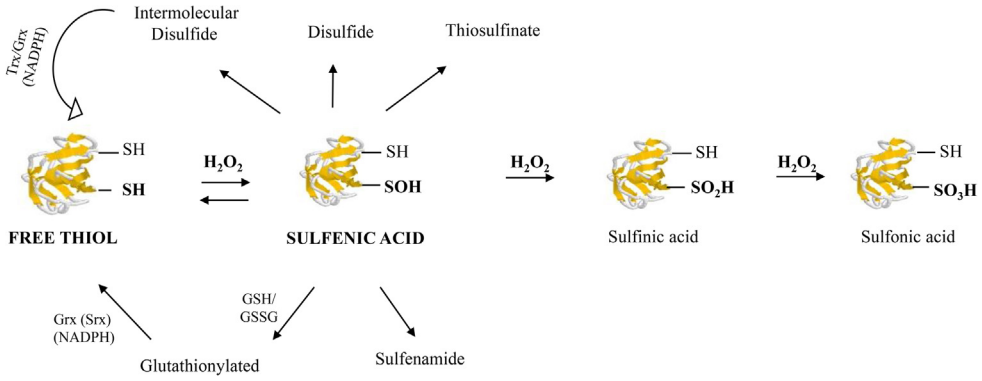

Fig. 2. Schematic representation of redox state of proteins. ROS can interact with thiol groups of proteins to produce a sulfenic acid (Cys-SOH). Sulfenic acids can readily react with nearby thiols of the same protein to form intramolecular disulfide bonds (Cys-S-S-Cys), or with thiols from other proteins or small low-molecular-weight thiols to form mixed disulfide bonds. Sulfenic acids can also react with a backbone amide nitrogen of adjacent residues to form a sulfenamide or condense with another sulfenic acid to form a thiosulfinate. Reversible modifications like *S*-glutathionylation occur when the sulfenic forms react with free glutathione in cell (GSH). These oxidative thiol modifications are fully reversible, and their reduction is catalyzed by LMW thiols or by members of the glutaredoxin (Grx) or thioredoxin (Trx) system in the presence of a reducing power, such as NADPH. Overoxidation of thiols to irreversible sulfinic or sulfonic acid can occur.

PRR-associated kinase BIK1 has been proposed to be essential for PAMP-triggered ROS production (Kadota et al., 2014).

Yang et al. (2015), demonstrated that cytosolic ascorbate peroxidase (APX1), carried out the ROS balance, is regulated by S-nitrosylation at Cys-32 and Cys-49 residues. S-nitrosylation of APX1 at Cys-32 residue regulated its activity positively and, in consequence, increased resistance to oxidative stress (Fig. 3). Additionally, they demonstrated that Arabidopsis plant treated with flagellin elicitor peptide (flg22), a molecule derived from bacterial flagellin, increased the S-nitrosylation levels of APX1 indicating that PTM regulation of APX1 at Cys-32 is functionally important for redox homeostasis during immune responses (Yang et al., 2015). Regulation of APX by NO has been demonstrated in pea plant under salt stress (Begara-Morales et al., 2014). In contrast, APX-B recombinant protein (unicellular red alga *Galdieria. partita* APX-B) is a target protein of oxidation and glutathionylation at Cys-25 residue, a residue equivalent to Cys-32 of Arabidopsis APX1 and pea cytosolic APX, and both modifications provoked a rapid inactivation of the APX activity (Kitajima et al., 2008).

Another regulation point by PTMs are Prxs, antioxidant enzymes involved in multiple cellular functions such as peroxidases, molecular chaperone, enzyme activator, protein binding partner, transnitrosylases and redox sensor (Dietz et al., 2006; Lázaro et al., 2013). They have emerged as important factors in the ROS metabolism in redox-dependent signalling events (Rhee et al., 2012). Arabidopsis peroxiredoxin (PrxIIE) has been proposed as the key protein regulating the ONOO- concentration in cells during plant-*P. syringae avrB* pathogen interaction (Romero-Puertas et al., 2008). NO was capable of inhibiting the peroxidase and ONOO- reductase activities of PrxIIE by S-nitrosylation, so amplifying the deleterious effects of ONOO- and caused a drastic increase of ROS accumulation after biotic stress (Fig. 3). Recent studies have demonstrated that *Solanum tuberosum-P. infestans* (*avr*) model system exhibited a transient accumulation of ONOO- correlated in time with the nitrosative and oxidative "burst" detected 6 h after infesting with avirulent-pathogen (Arasimowicz-Jelonek et al., 2015). In the susceptible potato genotype, the ONOO- over-accumulation was related to enhanced levels of protein tyrosine nitration, while in the resistant potato genotype these changes were not observed. The biological role of ONOO- in resistance was tested when the susceptible genotype was previously treated with ONOO- followed by inoculation with *P. infestans*. Susceptible genotype treated with $ONOO^-$ showed an increase in the pathogen resistance controlling the pathogen colonization and up-regulation of the key defence markers such as *PR-1* gene (Arasimowicz-Jelonek et al., 2015). In this sense, it was proposed that the specific and fine regulation of NO and ROS generation in sites of pathogen infection could generate a sufficient threshold of ONOO- triggering defence responses (Arasimowicz-Jelonek et al., 2015).

The functional switch from peroxidase activity to transnitrosylase activity of the recombinant pea mitochondrial PrxIIF was induced by S-nitrosylation with NO donors (GSNO and SNP). S-nitrosylation of PrxIIF provoked changes in the protein conformation, in the oligomerization pattern and its cellular function under nitrosative stress conditions (Camejo et al., 2015b). Recent studies have demonstrated that both pea recombinant proteins, chloroplast 2CysPrx and mitochondrial PrxIIF, are S-glutathionylated by oxidized glutathione (GSSG) (Calderón et al., 2017). S-glutathionylation on Cys174 of the 2CysPrx and on Cys59 and Cys84 of the PrxIIF provoked a conformational change and a decrease in the peroxidase activity of both proteins (Calderón et al., 2017). Additionally, the authors observed that pea recombinant sulfiredoxin

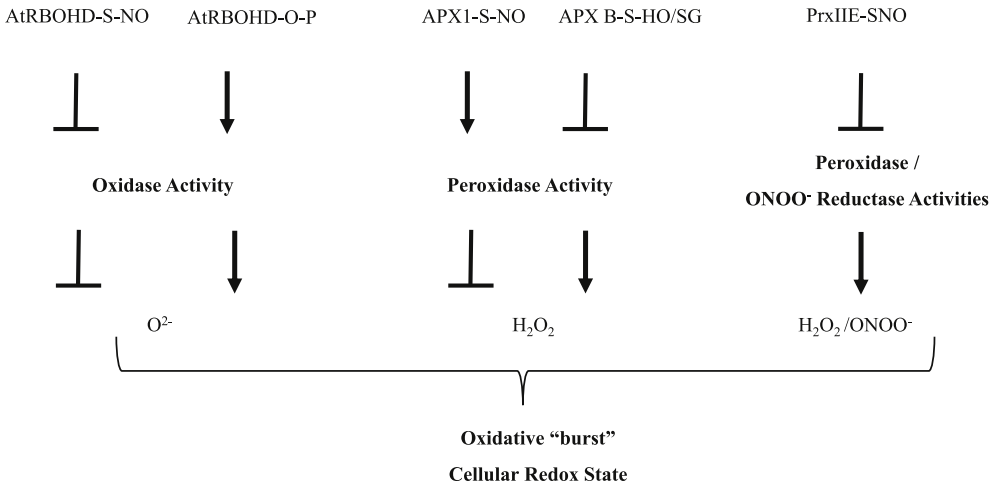

Fig. 3. Schematic representation of functional regulation of proteins involving in the oxidative "burst" and cellular redox-state. S-nitrosylation of Arabidopsis NADPHD oxidase (AtRBOHD-S-NO) inhibited oxidase activity, while its phosphorylation (AtRBOHD-O-P) is essential for ROS production. S-nitrosylation of Arabidopsis and pea cytosolic ascorbate peroxidase 1 (APX1-S-NO) positively regulated its activity while, S-nitrosylation of *G. partita* cytosolic ascorbate peroxidase-B (APX-B) inhibited the peroxidase activity. S-nitrosylation of Arabidopsis peroxiredoxin IIE (PrxIIE-S-NO) inhibit the peroxidase and ONOO- reductase activities.

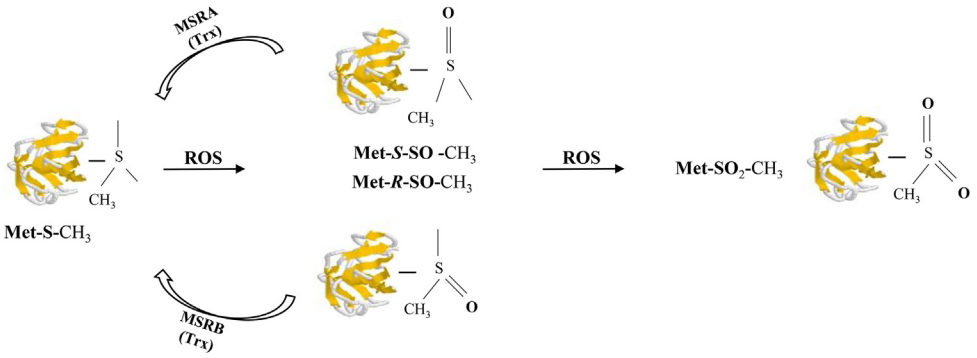

Fig. 4. Schematic representation of redox state of proteins. ROS may interact with Met residues (Met-S-CH_3) leads to the formation of Met sulfoxide (Met-*S*-SO-CH_3, Met-*R*-SO-CH_3), which can be further irreversibly oxidized to Met sulfone (Met-SO_2-CH_3). MetSO can be reduced by two distinct isozymes methionine sulfoxide reductases (MSRA and MSRB).

was able to deglutathionylate pea 2-CysPrx but not pea PrxIIF.

In summary, the results presented in this section demonstrate that oxidative "burst" and cellular redox balance during plant-pathogen interaction is controlled by PTMs of target proteins involved directly or indirectly in the ROS generation, determining the cellular redox state, which is strictly related with cellular protein function, the induction of defence genes and events linked to hypersensitive response (Fig. 3).

2.3. Oxidative PTMs of Met residues

The attack of ROS on Met residues (Met-S-CH_3) leads to the formation of Met sulfoxide (Met-*S*-SO-CH_3,Met-*R*-SO-CH_3),which can be further irreversibly oxidized to Met sulfone (Met-SO_2-CH_3) (Fig. 4). The oxidation of Met to methionine sulfoxide (MetSO) can cause changes in the physicochemical properties of the whole protein, which, in turn, can affect the stability and/or the activity of the oxidized protein (Jacques et al., 2015; Lee et al., 2014). Subsequently, the MetSO can be reduced by two distinct isozymes methionine sulfoxide reductases (MSRA and MSRB), which exhibit stereo selectivity toward S- and R-isomers of MetSO (Met-*R*-SO or Met-*S*-SO) (Tarrago et al., 2009). Differential affinity by substrate has been described for both MSRA and MSRB enzymes, while MSRAs generally reduce both the peptide-bound MetSO and the free form efficiently. MSRBs are generally more efficient in reducing the peptide-bound form, except for some isoforms in plants (Le et al., 2013; see Rey and Tarrago, 2018). As part of the catalytic cycle, MSRs utilize Trx as the electron donor and their reactivity is determined by the availability of reducing equivalents, such as NADPH (Fig. 4).

2.3.1. Oxidative PTMs of Met residues functions as redox signalling

The biological significance of the MetSO remains largely uncharacterized, but a lot of evidence suggests that cyclic oxidation of Met is emerging as a mechanism by which proteins perceive oxidative stress and function in redox signalling (Rey and Tarrago, 2018). For example, in animals, the reversible oxidation of Met residue by ROS has been identified in Ca^{2+} regulatory proteins of heart cells and it functions as a switch that modulates signals and regulates apoptosis (Erickson et al., 2008). Met oxidation can also affect protein function indirectly by coupling oxidative signals to protein phosphorylation-dephosphorylation. A specific Met oxidation was reported that modulates the activities of calcineurin, a protein phosphatase, as well as Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) (Carruthers et al., 2008; Erickson et al., 2008). Other studies have shown the susceptibility of calmodulin (CaM) to Met oxidation in different conformations (Snijder et al., 2011). The authors demonstrated that the oxidation of Met 144 and 145 affected structural integrity and inhibited CaM-CaMKII interaction (Snijder et al., 2011). In contrast, oxidation of Met 71, 72 and 145 or of methionines in the C-terminal lobe Met 109, 124 and 145 affected specific functions of protein. Thus, oxidation on specific Met residues in CaM is tightly linked to its function and conformation, which has direct implications for calcium/CaM-CaMKII related signalling (Snijder et al., 2011).

Although reversible Met oxidation is generally considered as an inevitable damage caused by oxidative stress, experimental evidence indicates it may be a mechanism to couple oxidative signals to changes in the function of the proteins during stress conditions (Hung et al., 2013; Veredas et al., 2017). It has been shown that the actin is a protein susceptible to PTM by oxidation in its conserved Met 44 residue and it alters the actin's polymerization activity (Hung et al., 2013). Recently, the crosstalk between Met oxidation and phosphorylation has been addressed within the human proteome, observing that nearly 98% of the proteins containing oxidized Met were phosphoproteins (Veredas et al., 2017). The authors demonstrated also that the oxidation of Met located within phosphorylation motifs is a highly selective process among stress-related proteins, supporting the idea that crosstalk between Met oxidation and phosphorylation is part of the cellular defence against oxidative stress. The authors observed a high overlap between proteins containing MetSO and those exhibiting PTMs such as phosphorylation, ubiquitination and acetylation (Veredas et al., 2017).

In plant cells, the methionine oxidation has been described under stress and non-stress conditions. Accordingly, a proteomic study of *A. thaliana* demonstrated that 403 proteins were susceptible to methionine oxidation under oxidative stress, with the peroxisomal and chloroplast proteins being the most abundant proteins (Jacques et al., 2015). The comparative proteomic analysis between wild type and cat 2-2 knockout plant showed that 51 proteins were significantly more oxidized in cat 2-2 knockout plants in comparison to wild type genotype, after 3 h of high light stress (Jacques et al., 2015). Other studies have demonstrated the activation of the hypochlorite-responsive transcription factor by Met oxidation to MetSO, have been related with an increase of the viability of *E. coli* cells upon HOCl stress (Drazic et al., 2013).

In plants, the common occurrence of Met adjacent to Ser/Thr/Tyr residues and the frequent occurrence of MetSO near *O*-phosphorylation-sites suggests that crosstalk between these two PTMs is widespread (Rao et al., 2015). Hardin et al. (2009), who demonstrated that when a Met residue functioned as a hydrophobic recognition element within a phosphorylation motif, its oxidation inhibited peptide phosphorylation of recombinant calcium-dependent protein kinases, carried out a representative study. Additionally, the *in vitro* inhibition of human adenosine 3':5′-monophosphate-dependent protein kinase was also demonstrated (Hardin et al., 2009). This mechanism was also assayed on Arabidopsis leaf nitrate reductase, which was a candidate protein for this mechanism because the Met538 functions as a hydrophobic recognition site for phosphorylation Ser 534 and the oxidation of Met538 residue can inhibit phosphorylation of Ser 534 residue. Consistent with these results, it has been shown that the oxidation of Met residues within the phosphorylation motif of pyruvate dehydrogenase also inhibits the phosphorylation of nearby sites, suggesting that reversible methionine oxidation might serve as a rheostat to control the phosphorylation of proximal phospho-acceptors (Miernyk et al., 2009). Other studies have shown that a papaya MSRB1 (PaMsrB1) interacts

with the potyviral nuclear inclusion-a protease (NIaPro), which plays many roles during infection of papaya ringspot virus (PRSV; genus *Potyvirus*, family Potyviridae), and this interaction disrupts the import of PaMSRB1 into the chloroplast (Gao et al., 2012).

Several studies report that during the plant-pathogen interaction the MSRA and MSRB are involved in the virulence of bacterial pathogens. It has been demonstrated that genes encoding the MSRA and MSRB enzymes exist in bacteria and both are involved in the virulence of bacterial pathogens (Sasindran et al., 2007). In this sense, it has been demonstrated that pathogens deficient in MSR have a reduced ability to adhere to eukaryotic cells, to survive inside hosts and to resist *in vitro* oxidative stress (Sasindran et al., 2007).

3. Oxidative PTMs controlling the defence signalling pathways

Pathogen infection often results in the accumulation of ROS, and these molecules contribute to the local and systemic induction of defence genes (Hakmaoui et al., 2012; Yoshioka et al., 2011; Agurla et al., 2014).

Some of the best characterized defence signalling pathways regulated by oxidation events are the induction of SA-dependent responses and the regulation of two key regulators: the SA receptor NPR1 (non-expresser of PR genes 1) and TGA transcription factors in *Arabidopsis thaliana*. Redox state of NPR1 and TGA Cys residues defines the cellular localisation, structure and function of the protein (Lindermayr et al., 2010; Spoel et al., 2010; Tada et al., 2008). Arabidopsis NPR1 appears as S-nitrosylated oligomers in the cytoplasm (Fig. 5). However, SA-mediated redox changes that take place upon a pathogen attack provoke a reduction in the disulphide bonds in the NPR1 protein catalyzed by cytoplasmic Trxs (Trx-h3 and Trx-h5) (Tada et al., 2008). Reduced NPR1 monomers are translocated to the nucleus to interact with the oxidized TGA transcription factors triggering the target genes expression (Spoel et al., 2010; Tada et al., 2008). Previously, it had been demonstrated that the interaction of both NPR1 and TGA transcription factors is dependent on the SA-mediated redox changes that directly affect the oxidation state of Cys residues of TGA transcription factors (Despres et al., 2003). SA-mediated redox changes break intramolecular disulphide bonds in TGA1 and TGA4, allowing these TGAs to form a transcriptionally active complex with NPR1 in the nucleus (Despres et al., 2003). Moreover, it has been demonstrated that the translocation of NPR1 to the nucleus depends on the cytosol redox-state, which suppresses pathogenesis-related gene expression (Peleg-Grossman et al., 2010, 2012). Recent advances indicate that NO also regulates NPR1/TGA1 system. S-nitrosylation and S-glutathionylation of TGA1 were achieved after treatment with GSNO at Cys260 and Cys266, respectively (Lindermayr et al., 2010). Interestingly, Trxh5 catalyzed the denitrosylation of TGA1 during plant immune response (Kneeshaw et al., 2014). This regulation by NO was suggested as a protection mechanism for TGA1 from oxygen-mediated modifications, which improves the DNA binding activity of TGA1 to the sequence- 1 (as-1) element when NPR1 is translocated into nucleus (Fig. 5). S-nitrosylation of NPR1, promoted by NO, leads to the translocation of NPR1 into the nucleus, underlining an important role of NO as a redox regulator of the NPR1/TGA1 system during Arabidopsis plant defence response (Lindermayr et al., 2010). The results reveal high complexity in the regulation of NPR1-TGA1 by NO and ROS, which needs further research to clearly elucidate the exact mechanism involved in the plant immunity response.

The most relevant results were obtained by Asai et al. (2008), who found that NADPH oxidase and NO ASSOCIATED1 (NOA1) were keys in the oxidative and nitrosative "burst", respectively, elicited by INF1 elicitin during *P. infestans-N. benthamiana* interaction. The authors demonstrated that mitogen-activated protein kinase cascades, MEK2-SIPK/NTF4 and MEK1-NTF6, regulated ROS and NO accumulation. In this way, they identified that the ROS generation was induced by either MEK1-NTF6 or MEK2-SIPK/NTF4, whereas NO generation was induced only by conditional activation of MEK2-SIPK/NTF4, and not by MEK1-NTF6. Conversely, INF1- and mitogen-activated protein kinase (MAPK)-mediated ROS generation were eliminated by the silencing of RBOHB, and this was related to decreased resistance to *P. infestans*, but not to *Colletotrichum orbiculare* (Asai et al., 2008). Another MAP kinase has been best characterized in plants, as exemplified by NtWIPK and NtSIPK from tobacco (Liu et al., 2003), AtMAPK3, AtMAPK6 from Arabidopsis (Meng et al., 2013), and LeMAPK1, LeMAPK2, and LeMAPK3 from tomato (Kandoth et al., 2007). Recent studies have demonstrated that LeMAPK1, LeMAPK2, and LeMAPK3 play a critical role in disease resistance, and mediate the NO-induced defence response against interaction between necrotrophs *B. cinerea*-tomato (Zheng et al., 2014). Using the NO donor (sodium nitroprusside dehydrate, SNP) the authors found increased resistance to necrotrophs *B. cinerea* via mechanisms that, at least in part, were influenced by MAP kinase.

Experimental evidence has demonstrated that NO and reduced ROS generation accumulation are also involved downstream from the Ca^{2+} signal transduction cascade elicited from the endogenous plant elicitor peptides (Peps) during plant immune response (Ma et al., 2013). The authors characterized the Pep immune response and identified new molecular steps in the signal transduction cascade which are required for Pep immune activation that limits invasion of a virulent bacterial

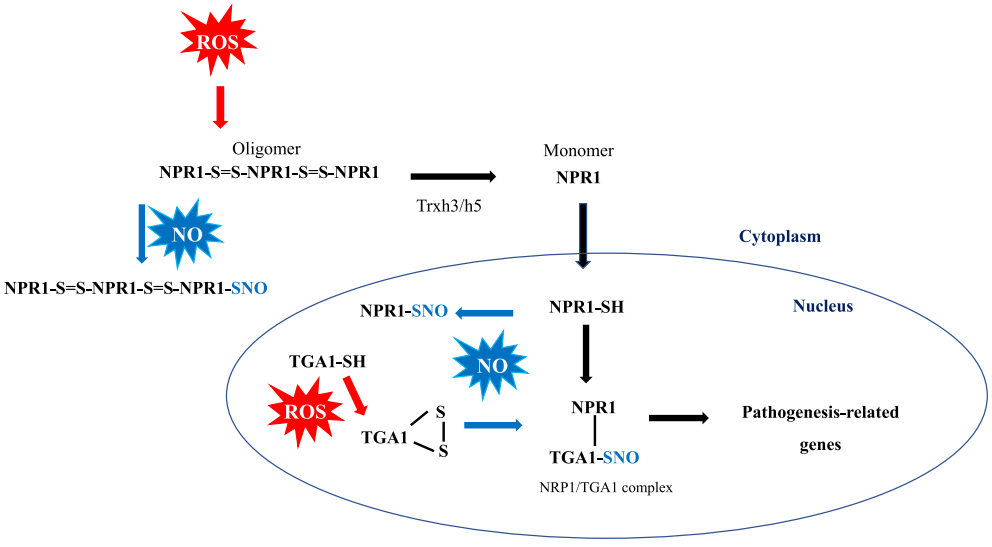

Fig. 5. Schematic representation of oxidative and nitrosative PTMs controlling the function and spatial localisation of non-expresser of pathogen related gene 1 (NPR1) and the transcription factor TGA1 involved in the pathogen-related gene expression. Oxidized or S-nitrosylated oligomer NPR1 is localised in cytoplasm. Salicylic acid-induced redox changes provoke a reduction of disulphide bonds of NPR1 catalyzed by thioredoxins (Trxh3/h5) and the NPR1 monomerization. NPR1 monomers translocate to the nucleus to interact with S-nitrosylated TGA1, inducing pathogen-related gene expression.

pathogen in the plant. It has been documented that both hetero and monomeric small G-proteins could trigger plant immune responses by activating the MAPK signalling cascade (Vidhyasekaran, 2014). ROS generation by activating NADPH oxidase, the activation of NO signalling, the polyamines and phosphatidic acid biosynthesis and programmed cell death are events that also accompany the plant immune response (Vidhyasekaran, 2014). Likewise, other studies have demonstrated that NO production induced by the elicitin cryptogein (produced by the oomycete *P.* cryptogea) in tobacco cell suspensions is partly under the control of a ROS-dependent pathway involving the NADPH oxidase, NtRBOHD (Kulik et al., 2015).

Other metabolites, such as pipecolic acid (PiP) - a non-protein amino acid produced from lysine catabolism - accumulates in local infested tissues, undergoing a gene-for-gene recognition response, and has been associated with systemic acquired resistance (SAR) (Návarová et al., 2012). Recent studies have also demonstrated that PiP accumulation upon infection induces SAR, increasing the accumulation of ROS, NO, as well as azelaic acid and glycerol-3-phosphate (G3P) (Wang et al., 2018). De novo synthesis of Pip in distal tissues was dependent on the accumulation of SA and G3P in the distal tissues, suggesting that several metabolites may be triggering the signalling cascade stimulating the biosynthesis of the other metabolites depending on their levels and their cellular localization (Wang et al., 2018).

4. Conclusions

There is a lot of evidence that ROS generation is an early event in the plant defence response against pathogen attack. Oxidative “burst” is involved in programmed cell death, hypersensitive response, defence gene activation and hormonal signalling. The existing evidence indicates that ROS largely signal through PTMs, providing strict spatial and temporal control of protein conformation to fine-tune activity. Biological significance of oxidation of Cys is particular related with function and localization of the proteins. In contrast, the Met oxidation has received little attention, so in plants it is still necessary to clarify the biological significance of the oxidative PTMs. Considerable evidence suggests that target proteins of oxidative modifications, such as sulfoxidation or methionylation, are more likely to have a second PTM when compared to other proteins that are not oxidized. Thus, ROS generation is sometimes accompanied by NO synthesis and the crosstalk between NO and ROS is of particular importance in plant-pathogen interactions due to their contribution to the local and systemic induction of defence genes. Thus, the understanding of ROS and NO interplay and the signalling functions of ROS driving PTMs can contribute to the elucidation of the molecular and biochemical mechanisms governing plan-pathogen interactions.

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References

Adachi, H., Yoshioka, H., 2015. Kinase-mediated orchestration of NADPH oxidase in plant immunity. Brief. Funct. Genomics 14, 253–259.
Agurla, S., Gayatri, G., Raghavendra, A.S., 2014. Nitric oxide as a secondary messenger during stomatal closure as a part of plant immunity response against pathogens. Nitric Oxide 43, 89–96.
Akter, S., Huang, J., Waszczak, C., Jacques, S., Gevaert, K., et al., 2015. Cysteines under ROS attack in plants: a proteomics view. J. Exp. Bot. 66, 2935–2944.
Arasimowicz-Jelonek, M., Floryszak-Wieczorek, J., Izbiańska, K., Gzyl, J., Jelonek, T., 2015. Implication of peroxynitrite in defense responses of potato to Phytophthora infestans. Plant Pathol. 65, 754–766.
Asai, S., Ohta, K., Yoshioka, H., 2008. MAPK signaling regulates nitric oxide and NADPH oxidase-dependent oxidative bursts in Nicotiana benthamiana. Plant Cell 20, 1390–1406.
Begara-Morales, J.C., Sánchez-Calvo, B., Chaki, M., Valderrama, R., Mata-Pérez, C., López-Jaramillo, J., Padilla, M.N., Carreras, A., Corpas, F.J., Barroso, J.B., 2014. Dual regulation of cytosolic ascorbate peroxidase (APX) by tyrosine nitration and S-nitrosylation. J. Exp. Bot. 65, 527–538.
Calderón, A., Lázaro-Payo, A., Iglesias-Baena, I., Camejo, D., et al., 2017. Glutathionylation of pea chloroplast 2CysPrx and mitocondrial PrxIIF affects their structure and peroxidase activity and sulfiredoxin deglutathionylates only the 2CysPrx. Front. Plant Sci. 8, 118.
Camejo, D., Ortíz-Espín, A., Lázaro, J.J., Romero-Puertas, M.C., Lázaro-Payo, A., et al., 2015b. Functional and structural changes in plant mitochondrial PrxIIF caused by NO. J. Proteomics. 119, 112–125.
Camejo, D., Guzmán-Cedeño, A., Moreno, A., 2016. Reactive oxygen species, essential molecules, during plant-pathogen interactions. Plant Physiol. Biochem. (Paris) 103, 10–23.
Camejo, D., Jiménez, A., Palma, J.M., Sevilla, F., 2015a. Proteomic identification of mitochondrial carbonylated proteins in two maturation stages of pepper fruits. Proteomics 15, 2634–2642.
Camejo, D., Romero-Puertas, M.C., Rodríguez-Serrano, M., Sandalio, L.M., Lázaro, A., et al., 2013. Salinity-induced changes in S-nitrosylation of pea mitochondrial proteins. J. Proteomics. 79, 87–99.
Carruthers, N.J., Stemmer, P.M., 2008. Methionine oxidation in the calmodulin-binding domain of calcineurin disrupts calmodulin binding and calcineurin activation. Biochemistry 47, 3085–3095.
Damiani, I., Pauly, N., Puppo, A., Brouquisse, R., Boscari, A., 2016. Reactive oxygen species and nitric oxide control early steps of the legume-Rhizobium symbiotic interaction. Front. Plant Sci. 7, 454.
Despres, C., Chubak, C., Rochon, A., Clark, R., Bethune, T., et al., 2003. The Arabidopsis NPR1 disease resistance protein is a novel cofactor that confers redox regulation of DNA binding activity to the basic domain/leucine zipper transcription factor TGA1. Plant Cell 15, 2181–2191.
Dietz, K.J., Jacob, S., Oelzeml, M.L., Laxz, M., Tognetti, V., et al., 2006. The function of peroxiredoxin in plant organelle redox metabolism. J. Exp. Bot. 57, 1697–1709.
Drazic, A., Miura, H., Peschek, J., Le, Y., Bach, N.C., et al., 2013. Methionine oxidation activates a transcription factor in response to oxidative stress. Proc. Natl. Acad. Sci. 110, 9493–9498.
Drazic, A., Winter, J., 2014. The physiological role of reversible methionine oxidation. Biochim. Biophys. Acta. 1844, 1367–1382 2014.
Erickson, J.R., Joiner, M.L., Guan, X., Kutschke, W., Yang, J., Oddis, C.V., Bartlett, R.K., Lowe, J.S., O'Donnell, S.E., Aykin-Burns, N., et al., 2008. A dynamic pathway for calcium-independent activation of CaMKII by methionine oxidation. Cell 133, 462–474.
Floryszak-Wieczorek, J., Arasimowicz-Jelonek, M., 2016. Contrasting regulation of NO and ROS in potato defense-associated metabolism in response to pathogens of different lifestyles. PLoS One 11. https://doi.org/10.1371/journal.pone.0163546.
Gao, L., Shen, W., Yan, P., Tuo, D., Li, X., Zhou, P., 2012. NIa-Pro of Papaya ringspot virus interacts with papaya methionine sulfoxide reductase B1. Virology 434, 78–87.
Hakmaoui, A., Pérez-Bueno, M.L., García-Fontana, B., Camejo, D., Jiménez, A., et al., 2012. Analysis of the antioxidant response of *Nicotiana benthamiana* to infection with two strains of pepper mild mottle virus. J. Exp. Bot. 63, 5487–5496.
Hardin, S.C., Larue, C.T., Oh, M.-H., Jain, V., Huber, S.C., 2009. Coupling oxidative signals to protein phosphorylation via methionine oxidation in Arabidopsis. Biochem. J. 422, 305–312.
Hung, R.J., Spaeth, C.S., Yesilyurt, H.G., Terman, J.R., 2013. SelR reverses Mical-mediated oxidation of actin toregulate F-actin dynamics. Nat. Cell Biol. 15, 1445–1454.
Iglesias-Baena, I., Barranco-Medina, S., Sevilla, F., Lázaro, J.J., 2011. The dual targeted plant sulfiredoxin retroreduces the sulfinic form of atypical mitochondrial peroxiredoxin. Plant Physiol. 155, 944–955.
Jacques, S., Ghesquière, B., De Bock, P.J., Demol, H., Wahni, K., Willems, P., Messens, J., Van Breusegem, F., Gevaert, K., 2015. Protein methionine sulfoxide dynamics in Arabidopsis thaliana under oxidative stress. Mol. Cell. Proteom. 14, 1217–1229.
Jwa, N.-S., Byung Kook Hwang, B.K., 2017. Convergent evolution of pathogen effectors toward reactive oxygen species signalling networking in plants. Front. Plant Sci. https://doi.org/10.3389/fpls.2017.01687.
Kadota, Y., Shirasu, K., Zipfel, C., 2015. Regulation of the NADPH oxidase RBOHD during plant immunity. Plant Cell Physiol. 56, 1472–1480. https://doi.org/10.1093/pcp/pcv063.
Kadota, Y., Sklenar, J., Derbyshire, P., Stransfeld, L., Asai, S., Ntoukakis, V., et al., 2014. Direct regulation of the NADPH oxidase RBOHD by the PRR-associated kinase BIK1 during plant immunity. Mol. Cell 54, 43–55. https://doi.org/10.1016/j.molcel.2014.02.021.
Kandoth, P.K., Ranf, S., Pancholi, S.S., Jayanty, S., Walla, M., et al., 2007. Tomato MAPKs LeMPK1, LeMPK2, and LeMPK3 function in the systemin-mediated defense response against herbivorous insects. Proc. Natl. Acad. Sci. 104, 12205–12210.
Kitajima, S., Kurioka, M., Yoshimoto, T., Shindo, M., Kanaori, K., Tajima, K., Oda, K., 2008. Acysteine residue near the propionate side chain of heme is the radical site in ascorbate peroxidase. FEBS J. 275, 470–480.
Kneeshaw, S., Gelineau, S., Tada, Y., Loake, G.J., Spoel, S.H., 2014. Selective protein denitrosylation activity of thioredoxin-h5 modulates plant immunity. Mol. Cell 56, 153–162.
Kulik, A., Noirot, E., Grandperret, V., Bourque, S., Fromentin, J., et al., 2015. Interplays between nitric oxide and reactive oxygen species in cryptogein signalling. Plant Cell Environ. 38, 331–348.
Lázaro, J.J., Jiménez, A., Camejo, D., Iglesias-Baena, I., Martí, M.C., et al., 2013. Dissecting the integrative antioxidant and redox systems in plant mitochondria.

Effect of stress and S-nitrosylation. Front. Plant Sci. 4, 460.
Le, D.T., Tarrago, L., Watanabe, Y., Kaya, A., Lee, B.C., Tran, U., Nishiyama, R., Fomenko, D.E., Gladyshev, V.N., Tran, L.S., 2013. Diversity of plant methionine sulfoxide reductases B and evolution of a form specific for free methionine sulfoxide. PLoS One 8, e65637.
Lee, S.-H., LiC, -W., Koh, K.W., Chuang, H.-Y., Chen, Y.-R., et al., 2014. MSRB7 reverses oxidation of GSTF2/3 to confer tolerance of Arabidopsis thaliana to oxidative stress. J. Exp. Bot. 65, 5049–5062.
Lindermayr, C., Sell, S., Muller, B., Leister, D., Durner, J., 2010. Redox regulation of the NPR1-TGA1 system of Arabidopsis thaliana by nitric oxide. Plant Cell 22, 2894–2907.
Liu, Y.D., Jin, H.L., Yang, K.Y., Kim, C.Y., Baker, B., et al., 2003. Interaction between two mitogen-activated protein kinases during tobacco defense signalling. Plant J. 34, 149–160.
López-Vidal, O., Camejo, D., Rivera-Cabrera, F., Konigsberg, M., Villa-Hernández, J.M., et al., 2016. Mitochondrial ascorbate-glutathione cycle and proteomic analysis of carbonylated proteins during tomato (*Solanum lycopersicum*) fruit ripening. Food Chem. 194, 1064–1072.
Ma, Y., Zhao, Y., Walker, R.K., Berkowitz, G.A., 2013. Molecular steps in the immune signaling pathway evoked by plant elicitor peptides: Ca^{2+}-dependent protein kinases, nitric oxide, and reactive oxygen species are downstream from the early Ca^{2+} signal. Plant Physiol. 163, 1459–1471.
Marroquin-Guzman, M., Sun, G., Wilson, R.A., 2017. Glucose-ABL1-TOR signaling modulates cell cycle tuning to control terminal appressorial cell differentiation. PLoS Genet. 13, e1006557.
Martí, M.C., Olmos, E., Calvete, J.J., Díaz, I., Barranco-Medina, S., et al., 2009. Mitochondrial and nuclear localization of a novel pea thioredoxin: identification of its mitochondrial target proteins. Plant Physiol. 150, 646–657.
Meng, X.Z., Xu, J., He, Y.X., Yang, K.-Y., Mordorski, B., et al., 2013. Phosphorylation of an ERF transcription factor by ArabidopsisMPK3/MPK6 regulates plant defense gene induction and fungal resistance. Plant Cell 25, 1126–1142.
Meyer, Y., Siala, W., Bashandy, T., Riondet, C., Vignols, F., et al., 2008. Glutaredoxins and thioredoxins in plants. Biochim. Biophys. Acta 1783, 589–600.
Miernyk, J.A., et al., 2009. Oxidation of an adjacent methionine residue inhibits regulatory seryl-phosphorylation of pyrubate dehydrogenase. Proteomics Insights 2, 15–22.
Mittler, R., 2017. ROS are good. Trends Plant Sci. 22, 11–19.
Moreau, M., Lindermayr, C., Durner, J., Klessig, D.F., 2010. NO synthesis and signaling in plants-where do we stand? Physiol. Plant. 138, 372–383.
Návarová, H., F. Bernsdorff, F., Döring, A.-C., Zeier, J., 2012. Pipecolic acid, an endogenous mediator of defense amplification and priming, is a critical regulator of inducible plant immunity. Plant Cell 24, 5123–5141.
Park, S.Y., Choi, J., Lim, S.E., Lee, G.W., Park, J., Kim, Y., et al., 2013. Global expression profiling of transcription factor genes provides new insights into pathogenicity and stress responses in the rice blast fungus. PLoS Pathog. 9, e1003350. https://doi.org/10.1371/journal.ppat.1003350.
Peleg-Grossman, S., Melamed-Book, N., Cohen, G., Levine, A., 2010. Cytoplasmic H_2O_2 prevents translocation of NPR1 to the nucleus and inhibits the induction of PR genes in Arabidopsis. Plant Signal. Behav. 5, 1401–1406.
Peleg-Grossman, S., Melamed-Book, N., Levine, A., 2012. ROS production during symbiotic infection suppresses pathogenesis-related gene expression. Plant Signal. Behav. 7, 409–415.
Perchepied, L., Balague, C., Riou, C., Claudel-Renard, C., Riviere, N., et al., 2010. Nitric oxide participates in the complex interplay of defense related signaling pathways controlling disease resistance to *Sclerotinia sclerotiorum* in *Arabidopsis thaliana*. Mol. Plant Microbe Interact. 23, 846–860.
Pietrowska, E., Różalska, S., Kaźmierczak, A., Nawrocka, J., Małolepsza, U., 2015. Reactive oxygen and nitrogen (ROS and RNS) species generation and cell death in tomato suspension cultures-*Botrytis cinerea* interaction. Protoplasma 252, 307–319.
Rao, Moller, Thelen, Miernyk, 2015. Convergent signaling pathways—interaction between methionine oxidationand serine/threonine/tyrosine O-phosphorylation. Cell Stress Chaperones 20, 15–21.
Rey, P., Tarrago, L., 2018. Physiological roles of plant methionine sulfoxide reductases in redox homeostasis and signaling. Antioxidants 7, 114. https://doi.org/10.3390/antiox7090114.
Rhee, S.G., Woo, H.A., Kil, I.S., Bae, S.H., 2012. Peroxiredoxin functions as a peroxidase and a regulator and sensor of local peroxides. J. Biol. Chem. 287, 4403–4410.
Romero-Puertas, M.C., Campostrini, N., Mattè, A., Righetti, P.G., Perazzolli, M., et al., 2008. Proteomic analysis of S-nitrosylated proteins in *Arabidopsis thaliana* undergoing hypersensitive response. Proteomics 8, 1459–1469.
Roos, G., Messens, J., 2011. Protein sulfenic acid formation: from cellular damage to redox regulation. Free Radic. Biol. Med. 51, 314–326.
Roos, G., Foloppe, N., Messens, J., 2013. Understanding the pK a of redox cysteines: the key role of hydrogen bonding. Antioxidants Redox Signal. 18, 94–127.
RuizMay, E., Segura-Cabrera, A., Elizalde-Contreras, J.M., Shannon, L.M., Loyola-Vargas, V.M., 2018. A recent advance in the intracellular and extracellular redox post--translational modification of proteins in plants. J. Mol. Recognit., e2754.
Sasindran, S.J., Saikolappan, S., Dhandayuthapani, S., 2007. Methionine sulfoxide reductases and virulence of bacterial pathogens. Future Microbiol. 2. https://doi.org/10.2217/17460913.2.6.619.
Schürmann, P., Buchanan, B.B., 2008. The ferredoxin/thioredoxin system of oxygenic photosynthesis. Antioxidants Redox Signal. 10, 1235–1274.
Segonzac, C., Zipfel, C., 2011. Activation of plant pattern-recognition receptors by bacteria. Curr. Opin. Microbiol. 14, 54–61.
Snijder, J., Rose, R.J., Raijmakers, R., Heck, A.J.R., 2011. Site-specific methionine oxidation in calmodulin affects structural integrity and interaction with Ca2+/calmodulin-dependent protein kinase II. J. Struct. Biol. 174, 187–195.
Spoel, S.H., Tada, Y., Loake, G.J., 2010. Post-translational protein modification as a tool for transcription reprogramming. New Phytol. 186, 333–339.
Svoboda, Reddie, Zhang, Vesely, Williams, et al., 2012. Redox-sensitive sulfenic acid modification regulates surface expression of the cardiovascular voltage-gated potassium channel Kv1.5. Circ. Res. 111, 842–853. https://doi.org/10.1161/CIRCRESAHA.111.263525.
Tada, Y., Spoel, S.H., Pajerowska-Mukhtar, K., Mou, Z., Song, J., et al., 2008. Plant immunity requires conformational changes (corrected) of NPR1 via S-nitrosylation and thioredoxins. Science 321, 952–956.
Tarrago, L., Laugier, E., Rey, P., 2009. Protein-repairing methionine sulfoxide reductases in photosynthetic organisms: gene organization, reduction mechanisms, and physiological roles. Mol. Plant 2, 202–217.
Torres, M.A., 2010. ROS in biotic interactions. Physiol. Plant. 138, 414–429.
Torres, M.A., Jones, J.D., Dangl, J.L., 2006. Reactive oxygen species signalling in response to pathogens. Plant Physiol. 141, 373–378.
Veredas, F.J., Cantón, F.R., Aledo, J.C., 2017. Methionine residues around phosphorylation sites are preferentially oxidized in vivo under stress conditions. Sci. Rep. 7, 40403. https://doi.org/10.1038/srep40403.
Vidhyasekaran, P., 2014. PAMP Signals in Plant Innate Immunity. Springerhttps://doi.org/10.1007/978-94-007-7426-1.
Wang, C., Liu, R., Lim, G.-H., de Lorenzo, L., Yu, K., 2018. Pipecolic acid confers systemic immunity by regulating free radicals. Sci. Adv. 4, eaar4509 2018.
Waszczak, Akter, Eeckhout, Persiau, Wahni, et al., 2014. Sulfenome mining in Arabidopsis thaliana. PNAS 111, 11545–11550. https://doi.org/10.1073/pnas.1411607111.
Waszczak, C., Carmody, M., Kangasjarvi, J., 2018. Reactive oxygen species in plant signaling. Annu. Rev. Plant Biol. 69, 209–236.
Withers, J., Dong, X., 2017. Post-translational regulation of plant immunity. Curr. Opin. Plant Biol. 38, 124–132 2017.
Yang, H., Mu, J., Chen, L., Feng, J., Hu, J., Li, L., Zhou, J.-M., 2015. ZuoJ. S-nitrosylation positivelyregulates ascorbate peroxidase activity during plant stress responses. Plant Physiol. 167, 1604–1615.
Yoshioka, H., Adachi, H., Ishihama, N., Nakano, T., Shiraishi, Y., et al., 2015. Molecular mechanisms of ROS burst conferred by protein phosphorylation. J. Phytopathol. 81, 1–8.
Yoshioka, H., Mase, K., Yoshioka, M., Kobayashi, M., Asai, S., 2011. Regulatory mechanisms of nitric oxide and reactive oxygen species generation and their role in plant immunity. Nitric Oxide 25, 216–221.
Yuan, H.-M., Liu, W.-C., Lu, Y.-T., 2017. CATALASE2 coordinates SA-mediated repression of both auxin accumulation and JA biosynthesis in plant defenses. Cell Host Microbe 21, 143–155.
Yun, B.W., Feechan, A., Yin, M., Saidi, N.B., Le, Bihan, et al., 2011. S-nitrosylation of NADPH oxidase regulates cell death in plant immunity. Nature 478, 264–268.
Zhang, Z., Wang, J., Chai, R., Qiu, H., Jiang, H., et al., 2015. An S-(Hydroxymethyl) glutathione dehydrogenase is involved in conidiation and full virulence in the rice blast fungus magnaporthe oryzae. PLoS One. https://doi.org/10.1371/journal.pone.0120627.
Zheng, Y., Hong, H., Chen, L., Li, J., Sheng, J., Shen, L., 2014. LeMAPK1, LeMAPK2, and LeMAPK3 are associated with nitric oxide-induced defense response against Botrytis cinerea in the Lycopersicon esculentum fruit. J. Agric. Food Chem. 62, 1390–1396.
Zhou, J., He, P., Shan, L., 2014. Ubiquitination of plant immune receptors. Methods Mol. Biol. 1209, 219–231.