



## Graphical Review

## Oxylipins in plastidial retrograde signaling

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## ABSTRACT

Oxylipins (compounds derived from the oxidation of polyunsaturated fatty acids) are essential in retrograde signaling emanating from plastids to the nucleus during plant developmental and stress responses. In this graphical review, we provide an overview of the chemical structure, biosynthesis and role of oxylipins, as both redox and hormonal signals, in controlling plant development and stress responses. We also briefly summarize current gaps in the understanding of the involvement of oxylipins in plastidial retrograde signaling to highlight future avenues for research.

## 1. Introduction

Plants are unique organisms due to their capacity to perform photosynthesis and sustain all life on Earth, and improving our understanding of the redox signals modulating plastid-to-nucleus retrograde signaling will help us not only understand better basic aspects of plant development and stress responses but also improve current biotechnological approaches to achieve a more sustainable agriculture. The presence of cell walls, vacuoles and plastids are the most prominent features of plants at the subcellular level. Plastids are plant cell-specific organelles of endosymbiotic origin which are surrounded by a double membrane and display a high flexibility in their morphology and function. They are inherited as an undifferentiated precursor form, the so-called proplastid, which develops into a mature form during the growth and development of the plant. Like their cyanobacterial ancestors, plastids multiply by fission in a coordinated way with the division of the cell in which they reside, which guarantees that all cells during plant growth will be provided with their own set of plastids [1]. The most prominent representative of these organelles is the chloroplast in the aerial parts of the plant which is the site of photosynthesis and many other important metabolic reactions involved in, e.g., nitrate or sulfate reduction, purine and pyrimidine biosynthesis or amino acid production. Other forms are colorless amyloplasts or elaioplasts in the roots and storage organs, which serve as starch or oil storage compartments, respectively, or colored chromoplasts in fruits or flowers, which serve an important role in fruit ripening or pollinators' attraction, respectively. Chloroplasts can also trigger and undergo important morphological and

metabolic changes leading to the formation of gerontoplasts during leaf senescence. Therefore, plastids are unique organelles that play essential roles in plant development and stress responses (Fig. 1).

The presence of plastidial organelles in plant cells also provides several advantages in terms of energy usage and compartmentalization of biochemical pathways, allowing accumulation and storage of specific metabolites. Since plastids, in particular chloroplasts, are site sensors of environmental and developmental changes, communication from these organelles to the nucleus is essential to grant plant acclimation and metabolic adjustments. This form of signal transduction is known as retrograde signaling, opposite to anterograde signaling that refers to signals emanating from the nucleus to other organelles, and was firstly evidenced by studies on plastid ribosome deficient mutants of barley in the early 1970s [2,3]. From this pioneer work, much information is now available on retrograde signals, which can be divided into two classes: (i) those related to plastid biogenesis or differentiation (either of chloroplasts, gerontoplasts, amyloplasts, elaioplasts or chromoplasts) and the consequent development of specific morphological and functional characteristics (biogenic control), and (ii) those related to the function of the corresponding plastids in the plant response to environmental stimuli (operational control) [3]. Although lipid peroxidation has been studied in detail in plants and recently reviewed [4,5] and the differentiation of chloroplasts to either gerontoplasts (in senescing leaves) or chromoplasts (during fruit ripening) has been characterized in some detail [6], less attention has been paid on the focus on how signals emanating from chloroplasts modulate plastid interconversion.

Oxylipins arising from plastid lipid membranes illustrate the

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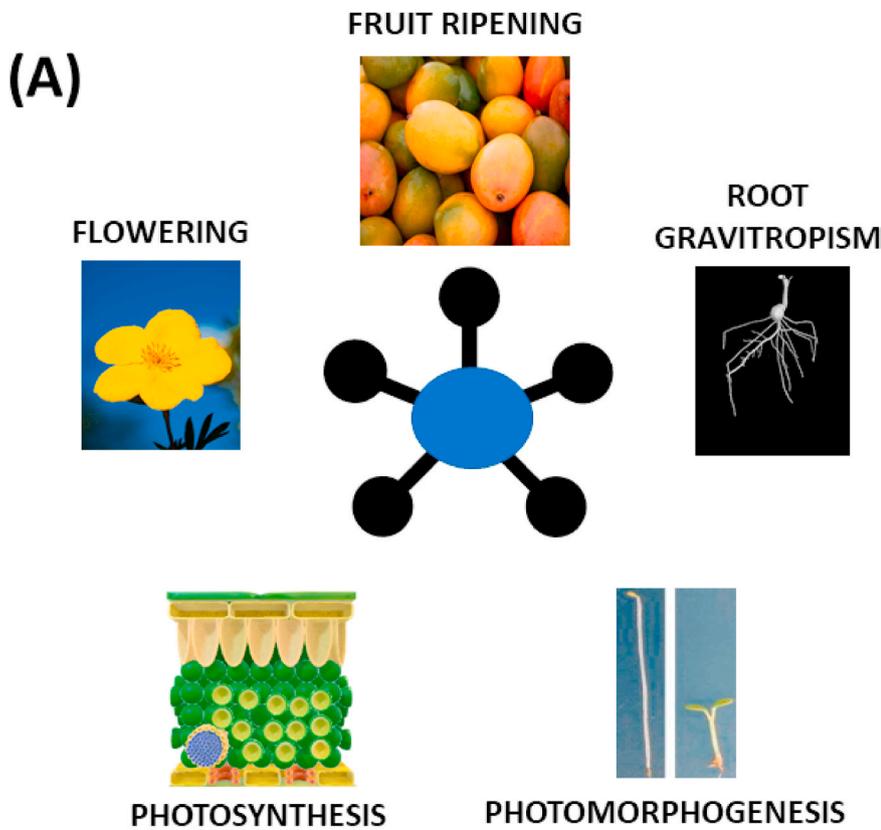
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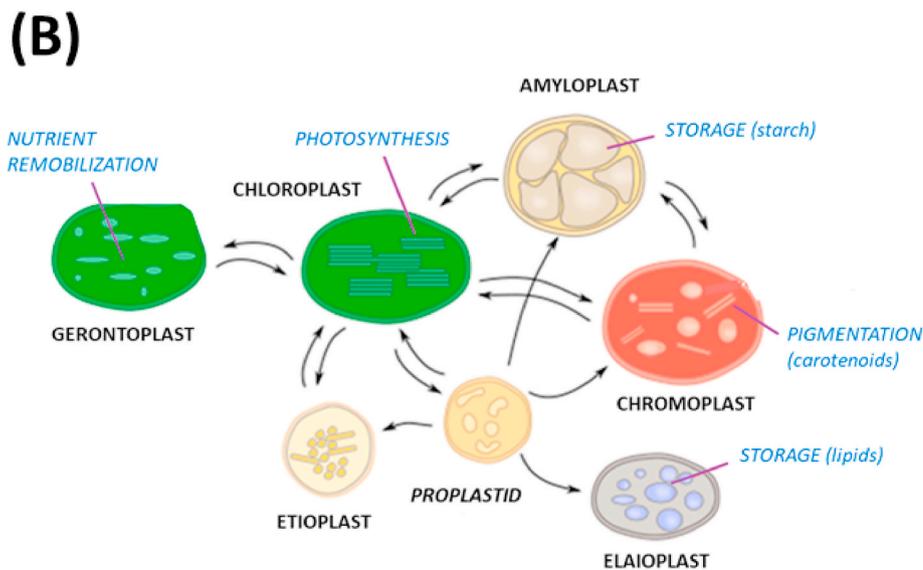
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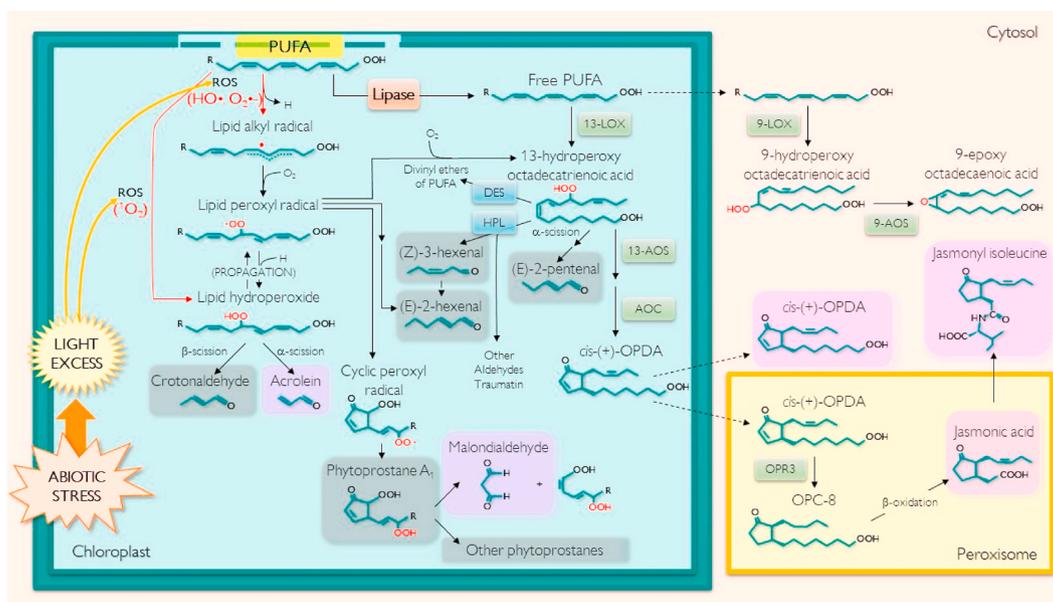


**Fig. 1.** Plastids play a major role in the modulation of plant development and stress responses. **(A)** Plastids play a major role during plant development, including the regulation of root gravitropism (by sensing and signaling gravity with amyloplasts), photomorphogenesis (with the conversion of etioplasts to chloroplasts), harnessing and converting light energy into chemical energy in photosynthetic chloroplasts (capacity that is progressively lost during leaf senescence with the conversion of chloroplasts to gerontoplasts), and flower and fruit formation (with coloring chromoplasts for attraction). **(B)** Development and interconversion of plastids in plants. Proplastids can give rise to several plastids, not only including chloroplasts (with a photosynthesis function and that can give rise to gerontoplasts in senescing leaves), but also to storage plastids (such as amyloplasts and elaioplasts) and coloring plastids (chromoplasts) in flowers and fruits. Etioplasts are plastids that have developed in darkness (skotomorphogenesis).



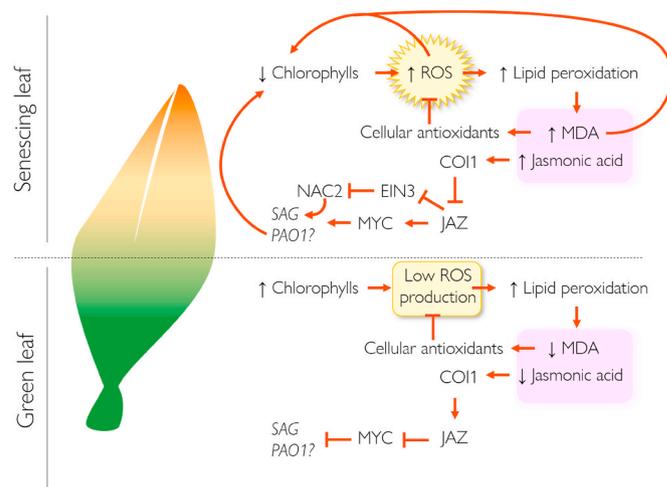
relevance of plastid-derived compounds in retrograde signaling during developmental and stress responses. Oxylipins origin in plants from both enzymatic and chemical reactions by addition of molecular oxygen in the structure of polyunsaturated fatty acids of lipid membranes, namely  $\alpha$ -linolenic acid (18:3) and linoleic acid (18:2) (Fig 2). The nature of these molecules makes oxylipins a diverse family with more than 650 compounds, including the well-characterized jasmonate-related compounds together with other hormone-like and redox signal molecules. Lipases or other unspecific acyl-lipid hydrolases [7], provide free fatty acids to 9- and 13-lipoxygenases (LOX) that initiate oxylipin formation through enzymatic pathways. Differential subcellular localization of these LOXs suggests site-specialization in oxylipin production,

determining their function in development and plant acclimation processes [8]. The jasmonate branch by plastidial 13-LOX includes the formation of intermediate molecules with known signaling functions like 12-oxo-phytodienoic acid (OPDA), which has been reported to trigger specific set of genes in *Arabidopsis* [9]. For further detail on oxylipin formation and signaling via LOX pathway, see a recent review by Wasternack and Feussner [10]. On the other hand, excess excitation energy in plant photosystems due to abiotic stress prompts the production of reactive oxygen species (ROS) in chloroplasts (Fig. 2), in particular singlet oxygen ( $^1O_2$ ), responsible of most part of lipid peroxidation taking place in chloroplast membranes [11]. Subsequent formation of lipid hydroperoxides and cyclic peroxy radicals elicits the



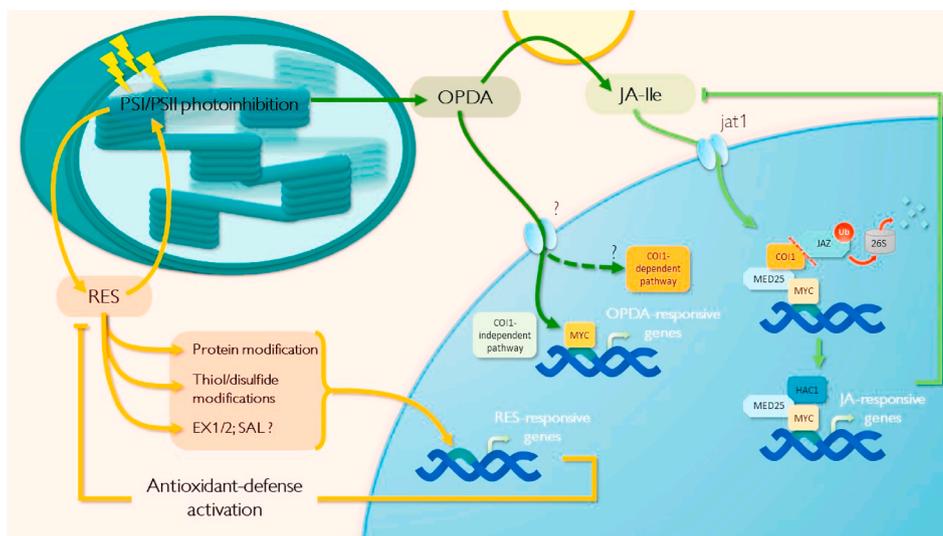
**Fig. 2.** Schematic representation of oxylipin biosynthesis from chloroplasmic polyunsaturated fatty acids (PUFA) triggered by abiotic stress. Reactive oxygen species (ROS) produced from excessive light at the reaction centers of chloroplast photosystems together with the excision of free fatty acids by lipases promote oxylipin formation, including reactive electrophilic species (RES) and the jasmonic acid branch. Purple squares represent oxylipins with a described function in retrograde signaling under abiotic stress, while grey squares represent RES with putative signaling functions. AOC, allene oxide cyclase; AOS, allene oxide synthase; DHS, divinyl ether synthase; HPL, hydroperoxide liase; LOX, lipoxygenase; OPC-8, (1R, 2S)-3-oxo-2-[(Z)pent-2'-enyl]-cyclopentan-1-octanoic acid; OPDA, 12-oxo-phytodienoic acid; OPR, oxo-phytodienonate reductase. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

production of reactive electrophilic species (RES) as secondary lipid peroxidation products. The oxygenated structure and mild-stability of these RES makes it feasible to react with cellular proteins and nucleic acids and therefore, may be positioned at the interface between ROS and chloroplast-to-nucleus signal transduction. Even though studies on RES are scarce, partially due to the complexity to differentiate between specific RES signaling and the overall redox processes taking place after ROS production, exogenous application of singular RES such as malondialdehyde [12] and acrolein [13] have shown indeed that RES activate nuclear gene expression and contribute to plant stress acclimation. Other intermediate molecules such as plant phytoosteranes with a cyclopentenone structure, highly resembles that of OPDA and induce a similar subset of genes in stress responses that could be mediated by activation of TGA transcription factors family [14]. Nevertheless, our understanding in RES signaling is much limited and it is necessary to uncover specific mechanisms led by specific oxylipins in retrograde signaling in plant developmental processes is on their role to modulate leaf senescence. Leaf senescence is the final stage in the development of leaves, and typically includes three phases: (i) an initial stage in which senescence is initiated by external signals or internal developmental factors (induction phase), (ii) a second phase characterized by the remobilization of photoassimilates and nutrients from senescing leaves (source) to developing flowers or fruits, buds at initial stages of development, roots or storage organs, which all act as sinks (remobilization or transdifferentiation phase), and (iii) a third, last phase in which programmed cell death is finally executed (terminal phase) [15]. The first visual sign of leaf senescence is yellowing due to chlorophyll degradation, which often begins at the tip and margins of the leaf, and chloroplasts to gerontoplasts differentiation occurs during the re-organization phase. Although senescence is often considered as a degenerative process, it is in fact an active stage of development in which the expression of many genes is drastically altered, and new biochemical and physiological processes are activated to enable an efficient remobilization [16, 17]. The oxylipin jasmonic acid (JA) is involved in plant leaf senescence as it has been stated by studies performing both exogenous applications of these compounds [18], as well as JA mutant-deficient plants [19]. In



**Fig. 3.** Schematic representation of the role of oxylipins in the control of leaf senescence. Under optimal growing conditions (lower panel) leaves only produce small amounts of oxylipins as a result of low lipid peroxidation induced by mild levels of reactive oxygen species (ROS). Such conditions inhibit the jasmonic acid signaling pathway and JASMONATE ZIM-DOMAIN PROTEIN (JAZ) represses expression of MYC transcription factors, while low levels of lipid hydroperoxides and malondialdehyde (MDA) induce the production of antioxidants that enable ROS control in plant cells. During senescence (upper panel), jasmonic acid plays a prominent role in the activation of senescence-associated genes (SAGs) and expression of chlorophyll catabolic enzymes such as *pheophorbide a* (PAO1) that contribute to chlorophyll degradation and programmed cell death with a tight control of ROS production and oxylipin formation by antioxidant systems.

senescing leaves, jasmonic acid activates the transduction of MYC transcription factors that positively induce the expression of senescence-associated genes (SAGs) [19] and chlorophyll catabolic genes such as PAO1 [20]. Likewise, crosstalk of jasmonic acid with other senescence-related phytohormones like ethylene has also been reported



**Fig. 4.** Schematic representation of the oxylipin signaling pathways. Green lines represent hormonal pathways including the jasmonic acid branch, where jasmonyl isoleucine (JA-Ile) promotes JASMONATE ZIM-DOMAIN PROTEIN (JAZ) binding to the CORONATINE INSENSITIVE1 (COI1) and there is subsequently ubiquitination and degradation of JAZ by the 26S proteasome, thereby inducing the expression of jasmonic acid (JA)-responsive genes. Several studies have reported COI1-independent pathways for OPDA signaling, including for the induction of the expression of several heat-shock proteins. Nevertheless, the COI1–JAZ receptor system could be modulated by OPDA with particular isoforms of COI1 and JAZ. On the other hand, the yellow lines represent the induction of RES-responsive genes in retrograde signalling by RES produced in chloroplast and mediated by protein and thiol/disulfide modifications. However, it remains elusive whether this RES could interact with other oxidative sensors such as EXECUTER1/2 (EX1/2) or 3'-phosphoadenosine 5'-phosphate (PAP) phosphatase SAL1 (SAL1). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

for several models and together constitute an intricate network of regulatory signals that positively induce programmed cell death [21] (Fig. 3). Accumulation of other RES oxylipins such as malondialdehyde has also been shown to occur during organ senescing programs [12]. However, the involvement of these molecules has mainly been associated with its harmful properties and no specific function has been described at molecular level contributing to the regulation of programmed cell death in senescing organs.

In line with this, the best recognized oxylipin signaling pathway at molecular level is mediated by jasmonate-isoleucine (Ja-Ile) (Fig. 4), where these lipid-derived phytohormones interact with CORONATINE INSENSITIVE1 (COI1), a nuclear protein with an F-box domain, that induces ubiquitination of the jasmonate ZIM-domain (JAZ) and the subsequent degradation by the 26S proteasome. JAZ degradation allows additional coactivators recruitment and induce the expression of MYC transcription factors that participate in the activation of jasmonate-responsive genes [22]. Even though it has been stated for several years a JA-independent role of OPDA in plant stress acclimation [8], the exact mechanism remained unknown. A recent study in the bryophyte *Marchantia polymorpha* lacking biosynthetic functions for JA-Ile has identified an ancient JA-COI1-independent pathway that can mediate heat stress acclimation and is also conserved in the angiosperm *A. thaliana* [23]. This study highlights a differential mechanism for OPDA signal transduction that puts in relevance specific oxylipin profiles dealing with chloroplast-to-nucleus signaling (Fig. 4). In contrast, there is very limited data on the signal transductions that lead specific signatures by RES production. If considered as ROS-derived compounds with chemical reactive structures, one may expect that pathways activated by RES may be similar to those described by ROS signaling, such as protein and thiol/disulfide modifications, or even the regulation of specific proteins involved in retrograde signaling, such as EXECUTER 1 (EX1) or 3'-phosphoadenosine 5'-phosphate (PAP) phosphatase SAL1 (SAL1) that have been related to  $^1\text{O}_2$  production [24]. In this context, even RES oxylipins and ROS may induce differential genes subsets [25], current knowledge fails to address specific regulation of these cascades due to overlapping chemical reactions. However, the venture of new editing tools such as CRISPR/CAS9 may provide a better approach to study the role of RES oxylipins in acclimation and developmental processes of plants by targeting specific transcription factors activated by these molecules.

In conclusion, major advances have taken place in our understanding of the role of various oxylipins in chloroplast-to-nucleus retrograde signaling in plants. In particular, the role of jasmonates in the regulation of plant development and stress responses have been reported in detail at the physiological and molecular levels. There are still, however, many gaps in our knowledge of the physiological processes and mechanisms underlying retrograde signaling by oxylipins from plastids to the nucleus, more specifically in chromoplasts, amyloplasts and elaioplasts. Better understanding of how redox signals emanating from these plastids is regulated is not only essential to expand our knowledge of basic biology, but it will also have important economic implications in the agri-food biotechnology sector.

#### Declaration of competing interest

The authors declare no conflict of interest.

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#### References

- [1] K.A. Pyke, Plastid Division, *AoB Plants* 2010, 2010, p. plq016.
- [2] T. Börner, The discovery of plastid-to-nucleus retrograde signaling—a personal perspective, *Protoplasma* 254 (2017) 1845–1855.
- [3] T. Pfannschmidt, M.J. Terry, O. Van Aken, P.M. Quiros, Retrograde signals from endosymbiotic organelles: a common control principle in eukaryotic cells, *Philos. Trans. R. Soc. Lond. Ser. B* 375 (2020) 20190396.
- [4] J.D. Alché, A concise appraisal of lipid oxidation and lipoxidation in higher plants, *Redox Biol.* 23 (2019) 101136.
- [5] E.E. Farmer, M.J. Mueller, ROS-mediated lipid leroxidation and RES-activated signaling, *Annu. Rev. Plant Biol.* 64 (2013) 429–450.
- [6] U.C. Biswal, B. Biswal, M.K. Raval, *Chloroplast Biogenesis*, Springer, Dordrecht, The Netherlands, 2003.
- [7] D. Ellinger, N. Stingl, I.I. Kubigsteltig, T. Bals, M. Juenger, S. Pollmann, S. Berger, D. Schuenemann, M.J. Mueller, DONGLE and DEFECTIVE IN ANTHOR DEHISCENCE1 lipases are not essential for wound- and pathogen-induced jasmonate biosynthesis: redundant lipases contribute to jasmonate formation, *Plant Physiol.* 153 (2010) 114–127.
- [8] J.P. Tolley, Y. Nagashima, Z. Gorman, M.V. Kolomiets, H. Koiwa, Isoform-specific subcellular localization of *Zea mays* lipoxygenases and oxo-phytyldienoate reductase 2, *Plant Gene* 13 (2018) 36–41.

- [9] N. Taki, Y. Sasaki-Sekimoto, T. Obayashi, A. Kikuta, K. Kobayashi, T. Aina, K. Yagi, N. Sakurai, H. Suzuki, T. Masuda, K. Takamiya, D. Shibata, Y. Kobayashi, H. Ohta, 12-oxo-phytodienoic acid triggers expression of a distinct set of genes and plays a role in wound-induced gene expression in Arabidopsis, *Plant Physiol.* 139 (2005) 1268–1283.
- [10] C. Wasternack, I. Feussner, The oxylipin pathways: biochemistry and function, *Annu. Rev. Plant Biol.* 69 (2018) 363–386.
- [11] C. Triantaphylidès, M. Krischke, F.A. Hoerberichts, B. Ksas, G. Gresser, M. Havaux, F. Van Breusegem, M.J. Mueller, Singlet oxygen is the major reactive oxygen species involved in photooxidative damage to plants, *Plant Physiol.* 148 (2008) 960–968.
- [12] H. Weber, A. Chételat, P. Reymond, E.E. Farmer, Selective and powerful stress gene expression in Arabidopsis in response to malondialdehyde, *Plant J.* 37 (2004) 877–888.
- [13] T. Roach, C. Sun, W. Stöggli, A. Krieger-Liszkay, The non-photochemical quenching protein LHCSR3 prevents oxygen-dependent photoinhibition in *Chlamydomonas reinhardtii*, *J. Exp. Bot.* 71 (2020) 2650–2660.
- [14] H.U. Stotz, S. Mueller, M. Zoeller, M.J. Mueller, S. Berger, TGA transcription factors and jasmonate-independent COI1 signaling regulate specific plant responses to reactive oxylipins, *J. Exp. Bot.* 64 (2013) 963–975.
- [15] S. Munné-Bosch, L. Alegre, Die and let live: leaf senescence contributes to plant survival under drought stress, *Funct. Plant Biol.* 31 (2004) 203–213.
- [16] A. Guiboileau, R. Sormani, C. Meyer, C. Masclaux-Daubresse, Senescence and death of plant organs: nutrient recycling and developmental regulation, *C. R. Biol.* 333 (2013) 382–391.
- [17] H. Rogers, S. Munné-Bosch, Production and scavenging of reactive oxygen species and redox signaling during leaf and flower senescence: similar but different, *Plant Physiol.* 171 (2016) 1560–1568.
- [18] L. Liu, H. Li, H. Zeng, Q. Cai, X. Zhou, C. Yin, Exogenous jasmonic acid and cytokinin antagonistically regulate rice flag leaf senescence by mediating chlorophyll degradation, membrane deterioration, and senescence-associated genes expression, *J. Plant Growth Regul.* 35 (2016) 366–376.
- [19] T. Qi, J. Wang, H. Huang, B. Liu, H. Gao, Y. Liu, S. Song, D. Xie, Regulation of jasmonate-induced leaf senescence by antagonism between bHLH subgroup IIIe and IIIc factors in Arabidopsis, *Plant Physiol.* 27 (2015) 1634–1649.
- [20] S. Aubry, N. Fankhauser, S. Ovinnikov, A. Průžinská, M. Stirnemann, K. Zienkiewicz, C. Herrfurth, I. Feussner, S. Hörtensteiner, Pheophorbide a may regulate jasmonate signaling during dark-induced senescence, *Plant Physiol.* 182 (2020) 776–791.
- [21] J. Kim, S.E. Patterson, B.M. Binder, Reducing jasmonic acid levels causes ein2 mutants to become ethylene responsive, *FEBS Lett.* 587 (2013) 226–230.
- [22] G.A. Howe, I.T. Major, A.J. Koo, Modularity in jasmonate signaling for multistress resilience, *Annu. Rev. Plant Biol.* 69 (2018) 387–415.
- [23] I. Monte, S. Kneeshaw, J.M. Franco-Zorrilla, A. Chini, A.M. Zamarreño, J. M. García-Mina, R. Solano, An ancient COI1-independent function for reactive electrophilic oxylipins in thermotolerance, *Curr. Biol.* 30 (2020) 962–971.
- [24] P. Muñoz, S. Munné-Bosch, Photo-oxidative stress during leaf, flower and fruit development, *Plant Physiol.* 176 (2018) 1004–1014.
- [25] M.J. Mueller, S. Berger, Reactive electrophilic oxylipins: pattern recognition and signalling, *Phytochemistry (Oxf.)* 70 (2009) 1511–1521.