Microbial Pathogenesis 145 (2020) 104224

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

Review

Plant hypersensitive response vs pathogen ingression: Death of few gives life to others

Ali Noman[a,*], Muhammad Aqeel[b], Sameer Hasan Qari[c], Ameena A. Al Surhanee[d], Ghulam Yasin[e], Saad Alamri[f,g], Mohamed Hashem[f,h], Abdullah M Al-Saadi[i]

[a] Department of Botany, Government College University Faisalabad, Pakistan
[b] School of Life Sciences, Lanzhou University, Lanzhou, PR China
[c] Biology Department, Al-jumum University College, Umm Al Qura University, Makkah, Saudi Arabia
[d] Biology Department, College of Science, Jouf University, Sakaka, 2014, Saudi Arabia
[e] Institute of Pure and Applied Biology, Bahau ud din Zakria University, Multan, Pakistan
[f] King Khalid University, College of Science, Department of Biology, Abha, 61413, Saudi Arabia
[g] Research center for advance materials science (RCAMS), King Khalid University, PO Box 9004 Abha, 61413, Saudi Arabia
[h] Assuit University, Botany and Microbiology department, Assuit. 71516, Egypt
[i] College of Agriculture and Marine Science, Sultan Qaboos University, Oman

ARTICLE INFO

Keywords:
Microbial pathogenesis
Plants
PTI
SAR
HR

ABSTRACT

The hypersensitive response (HR) is a defense action against pathogen ingression. Typically, HR is predictable with the appearance of the dead, brown cells along with visible lesions. Although death during HR can be limited to the cells in direct contact with pathogens, yet cell death can also spread away from the infection site. The variety in morphologies of plant cell death proposes involvement of different pathways for triggering HR. It is considered that, despite the differences, HR in plants performs the resembling functions like that of animal programmed cell death (PCD) for confining pathogen progression. HR, in fact, crucially initiates systemic signals for activation of defense in distal plant parts that ultimately results in systemic acquired resistance (SAR). Therefore, HR can be separated from other local immune actions/responses at the infection site. HR comprises of serial events inclusive of transcriptional reprograming, Ca^{2+} influx, oxidative bursts and phyto-hormonal signaling. Although a lot of work has been done on HR in plants but many questions regarding mechanisms and consequences of HRs remain unaddressed.We have summarized the mechanistic roles and cellular events of plant cells during HR in defense regulation. Roles of different genes during HR have been discussed to clarify genetic control of HR in plants. Generally existing ambiguities about HR and programmed cell death at the reader level has been addressed.

1. Introduction

Plant resistance to attacking pathogens is escorted by the fast and multilayered defense responses. The distinct constituents of defense responses include use of chemical arsenal and structural barriers e.g. hydrolytic enzymes, lignin deposition and changes in cell wall proteins etc. [1]. The Array of defense actions is activated after recognition of pathogen elicitors by specific receptors. A defense response can be specifically or nonspecifically induced by multiple types of biotic or abiotic elicitors. Pathogen Associated Molecular Patterns (PAMPs) is the prime tier of the plant innate immunity that involves the recognition of microbial patterns by different types of host extracellular Pattern Recognition Receptors (PRRs) such as Receptor Kinases (RKs), Receptor Like Kinases (RLKs) and Receptor-Like Proteins (RLPs) [2]. The elicitors from pathogens include carbohydrates, glycoproteins or lipids and effectors are coded by particular strains. In case of suppression of PTI (PAMPs triggered immunity) by invading pathogens through effectors, plants employ Effector Triggered Immunity (ETI) that is second line of defense [3,4]. The pathogenic effectors are recognized by resistance proteins (R) [5]. This recognition complex triggers downstream signals that results in the activation of ETI [6]. PTI and ETI may protect the plants from the attack of approximately 99% phytopathogens (Table 1) [7].

As a survival strategy, recognition of invading biotrophic pathogens by the plant trigger immune responses frequently complemented by a type of cell death called as the hypersensitive response (HR) [8,9]. Very

* Corresponding author.
E-mail address: alinoman@gcuf.edu.pk (A. Noman).

https://doi.org/10.1016/j.micpath.2020.104224
Received 22 March 2020; Received in revised form 15 April 2020; Accepted 20 April 2020
Available online 29 April 2020

Table 1
Genes located at different sites in plant tissues are induced by different molecules and play crucial role in HR. The key functions of these genes have been elaborated by different workers. Starting from pathogen recognition by receptor and finalizing HR to restrict infection is categorically attributed to putative functions of these genes [90–93,96–98,100–108,110,111].

Sr. No.	Gene name	Putative function	Localization									Induced by									Reference
			C	N	M	P	V	PM	EM	ER	Mb	SA	JA	ET	ABA	MV	TMV	H_2O_2	Xcv	ND	
1	CaRLK1	Receptor						■										√	√		[51]
2	ELR	Recognition of Elicitin						■				√									[90]
3	LysM RLK1	chitin signaling						■													[91]
4	NbWIPK and NbSIPK	Activates downstream defense signaling against pathogen derived elicitors		■								√	√								[49, 92]
5	CaPIK1	Receptor-like cytoplasmic Kinase	■					■				√	√	√		√			√		[93]
6	SlMKK2	Positive redulation of defense						■													[94]
7	OsNPR1/NH1	Regulate SA-mediated immunity		■								√									[95]
8	CaCDPK4	Ca^{2+}-dependent protein kinase		■				■				√	√	√	√						[96]
9	CaATL1	AT-hook motif-containing		■								√		√			√		√		[97]
10	CaCAF1	CCR4-associated factor				■														√	[98]
11	SlSRN1	Positive regulation of defense				■						√	√								[99]
12	GaWRKY1	Control sesquiterpene phytoalexins biosynthesis		■								√									[100]
13	OsWRKY89	Regulate biosynthesis of wax and lignin		■									√								[101]
14	CaGL1	Lipase activity							■				√				√				[97]
15	CaLOX1	9-Lipoxygenase				■						√	√	√		√			√		[102]
16	CaLTP1	Lipid transfer protein	■									√	√	√	√				√		[98]
17	Lipoxygenase (LOX)	Lipid oxidation	■										√								[103]
18	CaPRP1	Proline-rich protein						■												√	[104]
19	CaAMP1	Antimicrobial action	■						■			√	√	√				√	√		[105]
20	CaPMEI1	Pectin methylesterase inhibitor	■									√	√	√	√			√			[91]
21	CaLRR1	Leucine-rich repeat protein							■						√				√		[106]
22	CaHIR1	SPFH domain-containing protein	■					■				√	√	√	√				√		[106]
23	CaABR1	ABA-responsive protein	■								■								√		[107]
24	TaMYB4	Induceimmune response																			[108]
25	NtERF3	Induces HR-like cell death		■																	[109]
26	CaPR4b	PR 4						■		■									√		[110]
27	CaPR10	Ribonuclease	■		■							√	√	√					√		[106]
28	Chitinase and β-1,3 glucanase	PR protein					■						√	√							[111]

PM: Plasma membrane, C: cytoplasm, Ch: Chloroplast, EM: Extracellular Matrix, N: Nucleus, P: Peroxisome, ER: Endoplasmic reticulum, G: Golgi Body, V: Vacuole, M: Mitochondria, Mb: Micro Body, SA: Salicylic Acid, JA: Jasmonic Acid, ET: Ethylene, ABA: Abscisic Acid, MV: Methyl Violgen: H_2O_2: Water, Xcv: Avirulent strains of X. *campestris* pv. *vesicatoria*, ND: Not Determined

commonly, fungi, oomycetes, bacteria and viruses are inducers of HRs but it can also be induced by insects or nematodes [10]. Similarly, contacts between parasitic plants and their hosts have also presented evidence of cell death although it is unclear that whether it is an absolute HR or not [11,12]. Generally, the dead, brown cells, with visible lesions are attributes of HR. Although death during HR can be limited to the tissue region in direct interaction with a pathogen yet it can also inflate away from the original infection site [13]. Genetic manipulation of HR reveals that it is widespread phenomenon under strict control toprevent cell death away from the infection site and exhibit apoptosis resembling attributes [8,14]. As a part of the immune plan, leakage of cellular contents during HR alerts neighboring cells to be ready for dealing with the potential invasion(s). Mostly, HR cell death in plants has been focused in plant defense against biotrophic or hemibiotrophic

pathogens. However, necrotrophic pathogens are well able to hijack HR for benefit. HR, in fact, crucially initiates systemic signals for defense activation in distal parts of plant that ultimately results in resistance. This is called as systemic acquired resistance (SAR) [15]. Therefore, HR can be separated from other local immune actions/responses at the infection site. HR comprises of serial events inclusive of transcriptional reprograming, Ca^{2+} influx, oxidative bursts, phyto-hormonal signaling, mitogen activated protein kinases (MAPK) etc. [16].

The understanding of HR has also been complicated since cell death due to different causes is a common phenomenon in plants. However, the fundamentals of HR along with its all consequences are considered as very conserved among angiosperms during their interactions with pathogens [17]. In diverse interactions, aspects of HR may change noticeably [18].

To avoid confusion and bring more clarity, often used term is 'hypersensitive-like cell death' in case of plant cell death without any categorical connection to R-genes, the defense response or disease resistance [19,20]. A growing body of literature about HR has presented overarching inferences. However, many questions regarding the mechanisms and consequences of HRs remain unaddressed. In this review, we aimed to precisely summarize the existing knowledge about HR and attempted to throw light on different aspects of HR as a key component of plant defense responses. Usual ambiguities regarding HR and programmed cell death (PCD) at reader level has been addressed. The prospective mechanistic variations in HRs among same/different host species with interacting pathogens have also been focused.

2. Is HR really needed for plant defense?

The HR in plants leads to rapid cell death in the region of invasion that limits the pathogen and prepares the plant defense for successive assaults. Being a very controlled phenomenon, HR involves concerted metabolic actions and reactions as well as regulators at different levels that make it efficient defense response [9,21]. A deep look into HR phenomenon reveals two basic functions attributed to this i.e. Resistance and death (Fig. 1) [22]. Over the years, it has been discussed intensively whether cell death is a complete and only prerequisite for HR mediated resistance in plants. An initial and quick defense rejoinder results in the development of large symptomless resistance, whilst a moderately primary defense reaction leads to resistance with controlled and limited HR cell-tissue death. Consequently, a deferred or futile host challenge to a pathogen for eliciting resistance responses may ends in systemic HR i.e. heavily stressed plant tissues as well as the partial or complete defeat of control over invading pathogen(s) [22–24]. The active plant resistance responses suggests that fight against pathogen can be effective in presence or absence of PCD but its result may principally dependent upon the timing and speed of the host responses (s). Therefore, it can be inferred that plant resistance can be effective with or without cell death. Generally, in HR, cell death -resistance coupling can be observed in terms of physiology and genetics (Tables 1 and 2) [9,21,25,26]. So we agree over the essential involvement of cell death in resistance against biotrophic pathogens [27]. Hence, HR cell

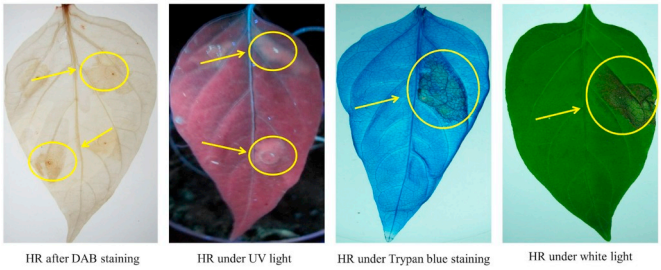

Fig. 1. HR in pepper plants after inoculation of *Agrobacterium* harbouring different TFs.

Table 2
Different genes of one or the other type behave differentially against diverse pathogens. The functions of these molecular regulators are critical in determining plant defense response. Some of the genes regulate immunity positively while many can be negative regulators of plant immunity.

Sr. No.	Gene Type	Plant	Gene name	Interacting Pathogen	Gene Activity	References
1	**RECEPTOR GENE**	*Arabidopsis thaliana*	LecRK-V1.2	*Pseudomonas syringae* pv tomato	Triggers PTI	[112]
2			CERK1	*Alternaria brassicicola*	Crucial for chitin elicitor	[113]
3			LysM RLK1	*Erysiphe cichoracearum*	Essential for chitin signaling	[113]
4			BOTRYTISSUSCEPTIBLE1(BOS1)	*Botrytis cinerea*	Mediates ROS signals and regulates JA signaling	[114]
5		*Nicotiana tabacum*	NtERF3	*Tobacco mosaic virus*	Induces hypersensitive- response-like cell death	[109]
6		*Triticum aestivum*	TaPIE1	*Rhizoctonia cerealis*	Regulates ethylene-dependent defense response	[115]
7			TaNAC4	*Puccinia striiformis* f. sp. tritici	Transcriptional activator	[116]
8	**TRANSCRIPTION FACTOR**	*Arabidopsis thaliana*	WRKY8	*Tobacco mosaic virus*	Regulates abscisic acid and ethylene signaling pathways	[117]
9		*Nicotiana benthamiana*	GhWRKY44	*Ralstonia solanacearum,*	Positive regulation of plant- pathogen interaction	[118]
10		*Oryza sativa*	OsWRKY13	*Xanthomonas oryzae* pv. Oryzae	Activator and suppressor of SA and JA pathways, respectively	[119]
11			OsWRKY30	*Pectobacterium carotovora*	Positively regulates PR10 defense gene	[120]
12		*Solanum lycopersicum*	SlSRN1	*Botrytis cinerea, Pseudomonas*	Positive regulator of defense response syringae pv. Tomato	[99]
13			SlDRW1	*Botrytis cinerea*	Positive regulator of defense response	[121]
14		*Triticum aestivum*	TaPIMP1	*Bipolaris sorokiniana*	Regulation of Abscisic acid (ABA) and SA signaling pathway genes	[122]
15	**REGULATORY GENES**	*Triticum aestivum*	TaNPSN SNARE	*Puccinia striiformis* f. sp. tritici	Vesicle-mediated resistance	[123]
16		*Nicotiana tabacum*	NtERF3	*Tobacco mosaic virus, Phytophthora*	Diacylglycerol kinase activity	[124]
17	**PROTEIN KINASES**	*Arabidopsis thaliana*	CML9	*Pseudomonas syringae*	Regulates flagellin-dependent signaling pathway	[125]
18			OXI1 protein kinase	*Hyaloperonospora parasitica,*	Regulates effector-triggered immunity	[126]
19			GhMPK16	*Colletotrichum nicotianae*	Activation of multiple signal transduction pathways	[127]
20		*Oryza sativa*	OsNPR1/NH1	*Xanthomonas oryzae* pv. oryzae	Regulator of SA-mediated resistance	[95]
21		*Solanum lycopersicum*	SlMKK2 and SlMKK4	*Botrytis cinerea*	Positive regulator of defense response	[94]

death can be regarded as a result of intense defense responses throughout the resistance.

3. Biochemical and cellular signals involved in HR

After pathogen recognition, host plants experience multi types of biochemical and cellular signals as well as defense responses inclusive of ionic flux, activation of kinase cascades, ROS (reactive oxygen species) burst, variations in phyto-homonal levels, transcriptional reprogramming [28–33]. However, it is not easy to evaluate the individual differentiated role of any of the earlier mentioned processes as fully accountable for cell death and resistance during HR. The ion fluxes are initial obvious cellular proceedings taking place across the plasmalemma and a ROI (reactive oxygen intermediates) burst [34]. Oxidative burst is induced by ion fluxes and sequentially needed for induction of defense marker genes and production of antimicrobial metabolites [34–36]. An important clue in understanding this phenomenon is exclusively yielded by plant-biotrophic pathogen interaction as this cannot be observed in the case of necrotrophic pathogens. The dying plant cells after biotrophic pathogen attack might discharge few of the mentioned signals that themselves may be antibiotics or disinfectants [37]. In hand evidence suggests presence of some pathogenic particles in living plant cells adjacent to necrotic area. Besides, antioxidants can also control number of HR-lesions in case of TMV attack [38]. Such findings highlight that resistance as well as cell death can be separated physiologically. Vacuolar processing enzyme (VPE) is essentially required for vacuolar collapse triggered PCD during N gene-mediated HR in TMV attack. Loss of function of VPE distinctly blocked HR-type necrosis and enhanced TMV growth [39]. This proposes that some PCD types would also limit virus attack. Likewise, nutrient adjustment i.e., addition of sulfate to growing tobacco plants can also reduce number of necrotic lesions as compared to lesion number in plants growing in sulfate deficiency [40]. In *Erwinia amylovora* inoculated apple leaves, cell death in the HR continued through ROS, ethylene and VPE pathways mediated signaling cascade. So we see the commonality despite obvious differences in terms of HR among genetically different cultivars. Interestingly, HR phenotypically resembled in both resilient and vulnerable apple cultivars along with ROS mediated development of micro as well as macro lesions but maximum VPE expression was detected in resistant cultivar [41]. It was also documented that in vitro bacterial survival could be reduced by H_2O_2 [42]. Besides oxidative burst, pathogen like *E. amylovora* may also cause cell death effects linked with modifications of plasmalemma H + -ATPase, the reduced ATP production and fast obliteration of mitochondrial functions [43]. Such physiological changes collectively or individually perturb attributes of living cells and culminate in their death. So any increase/decrease in mentioned physiological attributes may check HR and confirmed that cell death is a consequence not the cause of plant resistance to a pathogen. It means that if we manage physiological attributes by chemical means or some genetic manipulation, HR type -cellor -tissue death would control pathogen invasion by inhibiting its growth. Such uncoupling of cell death and immunity has been observed in fungus/bacteria-plant interactions [40,44,45]. The experimental procedures have also elaborated that strengthened cell wall during HR cell death plays positive role in plant-pathogen interactions. Histochemical analyses demonstrate the strengthening of the cell wall as a fragment of HR PCD-mediated defense [46]. The relative expression level of *xyloglucan-specific endo-β-1,4-glucanase inhibitor-protein 1* gene (*CaXEGIP1*) validate molecular mechanism of cell wall reinforcement and signaling during HR mediated PCD [47]. The target of *CaXEGIP1* is plant xyloglucan-modifying enzymes. Therefore, its expression starts cell death and related defense signaling. Similarly, *CaPKc1* is induced by pathogen attack and take part in ATP production for catering energy needs of HR and defense responses [21].

Topical advances in genomics and proteomics techniques facilitate us in observing modulations in plant gene expression and proteins. High throughput transcriptomic and proteomic analyses unveiled the various molecular and biochemical alterations during plant-pathogen interaction. Several defense linked genes have been discovered, cloned and even their ectopic expressions have been recorded. This strategy of isolating HR-related genes and measurement of their relative expression levels is an effective strategy in plants (Tables 1 and 2). For instance, specific cDNAs from *Xcv* or *P. capsici* infected leaves presented several induced transcripts of *Capsicum annuum* encoding LRR, chitinase, stellacyanin, PR-5 and by abiotic elicitor treatment [48]. Spatio-temporal expression arrays of some defense linked and HR-related genes in different plants have been noticed as inducible defense responses i.e. *CabZIP53, CaZNF830, CaWRKY40b, CaWRKY22* [2,3,19,26,28–30]. Besides, many genes are not constitutively expressed in plants with special reference to HR. Many membrane-localized receptor protein and genes are exclusively expressed during HR and regulate defense. Such genes and proteins include *Membrane-Located Receptor-Like Protein 1(MRP1),* receptor-like kinase 1 (*RLK1*), *Mildew Resistance Locus O* (*CaMLO1-2) etc.*(Table 1) [49,50]. Transgenic expression of *RLK1* in pepper pointedly conceded virulent and avirulent bacterial pathogen-induced cell death in *tobacco,* complemented by superoxides production and induction of *Lesions Simulating Disease* (*LSD*) gene [51]. Nevertheless, the transcriptional fluctuations may not reveal regulatory processes at the whole cell level due to different alterations at the post-transcriptional and post-translational level [21]. Micro- or macro-arrays of the plant transcriptome and proteome help in quantitative appraisals of protein expressions among infected and healthy plants. Combined genetic and proteomic strategies exposes incompatible interfaces regulating the plant resistance responses to pathogens.

4. Morpho-ultrastructural modifications during HR

It is not easy to arrange cytological events in a proper order that lead to HR. In plant-biotrophic pathogen interaction i.e. *Vigna unguiculata-Uromyces vignae*, the events have been observed in a sequence. In the first step, nucleus migrated to the site of penetration causing streaming of the cytoplasm. Later on, organelles presented Brownian movement with condensation of the nucleus and dismantling of the protoplast. Finally, cytoplasm was collapsed ending at death of infected cell [52–54]. The apoptotic bodies had also been observed in isolated plant protoplasts [55]. The timing of these events is very quick. Such time limitations parallel to quick responses render it difficult to observe intermediate events in fixed tissues.

During hypersensitive response, plant cells facing pathogen attack reinforce their cell walls by deposition of some phenolic compounds, phytoalexins production, and accrual of pathogenesis-related (PR) proteins. The understanding of the pathogen plant interactions that result in the HR may lead to the discovery of effective methods for disease control [56] and plant-herbivore interactions. Genetic control over HR cell death is unveiled by the activation of plant defense associated genes and defense responses upon recognition of pathogen [57–59]. The morpho-ultrastructural modifications accompanying PCD during plant-microbe interactions are limited to some model plants and pathogens. It has been confirmed that autophagy also performs a prominent function in plant immune responses and impeding autophagy enhanced susceptibility virus attack by enhancing its propagation [60]. Similarly, elicitors i.e. Fumonisin B1 or harpins can also initiate HR and induce physiological alterations related to disease resistance [61]. Pathogens virulence factors e.g. harpins (involved in type III secretion system, T3S) impairs the integrity of the plant cell. Type III proteins results in compromised the plant cell physiology of and promote the disease [2,62]. The available evidence reveals that exogenous application of harpin coordinately induce micro-HR and systemic resistance to pathogens [63]. The comparative account of plant molecular as well as cytological markers may offer distinction between HR and necrosis (Fig. 1). These events do support fate of living cells till death but still the question is what to do of dead cells? Where those dead cells would

be disposed off? Resistance is associated with cell death but it never means that cell death is total resistance. Therefore, the correlation between cytological events, PCD and HR must be focused for functional evaluation and mechanistic assessments. Furthermore, signals from the plant as well as the pathogen can interfere to distress progress to death of cells. Consequently, evaluating cell death in the interaction perspective may help in our understanding.

5. Plant HR like cell death is different from developmental PCD and mammalian apoptosis

Programmed cell death (PCD) is the term used for organized annihilation of a cell that is very significantly important in different plant developmental pathways such as embryogenesis, senescence etc. [64,65]. During HR, it offers a defense reaction against pathogens ingression and takes part in plants responses to environmental stresses [66]. Apoptosis is a genetically controlled type of PCD in mammals that is characteristically recognizable. Even though different pathogens of plants and fungi display developmental PCD with confirmed morphological as well as genetic resemblances yet some questions on homology with mammalian apoptosis are still need to be answered [9,13]. Based on its ubiquitous nature and involvement in plant metabolism [67], as well as some common attributes with apoptosis, it is considered HR cell death is endogenously regulated. But a robust and constant association of HR with immunity differentiates it from the PCD taking part in plant development [9,68]. This gives rise to a cross-talk between developmental PCD and defense HR. The first evidence of discriminated response comes from genetic regulation of processes. The gene works individually or as a web may activate defense or developmental processes and vice versa. For instance, Pontier et al. [67] described low transcript levels of *SAG12* in transgenic tobacco cells around the HR lesions induced by bacteria and TMV. Oppositely this gene is considered as a marker gene for senescence in *Arabidopsis*. This reveals an obvious difference in response leading to differential contribution of this gene in plants. Corroboration of available data helps us to agree that HR is a precise kind of plant PCD progressed as a defense.

Conceivably, the most convincing proof of HR as a PCD process is the presence of disease lesion mimics mutants [56]. Similarly, immunity in *A. thaliana* is triggered by a bacterial acetyltransferase without HR [69]. These are different but parallel lines of facts confirming dependence/independence of HR over some other process. Facts advocate discrete signaling pathways may possibly lead to the cell death and trigger defense gene(s) that characterize parasite/pathogen-specific immunity associated genes taking part in regulation of responses. For example, the promoter of *BnLSC54* has been detected active in *Arbidopsis thaliana* before *Peronospora parasitica* mediated HR. It is noteworthy that this gene is inducible by senescence [70]. It is noteworthy that studies using cell death inhibition support that PCD can be uncoupled from the activation of defense genes [71]. Researchers believe that PCD in HR and pathogen confinement are two distinct plant defense responses [72,73]. So we can consider that HR is a kind of PCD and can be described as default state upon pathogen invasion into cell. It seems that biotrophic plant pathogens resemble intra-cellularly with some animal viruses that can surmount HR in susceptible hosts [9,74]. Thorough investigations unveiling gene regulatory mechanisms would offer an in depth elucidation of interconnected pathways involved in the regulation of HR and PCD. Experimentation by using transgenic/mutant plants may shed more light on the interconnected phenomena regulated by a diverse range of biochemicals.

6. Plant proteases and hypersensitive response

Living cells require Proteases at the post-translational level to carry on irreversible hydrolytic reactions for the production of new protein products [72,75]. The proteases perform hydrolysis functions but very significantly these ubiquitous enzymes can also impact the activity of proteins, regulate their localization, manage protein-protein interactions, and take part in cellular information processing, cell death and immunity [75–77]. The plant proteases are associated with the regulation of host immune reactions to microbial infection including PCD [78]. Apoptosis in animal and HR in plants shares specific characteristics. This provided a clue that some sort of conservation of the molecular components involved in PCD is present across the both kingdoms [72]. Approximately 140 cysteine proteases have been observed in plant genomes and categorized into five discrete clans. Misas-Villamil et al. [79], have documented the CA and the CD clan in context of plant-pathogen interactions. Belonging to CA clan, PLCPs (papain-like cysteine proteases) are mainly secreted into the apoplast that determines the success of infection or a plant defense response [80]. For instance, the plant CathB (Cathepsin B) is activated in apoplast and regulates defense-associated HR and basal disease resistance [81,82]. It was proved that *E. amylovora* and *Psuedomonas syringae* elicited HR was interrupted by loss of function of CathB that enhanced disease severity. Likewise, a decline in *CathB t*ranscripts can also impair functioning of NB-LRR in potato and compromise HR [83]. Importantly, *AtCathB1-3* genes work excessively for positive regulation of HR [82]. Although *CathB* is not regarded as a universal regulator of HR yet its involvement in defense HR appears to be pathogen-specific. Additionally, Pip1 and Rcr3 also mediate pathogen perception in tomato. *C. fulvum* secretes Avr 2 (effector) into the apoplast and it make complexes with Rcr3 and Pip1. The mentioned complexes perceived by the Cf-2, a receptor-like protein (RLP) trigger HR which helps in resistance to *C. fulvum* [84]. Correspondingly, VPEs are also needed for an HR-like cell death triggered by *Fusarium moniliforme* [85].Interestingly, VPEs may be reckoned as player during compatible interactions not dependent upon cell death [86]. Metacaspases also belong to CD clan and [72] found in plants, fungi and bacteria. In Arabidopsis, *AtMC1* has been found upregulated upon pathogen encounter and required for cell death phenotype. *AtMC2*, in contrast to MC1, work as a negative regulator of HR [87]. Because *MC1* is a strong HR mediator, plant cells require its apt activation under discrete stress conditions. Correspondingly *AtMC4*, take part in HR-like cell death response triggered by *P. syringae* as well as fungal mycotoxin FB1 [88,89].

7. Conclusion

The research focus upon improvement in plant resistance to pathogens and pests has significantly enhanced interest in signal transduction and related responses at all levels during HR against disease attack. Particularly the molecular as well as biochemical events during the defense activation against pathogen invasion has led to the identification and functional characterization of genes and metabolic pathways taking part in PCD and HR for better understanding the process. But many questions remain to be addressed. So far, despite resemblances in PCD among animals and plants, need is to explore the therapeutic significance of these resemblances and differences for managing microbial ingression in different crops. Likewise, expression of anti-PCD genes in plants should be focused to search for broad-spectrum resistance patterns among different plant-microbe interactions. Engineering of pro-PCD genes for induction of HR is also a viable option for improving plant defense against biotrophic pathogens. The exogenous application of synthetic compounds already detected in plant HR induction can be applied for plant protection and durable resistance.

Declaration of competing interest

The Authors declare no conflict of interest.

Acknowledgement

The authors extend their appreciation to Research Centre of Advanced Materials - King Khalid University, Saudi Arabia for support by grant number RCAMS/KKU/002–19.

References

[1] R. Dixon, M. Harrison, C. Lamb, Early events in the activation of plant defense responses, Annu. Rev. Phytopathol. 32 (1994) 479–501.
[2] A. Noman, M. Aqeel, Y. Lou, PRRs and NB-LRRs: from signal perception to activation of plant innate immunity, Int. J. Mol. Sci. 20 (2019) 1882.
[3] A. Hussain, X. Li, Y. Weng, Z. Liu, M.F. Ashraf, A. Noman, et al., CaWRKY22 acts as a positive regulator in pepper response to *Ralstonia solanacearum* by constituting networks with CaWRKY6, CaWRKY27, CaWRKY40, and CaWRKY58, Int. J. Mol. Sci. 19 (2018) 1426.
[4] S.T. Chisholm, G. Coaker, B. Day, B.J. Staskawicz, Host-microbe interactions: shaping the evolution of the plant immune response, Cell 124 (2006) 803–814.
[5] F. Cui, S. Wu, W. Sun, G. Coaker, B. Kunkel, P. He, et al., The Pseudomonas syringae type III effector AvrRpt2 promotes pathogen virulence via stimulating *Arabidopsis* auxin/indole acetic acid protein turnover, Plant Physiol. 162 (2013) 1018–1029.
[6] T. Boller, G. Felix, A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors, Annu. Rev. Plant Biol. 60 (2009) 379–406.
[7] P. Poltronieri, A. Brutus, I.B. Reca, F. Francocci, X. Cheng, E. Stigliano, Chapter 1 - engineering plant leucine rich repeat-receptors for enhanced pattern-triggered immunity (PTI) and effector-triggered immunity (ETI), in: P. Poltronieri, Y. Hong (Eds.), Applied Plant Biotechnology for Improving Resistance to Biotic Stress, Academic Press, 2020, pp. 1–31.
[8] E. Pitsili, U.J. Phukan, N.S. Coll, Cell death in plant immunity, Cold Spring Harbor Perspectives in Biology (2019) a036483.
[9] E.T. Iakimova, L. Michalczuk, E.J. Woltering, Hypersensitive cell death in plants-its mechnisms and role in plant defence against pathogens, J. Fruit Ornam. Plant Res. 13 (2005) 135.
[10] M. Rossi, F.L. Goggin, S.B. Milligan, I. Kaloshian, D.E. Ullman, V.M. Williamson, The nematode resistance gene Mi of tomato confers resistance against the potato aphid, Proc. Natl. Acad. Sci. Unit. States Am. 95 (1998) 9750–9754.
[11] S.B. Saucet, K. Shirasu, Molecular parasitic plant–host interactions, PLoS Pathog. 12 (2016).
[12] A. Mohamed, A. Ellicott, T. Housley, G. Ejeta, Hypersensitive response to Striga infection in sorghum, Crop Sci. 43 (2003) 1320–1324.
[13] J. Kacprzyk, C.T. Daly, P.F. McCabe, Chapter 4 - the botanical dance of death: programmed cell death in plants, in: J.-C. Kader, M. Delseny (Eds.), Adv Bot Res, Academic Press, 2011, pp. 169–261.
[14] L. Galluzzi, I. Vitale, S.A. Aaronson, J.M. Abrams, D. Adam, P. Agostinis, et al., Molecular mechanisms of cell death: recommendations of the nomenclature committee on cell death 2018, Cell Death Differ. 25 (2018) 486–541.
[15] M. Shine, X. Xiao, P. Kachroo, A. Kachroo, Signaling mechanisms underlying systemic acquired resistance to microbial pathogens, Plant Sci. 279 (2019) 81–86.
[16] H. Adachi, K. Tsuda, Convergence of cell-surface and intracellular immune receptor signalling, New Phytol. 221 (2019) 1676–1678.
[17] P. Balint-Kurti, The plant hypersensitive response: concepts, control and consequences, Mol. Plant Pathol. 20 (2019) 1163–1178.
[18] L.A. Mur, P. Kenton, A.J. Lloyd, H. Ougham, E. Prats, The hypersensitive response; the centenary is upon us but how much do we know? J. Exp. Bot. 59 (2008) 501–520.
[19] A. Noman, Z. Liu, S. Yang, L. Shen, A. Hussain, M.F. Ashraf, et al., Expression and functional evaluation of CaZNF830 during pepper response to *Ralstonia solanacearum* or high temperature and humidity, Microb. Pathog. 118 (2018) 336–346.
[20] Z. Liu, L. Shi, S. Yang, Y. Lin, Y. Weng, X. Li, et al., Functional and promoter analysis of ChiIV3, a chitinase of pepper plant, in response to *Phytophthora capsici* infection, Int. J. Mol. Sci. 18 (2017) 1661.
[21] H.W. Choi, B.K. Hwang, Molecular and cellular control of cell death and defense signaling in pepper, Planta 241 (2015) 1–27.
[22] A. Künstler, R. Bacsó, G. Gullner, Y.M. Hafez, L. Király, Staying alive – is cell death dispensable for plant disease resistance during the hypersensitive response? Physiol. Mol. Plant Pathol. 93 (2016) 75–84.
[23] R.N. Goodman, Z. Király, K.R. Wood, The Biochemistry and Physiology of Plant Disease, University of Missouri Press, 1986.
[24] J.T. Greenberg, N. Yao, The role and regulation of programmed cell death in plant–pathogen interactions, Cell Microbiol. 6 (2004) 201–211.
[25] J.-H. Jin, H.-X. Zhang, M. Ali, A.-M. Wei, D.-X. Luo, Z.-H. Gong, The CaAP2/ERF064 regulates dual functions in pepper: plant cell death and resistance to *Phytophthora capsici*, Genes 10 (2019) 541.
[26] M. Ifnan Khan, Y. Zhang, Z. Liu, J. Hu, C. Liu, S. Yang, et al., CaWRKY40b in pepper acts as a negative regulator in response to *Ralstonia solanacearum* by directly modulating defense genes including CaWRKY40, Int. J. Mol. Sci. 19 (2018) 1403.
[27] N. Coll, P. Epple, J. Dangl, Programmed cell death in the plant immune system, Cell Death Differ. 18 (2011) 1247–1256.
[28] A. Noman, A. Hussain, M.F. Ashraf, M.I. Khan, Z. Liu, S. He, CabZIP53 is targeted by CaWRKY40 and act as positive regulator in pepper defense against *Ralstonia solanacearum* and thermotolerance, Environ. Exp. Bot. 159 (2019) 138–148.
[29] A. Noman, M. Aqeel, M. Qasim, I. Haider, Y. Lou, Plant-insect-microbe interaction: a love triangle between enemies in ecosystem, Sci. Total Environ. (2019) 134181.
[30] A. Hussain, A. Noman, M.I. Khan, M. Zaynab, M. Aqeel, M. Anwar, et al., Molecular regulation of pepper innate immunity and stress tolerance: an overview of WRKY TFs, Microb. Pathog. (2019) 103610.
[31] J.L. Dangl, J.D. Jones, Plant pathogens and integrated defence responses to infection, Nature 411 (2001) 826–833.
[32] M.A. Torres, ROS in biotic interactions, Physiol. Plantarum 138 (2010) 414–429.
[33] Y.Y. Chen, Y.M. Lin, T.C. Chao, J.F. Wang, A.C. Liu, F.I. Ho, et al., Virus-induced gene silencing reveals the involvement of ethylene-, salicylic acid-and mitogen--activated protein kinase-related defense pathways in the resistance of tomato to bacterial wilt, Physiol. Plantarum 136 (2009) 324–335.
[34] J.M. McDowell, J.L. Dangl, Signal transduction in the plant immune response, Trends Biochem. Sci. 25 (2000) 79–82.
[35] T. Jabs, C. Colling, M. Tschöpe, K. Hahlbrock, D. Scheel, Elicitor-stimulated ion fluxes and reactive oxygen species from the oxidative burst signal defense gene activation and phytoalexin synthesis in parsley, Proc. Natl. Acad. Sci. U.S.A. 94 (1997) 4800–4805.
[36] D. Scheel, Resistance response physiology and signal transduction, Curr. Opin. Plant Biol. 1 (1998) 305–310.
[37] C. Lamb, R.A. Dixon, The oxidative burst in plant disease resistance, Annu. Rev. Plant Biol. 48 (1997) 251–275.
[38] K.M. Wright, G.H. Duncan, K.S. Pradel, F. Carr, S. Wood, K.J. Oparka, et al., Analysis of the N gene hypersensitive response induced by a fluorescently tagged tobacco mosaic virus, Plant Physiol. 123 (2000) 1375–1386.
[39] N. Hatsugai, K. Yamada, S. Goto-Yamada, I. Hara-Nishimura, Vacuolar processing enzyme in plant programmed cell death, Front. Plant Sci. 6 (2015) 234.
[40] L. Király, A. Künstler, K. Höller, M. Fattinger, C. Juhász, M. Müller, et al., Sulfate supply influences compartment specific glutathione metabolism and confers enhanced resistance to Tobacco mosaic virus during a hypersensitive response, Plant Physiol. Biochem. 59 (2012) 44–54.
[41] E.T. Iakimova, P. Sobiczewski, L. Michalczuk, E. Węgrzynowicz-Lesiak, A. Mikiciński, E.J. Woltering, Morphological and biochemical characterization of *Erwinia amylovora*-induced hypersensitive cell death in apple leaves, Plant Physiol. Biochem. 63 (2013) 292–305.
[42] M. Viljevac, K. Dugalić, I. Štolfa, E. Đermić, B. Cvjetković, R. Sudar, et al., Biochemical basis of apple leaf resistance to Erwinia amylovora infection, Food Technol. Biotechnol. 47 (2009) 281–287.
[43] M. Krause, J. Durner, Harpin inactivates mitochondria in Arabidopsis suspension cells, Molecular plant-microbe interactions 17 (2004) 131–139.
[44] R. Schiffer, R. Görg, B. Jarosch, U. Beckhove, G. Bahrenberg, K.-H. Kogel, et al., Tissue dependence and differential cordycepin sensitivity of race-specific resistance responses in the barley—powdery mildew interaction, Molecular plant-microbe interactions 10 (1997) 830–839.
[45] R. Hückelhoven, J. Fodor, C. Preis, K.-H. Kogel, Hypersensitive cell death and papilla formation in barley attacked by the powdery mildew fungus are associated with hydrogen peroxide but not with salicylic acid accumulation, Plant Physiol. 119 (1999) 1251–1260.
[46] B. Hwang, W. Kim, W. Kim, Ultrastructure at the host-parasite interface of *Phytophthora capsici* in roots and stems of *Capsicum annuum*, J. Phytopathol. 127 (1989) 305–315.
[47] H.W. Choi, N.H. Kim, Y.K. Lee, B.K. Hwang, The pepper extracellular xyloglucan-specific endo-β-1, 4-glucanase inhibitor protein gene, CaXEGIP1, is required for plant cell death and defense responses, Plant Physiol. 161 (2013) 384–396.
[48] H.W. Jung, B.K. Hwang, Isolation, partial sequencing, and expression of pathogenesis-related cDNA genes from pepper leaves infected by *Xanthomonas campestris* pv. vesicatoria, Mol. Plant Microbe Interact. 13 (2000) 136–142.
[49] D.S. Kim, B.K. Hwang, The pepper MLO gene, CaMLO2, is involved in the susceptibility cell-death response and bacterial and oomycete proliferation, Plant J. 72 (2012) 843–855.
[50] I.S. Hwang, B.K. Hwang, The pepper mannose-binding lectin gene CaMBL1 is required to regulate cell death and defense responses to microbial pathogens, Plant Physiol. 155 (2011) 447–463.
[51] S.Y. Yi, D.J. Lee, S.I. Yeom, J. Yoon, Y.H. Kim, S.Y. Kwon, et al., A novel pepper (*Capsicum annuum*) receptor-like kinase functions as a negative regulator of plant cell death via accumulation of superoxide anions, New Phytol. 185 (2010) 701–715.
[52] J.-B. Morel, J.L. Dangl, The hypersensitive response and the induction of cell death in plants, Cell Death Differ. 4 (1997) 671–683.
[53] C. Chen, M.C. Heath, Cytological studies of the hypersensitive death of cowpea epidermal cells induced by basidiospore-derived infection by the cowpea rust fungus, Can. J. Bot. 69 (1991) 1199–1206.
[54] S. Freytag, N. Arabatzis, K. Hahlbrock, E. Schmelzer, Reversible cytoplasmic rearrangements precede wall apposition, hypersensitive cell death and defense-related gene activation in potato/Phytophthora infestans interactions, Planta 194 (1994) 123–135.
[55] W. Wang, C. Jones, J. Ciacci-Zanella, T. Holt, D.G. Gilchrist, M.B. Dickman, Fumonisins and Alternaria alternata lycopersici toxins: sphinganine analog mycotoxins induce apoptosis in monkey kidney cells, Proc. Natl. Acad. Sci. Unit. States Am. 93 (1996) 3461–3465.
[56] J.L. Dangl, R.A. Dietrich, M.H. Richberg, Death don't have no mercy: cell death programs in plant-microbe interactions, Plant Cell 8 (1996) 1793.
[57] A. Noman, A. Hussain, M. Adnan, M.I. Khan, M.F. Ashraf, M. Zainab, et al., A novel MYB transcription factor CaPHL8 provide clues about evolution of pepper immunity againstsoil borne pathogen, Microb. Pathog. 137 (2019) 103758.

[58] M.F. Ashraf, S. Yang, R. Wu, Y. Wang, A. Hussain, A. Noman, et al., *Capsicum annuum* HsfB2a positively regulates the response to *Ralstonia solanacearum* infection or high temperature and high humidity forming transcriptional cascade with CaWRKY6 and CaWRKY40, Plant Cell Physiol. 59 (2018) 2608–2623.

[59] M.C. Suh, S.-K. Oh, Y.-C. Kim, H.-S. Pai, D. Choi, Expression of a novel tobacco gene, NgCDM1, is preferentially associated with pathogen-induced cell death, Physiol. Mol. Plant Pathol. 62 (2003) 227–235.

[60] Y. Liu, M. Schiff, K. Czymmek, Z. Tallóczy, B. Levine, S. Dinesh-Kumar, Autophagy regulates programmed cell death during the plant innate immune response, Cell 121 (2005) 567–577.

[61] T. Nürnberger, D. Nennstiel, T. Jabs, W.R. Sacks, K. Hahlbrock, D. Scheel, High affinity binding of a fungal oligopeptide elicitor to parsley plasma membranes triggers multiple defense responses, Cell 78 (1994) 449–460.

[62] R.B. Abramovitch, G.B. Martin, Strategies used by bacterial pathogens to suppress plant defenses, Curr. Opin. Plant Biol. 7 (2004) 356–364.

[63] J.-L. Peng, H.-S. Dong, H.-P. Dong, T. Delaney, J. Bonasera, S. Beer, Harpin-elicited hypersensitive cell death and pathogen resistance require the NDR1 and EDS1 genes, Physiol. Mol. Plant Pathol. 62 (2003) 317–326.

[64] T.J. Reape, P.F. McCabe, Apoptotic-like regulation of programmed cell death in plants, Apoptosis 15 (2010) 249–256.

[65] J. Kacprzyk, C.T. Daly, P.F. McCabe, The Botanical Dance of Death: Programmed Cell Death in Plants, Adv Bot Res: Elsevier, 2011, pp. 169–261.

[66] M.C. Heath, Hypersensitive Response-Related Death. Programmed Cell Death in Higher Plants, Springer, 2000, pp. 77–90.

[67] D. Pontier, S. Gan, R.M. Amasino, D. Roby, E. Lam, Markers for hypersensitive response and senescence show distinct patterns of expression, Plant Mol. Biol. 39 (1999) 1243–1255.

[68] F. Zaninotto, S.L. Camera, A. Polverari, M. Delledonne, Cross talk between reactive nitrogen and oxygen species during the hypersensitive disease resistance response, Plant Physiol. 141 (2006) 379–383.

[69] J. Jayaraman, S. Choi, M. Prokchorchik, D.S. Choi, A. Spiandore, E.H. Rikkerink, et al., A bacterial acetyltransferase triggers immunity in Arabidopsis thaliana independent of hypersensitive response, Sci. Rep. 7 (2017) 3557.

[70] V. Buchanan-Wollaston, The molecular biology of leaf senescence, J. Exp. Bot. 48 (1997) 181–199.

[71] I-c Yu, J. Parker, A.F. Bent, Gene-for-gene disease resistance without the hypersensitive response in Arabidopsis dnd1 mutant, Proc. Natl. Acad. Sci. Unit. States Am. 95 (1998) 7819–7824.

[72] O. Del Pozo, E. Lam, Caspases and programmed cell death in the hypersensitive response of plants to pathogens, Curr. Biol. 8 (1998) 1129–1132.

[73] A. Bendahmane, K. Kanyuka, D.C. Baulcombe, The Rx gene from potato controls separate virus resistance and cell death responses, Plant Cell 11 (1999) 781–791.

[74] M.C. Heath, Apoptosis, programmed cell death and the hypersensitive response, Eur. J. Plant Pathol. 104 (1998) 117–124.

[75] R.A. Van der Hoorn, Plant proteases: from phenotypes to molecular mechanisms, Annu. Rev. Plant Biol. 59 (2008) 191–223.

[76] M.H. Glickman, A. Ciechanover, The ubiquitin-proteasome proteolytic pathway: destruction for the sake of construction, Physiol. Rev. 82 (2002) 373–428.

[77] B. Turk, Targeting proteases: successes, failures and future prospects, Nat. Rev. Drug Discov. 5 (2006) 785–799.

[78] J. Salguero-Linares, N.S. Coll, Plant proteases in the control of the hypersensitive response, J. Exp. Bot. 70 (2019) 2087–2095.

[79] J.C. Misas-Villamil, R.A. van der Hoorn, G. Doehlemann, Papain-like cysteine proteases as hubs in plant immunity, New Phytol. 212 (2016) 902–907.

[80] Y. Du, M. Stegmann, J.C. Misas Villamil, The apoplast as battleground for plant–microbe interactions, New Phytol. 209 (2016) 34–38.

[81] E.M. Gilroy, I. Hein, R. Van Der Hoorn, P.C. Boevink, E. Venter, H. McLellan, et al., Involvement of cathepsin B in the plant disease resistance hypersensitive response, Plant J. 52 (2007) 1–13.

[82] H. McLellan, E.M. Gilroy, B.W. Yun, P.R. Birch, G.J. Loake, Functional redundancy in the *Arabidopsis Cathepsin* B gene family contributes to basal defence, the hypersensitive response and senescence, New Phytol. 183 (2009) 408–418.

[83] M.R. Armstrong, S.C. Whisson, L. Pritchard, J.I. Bos, E. Venter, A.O. Avrova, et al., An ancestral oomycete locus contains late blight avirulence gene Avr3a, encoding a protein that is recognized in the host cytoplasm, Proc. Natl. Acad. Sci. Unit. States Am. 102 (2005) 7766–7771.

[84] M. Shabab, T. Shindo, C. Gu, F. Kaschani, T. Pansuriya, R. Chintha, et al., Fungal effector protein AVR2 targets diversifying defense-related cys proteases of tomato, Plant Cell 20 (2008) 1169–1183.

[85] H. Zhang, S. Dong, M. Wang, W. Wang, W. Song, X. Dou, et al., The role of vacuolar processing enzyme (VPE) from Nicotiana benthamiana in the elicitor-triggered hypersensitive response and stomatal closure, J. Exp. Bot. 61 (2010) 3799–3812.

[86] J.C. Misas-Villamil, G. Toenges, I. Kolodziejek, A.M. Sadaghiani, F. Kaschani, T. Colby, et al., Activity profiling of vacuolar processing enzymes reveals a role for VPE during oomycete infection, Plant J. 73 (2013) 689–700.

[87] N.S. Coll, D. Vercammen, A. Smidler, C. Clover, F. Van Breusegem, J.L. Dangl, et al., Arabidopsis type I metacaspases control cell death, Science 330 (2010) 1393–1397.

[88] N. Watanabe, E. Lam, Two Arabidopsis metacaspases AtMCP1b and AtMCP2b are arginine/lysine-specific cysteine proteases and activate apoptosis-like cell death in yeast, J. Biol. Chem. 280 (2005) 14691–14699.

[89] N. Watanabe, E. Lam, Arabidopsis metacaspase 2d is a positive mediator of cell death induced during biotic and abiotic stresses, Plant J. 66 (2011) 969–982.

[90] J.K. Hong, D.S. Choi, S.H. Kim, S.Y. Yi, Y.J. Kim, B.K. Hwang, Distinct roles of the pepper pathogen-induced membrane protein gene CaPIMP1 in bacterial disease resistance and oomycete disease susceptibility, Planta 228 (2008) 485–497.

[91] S.H. An, H.W. Choi, I.S. Hwang, J.K. Hong, B.K. Hwang, A novel pepper membrane-located receptor-like protein gene CaMRP1 is required for disease susceptibility, methyl jasmonate insensitivity and salt tolerance, Plant Mol. Biol. 67 (2008) 519.

[92] C. Segonzac, D. Feike, S. Gimenez-Ibanez, D.R. Hann, C. Zipfel, J.P. Rathjen, Hierarchy and roles of pathogen-associated molecular pattern-induced responses in Nicotiana benthamiana, Plant Physiol. 156 (2011) 687–699.

[93] D.S. Kim, B.K. Hwang, The pepper receptor-like cytoplasmic protein kinase CaPIK1 is involved in plant signaling of defense and cell-death responses, Plant J. 66 (2011) 642–655.

[94] X. Li, Y. Zhang, L. Huang, Z. Ouyang, Y. Hong, H. Zhang, et al., Tomato SlMKK2 and SlMKK4 contribute to disease resistance against Botrytis cinerea, BMC Plant Biol. 14 (2014) 166.

[95] L. Gallego-Giraldo, Y. Jikumaru, Y. Kamiya, Y. Tang, R.A. Dixon, Selective lignin downregulation leads to constitutive defense response expression in alfalfa (*Medicago sativa* L.), New Phytol. 190 (2011) 627–639.

[96] E.-S. Chung, S.-K. Oh, J.-M. Park, D.-I. Choi, Expression and promoter analyses of pepper CaCDPK4 (*Capsicum annuum* calcium dependent protein kinase 4) during plant defense response to incompatible pathogen, Plant Pathol. J. 23 (2007) 76–89.

[97] S.-Y. Kim, Y.-C. Kim, E.S. Seong, Y.-H. Lee, J.M. Park, D. Choi, The chili pepper CaATL1: an AT-hook motif-containing transcription factor implicated in defence responses against pathogens, Mol. Plant Pathol. 8 (2007) 761–771.

[98] S. Sarowar, H.W. Oh, H.S. Cho, K.H. Baek, E.S. Seong, Y.H. Joung, et al., *Capsicum annuum* CCR4-associated factor CaCAF1 is necessary for plant development and defence response, Plant J. 51 (2007) 792–802.

[99] B. Liu, Z. Ouyang, Y. Zhang, X. Li, Y. Hong, L. Huang, et al., Tomato NAC transcription factor SlSRN1 positively regulates defense response against biotic stress but negatively regulates abiotic stress response, PloS One 9 (2014).

[100] Y.-H. Xu, J.-W. Wang, S. Wang, J.-Y. Wang, X.-Y. Chen, Characterization of GaWRKY1, a cotton transcription factor that regulates the sesquiterpene synthase gene (+)-δ-cadinene synthase-A, Plant Physiol. 135 (2004) 507–515.

[101] H. Wang, J. Hao, X. Chen, Z. Hao, X. Wang, Y. Lou, et al., Overexpression of rice WRKY89 enhances ultraviolet B tolerance and disease resistance in rice plants, Plant Mol. Biol. 65 (2007) 799–815.

[102] I.S. Hwang, B.K. Hwang, The pepper 9-lipoxygenase gene CaLOX1 functions in defense and cell death responses to microbial pathogens, Plant Physiol. 152 (2010) 948–967.

[103] S.A. Christensen, A. Nemchenko, Y.-S. Park, E. Borrego, P.-C. Huang, E.A. Schmelz, et al., The novel monocot-specific 9-lipoxygenase ZmLOX12 is required to mount an effective jasmonate-mediated defense against *Fusarium verticillioides* in maize, Mol. Plant Microbe Interact. 27 (2014) 1263–1276.

[104] S.I. Yeom, E. Seo, S.K. Oh, K.W. Kim, D. Choi, A common plant cell-wall protein HyPRP1 has dual roles as a positive regulator of cell death and a negative regulator of basal defense against pathogens, Plant J. 69 (2012) 755–768.

[105] S.C. Lee, I.S. Hwang, H.W. Choi, B.K. Hwang, Involvement of the pepper antimicrobial protein CaAMP1 gene in broad spectrum disease resistance, Plant Physiol. 148 (2008) 1004–1020.

[106] D.S. Choi, I.S. Hwang, B.K. Hwang, Requirement of the cytosolic interaction between PATHOGENESIS-RELATED PROTEIN10 and LEUCINE-RICH REPEAT PROTEIN1 for cell death and defense signaling in pepper, Plant Cell 24 (2012) 1675–1690.

[107] D.S. Choi, B.K. Hwang, Proteomics and functional analyses of pepper abscisic acid–responsive 1 (ABR1), which is involved in cell death and defense signaling, Plant Cell 23 (2011) 823–842.

[108] M.N. Al-Attala, X. Wang, M. Abou-Attia, X. Duan, Z. Kang, A novel TaMYB4 transcription factor involved in the defence response against *Puccinia striiformis* f. sp. tritici and abiotic stresses, Plant Mol. Biol. 84 (2014) 589–603.

[109] T. Ogata, Y. Kida, T. Arai, Y. Kishi, Y. Manago, M. Murai, et al., Overexpression of tobacco ethylene response factor NtERF3 gene and its homologues from tobacco and rice induces hypersensitive response-like cell death in tobacco, J. Gen. Plant Pathol. 78 (2012) 8–17.

[110] I.S. Hwang, D.S. Choi, N.H. Kim, D.S. Kim, B.K. Hwang, Pathogenesis-related protein 4b interacts with leucine-rich repeat protein 1 to suppress PR 4b-triggered cell death and defense response in pepper, Plant J. 77 (2014) 521–533.

[111] A. Anand, T. Zhou, H.N. Trick, B.S. Gill, W.W. Bockus, S. Muthukrishnan, Greenhouse and field testing of transgenic wheat plants stably expressing genes for thaumatin-like protein, chitinase and glucanase against *Fusarium graminearum*, J. Exp. Bot. 54 (2003) 1101–1111.

[112] Y.-H. Yeh, Y.-H. Chang, P.-Y. Huang, J.-B. Huang, L. Zimmerli, Enhanced Arabidopsis pattern-triggered immunity by overexpression of cysteine-rich receptor-like kinases, Front. Plant Sci. 6 (2015) 322.

[113] A. Miya, P. Albert, T. Shinya, Y. Desaki, K. Ichimura, K. Shirasu, et al., CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in Arabidopsis, Proc. Natl. Acad. Sci. Unit. States Am. 104 (2007) 19613–19618.

[114] T. Mengiste, X. Chen, J. Salmeron, R. Dietrich, The BOTRYTIS SUSCEPTIBLE1 gene encodes an R2R3MYB transcription factor protein that is required for biotic and abiotic stress responses in Arabidopsis, Plant Cell 15 (2003) 2551–2565.

[115] X. Zhu, L. Qi, X. Liu, S. Cai, H. Xu, R. Huang, et al., The wheat ethylene response factor transcription factor pathogen-induced ERF1 mediates host responses to both the necrotrophic pathogen *Rhizoctonia cerealis* and freezing stresses, Plant Physiol. 164 (2014) 1499–1514.

[116] N. Xia, G. Zhang, X.-Y. Liu, L. Deng, G.-L. Cai, Y. Zhang, et al., Characterization of a novel wheat NAC transcription factor gene involved in defense response against stripe rust pathogen infection and abiotic stresses, Mol. Biol. Rep. 37 (2010)

3703–3712.
[117] L. Chen, L. Zhang, D. Li, F. Wang, D. Yu, WRKY8 transcription factor functions in the TMV-cg defense response by mediating both abscisic acid and ethylene signaling in *Arabidopsis*, Proc. Natl. Acad. Sci. Unit. States Am. 110 (2013) E1963–E1971.
[118] J. Li, J. Wang, N. Wang, X. Guo, Z. Gao, GhWRKY44, a WRKY transcription factor of cotton, mediates defense responses to pathogen infection in transgenic *Nicotiana benthamiana*, Plant Cell Tissue Organ Cult. 121 (2015) 127–140.
[119] S. Giberti, C.M. Bertea, R. Narayana, M.E. Maffei, G. Forlani, Two phenylalanine ammonia lyase isoforms are involved in the elicitor-induced response of rice to the fungal pathogen *Magnaporthe oryzae*, J. Plant Physiol. 169 (2012) 249–254.
[120] H. Lee, Y.J. Ko, J.-Y. Cha, S.R. Park, I. Ahn, D.-J. Hwang, The C-terminal region of OsWRKY30 is sufficient to confer enhanced resistance to pathogen and activate the expression of defense-related genes, Plant biotechnology reports 7 (2013) 221–230.
[121] B. Liu, Y.-B. Hong, Y.-F. Zhang, X.-H. Li, L. Huang, H.-J. Zhang, et al., Tomato WRKY transcriptional factor SlDRW1 is required for disease resistance against *Botrytis cinerea* and tolerance to oxidative stress, Plant Sci. 227 (2014) 145–156.
[122] B. Zhang, Y. Yang, T. Chen, W. Yu, T. Liu, H. Li, et al., Island cotton Gbve1 gene encoding a receptor-like protein confers resistance to both defoliating and non-defoliating isolates of *Verticillium dahliae*, PloS One 7 (2012).
[123] X. Wang, X. Wang, L. Deng, H. Chang, J. Dubcovsky, H. Feng, et al., Wheat TaNPSN SNARE homologues are involved in vesicle-mediated resistance to stripe rust (*Puccinia striiformis* f. sp. tritici), J. Exp. Bot. 65 (2014) 4807–4820.
[124] J. Zhang, Y. Peng, Z. Guo, Constitutive expression of pathogen-inducible OsWRKY31 enhances disease resistance and affects root growth and auxin response in transgenic rice plants, Cell Res. 18 (2008) 508–521.
[125] L.J. Leba, C. Cheval, I. Ortiz-Martín, B. Ranty, C.R. Beuzón, J.P. Galaud, et al., CML9, an Arabidopsis calmodulin-like protein, contributes to plant innate immunity through a flagellin-dependent signalling pathway, Plant J. 71 (2012) 976–989.
[126] L.N. Petersen, R.A. Ingle, M.R. Knight, K.J. Denby, OXI1 protein kinase is required for plant immunity against *Pseudomonas syringae* in Arabidopsis, J. Exp. Bot. 60 (2009) 3727–3735.
[127] J. Shi, L. Zhang, H. An, C. Wu, X. Guo, GhMPK16, a novel stress-responsive group D MAPK gene from cotton, is involved in disease resistance and drought sensitivity, BMC Mol. Biol. 12 (2011) 22.