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Redox and the circadian clock in plant immunity: A balancing act

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Abstract

Plants' reliance on sunlight for energy makes their light-driven circadian clock a critical regulator in balancing the energy needs for vital activities such as growth and defense. Recent studies show that the circadian clock acts as a strategic planner to prime active defense responses towards the morning or daytime when conditions, such as the opening of stomata required for photosynthesis, are favorable for attackers. Execution of the defense response, on the other hand, is determined according to the cellular redox state and is regulated in part by the production of reactive oxygen and nitrogen species upon pathogen challenge. The interplay between redox and the circadian clock further gates the onset of defense response to a specific time of the day to avoid conflict with growth-related activities. In this review, we focus on discussing the roles of the circadian clock as a robust overseer and the cellular redox as a dynamic executor of plant defense.

Keywords

Circadian clock; Redox rhythm; Plant immunity; Salicylic acid; Jasmonic acid; Cellular redox; Reactive oxygen species; Reactive nitrogen species; S-nitrosylation

1. Introduction

Plants lead challenging lives as sessile photosynthetic organisms: they cannot actively diversify their energy sources or escape from environmental challenges. This essentially turns their existence into an endeavor for better resource management. A well-established example is the tradeoff between growth and defense [1]: How are resources allocated towards defense without the risk of severely delayed growth and development? Since plants do not have specific immune cells against particular pathogens as do animals, they must also balance distinct defense mechanisms against attackers with contrasting infection strategies. When challenged by biotrophic pathogens, which thrive in living tissues, plants can kill infected cells to contain the invaders. However, this strategy may leave them vulnerable to necrotrophs that feed on dead cells. Therefore, immune responses need to be managed and balanced against each other, so that the most optimal defense strategy is deployed [2]. In this review, we present how the plant circadian clock and redox system respectively serve

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as a strategic planner and an executor of these immune strategies. For more comprehensive discussion on the interplay between the circadian clock and redox within the context of plant immunity, please see excellent reviews by Spoel and van Ooijen [3] and by Lu and colleagues [4].

The Earth's rotation around its axis and the sun results in robust rhythmic changes in its environment. Living organisms have evolved circadian clocks to exploit this predictable environmental information and synchronize internal processes with the daily cycles [5,6]. Disharmony with the environment can have dire consequences, with the disruption of the circadian rhythm being a risk factor for multitude of diseases in humans [7]. Considering that plants rely on photosynthesis for the generation of energy and reducing power, it is hard to overestimate the importance of the circadian clock in managing numerous aspects of plant physiology and improving plant's fitness [8–10], with at least 30% of the *Arabidopsis thaliana* transcripts showing the circadian rhythmicity [11]. Therefore, plants can use the circadian clock for the efficient planning of resource expenditure. For example, as a function of the clock, photosynthetic products (i.e., starch) accumulated during the day are exhausted in the service of growth-related activities at night right before dawn, demonstrating the “frugality” of plants in energy management [12]. As a high-cost and high-benefit trait, activation of plant immunity has also been found to be tightly regulated by the clock [4]. By using the circadian clock to schedule and gate defense to the time of high likelihood of an attack, plants can avoid energetically expensive and potentially deleterious effects of untimely immune induction [13].

In contrast to the regularity and robustness of the circadian clock, the cellular redox state is dynamic, determined by the current production of oxidized versus reduced metabolites. Plant immunity has long been associated with the production of reactive oxygen species (ROS), such as hydrogen peroxide (H₂O₂), and reactive nitrogen species (RNS), such as nitric oxide (NO) [14–16]. The balance between ROS and RNS production is crucial for a successful immune response [15], while their interplay is often a determinant of the fate of the infected cells [17]. As a major antioxidant in plants, glutathione plays a central role in regulating immunity [18–20]. In addition, the signaling of the two main plant defense hormones, salicylic acid (SA) and jasmonic acid (JA), responsible for defense against biotrophic and necrotrophic pathogens, respectively, are associated with opposing effects on cellular redox [21]. These redox-dependent mechanisms ultimately ensure that plant defense combats the appropriate attacker [16] while potentially minimizing the costs.

2. When to defend and when to attack: the role of the circadian clock

Upon pathogen challenge, plants must first determine how much energy can be diverted towards defense. Plant energy generation in nature is diurnal, with photosynthesis occurring only during the day. Predictably, the opening of the microscopic epidermal pores (i.e., stomata) involved in the gas exchange for photosynthesis, is regulated by the circadian clock [22,23]. The aperture of the stomata is bigger during the day and smaller at night. Because stomata are also entry points for some pathogens, plants show greater resistance against surface-inoculated bacteria at night, when stomata have a smaller aperture [24,25] (Fig. 1). Moreover, stomatal closure in response to pathogens is among the earliest plant

immune responses. After detecting pathogen-associated molecular patterns (PAMPs), such as flagellin, as a part of pattern-triggered immunity (PTI) [26], plants rapidly close the stomata [27]. Core morning clock genes *CIRCADIAN CLOCK ASSOCIATED 1 (CCA1)* and *LATE ELONGATED HYPOCOTYL (LHY)* have been found to regulate stomatal immunity through their target *GLYCINE-RICH RNA-BINDING PROTEIN 7 (GRP7)*, also known as *COLD AND CIRCADIAN REGULATED 2 (CCR2)* [24]. GRP7 is part of a peripheral loop of the circadian clock [28], which, besides being involved in stomatal defense, binds to some PAMP receptor transcripts and can upregulate the translation of at least one of them during an infection [29]. Additionally, night-expressed clock gene *TIME FOR COFFEE (TIC)* is required for both circadian oscillation of stomatal aperture and efficient stomatal defense [25]. Interestingly, darkness treatment by itself induces stronger stomatal closure than an infection under light [30], suggesting that other form of defense may be required in the presence of light to compensate for the weaker stomatal protection.

While stomatal closure after the infection during the daytime might be limited to prevent conflict with photosynthetic gas exchange, the light-dependent energy generation may allow plants to invest towards more proactive immune responses. Several *A. thaliana* genes involved in PTI and basal defense peak and/or are induced more strongly at dawn [13,25,31], when conditions such as high humidity and opened stomata are favorable for pathogen invasion [25,32]. Consequently, when a plant is infiltrated directly with bacteria, bypassing the stomata, it shows the highest resistance at dawn [25,31].

Certain pathogens have evolved specific proteins, called effectors, which are delivered into plant cells to overcome PTI and enhance virulence. As a counter act, plants express intracellular nucleotide-binding and leucine-rich repeat (NB-LRR) immune receptors to detect specific pathogen effectors or their activities to induce effector-triggered immunity (ETI) [33]. ETI is a more drastic defense response than PTI, normally involving programmed cell death (PCD) of the infected tissue. The immune receptor gene, *RECOGNITION OF PERONOSPORA PARASITICA 4 (RPP4)*, which recognizes an effector in the oomycete pathogen *Hyaloperonospora arabidopsidis (Hpa)* Emw1, is a target of the core clock component CCA1, and peaks in the morning, when the likelihood of *Hpa* infection is the highest [32]. This provides a direct genetic link between the circadian clock and defense.

Another direct clock target is the *ISOCHORISMATE SYNTHASE 1 (ICS1)* gene, which encodes a key enzyme in the defense hormone SA biosynthesis, and whose expression is driven by the evening-phased clock transcription factor CCA1 HIKING EXPEDITION (CHE) [34]. Both *ICS1* gene expression and the concentration of SA peak in the middle of the night as a result of this regulation, possibly to anticipate infection in the morning. SA is not only required for local defense against biotrophs, but also serves as a necessary and sufficient signal for inducing the broad-spectrum systemic acquired resistance (SAR) in the distal tissue [33]. Notably, the *che* mutant has compromised SAR, but intact local defense, suggesting that oscillation of SA might be involved in gating SAR because “immunizing” the entire plants against future infection is an extra energy expenditure that should only be “budgeted” when plants have excess to spare [34]. Altogether, the circadian clock primes costly defense responses (e.g., expression of immune genes) towards the morning, when

stomata must be opened to facilitate photosynthesis, coinciding with the infection window for some biotrophic pathogens (Fig. 1).

In contrast to SA, JA, the defense hormone against necrotrophs and herbivores, peaks in the middle of the day [35]. It is proposed that JA oscillation anticipates the activities of herbivores, such as *Trichoplusia ni* caterpillars, which peak just before dusk [35]. When such anticipation is disrupted by entraining plants' circadian clocks out of phase with caterpillar activities, more tissue loss to herbivory is observed. Similarly, clock-deficient plants have been shown to be preferred by the caterpillars over wild type plants [35,36]. In addition to JA levels, the JA signaling pathway is also influenced by the clock. The clock component TIC facilitates proteasome-mediated degradation of MYC2, a key component in the JA-mediated defense against herbivores [37], through the night, while additionally priming the expression of the JA receptor gene *CORONATINE INSENSITIVE 1 (COI1)* towards dawn [38]. Altogether, the strongest accumulation of MYC2 happens during the daytime [38], which might help combat the higher herbivore activity during the day [35]. The day time JA peak does not seem to coincide with resistance against the necrotrophic fungus *Botrytis cinerea*, which is the strongest when the pathogen is inoculated at dawn [39,40]. This discrepancy was explained by the approximate 12-h delay required for the germination of *B. cinerea* conidiospores and the formation of infectious hyphae [40]. Based on these observations, it is reasonable to speculate that the temporal separation of SA and JA oscillations by the circadian clock allows plants to prepare defense for a specific type of the attacker while avoiding potential antagonism between SA and JA [41].

3. How to defend: the role of redox

While the plant circadian clock anticipates imminent invasion by various attackers [3,4], redox signaling is used to choose and execute the appropriate defense for the pathogen at hand [3,16] (Fig. 2). Immune responses are efficiently triggered only when both ROS and RNS signaling are simultaneously activated, and the sources of ROS/RNS often determine the nature of the defense response. Upon pathogen challenge, superoxide radical produced from the NADPH oxidase RESPIRATORY BURST OXIDASE HOMOLOGUE D (RBOHD) facilitates *A. thaliana* stomatal closure during PTI [42,43], while another NADPH oxidase, RBOHF, is required for full accumulation of SA [44]. Additionally, ROS production by the apoplastic peroxidases PRX33 and PRX34 are needed specifically for the induction of SA-dependent defense genes [45–48]. Meanwhile, production of nitric oxide through NO synthase-like activity is required for both stomatal closure [27] and the induction of defense genes [49,50].

The interplay between ROS and RNS is more intricate during ETI when plants are forced to take the drastic measure of killing off the infected cells to contain the pathogen. Cell death is triggered when the NO/H₂O₂ ratio is between 0.25 and 2 [15], with both NO synthase-like activity [51] and nitrate reductases NR1 and NR2 [52] contributing to the generation of NO during ETI. The role of ROS signaling during ETI is complex. On one hand, RBOHD and RBOHF are required for the ROS production and cell death during ETI, respectively [53]. On the other hand, when *rbohD* and *rbohF* mutants were crossed with the *lesion simulation disease 1 (lsd1)* mutant, which exhibits superoxide-dependent runaway cell death (RCD)

upon SA treatment [54], they exacerbated the RCD phenotype [55]. This implies that in addition to initiating PCD during ETI, the ROS production by RBOHs can also prevent uncontrollable cell death during ETI.

S-nitrosylation, the covalent attachment of the NO moiety to the cysteine thiol group, is an important mediator of NO signaling and forms yet another layer of redox regulation on PCD. S-nitrosoglutathione (GSNO) acts as a mobile donor of SNOs and affects the balance of S-nitrosylation in the cell [56]. Both the GSNO reductase 1 mutant of *A. thaliana*, *gsnor1-3*, and the *nitrous oxide overexpressor 1 (nox1)* mutant, have increased levels of S-nitrosothiols (SNOs) and stronger PCD during ETI [17]. Remarkably, in *gsnor1-3* and *nox1* mutants, both SA accumulation and NADPH oxidase activity are reduced, the latter of which can be explained by the inhibitory S-nitrosylation of RBOHD. This results in increased susceptibility of the *gsnor1-3* and *nox1* mutants to infection [57]. Surprisingly, while THIOREDOXIN H-TYPE 5 (TRX-H5) can partially restore immunity in *nox1* plants through its denitrosylation activity, it is unable to do so in *gsnor1-3* mutants [58]. This indicates that TRX-H5 selectively targets the proteins which were S-nitrosylated due to excessive free NO but not GSNO. The restoration of the PCD in RBOH-deficient mutants by the *gsnor1-3* mutation suggests that S-nitrosylation may act as a backup mechanism for ETI even though it negatively affects basal resistance. Supporting this hypothesis, the *gsnor1-3* mutation could reestablish the PCD-dependent resistance to *Hpa* Emwa1 in the *salicylic acid induction deficient 2 (sid2)* mutant [17].

In addition to their role in defense against biotrophic pathogens, both ROS and RNS are also necessary for defense against necrotrophs and herbivores. The lack of ROS production by apoplastic peroxidases in *A. thaliana* renders the plants more susceptible to *B. cinerea* [45], while addition of NO donors induces JA-mediated defense against root knot nematodes in tomato [59]. NO is also produced in response to wounding [60]. However, full induction of JA-signaling by gaseous NO in *A. thaliana* happens only in the absence of SA. Considering that gaseous NO can also induce SA production, this exclusive induction likely serves as a mechanism to avoid unnecessary simultaneous activation of the opposing pathways [60].

Apart from the ROS/RNS bursts described above, plant immunity is often accompanied by alteration of the cellular redox state, reflected by changes in the ratio of reduced (GSH) and oxidized (GSSG) forms of glutathione, as well as in total glutathione levels. These changes are necessary for execution of the long-term immune response, SAR, which is accompanied by global transcriptional reprogramming mediated by the redox-sensitive transcription regulator NONEXPRESSER OF PATHOGENESIS-RELATED GENES 1 (NPR1) [61]. NPR1 is normally sequestered in the cytoplasm in an oligomer form through disulfide bridges, which are also affected by S-nitrosylation [62]. SA induces glutathione production and increases the GSH/GSSG ratio, reducing NPR1 oligomer primarily via thioredoxin TRX-H5 [62,63]. NPR1 monomer is then translocated into the nucleus [63,64], where it acts as a transcriptional coactivator for the TGA family of transcription factors and induces defense genes [65,66].

In contrast to SA, JA depletes glutathione pools and lowers the GSH/GSSG ratio, shifting the cellular redox towards oxidizing conditions [21]. Unsurprisingly, glutathione plays

a vital role in the regulation of the crosstalk between SA and JA. The suppression of JA signaling by SA depends on the changes in glutathione pools and is weakened in the presence of a glutathione synthesis inhibitor [67]. Additionally, the mutation in *GLUTATHIONE-DISULFIDE REDUCTASE 1 (GR1)* leads to oxidized cellular environment and attenuates SA-mediated defense while affecting JA signaling [68]. The redox-dependent SA-JA antagonism can also be manipulated by pathogens and herbivores to their advantage. Necrotrophic fungus *B. cinerea* increases SA levels to take advantage of the SA-mediated induction of glutaredoxin (a reducing enzyme which uses glutathione as a cofactor) *GRXS13* to repress JA-mediated defense and increase host susceptibility [69]. *Spodoptera exigua* caterpillars also secrete effectors from salivary glands to induce the SA pathway and prevent oxidation of the cellular redox state necessary for the activation of JA-mediated defense [70]. Remarkably, while glutathione acts as a centerpiece in redox-mediated SA-JA antagonism, a mutation in γ -glutamylcysteine synthetase (GSH1), which catalyzes the first step of glutathione synthesis, results in susceptibility to not only biotrophic pathogens [18,20], but also necrotrophs [18] and herbivores [19]. This underscores the importance of proper redox balance during immune responses.

4. Balancing growth and immunity: combined influence of the clock and redox

Despite being necessary for plant survival, defense induction often carries a great cost. Plant growth and defense are locked in an eternal struggle for resource allocation [1]. Constitutive induction of plant immunity results in dwarfism [71,72], whereas the plant growth hormone auxin suppresses defense [73]. Interestingly, the crosstalk between defense and growth is, at least partially, redox-mediated. The catalase mutant *cat2*, which is under constitutive oxidative stress, exhibits dwarfism but has increased resistance against biotrophic pathogens [74–76]. It was found that SA directly binds to plant catalases to inhibit their activity [77,78]. In *A. thaliana*, the inhibition of CAT2 activity by SA leads to an increase in H₂O₂ and subsequent sulfenylation (oxidation of a thiol -SH into sulfenic acid -SOH) of tryptophan synthetase β subunit 1 (TSB1) [76]. Reduced levels of tryptophan, the auxin precursor, cause reduced growth, but stronger immunity. These findings demonstrate how plant defense hormones could manipulate cellular redox to suppress growth.

The plant circadian clock also plays a central role in mediating growth-defense tradeoff. The clock-mediated stomatal closure at night and the gating of active defense towards the morning are good demonstrations of how the circadian clock prevents unsustainable redirection of energy towards immunity. Additionally, the morning core clock component CCA1 regulates the expression of catalases, including *CAT2*, to manage ROS homeostasis and possibly also to affect defense through redox changes [79]. Moreover, circadian clock gates the induction of immunity towards morning to prevent conflicts with growth at night through interactions with the metabolic circadian redox rhythm [13]. The circadian redox rhythm was initially discovered as oscillations in NADH and NADPH levels as well as in the oxidation state of ROS scavenger peroxiredoxins in anucleate red blood cells (RBCs), in which transcription and translation activities are considered absent [80]. Unlike the genetic circadian clocks consisting of distinct transcription and translation feedback loops,

the active site of peroxiredoxins, responsible for circadian redox rhythms, is conserved in all domains of life, hinting at a possible redox-based origin of circadian clocks [81]. Furthermore, the oscillations of NADH and NADPH in RBCs [80], in particular, hint at a more generic redox rhythm than simple oxidation/reduction cycles of peroxiredoxins. In plants, the circadian redox rhythm (i.e. NADP/H oscillation) is coupled to the genetic clock through the redox-sensitive immune regulator NPR1 [13]. This link is mediated through SA-induced cellular redox changes, which cause nuclear translocation of NPR1 [63]. However, acute perturbation of the redox rhythm by SA does not change the phase or the period of the genetic clock, but rather reinforces it through NPR1-mediated upregulation of both morning (*LHY* and *PSEUDO-RESPONSE REGULATOR 7 (PRR7)*) and evening (*TIMING OF CAB EXPRESSION 1 (TOC1)*) clock genes [13]. Since *LHY* is a positive regulator of defense genes while *TOC1* is a repressor, increases in their expression lead to the gating of defense with higher sensitivity to SA induction in the morning than in the evening [13]. The biological significance of this clock-mediated gating is demonstrated by the severe loss of fresh weight in plants whose immunity is untimely induced by SA in darkness [13]. It has been recently demonstrated that an aqueous environment is essential for pathogen virulence [82]. It is also known that SA treatment results in repression of several aquaporin genes, possibly as a defense mechanism [13,83]. If this repression on water transport activities occurs at night, it interferes with growth-related activities. Therefore, it can be argued that one of the benefits of clock-mediated gating of the SA immune response towards the morning is to avoid conflict with water transport activities required for growth that occurs at night.

5. Future directions

In this review, we present how plants utilize the robustness of the circadian clock to plan and the sensitivity of redox signaling to execute an appropriate defense response while minimizing the cost of this response. It should be noted, however, that there is a daily rhythmic accumulation of ROS in plants, accompanied by the circadian expression of ROS-dependent genes [79]. Because many of these genes, such as catalases and NADPH oxidases, are also involved in plant defense, redox might add an extra layer of regulation to the clock control of plant defense[3,4]. However, ROS-dependent genes which regulate immunity are also often directly induced in the presence of the pathogen, as demonstrated by the specific spatiotemporal regulation of *RBOHD* and *RBOHF* expression during plant defense [84]. Thus, it is likely that circadian expression of these redox genes does not serve to anticipate pathogens, but rather is tied to the rhythmic metabolic ROS production as shown in [79]. It is also unknown which circadian-clock-dependent redox genes are responsible for setting the circadian redox rhythm, especially considering that peroxiredoxin oscillations persist in clock-impaired *TOC1*-overexpressing (*TOC1-OX*) plants [81]. Thus, the source of the circadian redox rhythm (NADP/H oscillation) remains unclear at least in plants.

While we understand that acute perturbation of the redox rhythm during SA-mediated immune induction reinforces the genetic clock to gate the immune response, not much is known about the role of the redox rhythm itself. Levels of monomeric NPR1 protein peak at the same time as NADPH [13], implying that the redox rhythm might periodically

reduce NPR1. Nevertheless, the cause of the NPR1 monomer oscillations has not been unambiguously identified yet. Notably, SA levels also peak in phase with the NPR1 monomer, as a result of regulation by the clock component CHE [34]. Thus, it is possible that SA might influence oscillations of NPR1 monomer by affecting cellular redox [13,63]. Another possibility could be the stabilization of nuclear NPR1 at night by higher levels of SA [85]. Furthermore, the activity of CHE protein itself might be regulated by the cellular redox [86], closing the feedback loop between SA, circadian redox rhythm, NPR1 and the genetic circadian clock. A thorough investigation of the role of the immune hormone SA as a connecting signal between redox and the circadian clock might reveal the significance of having the ancient redox rhythm along with the comparatively modern genetic clock.

Similar to the interplay between the genetic circadian clock and the redox rhythm discussed above, integration of multiple ROS/RNS signals is required for efficient plant defense. This complexity allows the plant to select the appropriate defense strategy based on the source of ROS/RNS, preventing conflicting immune responses such as concurrent defense against herbivores and biotrophic pathogens. Furthermore, because ROS/RNS are required for defense against both biotrophs [27,42,48,50] and necrotrophs/herbivores [45,59], they could also play a significant role in limiting the SA-JA antagonism, which is often exploited by attackers [69,70]. For example, the *cat2* mutation increases defense against biotrophs but decreases resistance to necrotrophs by suppressing JA biosynthesis [76]. In contrast, plants without apoplastic peroxidase activity are unable to mount efficient defense against both types of pathogens [45], implying that the source of ROS/RNS also affects how the plants balance SA- and JA-dependent defenses. A possible strategy to prevent excessive antagonism between these two essential pathways could be a preemptive partial activation of the opposing pathway, recently demonstrated by the noncanonical activation of JA signaling through SA receptors [87]. Interestingly, gaseous NO does induce elements of both JA and SA signaling pathways [60]. Further dissection of these clues may give us better understanding of a plant's struggle to equipose contrasting defense strategies.

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Abbreviations

ROS	reactive oxygen species
H₂O₂	hydrogen peroxide
RNS	reactive nitrogen species
NO	nitric oxide
GSH1	γ -glutamylcysteine synthetase
SA	salicylic acid
JA	jasmonic acid

PAMP	pathogen-associated molecular pattern
PTI	pattern-triggered immunity
CCA1	CIRCADIAN CLOCK ASSOCIATED 1
LHY	LATE ELONGATED HYPOCOTYL
GRP7	GLYCINE-RICH RNA-BINDING PROTEIN 7
CCR2	COLD AND CIRCADIAN REGULATED 2
TIC	TIME FOR COFFEE
NB-LRR	nucleotide-binding and leucine-rich repeat
ETI	effector-triggered immunity
PCD	programmed cell death
Hpa	Hyaloperonospora arabidopsidis
RPP4	RECOGNITION OF PERONOSPORA PARASITICA 4
ICS1	ISOCHORISMATE SYNTHASE 1
CHE	CCA1 HIKING EXPEDITION
SAR	systemic acquired resistance
COI1	CORONATINE INSENSITIVE 1
NAD	nicotinamide dinucleotide
NADP	nicotinamide dinucleotide phosphate
RBOHD	RESPIRATORY BURST OXIDASE HOMOLOGUE D
RBOHF	RESPIRATORY BURST OXIDASE HOMOLOGUE F
PRX33	PEROXIDASE 33
PRX34	PEROXIDASE 34
NR1	NITRATE REDUCTASE 1
NR2	NITRATE REDUCTASE 2
nox1	nitrous oxide overexpressor 1
lsd1	lesion simulation disease 1
RCD	runaway cell death
GSNO	S-ni-trosoglutathione
GSNOR1	GSNO reductase 1

GSH	glutathione
GSSG	glutathione disulfide
SNO	S-nitrosothiol
TRX-H5	THIOREDOXIN H-TYPE 5
sid2	salicylic acid induction deficient 2
NPR1	NONEXPRESSER OF PATHOGENESIS-RELATED GENES 1
GRXS13	GLUTAREDOXIN 13
GR1	GLUTATHIONE-DISULFIDE REDUCTASE 1
CAT2	CATALASE 2
TSB1	tryptophan synthetase β subunit 1
PRR7	PSEUDO-RESPONSE REGULATOR 7
TOC1	TIMING OF CAB EXPRESSION 1
TOC1-OX	TOC1-overexpressing

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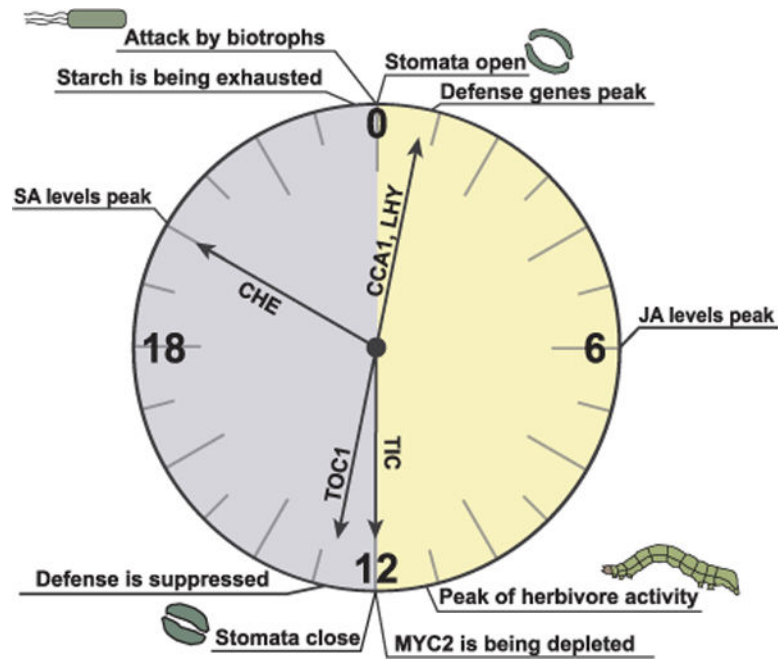


Fig. 1.

The many hands of the circadian clock. The circadian clock (genes represented by arrows in the figure) primes several active plant defenses against biotrophs towards the morning and daytime, when stomata are open, the energy is available due to photosynthesis and the conditions are favorable for pathogen invasion. The clock suppresses the active defense against biotrophs at night, relying on closed stomata to prevent pathogen invasion. JA signaling component MYC2 is depleted through the night and accumulates during the day. The nighttime peak of SA and the daytime peak of JA could anticipate the morning attack by biotrophs and peak herbivore activity just before dusk, respectively.

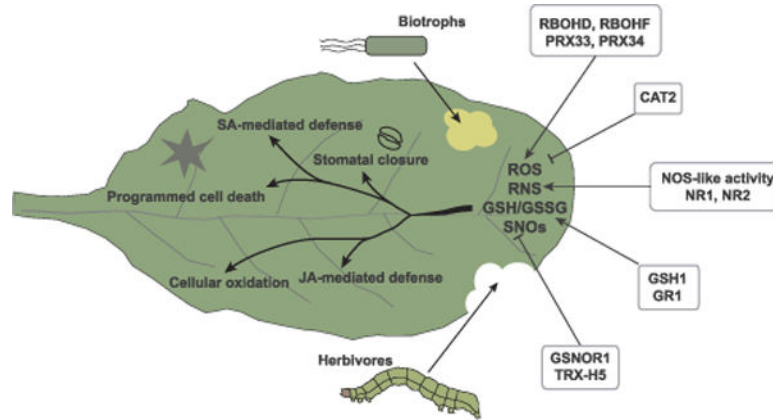


Fig. 2.

Cellular redox and ROS/RNS regulate plant immunity and balance potentially conflicting immune strategies against biotrophs versus herbivores/necrotrophs. Plants produce through NADPH oxidases RBOHD and RBOHF and apoplastic peroxidases PRX33 and PRX34 in response to pathogen challenge. Cellular ROS is scavenged by catalases, among CAT2 plays a significant role in regulating defense. RNS are produced through NOS-like activity or by nitrate reductases NR1 and NR2. The balance between oxidized (GSH) and (GSSG) forms of glutathione depends on glutathione reductase GR1 and γ -glutamylcysteine synthetase GSH1 activity. Cellular S-nitrosothiols are recycled partly by thioredoxin and are also affected by S-nitrosoglutathione (GSNO), which is recycled by the GSNO reductase, GSNOR1.