Chapter 10

Advances in Plant Tolerance to Biotic Stresses

Geoffrey Onaga and Kerstin Wydra

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/64351

Abstract

Plants being sessile in nature encounter numerous biotic agents, including bacteria, fungi, viruses, insects, nematodes and protists. A great number of publications indicate that biotic agents significantly reduce crop productivity, although there are some biotic agents that symbiotically or synergistically co-exist with plants. Nonetheless, scientists have made significant advances in understanding the plant defence mechanisms expressed against biotic stresses. These mechanisms range from anatomy, physiology, biochemistry, genetics, development and evolution to their associated molecular dynamics. Using model plants, e.g., Arabidopsis and rice, efforts to understand these mechanisms have led to the identification of representative candidate genes, quantitative trait loci (QTLs), proteins and metabolites associated with plant defences against biotic stresses. However, there are drawbacks and insufficiencies in precisely deciphering and deploying these mechanisms, including only modest adaptability of some identified genes or QTLs to changing stress factors. Thus, more systematic efforts are needed to explore and expand the development of biotic stress resistant germplasm. In this chapter, we provided a comprehensive overview and discussed plant defence mechanisms involving molecular and cellular adaptation to biotic stresses. The latest achievements and perspective on plant molecular responses to biotic stresses, including gene expression, and targeted functional analyses of the genes expressed against biotic stresses have been presented and discussed.

Keywords: Biotic stress, climate change, innate immunity, phytohormones

1. Introduction

Biotic stresses are the damage to plants caused by other living organisms such as bacteria, fungi, nematodes, protists, insects, viruses and viroids. Numerous biotic stresses are of historical significance, for instance, the potato blight in Ireland, coffee rust in Brazil, maize leaf blight caused by *Cochliobolus heterostrophus* in the United States and the great Bengal famine

in 1943 [1]. These are some of the major events that devastated food production and led to millions of human deaths and migration to other countries in the past. Presently, the occurrence of new pathogen races and insect biotypes poses further threat to crop production [2]. Pathogens account for about 15% losses in global food production, and are a major challenge in breeding resistant crops. Considering that genetic polymorphism is present in phytopathogenic agents and insect populations, changes in the climatic factors are considered to further influence/modify this polymorphism, causing evolution of aggressive strains or biotypes [3] that will alter the outcome of host-pathogen interaction. Thus, disease or insect pest outbreaks are expected to continue to cause food production losses or even worsen by expanding to the areas they were not prevalent before [4]. This has important implications for the management options available. Using a combination of options provides certainly more reliability. However, in areas where resources are limiting, e.g., the smallholder farming systems in rural Africa and South East Asia, plant breeders are compelled to make the best use of the diverse disease and pest resistance alleles existing in cultivated crop gene pools and their wild relatives. Thus, exploring the mechanisms of resistance regulated by these resistance alleles is required to enable their exploitation for improving the cultivated elite germplasm that support most of the rural poor livelihoods.

Plant mechanisms of resistance to various pathogens and insect pests are known to involve an array of morphological, genetic, biochemical and molecular processes [5]. These mechanisms may be expressed continuously (constitutively) as preformed resistance, or they may be inducible and deployed only after attack. Plant success in deploying these resistance mechanisms is an evolved ability to persist in unfavourable and variable environments [6]. The recent realization that plant mechanisms of disease/insect resistance or susceptibility are related to mechanistic animal immunity [7] has significantly reshaped our view of plant immunity. The identification of plant pattern recognition receptors (PRRs) that sense pathogens' or insect pests'conserved molecules termed pathogen-associated molecular patterns or herbivore-associated molecular patterns (PAMPs/MAMPs/HAMPs)—and the subsequent PAMP-triggered immunity (PTI) [8] is a paradigm for plant-pathogen interaction studies.

On the other hand, the ability of pathogens/insect pests to suppress or evade PTI, as a structural and functional basis of pathogen survival and evolutionary dynamics in their feeding mechanisms has revitalized research on the so-called 'gene-for-gene' effector induced resistance in plants. It is now clear that effectors are important determinants of pathogens' ability to evade the plant's arsenal targeted towards PAMPs/HAMPs. Effector induced resistance or vertical resistance, often interchangeably translated in modern terms as effector triggered immunity (ETI), is the most successful means of controlling pathogens able to evade PTI [6]. ETI engages a compensatory mechanism within the defense network to transcriptionally coordinate and boost the defense output against pathogens. ETI mostly relies on the endogenious NB-LRR protein products encoded by the resistance (R)-genes. Although R gene mediated resistance is generally not durable, ETI is now effectively deployed through pyramiding of several resistance (R)-genes in the same cultivar, which increases resistance durability and spectrum.

Another aspect of resistance that has gained significance in plant defence studies is the systemic acquired resistance (SAR), in which defence proteins accumulate not only at the site of infection

but also systemically in uninfected tissues and/or plants. SAR provides long-term defense against a broad-spectrum of pathogens and insects. Another form of induced resistance, which, in many aspects, is similar to SAR, is induced systemic resistance (ISR). ISR is potentiated by plant growth promoting rhizobacteria (PGPR), many of them belonging to *Pseudomonas* species. Obviously, the sessile nature of plants requires an efficient signalling system capable of detecting, transporting and interpreting signals produced at the plant-pathogen interface, and SAR and ISR provide a practical means to confer a fitness advantage to plants in conditions of high disease pressure, since plants are primed to more quickly and effectively activate their defences ahead of pathogen/ insect attack. Plants also defend themselves through RNA interference to target and inactivate invading nucleic acids from viruses, and more recently fungal pathogens.

These are the aspects that this chapter has addressed to provide background information for a more detailed discussion of the diverse aspects of plant defence patterns, including qualitative and quantitative mechanisms and their associated molecular patterns. Although pathogenic mechanisms would be interesting to the reader, this chapter does not delve extensively into this aspect, except to mention it as a consideration in emphasizing certain aspects of plant resistance. For additional background, the reader is referred to excellent reviews and the references therein that address plant-pathogen interaction.

2. Plant defence mechanisms in response to pathogens

Plants respond to various pathogens through an intricate and dynamic defence system. The mechanism of defence has been classified as innate and systemic plant response. The overview of plant defence response is represented in Figure 1. An innate defence is exhibited by the plant in two ways, viz., specific (cultivar/pathogen race specific) and non-specific (non-host or general resistance) [8]. The molecular basis of non-host resistance is not well studied, but presumably relies on both constitutive barriers and inducible responses that involve a large array of proteins and other organic molecules produced prior to infection or during pathogen attack [9, 10]. Constitutive defences include morphological and structural barriers (cell walls, epidermis layer, trichomes, thorns, etc.), chemical compounds (metabolites, phenolics, nitrogen compounds, saponins, terpenoids, steroids and glucosinolates), and proteins and enzymes [11, 12, 199]. These compounds confer tolerance or resistance to biotic stresses by not only protecting the plant from invasion, but also giving the plant strength and rigidity. The inducible defences, e.g., the production of toxic chemicals, pathogen-degrading enzymes e.g., chitinases and glucanases, and deliberate cell suicide are conservatively used by plants because of the high energy costs and nutrient requirements associated with their production and maintenance. These compounds may be present in their biologically active forms or stored as inactive precursors that are converted to their active forms by host enzymes in response to pathogen attack or tissue damage. Plant defence strategies involving these compounds can fall in either category, innate or SAR. Although innate immunity is of greater efficiency and is the most common form of plant resistance to microbes, both defence strategies depend on the

ability of the plant to distinguish between self and non-self molecules. The molecular bases of these defence mechanisms are discussed below.

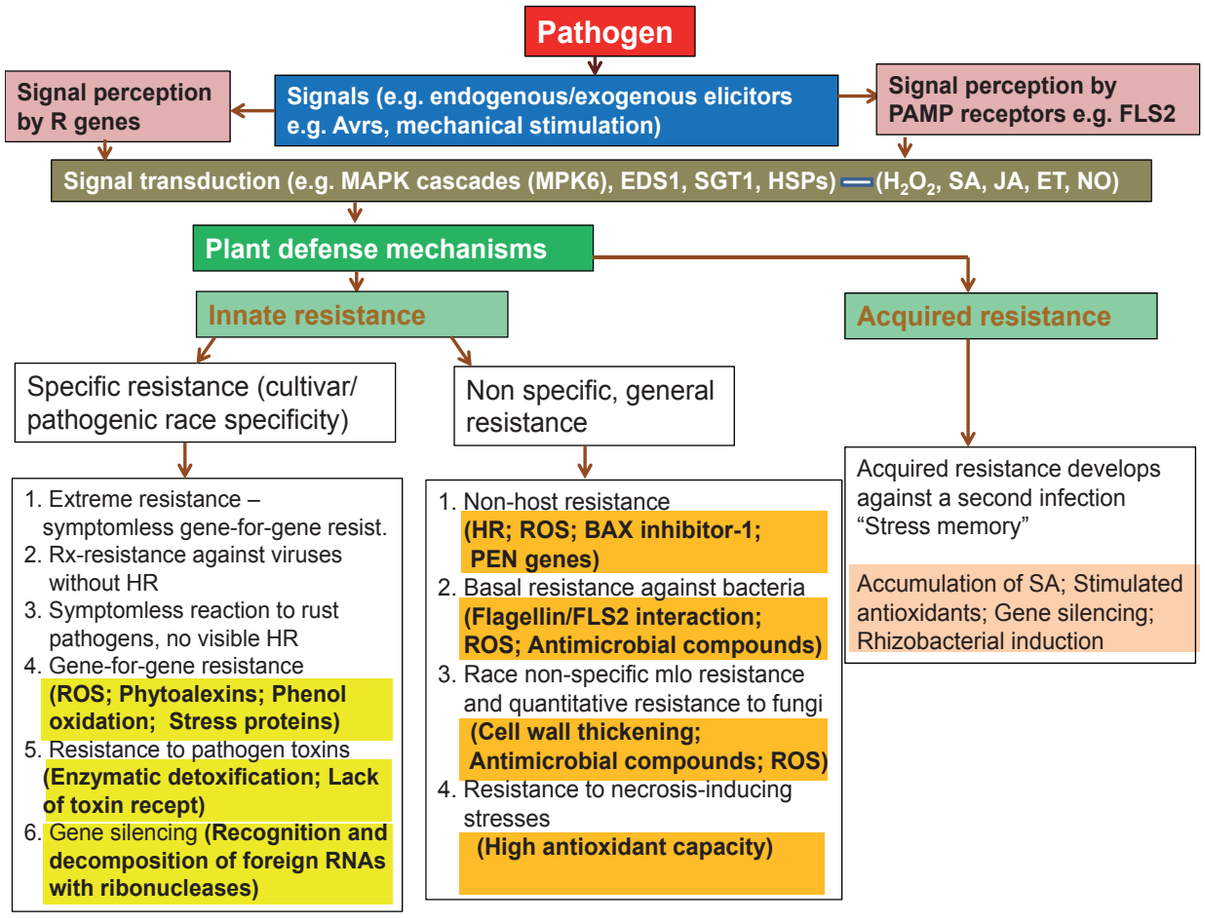

Figure 1. Overview of cellular mechanisms of biotic stress response leading to innate immunity and systemic acquired resistance. Plant PRRs or R-genes perceive PAMPS/DAMPs and effectors, respectively. Inside the cell, an overlapping set of downstream immune responses results from the PTI/ETI continuum. This includes the activation of multiple signaling pathways involving reactive oxygen species (ROS), defense hormones (such as salicylic acid, jasmonic acid and ethylene), mitogen activated protein kinases (MAPK), and transcription factor families, e.g., AP2/ERF, WRKY, MYB, bZIP etc. these signals activate either innate response or acquired immune response or both.

3. Innate immunity

Innate immunity in plants is divided into microbial-associated molecular-pattern-triggered immunity (MTI; also called PTI) and effector-triggered immunity (ETI). In MTI/PTI, innate immunity is defined by receptors for microbe-associated molecules, conserved mitogen-associated protein kinase signalling cascades and the production of antimicrobial peptides/compounds [13]. Recognition of microbes is divided into two branches, one involving slowly evolving microbial- or pathogen-associated molecular patterns, such as fungal chitin, xylanase or bacterial flagellin, lipopolysaccharides and peptidoglycans [14], and the other that responds

to a compromised 'self', also called damage-associated molecular patterns (DAMPs) [14, 15]. Both PAMPs and DAMPs are recognized by transmembrane pattern recognition receptors (PRRs).

A common strategy employed by adapted pathogens is to secrete effector proteins that avoid or regulate PTI recognition. To counter this stealth afforded by the microbial effectors, plants have evolved an intracellular surveillance involving polymorphic NB-LRR protein products encoded by resistance (R) genes, named after their characteristic feature due to the presence of nucleotide binding (NB) and leucine-rich repeat (LRR) domains [9]. This type of plant defence is referred to as ETI and is synonymous to pathogen race/host plant cultivar-specific plant disease resistance [8].

Generally, PTI and ETI trigger similar defence responses, but ETI is much faster and quantitatively stronger [16]. ETI is often associated with a localized cell death termed the hypersensitive response (HR) that functions to restrict further spread of microbial attack [9, 17]. Hence, the important feature of ETI is the ability to sense microbe-mediated modifications inferred on points of vulnerability in the host, whereas PTI is able to sense infectious-self and non-self. By guarding against weak points or even setting up decoys to confuse invaders, ETI is an efficient defence system for more progressed infections [15, 18], whereas PTI is important for non-host resistance and for basal immunity in susceptible host plant cultivars. In the following section, we will discuss novel insights and overviews on the dynamics of innate immunity in plant defence.

3.1. Pathogen- or microbial-associated molecular-pattern (PAMP/MAMP)-triggered immunity (PTI)

PTI (formerly called basal or horizontal disease resistance) is the first facet of active plant defence and can be considered as the primary driving force of plant-microbe interactions [19]. As discussed before, PTI involves the recognition of conserved, indispensable microbial elicitors known as PAMPs by PRRs of either the receptor-like kinase (RLK) or receptor-like proteins (RLPs) families, which are membranous bound extracellular receptors. RLPs resemble the extracellular domains of RLKs, but lack the cytosolic signalling domain, whereas RLKs have both extracellular and intracellular kinase domains [6]. Instances of hetero-oligomeric complexes between RLKs and RLPs have been reported to occur, and to complement each other in PAMP detection [8], as will be discussed in the following sections. Examples of RLPs include the S locus glycoprotein (*SLG*), *CLAVATA2* and *Xa21D*. RLKs are numerous, and some examples will also be discussed in the following sections. Despite different configurations, both RLKs and RLPs receptors contribute to blocking infection before the microbe gains a hold on the plant.

PAMPs occur throughout the pathogen classes, including bacterial flagellin (*flg22*) and EF-Tu (*elf18*), fungal chitin (*CEBiP*) and mannans of yeast, xylanase (*LeEIX1/2*) and Oomycetes' heptaglucan (*HG*) [17, 19–21]. The early responses induced by PAMPs occur within minutes to hours and are varied, ranging from rapid ion fluxes across the plasma membrane, oxidative burst, activation of mitogen-activated protein kinases (MAPKs) and calcium-dependent protein kinases (CDPKs) to local induction of defence -related genes or pathogen cell wall/cell

membranes lyasing enzymes/peptides, e.g., chitinases, glucanases and defensins (Figure 1) [22]. Other responses may include production of antimicrobial phytoalexins, plant cell wall modifications, e.g. deposition of papillae, enriched with (1,3)-β-glucan cell wall polymer, callose, lignin biosynthesis, or changes in cell wall proteins and pectic polysaccharide structures [14, 22, 89, 90, 200]. When the pathogen gains entry and initiates colonization, a concerted effort of both PTI and ETI may be required to restrict further colonization. In the event that ETI is not active, PTI could probably contribute to effective plant resistance as much as ETI, if the capacity to recognize undetected epitopes could be engineered into plants. Some of the examples of PTI that have been shown to contribute to resistance in plants are discussed in the following section.

3.1.1. Specific examples of PTI in plants

3.1.1.1. Flagellin-induced resistance

Flagellin constitutes the main building block of bacterial flagellum, and is so far the best characterized PAMP in plants. A 22 amino acid (*flg22*) peptide-spanning region in the N-terminal part of flagellin of *Pseudomonas syringae* is sufficient to elicit the whole array of typical immune responses in a broad variety of plants [23]. The PRR responsible for flagellin perception in the model plant *Arabidopsis thaliana* is the leucine-rich repeat receptor-like kinase (LRR-RLK) *FLAGELLIN-SENSING 2* (*FLS2*). Functional *FLS2* homologs have been identified in other major groups of higher plants, including tomato, grapevine, *Nicotiana benthamiana* and rice, suggesting that the receptors for the *flg22* epitope of bacterial flagellin are evolutionarily ancient and conserved [14, 24]. Despite evolutionary conservation, *FLS2* proteins from different plant species, such as tomato flagellin receptor (*LeFLS2)*, grapevine *(VvFLS2*) and *A. thaliana* (*AtFLS2*), still exhibit different perception specificities to elicitation determinants of flagellins [24–26]. This suggests that the domains found in *FLS* may have undergone some functional innovations that contribute to different perception specificities. Flagellin also seems to be recognized by other means in certain plant species. For instance, in rice, *flg22* epitope does not allow the activation of PRR, but flagellin induces cell death [26]. Moreover, the glycosylation status of flagellin proteins is emerging as a determinant of recognizing adapted and non-adapted bacteria by *Solanaceae* plants, such as tobacco and tomato [27, 28]. More recently, another flagellin, *flgII-28*, was identified in *Solanaceae* [29], though the corresponding PRR is yet to be identified. Both *flg22* and *flgII-28* are physically linked by a stretch of 33 amino acid residues, suggesting that both molecules are detected by the same receptor, *FLS2* [30].

The signalling events triggered in plant cells following *flg22* detection include rapid binding of *FLS2* to *BAK1* (*BRI1-associated kinase 1*) by reciprocal transphosphorylation of their kinase domains [31]. The plasma membrane localized receptor-like cytoplasmic kinase *BOTRYTIS-INDUCED KINASE 1* (*BIK1*) and related *PBS1-LIKE* (*PBL*) kinases associate with *FLS2*/*BAK1* [32]. The complex formed triggers multiple rapid phosphorylation events resulting in *BIK1* release. *BIK1* plays a central role in conveying signals from not only *FLS2* but also other PRRs, including *EFR*, *CERK1* and the DAMP receptor, *PEPR1*/*PEPR2*. The signal transduction downstream of *flg22* perception includes a Ca^{2+} burst, activation of *CDPKs* and *RbohD* required

http://dx.doi.org/10.5772/64351

for the ROS burst and induction of *MAPK* cascades. These signalling cascades activate transcriptional reprogrammers such as the *WRKY* TFs, which are required for induction of defence genes [201].

3.1.1.2. Elongation factor (EF-Tu) induced resistance

Elongation factor Tu (EF-Tu) is the most abundant bacterial protein originally isolated from *Escherichia coli*, and acts as PAMP in *Brassicaceae* family members including *A. thaliana* [33]. The conserved *N*-acetylated epitope *elf18* (first 18 amino acids of the protein) is sufficient to trigger defence responses in plants [33, 34]. The shorter peptide, *elf12* (first 12 N-terminal amino acids), comprising the acetyl group, is inactive as an elicitor but acts as a specific antagonist for EF-Tu–related elicitors. EF-Tu is recognized by the *LRR-RLK EF-TU RECEPTOR* (*EFR*) of the same subfamily (*LRRXII*) as *FLS2* [34]. Interestingly, the ability to perceive *elf18* epitope seems restricted to the plant family *Brassicaceae*. However, heterologous expression of *EFR* in the Solanaceae family, e.g., *N. benthamiana* and *Solanum lycopersicum*, makes them more resistant to a range of phytopathogenic bacteria, suggesting that *EFR* can be as well used to engineer broad-spectrum disease resistance in other families [35]. More recently, *EFa50* central region comprising *Lys176* to *Gly225* was found to be fully active as a PAMP in rice and induced H_2O_2 generation and callose deposition [36]. Moreover, *AtEFR*-transformed rice plants were shown to be well responsive to the *Xanthomonas oryzae* derived *elf18* peptide by strongly inducing ROS burst and expression of *OsPBZ1* in transgenic cell cultures [37], further suggesting that *EFR* confers stable resistance across plant families.

The mechanism of *EFR* resistance is mediated by heteromeric complex formation. For instance, in rice, the complex formed between *SOMATIC EMBRYOGENESIS RECEPTOR KINASEs* (*OsSERK2;* an ortholog of *BAK1*) and *XA21* binding protein 24 (*XB24*) is the most important component of *XA21*-mediated defence response. Four *SERK* co-receptor-like kinases interact with *EFR* within seconds to minutes of ligand binding [38], and once the ligand is perceived, *EFR* is rapidly phosphorylated, which triggers downstream signal activation, including the activation and release of *BIK1*. *BIK1* plays a central role in conveying signals, as discussed before (see discussion on flagellin-induced resistance). Interaction between *EFR* and *SERK* also triggers the activation and release of other members of the cytoplasmic receptor-like kinase subfamily VII from the complex. Downstream components of these responses include activation of a RING finger ubiquitin ligase (*XB3*), *MAPKs*, the plant-specific ankyrin-repeat (PANK) containing protein *XB25*, and *WRKY* TFs.

Notwithstanding the *FLS2* and *EFR* PRRs identified so far, relatively fewer PRR genes have been utilized to enhance plant resistance to bacterial pathogens through breeding and transgenic approaches [37], except a few that have been shown to be better adapted to defence signalling. The most famous example is that of *Xa21* gene transferred from *Oryza longistaminata*, which confers high resistance to *X. oryzae* in rice [39]. Heterologous expression of *XA21* in *Citrus sinensis*, *Lycopersicon esculentum* and banana (*Musa* sp.) also conferred moderate resistance to *Xanthomonas axonopodis pv. citri* and resistance to *Ralstonia solanacearum* and *Xanthomonas campestris pv. malvacearum* in experiments under controlled conditions [40–42]. The tomato *RLP Ve1*, which recognizes *Ave1* from *Verticillium dahliae race 1* is another interclass example that confers stable resistance when transferred and expressed in Arabidopsis for use as a model genetic system [43]. Taken together, *XA21* and *Ve1* are an example of

engineered resistance strategy under controlled conditions, despite their taxonomic restrictions. However, more PRRs recognizing conserved molecular signatures in bacteria will need to be discovered and their complex interaction with the plant's physiology and metabolism and the environment understood, if the ambition of improving crop plants through genetic engineering of broad-spectrum disease resistance by gene transfer is to become more convincing.

3.1.1.3. Plant perception of PAMPs from fungi and oomycetes

Chitin, a homopolymer of β-(1,4)-linked N-acetylglucosamine (GlcNAc) unit, is a major constituent of fungal cell walls and is a classical PAMP [17]. Chitin is an ideal point of attack during plant defence responses since glucosamine polymers are not found in plants. Upon pathogen contact with the host, plant chitinases (hydrolytic enzymes) break down microbial chitin polymers. Interestingly, different plants have evolved mechanisms that employ common factors for chitin perception, and this could be probably the reason for the evolution of pathogen counter measures, e.g., in the biotrophic fungal pathogen *Cladosporium fulvum* [44]. In this context, the reaction of tomato with induction of defense-related, signal transduction and transcription genes to external chitin application supports the role of the described mechanisms [202].

The first chitin-binding PRR was identified in rice as the *lysine motif* (*LysM*)-*RLP*, and was named *chitin*-elicitor *binding* protein (*CEBiP*) [45]. *CEBiP* is a glycoprotein that localizes in the plasma membrane. Upon chitin binding, *CEBiP* homodimerizes and forms a hetero-oligomeric complex with the *Chitin Elicitor Receptor Kinase 1* (*OsCERK1*), the rice ortholog of Arabidopsis *AtCERK1*. The binding thus forms a sandwich-type receptor system for chitin as described in [45, 46]. The mechanism of perception, however, varies between plant species. For example, *AtCERK1* does not seem to employ *CEBiP*-like *LysM-RLPs* to induce typical immune responses such as reactive oxygen species and immune gene expression upon chitin perception [47]. Instead, *AtCERK1* binds directly to octamers of chitin, which in turn induce *AtCERK1* homodimerization and the resultant immune signalling [48]. Arabidopsis *LysM (AtLYM2)*, the closest ortholog of *AtCEBiP*, and the rice *LysM RLPs* (*OsLYP4* and *OsLYP6*) are also able to bind chitin [49]. However, it is not clear whether *AtLYM2*/*LYK4* also display the putative homodimerization induced by chitin perception. Two other orthologs of *CEBiP*, *AtLYM1* and *AtLYM3*, which specifically bind *PGN,* but not chitin, interact with *AtCERK1*. This indicates that *AtCERK1* is a multifaceted *RLK* that also forms hetero-oligomeric complexes with ligand-binding *RLPs*, probably across different plant families.

Fungal xylanases also function as fungal PAMPs by eliciting defence responses and promoting necrosis [50, 51]. In tomato, ethylene-inducing xylanases (*EIXs*) produced by *Trichoderma* species are perceived by two specific LRR-RLPs receptors, *LeEix1* and *LeEix2* [52]. Both receptors bind *Eixs*, but o*LeEix2* is the primary mediator of defence responses. *LeEix1* heterodimerizes with *LeEix2* upon application of the *Eixs* and attenuates *Eix*-induced internalization and the subsequent signalling of the *LeEix2* receptor [53]. Microbial xyloglucan-specific endoglucanases (XEGs) have also been reported to induce plant defences. Fungal XEGs are inhibited by xyloglucan endoglucanase inhibiting proteins (*XEGIPs*), which so far have been characterized in tomato, carrot and tobacco [54, 55].

http://dx.doi.org/10.5772/64351

Other PRRs that have been identified in plants in response to fungal PAMPs include the *Brassica napus LepR3/Rlm2,* for blackleg resistance, which perceives *AVRLM1* [56]. In *Arabidopsis, Rlm2* interacts with *suppressor of BAK1-interacting receptor-like kinase 1* (*AtSOBIR1*), suggesting that *SOBIR1* is a component of LRR-RLP-mediated resistance against *Leptosphaeria maculans,* which is similar to that formed by rice *OsCERK1 and* Arabidopsis *AtCERK1* [57]. The tomato *Cf* proteins (*Cf2*, *Cf4* and *Cf9*) that recognize the corresponding effector proteins (*Avr2*, *Avr4* and *Avr9*) secreted by *C. fulvum* are other PRR-like receptors that were previously identified. *Cf4* interacts with *BAK1* in a manner similar to the rice ligand binding and associated receptor *OsSERK/EFR*.

Wheat and Arabidopsis *RLP1.1* and *RLP30* are also involved in antifungal defence, although the corresponding ligands are unknown so far [58]. Several orphan PAMPs with unknown PRRs, from fungi or oomycetes that can trigger immune signalling have also been identified, including fungal ergosterol [59], oomycete arachidonic acid [60], elicitins (*INF1*) [61], the transglutaminase-derived immunogenic epitope *Pep13* [62], cryptogein [63] and cellulose-binding elicitor lectin (*CBEL*) [64]. Thus, further research is required to understand mechanistically how these orphan PAMPs are involved in PTI.

Taken together, the identification of several potential host plant receptor targets and receptor complexes, and their stability across plant species and in the field will greatly help to improve plant protection. Moreover, identification of several potential microbial molecules that act as PAMPs would increase chances of identifying more potential host plant PRRs for developing crops with higher resistance or inducible resistance.

3.1.1.4. Plant perception of virus PAMPs

Although viral patterns inducing PTI are well known from animal systems, there is no similar pattern reported for plants [48]. Instead, plant resistance to viruses is mediated by post-transcriptional gene silencing of viral RNA or ETI. Nevertheless, infection by compatible viruses can also induce defence responses similar to PTI. Typical PTI cellular responses in plant-virus interactions include ion fluxes, ROS production, ethylene, salicylic acid (SA), MAPK signalling and callose deposition, for review see [65]. Commonly reported genes associated with PRRs in response to viruses include *PEPs* that encode longer peptides (*ProPEP*) from which small peptides (*PEP*) are derived. In Arabidopsis, *AtPEP* interact with two DAMP PRRs, *PEP*-receptor 1 (*PEPR1*) and *PEPR2* [66], both of which interact with *BAK1* upon recognition of *AtPEP*. Thus, *BAK1* is important for antiviral defence in *Arabidopsis.* Indeed, the *bak1* mutants show enhanced susceptibility to three different RNA viruses (*TMV-U1*, *ORMV* and *TCV*) during compatible interactions [67]. The immune response induced by *PEPR-BAK1* interaction is a classical PTI. Another viral resistance mechanism, which is highly similar to *BAK1* and *BAK1-like Kinase 1* (*BKK1*), is exhibited by the viral nuclear shuttle protein (NSP)-interacting kinases (*NIKs*) from leucine-rich repeats containing receptor-like serine/threonine kinase (LRR-RKs) subfamily [68].

Recent reviews have also suggested that the ribonuclease III-type DICER-like (DCL) enzymes could be acting as PRRs perceiving viral nucleic acids and triggering immune responses equivalent to the zig-zag model first layer [66]. The virus-derived molecules (e.g., dsRNAs)

act as PAMPs, which trigger PTI and RNA interference (RNAi). However, PTI is typically a form of innate immunity, whereas RNAi induces a form of adaptive immunity. Thus, it is clear that a lot remains to be discovered to prove that virus-derived molecules trigger PTI.

3.1.1.5. Plant perception of insect PAMPs

Molecular recognition via ligand-receptor binding phenomena is increasingly becoming important in insect-plant interactions [69]. As reported earlier, the concept of PAMPS has been expanded to include herbivore-associated molecular patterns or damaged-self compounds produced after insect attack [70]. HAMPs isolated and characterized to date include components found in insect oral secretions (proteins, fatty acid-amino acid conjugates (FACs), sulphur-containing fatty acids, as well as plant-derived molecules generated following insect herbivory, including degradation products of ATP synthase and cell walls [71, 72]. The insect oral secretion molecules are released by chewing insects and have been reported to induce ion imbalances, variations in membrane potential, changes in Ca^{2+} fluxes and the generation of reactive oxygen species (ROS), which stimulate downstream signalling events in plants [73]. Ca^{2+} influx is obviously preceded by the opening of calcium channels, and it is likely that these channels are associated with plant receptors tuned to insect elicitors. Recently, a mechanism similar to PTI was reported in Arabidopsis in which LRR-RK *BAK1* was shown to contribute to innate immunity against aphids [69]. Moreover, application of synthetic FACs on wounded *N. attenuate* leaves strongly induced *MAPK* activity, and subsequently wound-induced modifications in the transcriptome, proteome and defensive secondary metabolites [74, 75]. Insect egg ovipositional fluids have also been shown to induce plant defences [76, 77]. Moreover, insect egg deposition on one leaf could induce volatile emission in the other egg-free leaves [77], suggesting that SAR could be involved after detection of insect eggs' associated molecules. An interesting example was reported in the oviposition by *Pieris brassicae*, which triggered SA accumulation and the subsequent induction of PAMP responsive gene expression associated with lectin-domain RK (*LecRK*), *LecRK-I* [78]. Correspondingly, expression of the defence gene *PR-1,* which requires *EDS1*, *SID2* and *NPR1*, was also detected, implicating the SA pathway downstream of the insect egg recognition.

Another mechanism that is closely related to the PAMP receptors in plant resistance to insects is the *Mi-1* gene in tomato. The induction of *Mi-1* confers resistance to *Macrosiphum euphorbiae* [79]. A receptor-like kinase gene *OsLecRK* in rice, which confers basal resistance to *Nilaparvata lugens*, was recently suggested to be a PRR that recognizes molecules secreted by these insects [80]. A similar mechanism was demonstrated in aphid infestation of *Arabidopsis* in which the immune response was apparently triggered by infiltration of aphid saliva [81]. Consistent with this, infiltration of whole aphid extract from *M. persicae* was reported to activate PTI-like responses in *Arabidopsis* [69, 82].

This notwithstanding, the insect HAMP-receptor binding phenomenon that allows plants to detect insects still remains less clear as to whether these responses are exclusively due to the specific perception of herbivores or due to different damage patterns or both.

3.1.1.6. Infection self-perception DAMPs

As discussed before, plants can also sense self-molecules called damage-associated molecular patterns that are available for recognition only after cell/tissue damage. The striking similarities of DAMP perception in animals and plants have been reviewed [83]. A perfect example that was discussed earlier is the *Arabidopsis* plasma membrane LRR receptor kinase (LRR-RK), designated *PEPR1*/*PEPR2*, which perceives *AtPep* peptides derived from propeptide (Pro-PEPs) encoded by a seven-member multigenic family (*Pep1-Pep7*). Both *PEPR1* and *PEPR2* were reported to be transcriptionally induced by wounding, treatment with methyl jasmonate, *Pep* peptides and pathogen-associated molecular patterns [64, 84]. Moreover, *AtPep* perception is part of a PTI amplification loop and is important for the induction of systemic immunity [85]. In another example, hydroxyproline-containing glycopeptides (*HypSys*) and rapid alkalinization factor (*RALF*) peptides have been shown to induce an *MAPK* cascade in tomato cells [86]. The precursors of *HypSys* and *RALF* are constitutively present in the plant cell walls [14]. Microbial proteases or intracellular proteases release these peptides upon cell injury, making then to act as DAMPs.

Cell wall components derived from the enzymatic activity of highly specific microbial homogalacturonan (HGA) is another good example of DAMPs [87]. The enhanced production of oligogalacturonic acid (OGA) fragments from plant cell walls potentially acts as DAMP, which are perceived by receptors such as *RLK THESEUS1* (*THE1*), *ER* and *WAK1*. Plants may also rely on the recognition of cell wall degrading enzymes (CWDEs) by LRR-RLPs receptors, e.g., *RBPG1* and *LeEIX1-2* [88]. A decisive role of the composition and structure of plant cell wall polysaccharides, specifically of side chains of pectic polysaccharides, in elicitation of plant defence has also been described in tomato interaction with a bacterial pathogen, *R. solanacearum* [89, 90, 203]. Thus, studying the expression of endogenous molecules and microbial cell wall degrading enzymes and their inhibitors, e.g., polygalacturonases (PGs) and polygalacturonase-inhibiting proteins (PGIPs) [204] is a valuable approach to understanding the dynamics of plant-pathogen interactions as well as to develop a strategy to improve plant protection using induced plant endogenous molecules.

3.2. Effector-triggered immunity (ETI)

ETI (formerly called *R*-gene-mediated or vertical resistance) is based on the highly specific, direct or indirect interaction of pathogen effectors and the products of plant *R* genes according to the gene-for-gene theory [14]. As discussed before, R genes encode proteins of the intracellular nucleotide-binding leucine-rich repeat (NB-LRR) class [10]. The NB-LRR consist of N-terminal effector domain, central NB domain and C-terminal LRR domain, which largely vary in plants [91]. Two major subgroups that have distinct N-terminal domains are generally recognized: (1) one group with a Toll–interleukin 1 receptor (*TIR*) domain are called TNLs, and (2) those with a coiled-coil (CC) domain are called CNLs [92].

In Arabidopsis, the CNLs functionally interact with the glycosylphosphatidylinositol (GPI) anchored protein—*NON-RACE SPECIFIC DISEASE RESISTANCE 1* (*NDR1*), a positive regulator of SA accumulation, for signalling [93, 94]. Indeed, an *ndr1* mutation compromises resistance conferred by the CC-NBS-LRR proteins *RPS2*, *RPM1* or *RPS5* to *P. syringae* express-

ing the avirulence effectors *avrRpt2*, *avrB* and *avrRpm1*, or *avrPph3*, respectively [95]. In contrast, multiple TNLs functionally associate with *ENHANCED DISEASE SUCEPTIBILITY 1* (*EDS1*) and *PHYTOALEXIN DEFICIENT 4* (*PAD4*) for signalling. For instance, resistance conferred by the TIR–NBS–LRR protein *RPS4*, which recognizes *avrRps4* in *P. syringae* is compromised in *eds1* mutants [96]. However, resistance mediated by some R genes is independent of *EDS1*/*PAD4* and *NDR1* or require additional co-activating proteins, suggesting existence of additional components for signal transmission during plant-pathogen interaction. Some of the regulatory components functionally associated with R genes for an effective HR mediated resistance include *RAR1* (required for *Mla12* resistance) and *SGT1* (suppressor of the G_2 allele of *skp1*) proteins [97]. *RAR1* interacts with the N-terminal half of *HSP90* that contains the ATPase domain. *HSP90* also specifically interacts with *SGT1* that contains a tetratricopeptide repeat motif and a domain with similarity to the co-chaperone *p23* [98]. These observations suggest that R proteins require several co-activating proteins, although distinct downstream signalling pathways could be involved. There are also some NLRs containing N terminus other than the classical TIR and CC, either because their protein structures are not validated or due to lack of significant homology; they are referred to as non-TIR-type NLRs (nTNLs) or generally referred to as NLRs. Further work on non-sequenced genomes is likely to expand the number of NLRs, and probably refine functional difference associated with NLR repertoires.

Regardless of the NLR class, NB-ARC domain is the core nucleotide-binding fold in NB-LRR proteins. Four distinct subdomains constitute the NB-ARC domain, including nucleotide-binding (NB) fold and *ARC1, -2* and *-3* subdomains. *ARC1* is a four-helix bundle, *ARC2* is a winged-helix fold and *ARC3* is a helical bundle [99]. *ARC1* and *ARC2* are conserved in *Caenorhabditis elegans CED-4*, and plant NB-LRR R proteins, whereas *ARC3* is absent [99]. Throughout the NB-ARC domain in R proteins, numerous conserved motifs (e.g., *hhGRExE*, Walker A or P-loop, Walker B, GxP, *RNBS-A* to *D* and *MHD*) have been reported [100]. A mutation in these conserved motifs has shown their functional importance in the NB-LRR proteins [101], and is apparently a critical factor determining R gene functional effector recognition pattern differences. Generally, pathogen effector recognition by NLR and NLR expression are broadly characterized into (1) direct NLR-Effector interaction or (2) indirect NLR indirect surveillance of effector activities.

3.2.1. Direct NLR-effector interaction

NLRs maintain an ADP-binding inactive state in the absence of effectors. The binding of effectors induces conformational changes in NLRs, which allow ADP/ATP exchange. Consequently, the exchange of nucleotides triggers a second conformational change that activates the NB-LRRs' N-terminus (TIR or CC) to interact with and trigger downstream target processes [102]. However, there is no substantial evidence on direct NLR-effector interaction that underlies resistance specificity in the NLR-effector combinations, apart from the yeast two-hybrid (Y2H) and *in vitro* interaction assays [103, 104]. A few examples that attempt to show the NLR-effector interaction include the Arabidopsis NLR *RPP1* recognition of the oomycete effector *ATR1* leading to *Hyaloperonospora arabidopsidis (Hpa)* resistance [104]. Both the *RPP1*

receptor and *ATR1* alleles from *Hpa* strains can be diverse. This diversity contributes to a spectrum of resistance phenotypes and effectors. For instance, the recognition specificity of *RPP1-WsB* (from the Wassilewskija ecotype) and *RPP1-NdA* (from the Niederzenz ecotype) vary. The *RPP1-NdA* recognizes a small subset of the *ATR1* alleles recognized by *RPP1-WsB*, while the *RPP1-WsB* associates with the cognate *Hpa* effector protein, *Atr1*, through its LRR domain in a recognition-specific manner [105]. Another example is the Arabidopsis NLR *RRS1*, a domain with sequence similarity to *WRKY* TFs, positioned after the LRR. The cognate effectors *AvrRps4* and *PopP2* directly interact with this *WRKY*-like domain to activate the downstream resistance components [106].

Together, the different R proteins have functional domains that can occupy different positions in NLRs. The functional domain positioning differences could be the reason behind several R genes that have been identified in plants. For instance, in rice more than 100 NLRs encoding genes have been described to confer resistance to strains of *Magnaporthe oryzae* [107]. However, only few R proteins encoded by these genes have been characterized, which limits their deployment. A well-known structure for the recognition of *M. oryzae* effectors is that of *AVR-Piz-t*, which adopts a six-stranded β-sandwich structure and contains a single disulphide bond [108]. The *AVR-Pia* and *AVR1-CO39* have also been reported to be recognized by the *R GENE ANALOGs (RGA4/RGA5)* NLR pair [109, 110] through direct binding to a Heavy-Metal Associated domain (HMA; also known as RATX1) integrated into *RGA5* after the LRR position. *RGA4/RGA5* physically interact to prevent cell death mediated by *RGA4* in the absence of *AVR-Pia*; the presence of the effector relieves this suppression, and induces cell death response, a mechanism that could also be described as indirect NLR surveilance. More recently, Maqbool et al. [111] also found that recognition of *AVR-Pik* by *Pik* is by direct binding to the *HMA* domain of *Pik-1*. However, the positioning of the *HMA* domain between the CC and NB-ARC region of *Pik-1* and after the LRR in *RGA5* is a striking difference between *Pik-1* and *RGA5.* These conformational changes underlying direct effector binding could be causing immunity-related signalling differences. However, the intra- and/or inter-molecular complexes mediating output may be conserved [111].

3.2.2. Indirect NLR surveillance of effector activities

During indirect recognition, the NLR guards the host protein by recognizing (monitoring) the modifications caused by the pathogen effector on the guarded protein [10]. The guarded protein can either be the actual effector virulence target or a decoy inviting modification by the pathogen. An example of the indirect recognition of effectors by NLRs was demonstrated in the conserved Arabidopsis protein *RPM1*-interacting protein 4 (*RIN4*). *RIN4* is targeted by multiple bacterial effectors, e.g., *AvrRpt2*, *AvrRpm1* and *AvrB*, and is monitored for effector-induced modification by two plasma membrane CNL receptors, *RPM1* (resistance to *P. syringae* pv. *maculicola 1*) and *RPS2* (*resistance to P. syringae 2*) [112]. *AvrB*-induced phosphorylation and cis/trans isomerization coupled with conformational changes in *RIN4* are sensed by *RPM1* to activate immune signalling [112, 113]. *AvrRpt2*, being a cysteine protease, cleaves *RIN4* and induces *RIN4* degradation. In the absence of *RPM1* and *RPS2*, *RIN4* acts as a negative regulator of basal resistance, and in that capacity appears to be targeted for manipulation by multiple bacterial effectors [114].

The functioning of NLRs as genetically tightly linked pairs to deliver disease resistance was also recently reported [115]. Moreover, Williams et al. [116] demonstrated, by coupling crystal structure and functional analyses, that *RPS4* and *RESISTANT TO RALSTONIA SOLANACEARUM 1* (*RRS1*) TIR domains form homo- and hetero-dimers through a common conserved interface that includes a core serine-histidine (SH) motif. Transient expression assays in tobacco revealed that the *RPS4* TIR domain triggers an effector-independent cell death, which is dependent on the SH motif. Co-expression of the *RRS1* TIR domain and *RPS4* TIR impedes the auto-active cell death caused by *RPS4* TIR, and this was found to be dependent on the *RRS1* SH motif. This suggests that an inactive *RRS1*/*RPS4* TIR hetero-dimer and the formation of an active *RPS4* TIR homo-dimer compete to modulate signalling. As discussed before, Cesari et al. [109] investigated the mode of action of *RGA 4* and *5* that associate through their coiled-coil domains. *RGA4* and *RGA5* are tightly linked rice CC-NLRs, which functionally interact to modulate resistance to the rice pathogen *M. oryzae*. *RGA5* modulates an effector independent cell death constitutively induced by *RGA4* signalling. *RGA5* domain on the C-terminus has a heavy-metal-associated domain, which is related to the cytoplasmic copper chaperone *ATX1* from *Saccharomyces cerevisiae* (*RATX1* domain). This domain is an *AVR-Pia* effector interacting domain in *RGA5*. Thus, the formation of the *RGA4*/*RGA5* hetero-complex is crucial to regulate *RGA4* activity in the absence of pathogen in rice. Hence, *RGA4* acts as a signalling component regulated by its interaction with *RGA5* that acts both as a repressor and a receptor that directly binds the *AVR-Pia* proteins. The apparent striking similarity between the *RPS4*/*RRS1* and the *RGA4*/*RGA5* functional models suggests that similarities are likely to be frequent between the different R genes present in dicots and monocots.

3.2.3. Patterns of NLRs signalling in plant defence

Most NLRs respond to the presence of proteins (effectors) delivered by adapted pathogens/parasites. Using suppressor screens, Gabriels et al. [117], identified *NRC1* (*NLR protein required for HR-associated cell death 1*) as a component of fungal resistance modulated by the tomato plasma membrane receptor-like resistance protein *Cf-4* (*C. fulvum 4*). *NRC1* mediates resistance and cell death induced by both membrane receptors and intracellular NLRs. This indicates that *NRC1* is probably a downstream convergence point in ETI initiated at various cell locations. Indeed, silencing of *NRC1* in *N. benthamiana* impairs the HR mediated by several other R proteins including two NLRs, *Rx* and *Mi*. Members of a conserved class of non-canonical CNLs also function in ETI, downstream of NLR effector recognition and have been designated as helper NLRs [118]. Characterization of these non-canonical CNLs is required in order to track their interaction networks.

The downstream components of ETI signalling events partially overlap with PTI response, including activation of *MAPK* cascade and activation of TFs such as *WRKYs* [119]. In Arabidopsis, three CNLs—*activated disease resistance 1* (*ADR1*), *ADR1-L1* and *ADR1-L2*—transduce signals that lead to SA accumulation and induction of downstream *WRKYs* modulated resistance [118]. In rice, the CNL receptor, *panicle blast 1* (*Pb1*), also appears to mediate resistance against rice blast in a mechanism involving interaction with *WRKY45*, a TF involved in induced resistance via SA signalling pathway [120]. Some CNLs directly translocate or

localize in the nucleus to activate defence [121], e.g., *barley mildew A 10* (*MLA10*) and Arabidopsis *RPS4* and *RPS6*. In the nucleus, *MLA10* interacts with *Hordeum vulgare* (Hv) *WRKY1/2*, which are suppressors of basal defence, during incompatible interaction with powdery mildew fungus. A CNL designated as *MLA1*, also from barley, functions in Arabidopsis against *Blumeria graminis* f. sp. *hordei* (*Bgh*) [122]. The *MLA1*-triggered immunity, including host cell death response and disease resistance, is fully retained in Arabidopsis mutant plants that are simultaneously impaired in well-characterized defence-phytohormone pathways (ET, JA and SA). Similar to *MLA1*, co-acting Arabidopsis TNL pair, *RPS4* and *RRS1* (which encodes a WRKY DNA binding domain), confers resistance in cucumber, *N. benthamiana*, and tomato [122].

Another example supporting our understanding of the NLR nuclear activity is the interaction of N immune receptor with the TF *SQUAMOSA PROMOTER BINDING PROTEIN-LIKE 6* (*SPL6*) in *N. benthamiana* [123]. The N immune receptor is present in the nucleus, and confers resistance to tobacco mosaic virus (TMV) infection. N receptor associates with *SPL6* at the subnuclear bodies only when the cognate effector, *p50*, is present in the cell. A genetic requirement for *SPL6* was not only shown in *N. benthamiana* for N-mediated disease resistance using the yeast two-hybrid system, but also in *A. thaliana* for *RPS4* immune receptor mediated defence against *P. syringae* pv. *tomato* expressing *AvrRps4* effector. Moreover, a number of *RPS4*-mediated defence responsive genes were differentially regulated upon *AtSPL6* silencing, including some of the previously characterized defence responsive genes such as *PAD4*, *PR1*, *ALD1*, *AIG1*, *NUDT6* and *FMO1*. Additional evidence has been shown in Arabidopsis *RPW8* resistance protein, which encodes truncated CNL-like proteins conferring resistance to powdery mildews in *N. tabacum* and *N. benthamiana* as in Arabidopsis. *RPW8* requires SA, *EDS1*, *NPR1* and *PAD4* to be effective. The functional role of *RPW8* is typically similar to a TNL *ADR1*, a close homolog of *N Requirement Gene 1* (*NRG1*), which functions in and beyond innate immunity [124]. These findings present a unique opportunity to further understand how effector-activated immune receptors directly associate with TFs in the nucleus to activate immune responses. Overall, a resistance signalling framework appears to have emerged for plants in which certain specificity-determining (sensor) NLRs initiate the immune response and either auto-activate and contribute to defence or compliment with other signalling NLRs to contribute to defence by conveying or amplifying the signal.

4. Phytohormones in plant defence response to pathogens and insects

Plant defence against pathogen/herbivore attack involves many signal transduction pathways that are mediated by a network of phytohormones. Phytohormones also play a critical role in regulating plant growth and development. Three most reported plant defence response phytohormones against pathogens/insects include salicylic acid (SA), jasmonic acid (JA) and ethylene (ET) [125]. Salicylic acid, a benzoic acid derivative, is an extensively studied important phytohormone in the regulation of plant defence [13]. In Arabidopsis, activation of the SA pathway has been shown to be important in both basal and R gene mediated biotrophic and hemibiotrophic pathogen defence [126, 127]. As discussed before, *NDR1* and *EDS1* act

upstream of SA, while the downstream pathway is modulated by *NONEXPRESSOR OF PR GENES 1* (*NPR1*), and *WRKY45* in rice. *NPR1* is a transcriptional co-activator of a large set of defence-related genes downstream of SA, and it can conditionally regulate *PDF1.2* expression following treatment of plants with SA and MeJA [128]. SA also contributes to the HR-associated resistance via mechanisms that interact with *RBOHD*, a catalyst in ROS generation and cell death [128]. In tobacco, SA significantly increases in resistant plants infected with TMV [129]. A similar response was observed in Ny-1-resistant potatoes after infection with Potato virus Y (PVY) [130].

In response to insect attack, SA regulates plant defence signalling against aphids by modulating the activity of *PAD4*. Indeed, *pad4* mutants, with compromised SA signalling, have increased susceptibility to *Myzus persicae*. Correspondingly, there is a correlation between *pad4* susceptibility and a delay in aphid-induced senescence [131], indicating that SA defence pathways are compromised in *pad4* mutants. Basal SA defences have also been shown to decrease *M. euphorbiae* longevity in tomato. Moreover, SA is necessary for *Mi1.2*-mediated resistance to potato aphids [132]. SA is also a key derivative of SAR in plants. SAR is a 'whole-plant' broad-spectrum resistance response that occurs following an earlier localized exposure to a pathogen [133]. It is well known that ETI can trigger SAR through both local and systemic synthesis of SA, resulting in transcriptional reprogramming of a battery of genes encoding PR proteins [133, 134]. The reports published so far point to different compounds as potential SAR signals [135]. A change in amino acid homeostasis is one of the suggested components in SAR mediated by ETI [136]. Moreover, amino acids have been reported to be precursors of a large array of plant secondary metabolites involved in defence, including signal SA, cell wall components and anthocyanins. Further evidence on the involvement of amino acid homeostasis in plant defence was reported in Arabidopsis *agd2-like defence response protein 1* (*ald1*) mutants. Characterization of the Arabidopsis *ald1* suggested that an amino acid–derived defence signal was generated upstream of SA synthesis [135]. These findings reveal that plants likely employ amino acids and their derivatives to rapidly reprogram SA synthesis and cellular transcription in order to cope with pathogen invasion, even though it appears to be at the expense of growth and development.

SA also interacts with other phytohormones either synergistically or antagonistically [137–138]. There is an obvious cross-talk between JA and SA signalling pathways in pepper to control thionin synthesis as part of the PR response and other defence pathways [139]. Other synergistic examples include the treatment of *N. benthamiana* plants with JA or SA, which was shown to enhance systemic resistance to TMV [140]; Ellis et al. [141] have also shown that SA- and JA-signalling pathways are required to accomplish the defence response necessary to avert pathogen attack. More recently, Arabidopsis mutants with constitutive SA responses were reported to require JA and ethylene signalling for SA mediated resistance [142]. A dominant mutant named *suppressor of SA insensitivity* (*ssi1*), which has constitutive expression of *PR* genes and is resistant to *P. syringae*, was also shown to constitutively express *PDF1.2* and accumulate elevated levels of SA [143]. Although this finding may be intriguing, because SA does not normally induce *PDF1.2* in wild-type plants, it suggests the existence of an intricate signalling network involving SA and JA. Another mutant named *constitutive PR 5 (cpr5*) was shown to

have SA-mediated *NPR1*-independent resistance, which apparently required components of the JA and ET signal pathways [144]. The pre-treatment of plants with JA followed by SA was also shown to remarkably enhance resistance more than otherwise. Moreover, plants impaired in the JA pathway fail to accumulate SA in the leaves or phloem and become highly susceptible to TMV [145]. Conversely, impairing the SA pathway does not affect JA levels, although increased susceptibility is observed [141, 146]. During infection by the pathogen *P. syringae* pv. *tomato* (Pst) DC3000/*AvrRpm1*, JA as a systemic signal for SAR, increases significantly 6 hours after infection and returns to normal 11 hours after infection [147], which suggests that JA may be transiently required for SA accumulation. Further evidence indicates that SAR is compromised in JA-insensitive mutants, *sgt1b*/*jai4*, *opr3* (JA-biosynthesis mutant) and *jin1* (JA-response mutant). The JA-biosynthesis mutants *dde2* and *opr3* as well as the downstream signalling mutants *coi1*, *jar1* and *jin1*, though intact in SAR, partially require JA biosynthesis for an effective resistance response [148]. Thus, it is possible that JA probably modulates early components of the SA biosynthetic or signalling pathway. However, it seems likely that the synergistic mechanisms may require not only SA and JA, but also ethylene [149, 150], considering that *cpr5* phenotype is suppressed by the *ethylene-insensitive* (*ein2)* mutation.

The negative crosstalk between SA and JA/ET pathways is probably modulated by *TGA1A-RELATED GENE* (*TGA*) factors. *TGA* class of *bZIP* TFs are repressed by plant-specific glutaredoxins (e.g., *ROXY19*), which are in turn induced by SA. Co-expression of *ROXY19* with *OCTADECANOID-RESPONSIVE ARABIDOPSIS AP2/ERF-domain protein 59* (*ORA59*) and *ETHYLENE INSENSITVE 3* (*EIN3*) complex suppresses *ORA59* promoter activity. Moreover, a study by Van der Does et al. [137] indicated that SA negatively regulates *ORA59* protein accumulation in *35S:ORA59-GFP* overexpressing plants. *ORA59* is a transcriptional regulator of JA/ET-induced defence genes and is activated by either JA or ET and suppressed by SA. More recently, *TGA2*, *TGA5* and *TGA6* were shown to activate the SA-suppression of ET-inducible defence by regulating *ORA59* expression [150]. This suggests that SA-suppresses JA/ET-inducible defence by interfering with *ORA59* activity through regulation of *ROXY-TGA* interaction. Conversely, evidence of SA positive regulation of ET was proposed by Guan et al. [151]. These authors have shown that in Arabidopsis, SA modules ET by potentiating MITOGEN-ACTIVATED PROTEIN KINASE6 (MPK6) and MPK3, and involves two 1-aminocyclopropane-1-carboxylic acid synthase (*ACS*; *ACS2* and *ACS6*) isoforms, which are downstream components o MPK signalling pathway. This finding adds another level of complexity to the phytohormones regulatory network and will probably require further elucidation on how this pathway differs from the ORA59 regulated pathway.

On the other hand, most ET dependent defenses are positively modulated by JA. The *JASMONATE ZIM-DOMAIN* (*JAZ*) protein, which directly binds *EIN3*/*EIL1* and recruits *HISTONE DEACETYLASE 6* (*HDA6*) to repress ET responsive transcription, is repressed in the presence of JA. Thus, accumulation of JA degrades *JAZ* and allows the binding of *EIN3* to the *ERF1* promoter resulting in the transcription of *ERF1* [142, 152]. *EIN3* also directly activates the promoter of *ORA59* that regulates JA/ET-activated defence pathway. Studies on microarray analysis of Arabidopsis plants infected with *Alternaria brassicicola* revealed that nearly half of the genes induced by ET are also induced by JA [153]. This was substantiated by Lorenzo et

al. [154] who reported that JA and ET pathways indeed converge in the transcriptional activation of *ERF1*, which encodes a TF that regulates the expression of pathogen response genes. *ERF* TFs have been reported to exhibit different regulatory roles depending on the species. For instance, in wheat *ERF* gene *TaPIEP1*/*TaPIE1,* which belongs to the B3 subgroup within the *ERF* subfamily, confers enhanced resistance to the fungal pathogens, *Bipolaris sorokiniana* and *R. cerealis*, when overexpressed in transgenic wheat [155], whereas in cotton GhERF of group IX, which includes *ORA59*, confer resistance to *Xanthomonas campestris pv. malvacearum*. Because *ERF1* integrates signals from the JA and ET defence signalling pathways, the constitutive expression of *ERF* family members activates the expression of several JA/ET-dependent defence genes and induces resistance against necrotrophic pathogens. For instance, expression of several *PR genes* which confer resistance against several necrotrophs (e.g., *PR3* and *PR5d* and *PDF1.2*) is modulated by *ERFs*. These defence genes possess a GCC box in their promoters, which is a direct target for the action of *ERFs* [156].

Although ET has been shown to regulate plant defence responses against fungi and bacteria, ET is probably not essential in plant resistance against viruses. Recently, 1-aminocyclopropane-1- carboxylic acid (ACC) was shown to enhance *TMVcg* accumulation in treated plants [157], which increased susceptibility, suggesting that ET is required for viral infection.

Other phytohormones, such as ABA, gibberellins (GBs), auxins, brassinosteroids and cytokinins (CKs), have recently emerged as defence regulators [158]. ABA, a sesquiterpene compound resulting from the cleavage of γ-carotene, regulates numerous developmental processes and adaptive stress responses in plants. ABA can positively regulate plant defence at the early stages of infection by mediating stomatal closure against invaders, or inducing callose deposition if the pathogen evades the first line of defence [159]. If activated at later stages, ABA can suppress ROS induction and SA or JA signal transduction, thereby negating defences controlled by these two pathways [160].

Cytokinins promote cell division, and are known to play a role in the synthesis and maintenance of chlorophyll and chloroplast development and metabolism. CKs are also involved in the modulation of defence mechanisms, including the induction of resistance against viruses [161, 162], but are known to suppress HR [163]. Cytokinins can however act synergistically with SA signalling [164]. CKs activate the transcriptional regulator *ARABIDOPSIS RESPONSE REGULATOR 2* (*ARR2*), which positively modulates SA signalling by interacting with the SA-responsive factor *TGA3* [165]. *TGA3* induces the binding of *ARR2* to the promoters of *PR-1* and *PR-2* to induce cytokinin-dependent gene transcription. Correspondingly, the *npr1-1* or *NahG* mutants fail to modulate the induction of *ARR2* when treated with CK, indicating that CK modulates signaling components downstream of SA. Moreover, increased transcription of genes involved in SA-biosynthesis and signalling (e.g., *SID1*, *SID2*, *PR-1* and *PR-5*) is observed in *ARR2* over-expressing mutants challenged with *P. syringae* pv. *tomato* (*Pst DC3000*). Thus, CKs synergistically interacts not only with the SA signaling pathway to boost SA dependent induction of plant defence genes but also modulates SA biosynthesis. Cytokinins have also been shown to enhance the production of two antimicrobial phytoalexins, scopoletin and capsidiol in tobacco plants challenged with *P. syringae* pv. *tabaci* (*Pst*) independent of SA signalling [166]. Moreover, cytokinins induce the expression of cell wall invertase, a key

sucrose cleaving enzyme required for carbohydrates supply through an apoplasmic pathway [167]. Invertase is required for plant defence against pathogens, including *Pst*. The glucose target of rapamycin (*TOR*) signalling pathway involved in autophagy apparently modulates the transcriptional dynamics associated with cytokinin-invertase-induced defence pathway by providing the required energy, metabolites and the cell cycle machinery required for cytokinin signal transduction [168]. The link between autophagy and cytokinin signalling was previously suggested [169], but the cytokinin-induced defence system in this interplay is probably a protective mechanism to maintain plant growth and proliferation despite pathogen challenge [170].

Brassinosteroids (BRs) are a class of polyhydroxysteroids that affect many cellular processes including elongation, proliferation, differentiation, membrane polarization and proton pumping [171]. BRs are increasingly becoming important in plant defence against pathogens. The mechanism underlying BR signalling involves the direct binding of BRs such as BL and castasterone to the LRR-RLK (*BRI1*). This interaction is reported to unlock *BRI1* from the negative regulator *BKI1*, followed by heterodimerization of *BRI1* with a co-receptor *BAK1* and phosphorylation of the *BRI1*-interacting signalling kinase (*BSK1*). Other events include the activation of the protein phosphatase *BSU1*. These biochemical changes inhibit the shaggy-like kinase *BIN2*, which culminates into the activation of the homologous TFs, *BZR1* and *BES1*/*BZR2* [172]. These TFs translocate to the nucleus, interact with BR-responsive promoters, and cause transcriptional changes that eventually lead to defence response. BRs have been demonstrated to enhance plant defence against pathogens. In potato, BRs have been shown to be effective against viral infection from the starting planting materials to the second tuber generation [173]. Furthermore, application of BRs on tobacco plants decreases TMV viral load and restricts infection by other biotrophs [174]. The same authors reported that *BAK1* is essential for plant basal immunity during compatible interactions with RNA viruses. The *BAK1* mutants, *bak1-4* and *bak1-5*, accumulate *turnip crinkle virus* (TCV), *oilseed rape mosaic virus* (ORMV) and TMV to higher levels compared to the WT plants [174]. Thus, *BAK1* could probably be a general regulator of plant defence against biotrophs and hemibiotrophs. BRs have also been reported to interact with other phytohormones, such as GA and auxins, but independent of SA [175]. For details on auxin- and cytokinin-modulated immunity, and GA/BR interaction, the reader is referred to excellent reviews [176, 177]. Furthermore, details on the interaction of BRs and SA, including their effect on SAR marker genes (e.g., *PR-1*, *PR-2* and *PR-5*) can be found in [178].

Taken together, the intricate cross-talk among hormones to cooperate with other signals and to coordinate appropriate induction of defences against pathogens and/or insect pests depends on the pathogen type, physiological stage and environmental and probably circadian regulations.

5. RNAi-mediated plant defence

RNA interference or silencing is one of the emergent crop improvement strategies that involve sequence-specific gene regulation by small non-coding RNAs, which mainly belong to two

categories, i.e., small interfering RNA (siRNA) and microRNA (miRNA). Though these sRNAs differ in biogenesis [179], both regulate the target gene repression through ribonucleoprotein silencing complexes. Plant RNA silencing involves four basic steps, which include introduction of double-stranded RNA (dsRNA) into the cell, processing of dsRNA into 18–25-nt small RNA (sRNA), sRNA 2-O-methylation and sRNA incorporation into effector complexes that interact with target RNA or DNA [180]. The formation of RNA-induced silencing complex (*RISC*) and its incorporation into the antisense strand of siRNAs, which interacts with Argonaute and other effector proteins, precedes the cleavage of the target mRNA. For details about the formation of *RISC* and cleavage of the target mRNA, the reader is referred to comprehensive reviews [179, 181]. For sRNA to meet the target mRNA, it has to move from the point of initiation to the target. Thus, two main movement categories include cell-to-cell (short-range; symplastic movement through the plasmodesmata) and systemic (long-range; through the vascular phloem) movement. These mobile silencing strategies use sRNAs to target mRNA in a nucleotide sequence specific manner. By use of fluorescently labelled 21 and 24-nt siRNAs, Dunoyer et al. [182] demonstrated the movement of siRNAs from cell to cell and over long distances. Such systematic movements enhance systemic silencing of viruses as reported in *N. benthamiana* [183]. Similar systemic movements have been reported in the phloem sap of oilseed rape [184] and pumpkin [185]. Endogenous 21-nt miRNAs (miR399) were also reported to be mobile within the roots [186], and between shoots and roots of rapeseed and pumpkin [187]. Thus, sRNAs can be targeted to most active plant tissues, with transcription activity, to achieve a desirable consequence.

Several RNAi strategies have shown success in plant improvement against biotic stresses. Arabidopsis *miR393* was the first sRNA implicated in bacterial PTI [188], and enhanced *miR393* accumulation was found during sRNA profiling in Arabidopsis challenged with *Pst* [189]. The mechanism of *miR393*-induced resistance involves repression of auxin signalling by negatively regulating the F-box auxin receptors like *transport inhibitor response 1* (*TIR1*). This process restricts *Pst* infection, and, indeed, plants overexpressing *miR393* exhibit effective resistance against *Pst* [188].

RNAi in plant resistance to fungi has also shown promise. For instance, RNAi-mediated suppression of a rice gene *OsSSI2* enhances resistance towards *M. oryzae* and *X. oryzae* [189]. Moreover, RNAi suppression of *OsFAD7* and *OsFAD8,* the two genes encoding for *Ω*-3 fatty acid desaturase, also enhances resistance against *M. oryzae* [190]. RNAi targeting of lignin production pathway genes aimed at reducing lignin content has also been shown to enhance resistance against *Sclerotinia sclerotiorum* in soybean [191]. Increased resistance to *Blumeria graminis* f. sp. *tritici* in wheat was also demonstrated through RNAi using 24 miRNAs [192]. Nevertheless, the performance of these approaches under environmental conditions has often been unsatisfactory and environmental influences in expression of resistance often remain unpredictable [205].

In response to virus infection, several cases have shown successful crop improvement. For instance, resistance to *African Cassava Mosaic Virus* (CMV) was achieved in transgenic cassava plants producing dsRNA against PSTVd sequences [193]. A similar strategy was successful in transgenic tomato resistance against *Potato Spindle Tuber Viroid* (PSTVd) [194]. RNAi targeting

of the virus coat protein has also been successfully engineered into plants to induce resistance against viruses. For instance, transgenic tobacco plants expressing the CP gene of TMV are resistant to TMV. The resistance of *N. benthamiana* to *Cucumber Green Mottle Mosaic Virus* (CGMMV); and that of *Prunus domestica* to *Plum Pox virus* (PPV) are other examples documented; for review see [179].

In functional biology studies, virus-induced gene silencing (VIGS) has emerged to be one of the most powerful RNA-mediated post-transcriptional gene silencing (PTGS), not only in plant protection against viruses, but also for gene knockouts in functional genomic studies [195, 196].

Although RNAi has the potential to contribute to increased crop productivity, by generating crops with improved resistance against pests and diseases, it would be even better if interaction between sRNAs and their targets is validated in several backgrounds. This would provide valuable insight into mechanisms of post-transcriptional gene regulation and multiple molecular pathways controlling plant stress responses. However, the danger of unintentional silencing of genes with regions of homology to the intended target, and target mutations leading to easier escape from miRNA-directed silencing are still ethical issues. Certain biosafety concerns on the use of RNAi transgenics, especially transcriptional gene silencing by chromatin modification is even a more sensitive and contentious issue, as it is rumoured to lead to hereditary changes associated with adverse effects. Thus, the underlying mechanisms associated with RNAi require further investigations using well-controlled experiments.

6. Modern approaches for improving biotic stress tolerance in plants

Conventional breeding methods still play an important role in the selection of new varieties. However, emerging tools in biotechnology are much needed to maximize the probability of success. One area of biotechnology, molecular marker assisted breeding (MAB), has already made significant impact in improving efficiency of conventional breeding. There are, however, major gaps in the improvement of traits controlled by a large number of small effects, epistatic QTLs displaying significant genotype × environment (G × E) interactions. Thus, accurate indirect selections based on genomic tools that have emerged over the last few decades are continuously being employed to improve the breeding efficiency for such traits. The advantage is that, to date, the genome sequences for more than 55 plant species have been produced and many more are being sequenced [197]. The genome sequence information available enables the identification and development of genomewide markers. Availability of markers covering the whole genomic regions has already shown promise in the development of special populations, such as recombinant inbred lines (RILs), near isogenic lines (NILs), introgression lines (ILs) or chromosome segment substitution lines (CSSLs). Recently, heterogeneous inbred family (HIFs) and multi-parent advanced generation inter-cross (MAGIC) populations, which can serve the dual purpose of permanent mapping populations for precise QTL mapping and for direct or indirect use in variety development, have shown promise in plant breeding. Also, genomewide association (GWA) analysis has been successfully applied to rice, maize, barley, wheat, sesame and other plants. GWA has also been adapted to the "breeding by design"

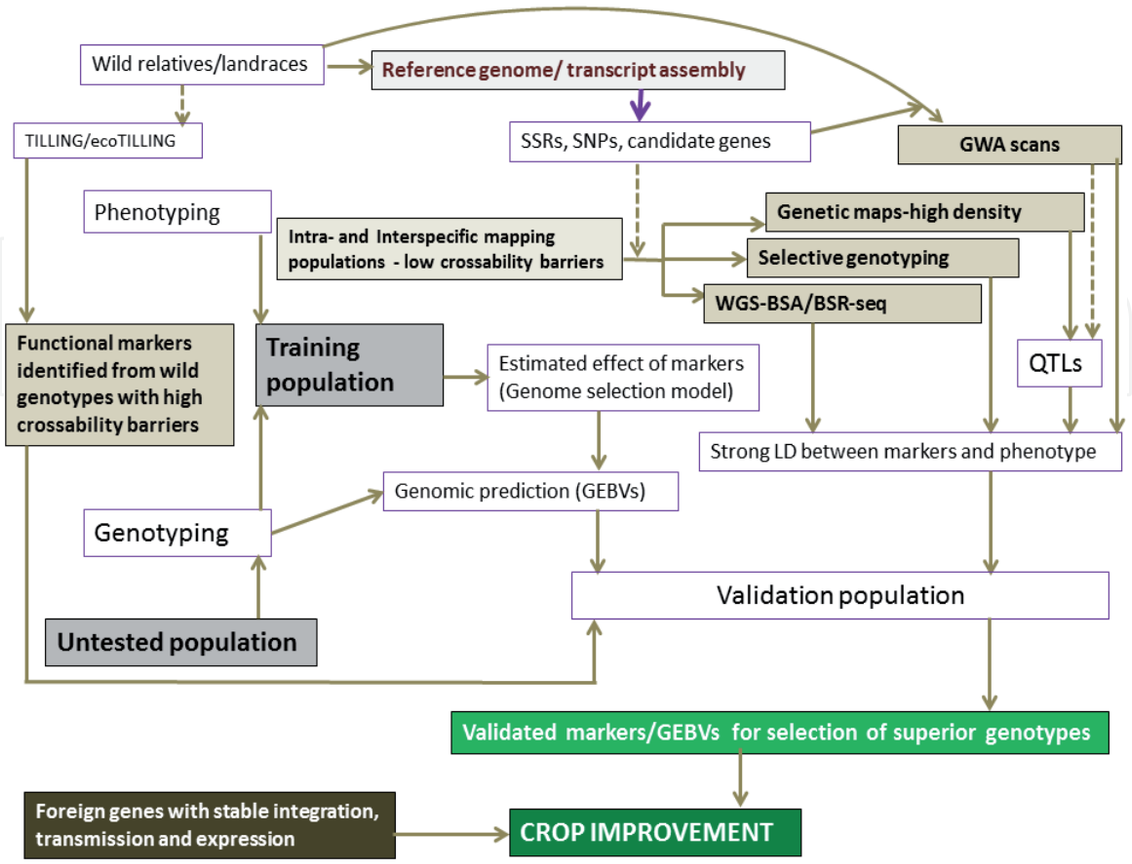

Figure 2. Principle of genomic selection. Two steps are involved; developing a training population to provide phenotypic and genotypic data; effects are estimated for all molecular markers. The second step involves genotyping untested populations and selecting superior genotypes based on their expected phenotypes according to the estimates obtained from the marker effects on the training population (bottom).

approach, often referred to as genome selection (Figure 2), which predicts the outcome of a set of crosses on the basis of molecular markers information.

Recently, a combination of different approaches has been used to develop new rice cultivars referred to as 'Green Super Rice', possessing resistance to multiple insects and diseases, high nutrient efficiency and drought resistance. If fully exploited, the integration of a similar approach with breeding by design or genome selection would help to design new plant types with not only a few selected major loci, but nearly all the functional loci of the genome controlling key desirable traits in commercial cultivars.

Expression studies also present a major area of interest for breeders. Among them, the NGS technologies have become the mainstay of studying complex traits, as direct sequencing of genomes and comparison with reference sequences is increasingly becoming more feasible. Re-sequencing has been performed for model species, e.g., *Arabidopsis*, to understand the whole genome sequence variation, and ultimately discover single nucleotide polymorphisms (SNPs). Similar re-sequencing efforts have been applied in rice, maize, soybean, grape and poplar. Combining re-sequencing with the recent developments in omic biology, including

http://dx.doi.org/10.5772/64351

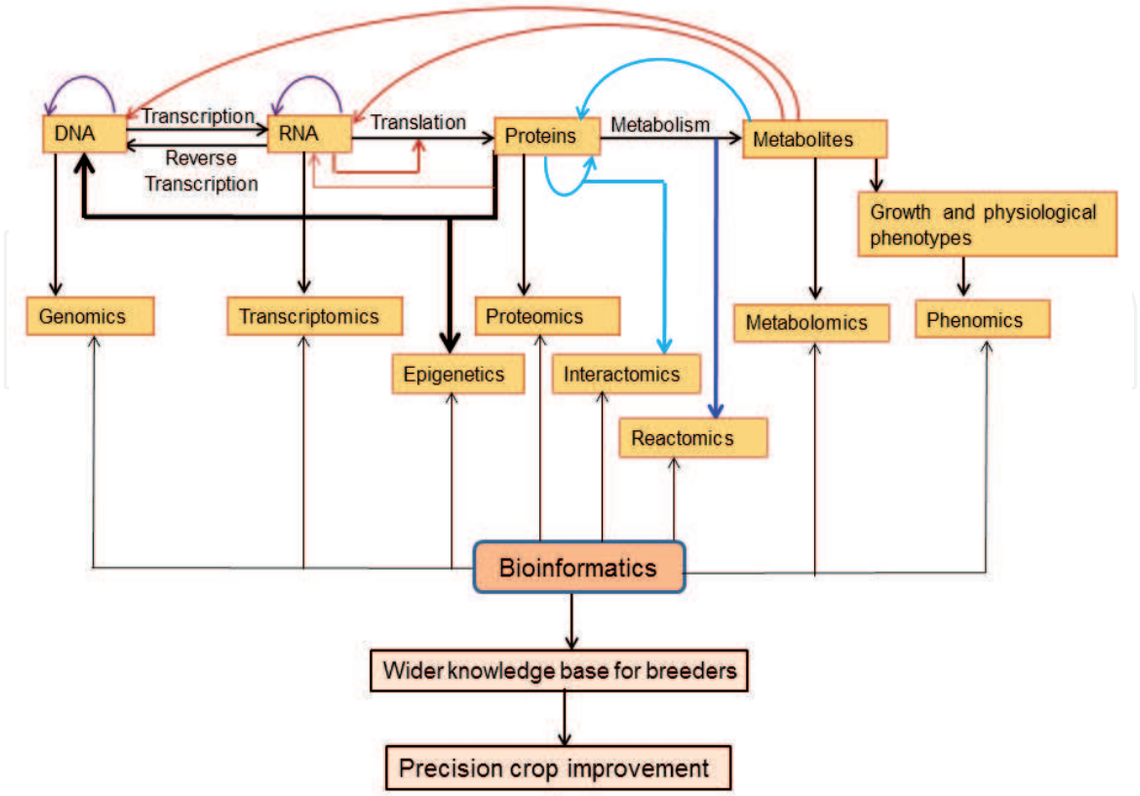

Figure 3. Supportive omic tools for increasing plant breeding efficiency against biotic stresses. Sky blue lines indicate interactions; largest bold black lines indicate epigenetic regulation; red lines indicate regulation; and blue line indicates metabolic reactions.

transcriptomics, proteomics, metabolomics, epigenetics and physiological and biochemical methods (Figure 3) will remarkably provide novel possibilities to understand the biology of plants and consequently to precisely develop stress tolerant crop varieties.

The recent advent of genotyping by sequencing (GBS) approach that minimizes ascertainment biases and the need for prior genome sequence information associated with traditional techniques has also enabled single nucleotide polymorphism marker detection, exposition of QTLs and the discovery of candidate genes controlling stress tolerance. Thus, genome/transcript profiling when combined with genome variation analysis is a potential area which could prove useful for breeders in the near future [205, 209]. Another newly developed approach, which combines genetical genomics and bulk segregant analysis (BSA) to identify markers linked to genes, shows the possibility of coupling BSA to high throughput sequencing methods. Although there are shortcomings, including errors introduced during NGS procedures, this method has proven to be useful in identifying stress tolerance genomic regions in crop plants. A more recent modification that exploits the power of deep sequencing of target-enriched SNP markers to increase the efficiency of BSA analysis is called target-enriched TEX-QTL mapping [197]. The authors propose that by combining a large F2 population size, deeply sequenced markers, and 10–20% bulk size, most QTLs can be identified within two generations. Although it does not currently detect very closely linked QTL, TEX-QTL method is

potentially a useful development in plant breeding. It is envisaged that BSA, by genotyping pooled-segregant sequencing, is likely to increase the reliability and reduce the time required to map all QTL defining the trait of interest and to identify causative superior alleles that can subsequently be used for crop improvement by targeted genetic engineering.

Desirable alleles are also being identified using functional genomic tools, including transformation, insertional mutagenesis, RNAi, the screening of either mutant or natural germplasm collections by means of targeting induced local lesions in genomes (TILLING) or ecotype TILLING (EcoTILLING) methodologies. These strategies enable plant scientists to predict gene functions and allow efficient prediction of the phenotype associated with a given gene, the so-called reverse genetics approach. The availability of a large volume of sequences generated through NGS technologies is significantly increasing the number and quality of candidates for TILLING and EcoTILLING studies. Thus, a number of crops have benefited from these technologies, including Arabidopsis, lotus, barley, maize, pea, melon and rice, for review see [198].

The use of improved recombinant DNA techniques to introduce new traits in early phases of cultivar selection is also currently gaining momentum in plant biology. Techniques such as oligonucleotide-directed mutagenesis (oDM) as well as those based on zinc finger nuclease (ZFN), transcription activator-like effector nuclease (TALeN) and clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated protein 9 (Cas9) system are all capable of specifically modifying a given target sequence leading to genotypes not substantially different from those obtained through traditional mutagenesis. The practical use of these techniques in developing countries and the performance of the germplasm developed through them under environmental conditions [206, 207, 208] is yet to be fully demonstrated.

7. Conclusion and perspective

Plant resistance to biotic stresses is jointly controlled by the plants' anatomy, physiology, biochemistry, genetics, development and evolution. Efforts to understand these mechanisms have generated a lot of data on candidate genes, quantitative trait loci (QTLs), proteins and metabolites associated with plant defences. This chapter has reviewed most of these aspects to provide a reader with background information on the diverse plant defence patterns. Some of the genes and methods that hold promise for improving plant defences are also discussed. Certainly, plant-pathogen/insect interaction is a complex phenomenon that involves various signalling pathways tracking and regulating the pathogens/insect ingress. The interactions leading to effective defence apparently involve activation of both innate and systemic acquired resistance, and require both direct and indirect pathways to rapidly limit the entry or proliferation of biotic agents in the plant. Identifying and harmonizing an efficient defence signalling pathway, which leads to activation of an effective defence strategy, is still a challenge, considering the large number of genes and proteins often expressed in most plant-pathogen/insect interaction studies. However, there are some resistance components that have shown promise, although further studies would be necessary to clarify the signalling patterns in

which such components are involved. Important examples include LRR-RK *BAK1*, which features in several signalling networks leading to plant resistance against a diversity of pathogens and insects, and *NRC1* which mediates resistance and cell death induced by both membrane receptors and intracellular NLRs. *BAK1* forms heteromeric complexes with other receptors, which indicates that BAK1 is a multifaceted receptor capable of PAMP detection, while *NRC1* is probably a downstream convergence point in ETI initiated at various cell locations. Thus, *BAK1* and *NRC1* could probably contribute to effective plant resistance to a diversity of pathogens and insects. However, identification of additional effective receptors will be necessary to counter the stealthy tendencies of most pathogens and insects, and to guarantee the transmission of signals to the downstream components. More studies on adaptability of defence genes or QTLs to changing biotic agents and climatic conditions also need to be conducted in order to limit boom and bust incidences frequently observed in pathosystems.

Acknowledgements

This publication was supported by Erfurt University of Applied Sciences.

Author details

Geoffrey Onaga[1] and Kerstin Wydra[2*]

*Address all correspondence to: kerstin.wydra@fh-erfurt.de

1 National Crops Resources Research Institute, Kampala, Uganda

2 Erfurt University of Applied Sciences, Faculty of Landscape Architecture, Horticulture and Forestry, Erfurt, Germany

References

[1] Hussain B. Modernization in plant breeding approaches for improving biotic stress resistance in crop plants. Turkish Journal of Agriculture and Forestry. 2015;39:515–530. DOI: 10.3906/tar-1406-176

[2] Sanghera GS, Wani SH, Singh G, Kashyap PL, Singh NB. Designing crop plants for bioticstresses using transgenic approach. International Journal of Plant Research. 2011;24:1–25

[3] Anderson PK, Cunningham AA, Patel NG, Morales FJ, Epstein PR, Daszak P. Emerging infectious diseases of plants: pathogen pollution, climate change and agrotechnolo-

gy drivers. Trends in Ecology & Evolution. 2004;19:535–544. DOI: 10.1016/j.tree.2004.07.021

[4] Ijaz S, Khan AI. Genetic pathways of disease resistance and plants-pathogens interactions. Molecular Pathogens. 2012;3(4):19–26. DOI: 10.5376/mp.2012.03.0004

[5] Howe GA, Jander G. Plant immunity to insect herbivores. Annual Reviews in Plant Biology. 2008;59:41–66. DOI: 10.1146/annurev.arplant.59.032607.092825

[6] Nurnberger T, Kemmerling B. Pathogen-associated molecular patterns (PAMP) and PAMP-triggered immunity. In: Parker J, editor. Molecular Aspects of Plant Disease Resistance. Annual Plant Reviews. Oxford, UK: Wiley. 2009;34:16–47. DOI: 10.1002/9781444301441.ch2

[7] Ausubel FM. Are innate immune signaling pathways in plants and animals conserved? Nature Immunology. 2005;6:973–979. DOI: 10.1038/ni1253

[8] Monaghan J, Zipfel C. Plant pattern recognition receptor complexes at the plasma membrane. Current Opinion in Plant Biology. 2012;15(4):349–357. DOI: 10.1016/j.pbi.2012.05.006

[9] Kiraly L, Barnaz B, Kiralyz Z. Plant resistance to pathogen infection: forms and mechanisms of innate and acquired resistance. Journal of Phytopathology. 2007;155:385–396. DOI: 10.1111/j.1439-0434.2007.01264.x

[10] Jones JD, Dangl JL. The plant immune system. Nature. 2006;444:323–29. DOI: 10.1038/nature05286

[11] Ferreira RB, Monteiro S, Freitas R, Santos CN, Chen Z, Batista LM, Duarte J, Borges A, Teixeira AR. The role of plant defence proteins in fungal pathogenesis. Molecular Plant Pathology. 2007;8:677–700. DOI: 10.1111/j.1364-3703.2007.00419.x

[12] Freeman BC, Beattie GA. An Overview of Plant Defenses against Pathogens and Herbivores. The Plant Health Instructor. 2008; DOI: 10.1094/PHI-I-2008-0226-01

[13] War AR, Paulraj MG, War MY, Ignacimuthu S. Herbivore and elicitor-induced resistance in groundnut to Asian armyworm, Spodoptera litura (Fab.) (Lepidoptera: Noctuidae). Plant Signaling & Behavior. 2011;6(11):1769–77. DOI: 10.4161/psb.6.11.17323

[14] Boller T, Felix G. A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. Annual Review in Plant Biology. 2009;60:379–406. DOI: 10.1146/annurev.arplant.57.032905.105346

[15] Malinovsky FG, Fangel JU, Willats WGT. The role of the cell wall in plant immunity. Frontiers in Plant Science. 2014;5:178. DOI: 10.3389/fpls.2014.00178

[16] Wei T, Ou B, Li J, Zhao Y, Guo D, Zhu Y, Guo D, Zhu Y, Chen Z, Gu H, Li C, Qin C, Qu LJ. Transcriptional profiling of rice early response to *Magnaporthe oryzae* identified OsWRKYs as important regulators in rice blast resistance. PLoS ONE. 2013;8(3):e59720. DOI: org/10.1371/journal.pone.0059720

[17] Dodds PN, Rathjen JP. Plant immunity: towards an integrated view of plant–pathogen interactions. Nature Reviews Genetics. 2010;11:539–548. DOI: 10.1038/nrg2812

[18] Van der Hoorn RA, Jones JD. The plant proteolytic machinery and its role in defence. Current Opinion in Plant Biology. 2004;7:400–407. DOI: 10.1016/j.pbi.2004.04.003

[19] Schwessinger B, Zipfel C. News from the frontline: recent insights into PAMP-triggered immunity in plants. Current Opinion in Plant Biology. 2008;11:389–395. DOI: 10.1016/j.pbi.2008.06.001

[20] Belien T, Van Campenhout S, Robben J, Volckaert G. Microbial endoxylanases: effective weapons to breach the plant cell-wall barrier or, rather, triggers of plant defense systems? Molecular Plant Microbe Interaction. 2006;19:1072–1081. DOI: 10.1094/MPMI-19-1072

[21] Mithöfer A, Fliegmann J, Neuhaus-Url G, Schwarz H, Ebel J. The hepta–beta–glucoside elicitor-binding proteins from legumes represent a putative receptor family. Biological Chemistry. 2000;381:705–713. DOI: 10.1515/BC.2000.091

[22] Zipfel C. Early molecular events in PAMP-triggered immunity. Current Opinion in Plant Biology. 2009;12:414–420. DOI: 10.1016/j.pbi.2009.06.003

[23] Felix G, Duran JD, Volko S, Boller T. Plants have a sensitive perception system for the most conserved domain of bacterial flagellin. The Plant Journal. 1999;18:265–276. DOI: 10.1046/j.1365-313X.1999.00265.x

[24] Trdá L, Fernandez O, Boutrot F, Héloir MC, Kelloniemi J, Daire X, Adrian M, Clément C, Zipfel C, Dorey S, Poinssot B. The grapevine flagellin receptor VvFLS2 differentially recognizes flagellin-derived epitopes from the endophytic growth-promoting bacterium *Burkholderia phytofirmans* and plant pathogenic bacteria. New Phytologist. 2014;201:1371–1384. DOI: 10.1111/nph.12592

[25] Robatzek S, Bittel P, Chinchilla D, Kochner P, Felix G, Shiu SH, Boller T. Molecular identification and characterization of the tomato flagellin receptor LeFLS2, an orthologue of Arabidopsis FLS2 exhibiting characteristically different perception specificities. Plant Molecular Biology. 2007;64:539–547. DOI: 10.1007/s11103-007-9173-8

[26] Takai R, Isogai A, Takayama S, Che F. Analysis of flagellin perception mediated by flg22 receptor OsFLS2 in rice. Molecular Plant Microbe Interaction. 2008;21:1635–1642. DOI: 10.1094/MPMI-21-12-1635

[27] Takeuchi K, Taguchi F, Inagaki Y, Toyoda K, Shiraishi T, Ichinose Y. Flagellin glycosylation island in *Pseudomonas syringae* pv. *glycinea* and its role in host specificity. Journal of Bacteriology. 2003;185:6658–6665. DOI: 10.1128/JB.185.22.6658-6665.2003

[28] Taguchi F, Takeuchi K, Katoh E, Murata K, Suzuki T, Marutani M, Kawasaki T, Eguchi M, Katoh S, Kaku H, Yasuda C, Inagaki Y,Toyoda K, Shiraishi T, Ichinose Y. Identification of glycosylation genes and glycosylated amino acids of flagellin in *Pseudomonas syringae* pv. *tabaci*. Cellular Microbiology. 2006;8:923–938. DOI: 10.1111/j.1462-5822.2005.00674.x

[29] Cai R, Lewis J, Yan S, Liu H, Clarke CR, Campanile F, Almeida NF, Studholme DJ, Lindeberg M, Schneider D, Zaccardelli M, Setubal JC, Morales-Lizcano NP, Bernal A, Coaker G, Baker C, Bender CL, Leman S, Vinatzer BA. The plant pathogen *Pseudomonas syringae* pv. *tomato* is genetically monomorphic and under strong selection to evade tomato immunity. PLoS Pathogens. 2011;7:e1002130. DOI: org/10.1371/journal.ppat.1002130

[30] Clarke CR, Chinchilla D, Hind SR, Taguchi F, Miki R, Ichinose Y, Martin GB, Leman S, Felix G, Vinatzer BA. Allelic variation in two distinct *Pseudomonas syringae* flagellin epitopes modulates the strength of plant immune responses but not bacterial motility. New Phytologist. 2013;200:847–860. DOI: 10.1111/nph.12408

[31] Chinchilla D, Zipfel C, Robatzek S, Kemmerling B, Nürnberger T, Jones JD, Felix G, Boller T. A flagellin-induced complex of the receptor FLS2 and BAK1 initiates plant defence. Nature. 2007;448:497–500. DOI: 10.1038/nature05999

[32] Lu D, Wu S, Gao X, Zhang Y, Shan L He P. A receptor-like cytoplasmic kinase, BIK1, associates with a flagellin receptor complex to initiate plant innate immunity. Proceedings of the National Academy of Science of the United States of America. 2010;107:496–501. DOI: 10.1073/pnas.0909705107

[33] Kunze G, Zipfel C, Robatzek S, Niehaus K, Boller T, Felix G. The N terminus of bacterial elongation factor Tu elicits innate immunity in Arabidopsis plants. The Plant Cell. 2004;16:3496–3507. DOI: 10.1105/tpc.104.026765

[34] Zipfel C, Kunze G, Chinchilla D, Caniard A, Jones JD, Boller T, Felix G. Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts Agrobacterium-mediated transformation. Cell. 2006;125:749–760. DOI: http://dx.doi.org/10.1016/j.cell.2006.03.037

[35] Lacombe S, Rougon-Cardoso A, Sherwood E, Peeters N, Dahlbeck D, van Esse HP, Smoker M, Rallapalli G, Thomma BP, Staskawicz B, Jones JD, Zipfel C. Interfamily transfer of a plant pattern-recognition receptor confers broad-spectrum bacterial resistance. Nature Biotechnology. 2010;28:365–369. DOI: 10.1038/nbt.1613

[36] Furukawa T, Inagaki H, Takai R, Hirai H, Che FS. Two distinct EF-Tu epitopes induce immune responses in rice and Arabidopsis. Molecular Plant Microbe Interaction. 2014;27(2):113–124. DOI: 10.1094/MPMI-10-13-0304-R

[37] Lu F, Wang H, Wang S, Jiang W, Shan C, Li B, Yang J, Zhang S, Sun W. Enhancement of innate immune system in monocot rice by transferring the dicotyledonous elongation factor Tu receptor EFR. Journal of Integrative Plant Biology. 2015;57(7):641–652. DOI: 10.1111/jipb.12306

[38] Schulze B, Mentzel T, Jehle AK, Mueller K, Beeler S, Boller T, Felix G, Chinchilla D. Rapid heteromerization and phosphorylation of ligand-activated plant transmembrane receptors and their associated kinase BAK1. Journal of Biological Chemistry. 2010;285:9444–9451. DOI: 10.1074/jbc.M109.096842

[39] Song WY, Pi LY, Wang GL, Gardner J, Holsten T, Ronald PC. Evolution of the rice Xa21 disease resistance gene family. The Plant Cell. 1997;9:279–287. DOI: 10.1105/tpc.9.8.1279

[40] Mendes BMJ, Cardoso SC, Boscariol-Camargo RL, Cruz RB, Mourão Filho FAA, Bergamin Filho A. Reduction in susceptibility to Xanthomonas axonopodis pv. citri in transgenic *Citrus sinensis* expressing the rice Xa21 gene. Plant Pathology. 2010;59:68–75. DOI: 10.1111/j.1365-3059.2009.02148.x

[41] Afroz A, Chaudhry Z, Rashid U, Ali GM, Nazir F, Iqbal J, Khan MR. Enhanced resistance against bacterial wilt in transgenic tomato (*Lycopersicon esculentum*) lines expressing the Xa21 gene. Plant Cell, Tissue and Organ Culture. 2011;104:227–237. DOI: 10.1007/s11240-010-9825-2

[42] Tripathi JN, Lorenzen J, Bahar O, Ronald P, Tripathi L. Transgenic expression of the rice Xa21 pattern-recognition receptor in banana (Musa sp.) confers resistance to *Xanthomonas campestris* pv. *musacearum*. Plant Biotechnology Journal. 2014;12(6):663–673. DOI: 10.1111/pbi.12170

[43] Fradin E, Adb-El-Haliem A, Masini L, van den Berg G, Joosten M, Thomma B. Interfamily transfer of tomato Ve1 mediates Verticillium resistance in Arabidopsis. Plant Physiology. 2011;156:2255–2265. DOI: 10.1104/pp.111.180067

[44] Jashni MK, Mehrabi R, Collemare J, Mesarich CH, de Wit PJGM. The battle in the apoplast: further insights into the roles of proteases and their inhibitors in plant–pathogen interactions. Frontiers in Plant Science. 2015;6:584. DOI: 10.3389/fpls.2015.00584.

[45] Shimizu T, Nakano T, Takamizawa D, Desaki Y, Ishii-Minami N, Nishizawa Y,Minami E, Okada K, Yamane H, Kaku H, Shibuya N. Two LysM receptor molecules, CEBiP and OsCERK1, cooperatively regulate chitin elicitor signaling in rice. The Plant Journal. 2010;64:204–214. DOI: 10.1111/j.1365-313X.2010.04324.x

[46] Hayafune M, Berisio R, Marchetti R, Silipo A, Kayama M, Desaki Y, Arima S, Squeglia F, Ruggiero A, Tokuyasu K, Molinaro A, Kaku H, Shibuya N. Chitin-induced activation of immune signaling by the rice receptor CEBiP relies on a unique sandwich-type dimerization. Proceedings of the National Academy of Science of the United States of America. 2014;111:404–413. DOI: 10.1073/pnas.1312099111

[47] Shinya T, Motoyama N, Ikeda A, Wada M, Kamiya K, Hayafune M, Kaku H, Shibuya N. Functional characterization of CEBiP and CERK1 homologs in Arabidopsis and rice reveals the presence of different chitin receptor systems in plants. Plant Cell Physiology. 2012;53:1696–1706. DOI: 10.1093/pcp/pcs113

[48] Zipfel C. Plant pattern-recognition receptors. Trends in Immunology. 2014;35:345–351. DOI: 10.1016/j.it.2014.05.004

[49] Liu T, Liu Z, Song C, Hu Y, Han Z, She J, Fan F, Wang J, Jin C, Chang J, Zhou JM, Chai J. Chitin-induced dimerization activates a plant immune receptor. Science. 2012;336:1160–1164. DOI: 10.1126/science.1218867

[50] Noda J, Brito N, González C. The Botrytis cinerea xylanase Xyn11A contributes to virulence with its necrotizing activity, not with its catalytic activity. BMC Plant Biology. 2010;10:1–15. DOI: 10.1186/1471-2229-10-38

[51] Sella L, Gazzetti K, Faoro F, Odorizzi S, D'Ovidio R, Schafer W, Favaron F. A *Fusarium graminearum* xylanase expressed during wheat infection is a necrotizing factor but is not essential for virulence. Plant Physiology and Biochemistry. 2013;64:1–10. DOI: 10.1016/j.plaphy.2012.12.008.

[52] Ron M, Avni A. The receptor for the fungal elicitor ethylene-inducing xylanase is a member of a resistance-like gene family in tomato. Plant Cell. 2004;16:1604–1615. DOI: 10.1105/tpc.022475

[53] Bar M, Sharfman M, Ron M, Avni A. BAK1 is required for the attenuation of ethylene-inducing xylanase (Eix)-induced defense responses by the decoy receptor LeEix1. The Plant Journal. 2010;63:791–800. DOI: 10.1111/j.1365-313X.2010.04282.x.

[54] Juge N. Plant protein inhibitors of cell wall degrading enzymes. Trends in Plant Science. 2006;11:359–367. DOI: 10.1016/j.tplants.2006.05.006

[55] Bellincampi D, Cervone F, Lionetti V. Plant cell wall dynamics and wall-related susceptibility in plant–pathogen interactions. Frontiers in Plant Science. 2014;5:228. DOI: 10.3389/fpls.2014.00228

[56] Larkan NJ, Lydiate DJ, Parkin IAP, Nelson MN, Epp DJ, Cowling WA, Rimmer SR, Borhan MH. The Brassica napus blackleg resistance gene LepR3 encodes a receptor-like protein triggered by the *Leptosphaeria maculans* effector AVRLM1. New Phytologist. 2013;197:595–605. DOI: 10.1111/nph.12043

[57] Ma L, Borhan MH. The receptor-like kinase SOBIR1 interacts with *Brassica napus* LepR3 and is required for *Leptosphaeria maculans* AvrLm1-triggered immunity. Frontiers in Plant Science. 2015;6:933. DOI: 10.3389/fpls.2015.00933

[58] Zhang W, Fraiture M, Kolb D, Löffelhardt B, Desaki Y, Boutrot FFG, Tör M, Zipfel C, Gust AA, Brunner F. Arabidopsis receptor-like protein30 and receptor-like kinase suppressor of BIR1-1/EVERSHED mediate innate immunity to necrotrophic fungi. The Plant Cell. 2013;25:4227–4241. DOI: 10.1105/tpc.113.117010

[59] Klemptner RL, Sherwood JS, Tugizimana F, Dubery IA, Piater LA. Ergosterol, an orphan fungal MAMP. Molecular Plant Microbe Interaction 2014;15(7):747–761. DOI: 10.1111/mpp.12127

[60] Bostock RM, Laine RA, Kuć JA. Factors affecting the elicitation of sesquiterpenoid phytoalexin accumulation by eicosapentaenoic and arachidonic acids in potato. Plant Physiology. 1982;70:1417–1424. DOI: http://dx.doi.org/10.1104/pp.70.5.1417

[61] Tyler BM. Molecular basis of recognition between Phytophthora pathogens and their hosts. Annual Reviews Phytopathology. 2002;40:137–167. DOI: 10.1146/annurev.phyto.40.120601.125310

[62] Brunner F, Rosahl S, Lee J, Rudd JJ, Geiler C, Kauppinen S, Rasmussen G, Scheel D, Nurnberger T. Pep-13, a plant defense-inducing pathogen-associated pattern from *Phytophthora transglutaminases*. The EMBO Journal. 2002;21:6681–6688. DOI: 10.1093/emboj/cdf667

[63] Garcia-Brugger A, Lamotte O, Vandelle C, Bourque S, Lecourieux D, Poinsot B, Wendehenne D, Pugin A. Early signaling events induced by elicitors of plant defenses. Molecular Plant Microbe Interaction. 2006;19:711–724. DOI: 10.1094/MPMI-19-0711.

[64] Gaulin E, Drame N, Lafitte C, Torto-Alalibo T, Martinez Y, Ameline-Torregrosa C, Khatib M, Mazarguil H, Villalba-Mateos F, Kamoun S, Mazars C, Dumas B, Bottin A, Esquerre-Tugaye MT, Rickauer M. Cellulose binding domains of a Phytophthora cell wall protein are novel pathogen-associated molecular patterns. The Plant Cell. 2006;18:1766–1777. DOI: 10.1105/tpc.105.038687

[65] Nicaise V. Crop immunity against viruses: outcomes and future challenges. Frontiers in Plant Science. 2014;5:660. DOI: 10.3389/fpls.2014.00660.

[66] Krol E, Mentzel T, Chinchilla D, Boller T, Felix G, Kemmerling B, Postel S, Arents M, Jeworutzki E, Al-Rasheid KA, Becker D, Hedrich R. Perception of the Arabidopsis danger signal peptide 1 involves the pattern recognition receptor AtPEPR1 and its close homologue AtPEPR2. Journal of Biological Chemistry. 2010;285:13471–13479. DOI: 10.1074/jbc.M109.097394

[67] Korner CJ, Klauser D, Niehl A, Domínguez-Ferreras A, Chinchilla D, Boller T, Heinlein M, Hann DR. The immunity regulator BAK1 contributes to resistance against diverse RNA viruses. Molecular Plant Microbe Interaction. 2013;26:1271–1280. DOI: 10.1094/MPMI-06-13-0179-R

[68] Fontes EP, Santos AA, Luz DF, Waclawovsky AJ, Chory J. The geminivirus nuclear shuttle protein is a virulence factor that suppresses transmembrane receptor kinase activity. Genes & Development. 2004;18:2545–2556. DOI: 10.1101/gad.1245904

[69] Prince DC, Drurey C, Zipfel C, Hogenhout SA. The leucine-rich repeat receptor-like kinase BAK1 and the cytochrome P450 PAD3 contribute to innate immunity to aphids in Arabidopsis. Plant Physiology. 2014;164:2207–2219. DOI: 10.1104/pp.114.235598

[70] Heil M, Ibarra-Laclette E, Adame-Alvarez RM, Martinez O, Ramirez-Chavez E,Molina-Torres J, Herrera-Estrella L. How plants sense wounds: damaged-self recognition is based on plant-derived elicitors and induces octadecanoid signaling. PLoS ONE. 2012;7(2):e30537. DOI: 10.1371/journal.pone.0030537

[71] Wu J, Baldwin IT. Herbivory-induced signaling in plants: perception and action. Plant Cell and Environment. 2009;32:1161–1174. DOI: 10.1111/j.1365-3040.2009.01943.x

[72] Foyer CH, Verrall SR, Hancock RD. Systematic analysis of phloem-feeding insect-induced transcriptional reprogramming in Arabidopsis highlights common features and reveals distinct responses to specialist and generalist insects. Journal of Experimental Botany. 2015;66:495–512. DOI: 10.1093/jxb/eru491

[73] Maffei ME, Mithöfer A, Boland W. Before gene expression: early events in plant–insect interaction. Trends in Plant Science. 2007;12:310–316. DOI: 10.1016/j.tplants.2007.06.001

[74] de Oliveira EF, Pallini A, Janssen A. Herbivores with similar feeding modes interact through the induction of different plant responses. Oecologia. 2016;180(1):1–10. DOI: 10.1007/s00442-015-3344-0

[75] Truitt CL, Wei HX, Pare PW. A plasma membrane protein from *Zea mays* binds with the herbivore elicitor volicitin. The Plant Cell. 2004;16:523–532. DOI: 10.1105/tpc.017723

[76] Hilker M, Meiners T. Early herbivore alert: insect eggs induce plant defense. Journal of Chemical Ecology. 2006;32:1379–1397. DOI: 10.1007/s10886-006-9057-4

[77] Tamiru A, Bruce TJA, Woodcock CM, Caulfield JC, Midega CAO, Ogol CKPO, MayonP, Birkett MA, Pickett JA, Khan ZR. Maize landraces recruit egg and larval parasitoids in response to egg deposition by a herbivore. Ecology Letters. 2011;14:1075–1083. DOI: 10.1111/j.1461-0248.2011.01674.x

[78] Gouhier-Darimont C, Schmiesing A, Bonnet C, Lassueur S, Reymond P. Signalling of *Arabidopsis thaliana* response to *Pieris brassicae* eggs shares similarities with PAMP-triggered immunity. Journal of Experimental Botany. 2013;64:665–674. DOI: 10.1093/jxb/ers362

[79] Rossi M, Goggin FL, Milligan SB, Kaloshian I, Ullman DE, Williamson VM. The nematode resistance gene Mi of tomato confers resistance against the potato aphid. Proceedings of the National Academy of Science of the United States of America. 1998;95:9750–9754. DOI: 10.1073/pnas.95.17.9750

[80] Du B, Zhang W, Liu B, Hu J, Wei Z, Shi Z, He R, Zhu L, Chen R, Han B, He G. Identification and characterization of Bph14, a gene conferring resistance to brown planthopper in rice. Proceedings of the National Academy of Science of the United States of America. 2009;106:22163–22168. DOI: 10.1073/pnas.0912139106

[81] De Vos M, Jander G. Myzus persicae (green peach aphid) salivary components induce defence responses in Arabidopsis thaliana. Plant, Cell and Environment. 2009;32:1548–1560. DOI: 10.1111/j.1365-3040.2009.02019.x

[82] Jaouannet M, Rodriguez PA, Thorpe P, Lenoir CJ, MacLeod R, Escudero-Martinez C, Bos JI. Plant immunity in plant-aphid interactions. Frontiers in Plant Science. 2014;5:663. DOI: 10.3389/fpls.2014.00663

[83] Lotze MT, Zeh HJ, Rubartelli A, Sparvero LJ, Amoscato AA, Washburn NR, Devera ME, Liang X, Tor M, Billiar T. The grateful dead: damage-associated molecular pattern molecules and reduction/oxidation regulate immunity. Immunological Reviews. 2007;220:60–81. DOI: 10.1111/j.1600-065X.2007.00579.x

[84] Yamaguchi Y, Huffaker A, Bryan AC, Tax FE, Ryan CA. PEPR2 is a second receptor for the Pep1 and Pep2 peptides and contributes to defense responses in Arabidopsis. The Plant Cell. 2010;22:508–522. DOI: 10.1105/tpc.109.068874

[85] Ross A, Yamada K, Hiruma K, Yamashita-Yamada M, Lu X, Takano Y, Tsuda K, Saijo Y. The Arabidopsis PEPR pathway couples local and systemic plant immunity. The EMBO Journal. 2014;33:62–75. DOI: 10.1002/embj.201284303

[86] Pearce G, Moura DS, Stratmann J, Ryan CA. RALF, a 5-kDa ubiquitous polypeptide in plants, arrests root growth and development. Proceedings of the National Academy of Science of the United States of America. 2001;98:12843–12847. DOI: 10.1073/pnas.201416998

[87] Liu H, Ma Y, Chen N, Guo S, Liu H, Guo X, Chong K, Xu Y. Overexpression of stress-inducible OsBURP16, the beta-subunit of polygalacturonase 1, decreases pectin contents and cell adhesion, and increases abiotic stress sensitivity in rice. Plant, Cell & Environment. 2014;37:1144–1158. DOI: 10.1111/pce.12223

[88] Bellincampi D, Cervone F, Lionetti V. Plant cell wall dynamics and wall-related susceptibility in plant–pathogen interactions. Frontiers in Plant Science. 2014;5:228. DOI: 10.3389/fpls.2014.00228

[89] Wydra, K. and Beri, H. 2007. Immunohistochemical changes in methyl-ester distribution of homogalacturonan and side chain composition of rhamnogalacturonan I as possible components of basal resistance in tomato inoculated with *Ralstonia solanacearum* Physiological and Molecular Plant Pathology 70: 13-24

[90] Wydra K, Beri H. Structural changes of homogalacturonan, rhamnogalacturonan I and arabinogalactan protein in xylem cell walls of tomato genotypes in reaction to *Ralstonia solanacearum*. Physiological and Molecular Plant Pathology. 2006;68:41–50. DOI: 10.1016/j.pmpp.2006.06.001

[91] Meyers BC, Kozik A, Griego A, Kuang H, Michelmore RW: Genome-wide analysis of NBS-LRR-encoding genes in Arabidopsis. Plant Cell. 2003;15(4):809–834. DOI: 10.1105/tpc.009308

[92] Griebel T, Maekawa T, Parker JE. NOD-like receptor cooperativity in effector-triggered immunity. Trends in Immunology. 2014;35:562–570. DOI: 10.1016/j.it.2014.09.005

[93] Lu H, Zhang C, Albrecht U, Shimizu R, Wang G, Bowman KD. Overexpression of a citrus NDR1 ortholog increases disease resistance in Arabidopsis. Frontiers in Plant Science. 2014;4:157. DOI: 10.3389/fpls.2013.00157

[94] Century KS, Holub EB, Staskawicz BJ. NDR1, a locus of *Arabidopsis thaliana* that is required for disease resistance to both a bacterial and a fungal pathogen. Proceedings of the National Academy of Science of the United States of America. 1995;92:6597–6601.

[95] Aarts N, Metz M, Holub E, Staskawicz BJ, Daniels MJ, Parker JE. Different requirements for EDS1 and NDR1 by disease resistance genes define at least two R gene-mediated signaling pathways in Arabidopsis. Proceedings of the National Academy of Science of the United States of America. 1998;95:10306–10311. DOI: 10.1073/pnas.95.17.10306

[96] Falk A, Feys BJ, Frost LN, Jones JD, Daniels MJ, Parker JE. EDS1, an essential component of R gene-mediated disease resistance in Arabidopsis has homology to eukaryotic lipases. Proceedings of the National Academy of Science of the United States of America. 1999;96:3292–3297. DOI: 10.1073/pnas.96.6.3292

[97] Rathjen JP, Moffett P. Early signal transduction events in specific plant disease resistance. Current Opinion in Plant Biology. 2003;6:300–306. DOI: 10.1016/S1369-5266(03)00057-8

[98] Takahashi A, Casais C, Ichimura K, Shirasu K. HSP90 interacts with RAR1 and SGT1 and is essential for RPS2-mediated disease resistance in Arabidopsis. Proceedings of the National Academy of Science of the United States of America. 2003;100:11777–11782. DOI: 10.1073/pnas.2033934100

[99] Albrecht M, Takken FLW. Update on the domain architectures of NLRs and R proteins. Biochemical and Biophysical Research Communication. 2006;339:459–462.

[100] Pan Q, Liu YS, Budai Hadrian O, Sela M, Carmel Goren L, Zamir D, Fluhr R. Comparative genetics of nucleotide binding site-leucine rich repeat resistance gene homologues in the genomes of two dicotyledons: tomato and Arabidopsis. Genetics. 2000;155:309–322.

[101] Van Ooijen G, van den Burg HA, Cornelissen BJC, Takken FLW. Structure and function of resistance proteins in solanaceous plants. Annual Reviews Phytopathology. 2007;45:43–72. DOI: 10.1146/annurev.phyto.45.062806.094430

[102] Cui H, Tsuda K, Parker JE. Effector-triggered immunity: from pathogen perception to robust defense. Annual Reviews in Plant Biology. 2015;66:487–511. DOI: 10.1146/annurev-arplant-050213-040012

[103] Deslandes L, Olivier J, Peeters N, Feng DX, Khounlotham M Boucher C, Somssich I, Genin S, Marco Y. Physical interaction between RRS1-R, a protein conferring resistance to bacterial wilt, and PopP2, a type III effector targeted to the plant nucleus.

Proceedings of the National Academy of Science of the United States of America. 2003;100:8024–29. DOI: 10.1073/pnas.1230660100

[104] Fabro G, Steinbrenner J, Coates M, Ishaque N, Baxter L, Studholme DJ, Körner E, Allen RL, Piquerez SJ, Rougon-Cardoso A,Greenshields D, Lei R, Badel JL, Caillaud MC, Sohn KH, Van den Ackerveken G, Parker JE, Beynon J, Jones JD. Multiple candidate effectors from the oomycete pathogen *Hyaloperonospora arabidopsidis* suppress host plant immunity. PLoS Pathogens. 2011;7:e1002348. DOI: 10.1371/journal.ppat.1002348. pmid:22072967

[105] Chou S, Krasileva K V, Holton JM, Steinbrenner AD, Alber T, Staskawicz BJ. Hyaloperonospora arabidopsidis ATR1 effector is a repeat protein with distributed recognition surfaces. Proceedings of the National Academy of Science of the United States of America. 2011;08:13323–13328. DOI: 10.1073/pnas.1109791108. pmid:21788488

[106] Sarris, Panagiotis F, Duxbury Z, Huh Sung U, Ma Y, Segonzac C, Sklenar J, Derbyshire P, Cevik, V, Rallapalli G, Saucet Simon B, Wirthmueller L, Menke Frank LH, Sohn Kee H, Jones Jonathan DG. A plant immune receptor detects pathogen effectors that target WRKY transcription factors. Cell. 2015;161:1089–1100. DOI: 10.1016/j.cell.2015.04.024

[107] Liu W, Liu J, Triplett L, Leach JE, Wang GL. Novel insights into rice innate immunity against bacterial and fungal pathogens. Annual Reviews in Phytopathology. 2014;52:213–241. DOI: 10.1146/annurev-phyto-102313-045926

[108] Zhang ZM, Zhang X, Zhou ZR, Hu HY, Liu M, Zhou B, Zhou J. Solution structure of the *Magnaporthe oryzae* avirulence protein AvrPiz-t. Journal of Biomolecular NMR. 2013; 55:219–223. DOI: 10.1007/s10858-012-9695-5

[109] Cesari S, Thilliez G, Ribot C, Chalvon V, Michel C, Jauneau A, Rivas S, Alaux L, Kanzaki H, Okuyama Y, Morel JB, Fournier E, Tharreau D, Terauchi R, Kroj T. The rice resistance protein pair RGA4/RGA5 recognizes the *Magnaporthe oryzae* effectors AVR-Pia and AVR1-CO39 by direct binding. The Plant Cell. 2013;25:1463–1481. DOI: 10.1105/tpc.112.107201

[110] Okuyama Y, Kanzaki H, Abe A, Yoshida K, Tamiru M, Saitoh H, Fujibe T, Matsumura H, Shenton M, Galam DC, Undan J, Ito A, Sone T, Terauchi RA. Multifaceted genomics approach allows the isolation of the rice Pia-blast resistance gene consisting of two adjacent NBS-LRR protein genes. The Plant Journal. 2011;66:467–479. DOI: 10.1111/j.1365-313X.2011.04502.x

[111] Maqbool A, Saitoh H, Franceschetti M, Stevenson C, Uemura A, Kanzaki H, Kamoun S, Terauchi R, Banfield MJ. Structural basis of pathogen recognition by an integrated HMA domain in a plant NLR immune receptor. eLife. 2015;4:e08709. DOI: 10.7554/eLife.08709

[112] Leister RT, Ausubel FM, Katagiri F. Molecular recognition of pathogen attack occurs inside of plant cells in plant disease resistance specified by the Arabidopsis genes

RPS2 and RPM1. Proceedings of the National Academy of Science of the United States of America. 1996;93:15497–15502.

[113] Li M, Ma X, Chiang YHH, Yadeta KA, Ding P, Dong L, Zhao Y, Li X, Yu Y, Zhang L, Shen QH, Xia B, Coaker G, Liu D,Zhou JM.. Proline isomerization of the immune receptor-interacting protein RIN4 by a cyclophilin inhibits effector-triggered immunity in Arabidopsis. Cell Host Microbe. 2014;16:473–483. DOI: 10.1016/j.chom.2014.09.007

[114] Wilton M, Subramaniam R, Elmore J, Felsensteiner C, Coaker G, Desveaux D. The type III effector HopF2 Pto targets Arabidopsis RIN4 protein to promote *Pseudomonas syringae* virulence. Proceedings of the National Academy of Science of the United States of America. 2010;107:2349–2354. DOI: 10.1073/pnas.0904739107

[115] Eitas TK, Dangl JL. NB– LRR proteins: pairs, pieces, perception, partners, and pathways. Current Opinion Plant Biology. 2013;13:472–477. DOI: 10.1016/j.pbi.2010.04.007

[116] Williams SJ, Sohn KH, Wan L, Bernoux M, Sarris PF, Segonzac C, Ve T, Ma Y, Saucet SB, Ericsson DJ, Casey LW, Lonhienne T, Winzor DJ, Zhang X, Coerdt A, Parker JE, Dodds PN, Kobe B, Jones JD. Structural basis for assembly and function of a heterodimeric plant immune receptor. Science. 2014; 344:299–303. DOI: 10.1126/science. 1247357

[117] Gabriels SH, Vossen JH, Ekengren SK, van Ooijen G, Abd-El-Haliem AM, van den Berg GC, Rainey DY, Martin GB, Takken FL, de Wit PJ, Joosten MH. An NB-LRR protein required for HR signaling mediated by both extra- and intracellular resistance proteins. The Plant Journal. 2007;50:14–28. DOI: 10.1111/j.1365-313X. 2007.03027.x

[118] Bonardi V, Tang S, Stallmann A, Roberts M, Cherkis K, Dangl JL. Expanded functions for a family of plant intracellular immune receptors beyond specific recognition of pathogen effectors. Proceedings of the National Academy of Science of the United States of America. 2011;108:16463–16468. DOI: 10.1073/pnas.1113726108

[119] Muthamilarasan M, Prasad M. Plant innate immunity: an updated insight into defense mechanism. Journal of Biosciences. 2013;38:433–449. DOI: 10.1007/ s12038-013-9302-2

[120] Inoue H, Hayashi N, Matsushita A, Xinqiong L, Nakayama A, Sugano S, Jiang CJ, Takatsuji H. Blast resistance of CC-NBLRR protein Pb1 is mediated by WRKY45 through protein-protein interaction. Proceedings of the National Academy of Science of the United States of America. 2013;110:9577–9582. DOI: 10.1073/pnas.1222155110

[121] Shen QH, Saijo Y, Mauch S, Biskup C, Bieri S, Keller B, Seki H, Ulker B, Somssich IE, Schulze-Lefert P.. Nuclear activity of MLA immune receptors links isolate-specific and basal disease-resistance responses. Science. 2007;315(5815):1098–1103. DOI: 10.1126/science.1136372

[122] Narusaka M, Kubo Y, Hatakeyama K, Imamura J, Ezura H, Nanasato Y, Tabei Y, Takano Y, Shirasu K, Narusaka Y. Interfamily transfer of dual NB-LRR genes confers

resistance to multiple pathogens. PLoS One. 2013;8:e55954. DOI: 10.1371/journal.pone.0055954

[123] Padmanabhan MS, Ma S, Burch-Smith TM, Czymmek K, Huijser P, Dinesh-Kumar SP. Novel positive regulatory role for the SPL6 transcription factor in the N TIR-NB-LRR receptor-mediated plant innate immunity. PLoS Pathogens. 2013;9:e1003235. DOI: 10.1371/journal.ppat.1003235

[124] Jacob F, Vernaldi S, Maekawa T. Evolution and conservation of plant NLR functions. Frontiers in Immunology. 2013;4:297. DOI: 10.3389/fimmu.2013.00297

[125] Bari R, Jones JD. Role of plant hormones in plant defence responses. Plant Molecular Biology. 2009;69:473–488. DOI: 10.1007/s11103-008-9435-0

[126] Glazebrook J. Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. Annual Reviews Phytopathology. 2005;43:205–227. DOI: 10.1146/annurev.phyto.43.040204.135923

[127] Spoel SH, Koornneef A, Claessens SM, Korzelius JP, Van Pelt JA, Mueller MJ, Buchala AJ, Métraux JP, Brown R, Kazan K, Van Loon LC, Dong X, Pieterse CM. NPR1 modulates cross-talk between salicylate- and jasmonate-dependent defense pathways through a novel function in the cytosol. The Plant Cell. 2003;15:760–770. DOI: 10.1105/tpc.009159

[128] Mur LA, Kenton P, Atzorn R, Miersch O, Wasternack C. The outcomes of concentration-specific interactions between salicylate and jasmonate signaling include synergy, antagonism, and oxidative stress leading to cell death. Plant Physiology. 2006;140:249–262.

[129] Vlot AC, Dempsey DA, and Klessig DF. Salicylic acid, a multifaceted hormone to combat disease. Annual Reviews Phytopathology. 2009;47:177–206. DOI: 10.1146/annurev.phyto.050908.135202

[130] Baebler Š, Witek K, Petek M, Stare K, Tušek-Žnidarič M, Pompe-Novak M, Renaut J, Szajko K, Strzelczyk-Żyta D, Marczewski W, Morgiewicz K, Gruden K, Hennig J.. Salicylic acid is an indispensable component of the Ny-1 resistance-gene-mediated response against Potato virus Y infection in potato. Journal of Experimental Botany. 2014;65:1095–1109. DOI: 10.1093/jxb/ert447

[131] Pegadaraju V, Knepper C, Reese J, Shah J. Premature leaf senescence modulated by the Arabidopsis PHYTOALEXIN DEFICIENT4 gene is associated with defense against the phloem-feeding green peach aphid. Plant Physiology. 2005;139(4): 1927-1934. DOI: 10.1104/pp.105.070433.

[132] Li Q, Xie QG, Smith-Becker J, Navarre DA, Kaloshian I. Mi-1-Mediated aphid resistance involves salicylic acid and mitogen-activated protein kinase signaling cascades. Molecular Plant Microbe Interaction. 2006;19(6):655-664. DOI: 10.1094/MPMI-19-0655

[133] Fu ZQ, Dong X. Systemic acquired resistance: turning local infection into global defense. Annual Reviews Plant Biology. 2013;64:839–863. DOI: 10.1146/annurev-arplant-042811-105606

[134] Park SW, Kaimoyo E, Kumar D, Mosher S, Klessig DF. Methyl salicylate is a critical mobile signal for plant systemic acquired resistance. Science. 2007;318:113–116. DOI: 10.1126/science.1147113

[135] Song JT, Lu H, McDowell JM, Greenberg JT. A key role for ALD1 in activation of local and systemic defenses in Arabidopsis. The Plant Journal. 2004;40:200–212. DOI: 10.1111/j.1365-313X.2004.02200.x

[136] Beckers GJM, Spoel SH. Fine-tuning plant defence signaling: salicylate versus jasmonate. Plant Biology. 2006;8:1–10. DOI: 10.1055/s-2005-872705

[137] Van der Does D, Leon-Reyes A, Koornneef A, Van Verk MC, Rodenburg N, Pauwels L, Goossens A, Körbes AP, Memelink J, Ritsema T, Van Wees SC, Pieterse CM. Salicylic acid suppresses jasmonic acid signaling downstream of SCFCOI1-JAZ by targeting GCC promoter motifs via transcription factor ORA59. The Plant Cell. 2013;25:744–761. DOI: 10.1105/tpc.112.108548

[138] De Vleesschauwer D, Xu J, Höfte M. Making sense of hormone-mediated defense networking: from rice to Arabidopsis, Frontiers in Plant Science. 2014;5:611. DOI: 10.3389/fpls.2014.00611

[139] Lee SC, Hong JK, Kim YJ and Hwang BK. Pepper gene encoding thionin is differentially induced by pathogens, ethylene and methyl jasmonate. Physiological and Molecular Plant Pathology. 2000;56:207–216. DOI: 10.1006/pmpp.2000.0269

[140] Zhu F, Xi D-H, Yuan S, Xu F, Zhang D-W, Lin H-H. Salicylic acid and jasmonic acid are essential for systemic resistance against tobacco mosaic virus in *Nicotiana benthamiana*. Molecular Plant Microbe Interaction. 2014;27:567–577. DOI: 10.1094/MPMI-11-13-0349-R

[141] Ellis C, Karafyllidis I, Turner JG. Constitutive activation of jasmonate signaling in an Arabidopsis mutant correlates with enhanced resistance to *Erysiphe cichoracearum*, *Pseudomonas syringae*, and *Myzus persicae*. Molecular Plant Microbe Interaction 2002a; 15:1025–1030. DOI: 10.1094/MPMI.2002.15.10.1025

[142] Xu E, Brosche M. Salicylic acid signaling inhibits apoplastic reactive oxygen species signaling. BMC Plant Biology. 2014;14:155. DOI: 10.1186/1471-2229-14-155

[143] Shah J, Kachroo P, Klessig DF. The Arabidopsis ssi1 mutation restores pathogenesis-related gene expression in npr1 plants and renders defensin gene expression salicylic acid dependent. The Plant Cell. 1999;11:191–206

[144] Clarke JD, Volko SM, Ledford H, Ausubel FM, Dong X. Roles of salicylic acid, jasmonic acid, and ethylene in cpr-induced resistance in Arabidopsis. The Plant Cell. 2000;12:2175–2190. DOI: 10.2307/3871113

[145] Alazem M, Lin NS. Roles of plant hormones in the regulation of host–virus interactions. Molecular Plant Pathology. 2014;16:529–540. DOI: 10.1111/mpp.12204

[146] Penninckx IA, Thomma BP, Buchala A, Metraux JP, Broekaert WF. Concomitant activation of jasmonate and ethylene response pathways is required for induction of a plant defensin gene in Arabidopsis. The Plant Cell. 1998;10:2103–2113. DOI: 10.1105/tpc.10.12.2103

[147] Truman W, Bennett MH, Kubigsteltig I, Turnbull C, Grant M. Arabidopsis systemic immunity uses conserved defense signaling pathways and is mediated by jasmonates. Proceedings of the National Academy of Science of the United States of America. 2007;104:1075–1080. DOI: 10.1073/pnas.0605423104

[148] Attaran E, Zeier TE, Griebel T, Zeier J. Methyl salicylate production and jasmonate signaling are not essential for systemic acquired resistance in Arabidopsis. The Plant Cell. 2009;21:954–971. DOI: 10.1105/tpc.108.063164

[149] Tuominen H, Overmyer K, Keinanen M, Kollist H, Kangasjarvi J. Mutual antagonism of ethylene and jasmonic acid regulates ozone-induced spreading cell death in Arabidopsis. The Plant Journal. 2004;39:59–69. DOI: 10.1111/j.1365-313X.2004.02107.x

[150] Zander M, Thurow C, Gatz C. TGA transcription factors activate the salicylic acid-suppressible branch of the ethylene-induced defense program by regulating ORA59 expression. Plant Physiology. 2014; 165:1671–1683. DOI: 10.1104/pp.114.243360

[151] Guan R, Su J, Meng X, et al. Multilayered Regulation of Ethylene Induction Plays a Positive Role in Arabidopsis Resistance against *Pseudomonas syringae*. Plant Physiology. 2015;169(1):299-312. doi:10.1104/pp.15.00659.

[152] Zhu Z, An F, Feng Y, Li P, Xue L, A M, Jiang Z, Kim JM, To TK, Li W, Zhang X, Yu Q, Dong Z, Chen WQ, Seki M, Zhou JM, Guo H. Derepression of ethylene-stabilized transcription factors (EIN3/EIL1) mediates jasmonate and ethylene signaling synergy in Arabidopsis. Proceedings of the National Academy of Science of the United States of America. 2011;108:12539–12544. DOI: 10.1073/pnas.1103959108

[153] Schenk PM, Kazan K, Wilson I, Anderson JP, Richmond T, Somerville SC, Manners JM. Coordinated plant defense responses in Arabidopsis revealed by microarray analysis. Proceedings of the National Academy of Science of the United States of America. 2000;97:11655–11660. DOI: 10.1073/pnas.97.21.11655

[154] Lorenzo O, Piqueras R, Sanchez-Serrano JJ, Solano R. *ETHYLENE RESPONSE FACTOR1* integrates signals from ethylene and jasmonate pathways in plant defense. The Plant Cell 2003;15:165–178. DOI: 10.1105/tpc.007468

[155] Dong N, Liu X, Lu Y, Du LP, Xu HJ, Liu HX, Xin ZY, Zhang ZY. Overexpression of TaPIEP1, a pathogen-induced ERF gene of wheat, confers host-enhanced resistance to fungal pathogen *Bipolaris sorokiniana*. Functional & Integrative Genomics 2010;10:215–226. 10.1007/s10142-009-0157-4

[156] Jia Y, Martin GB. Rapid transcript accumulation of pathogenesis-related genes during an incompatible interaction in bacterial speck disease-resistant tomato plants. Plant Molecular Biology. 1999;40:455–465. DOI: 10.1023/A:1006213324555

[157] Chen L, Zhang L, Li D, Wang F, Yu D. WRKY8 transcription factor functions in the TMV-cg defense response by mediating both abscisic acid and ethylene signaling in Arabidopsis. Proceedings of the National Academy of Science of the United States of America. 2013;110:E1963–E1971. DOI: 10.1073/pnas.1221347110

[158] Robert-Seilaniantz A, Grant M, Jones JDG. Hormone crosstalk in plant disease and defense: more than just JASMONATE-SALICYLATE antagonism. Annual Reviews Phytopathology. 2011; 49:317–343. DOI: 10.1146/annurev-phyto-073009-114447

[159] Asselbergh B, De Vleesschauwer D, Hofte M. Global switches and fine-tuning-ABA modulates plant pathogen defense. Molecular Plant Microbe Interaction. 2008; 21:709–719. DOI: 10.1094/MPMI-21-6-0709

[160] Ton J, Flors V, Mauch-Mani B. The multifaceted role of ABA in disease resistance. Trends in Plant Science. 2009;14:310–317. DOI: 10.1016/j.tplants.2009.03.006

[161] Pogany M, Koehl J, Heiser I, Elstner EF,Barna B. Juvenility of tobacco induced by cytokinin gene introduction decreases susceptibility to Tobacco necrosis virus and confers tolerance to oxidative stress. Physiological Molecular Plant Pathology. 2004;65:39–47. DOI: 10.1016/j.pmpp.2004.10.006

[162] Sano H, Seo S, Koizumi N, Niki T, Iwamura H, Ohashi Y. Regulation by cytokinins of endogenous levels of jasmonic and salicylic acids in mechanically wounded tobacco plants. Plant Cell Physiology. 1996;37:762–769.

[163] Barna B, Smigocki AC, and Baker JC. Transgenic production of cytokinin suppresses bacterially induced hypersensitive response symptoms and increases antioxidative enzyme levels in Nicotiana spp. Phytopathology. 2008;98:1242–1247. DOI: 10.1094/PHYTO-98-11-1242

[164] Pieterse CMJ, Van der Does D, Zamioudis C, Leon-Reyes A, Van Wees SCM. Hormonal modulation of plant immunity. Annual Reviews in Cell Development Biology. 2012;28:489–521. DOI: 10.1146/annurev-cellbio-092910-154055

[165] Choi J, Choi D, Lee S, Ryu CM, Hwang I. Cytokinins and plant immunity: old foes or new friends? Trends in Plant Science. 2011;16:388–394. 10.1016/j.tplants.2011.03.003

[166] Grosskinsky DK, Naseem M, Abdelmohsen UR, Plickert N, Engelke T, Griebel T, Zeier J, Novák O, Strnad M, Pfeifhofer H, van der Graaff E, Simon U, Roitsch T. Cytokinins mediate resistance against *Pseudomonas syringae* in tobacco through increased antimicrobial phytoalexin synthesis independent of salicylic acid signaling. Plant Physiology. 2011;157:815–830. DOI: 10.1104/pp.111.182931

[167] Ehness R, Roitsch T. Co-ordinated induction of mRNAs for extracellular invertase and a glucose transporter in *Chenopodium rubrum* by cytokinins. The Plant Journal. 1997;11:539–548. DOI: 10.1046/j.1365-313X.1997.11030539.x

[168] Xiong Y, Sheen J. The role of target of rapamycin signaling networks in plant growth and metabolism. Plant Physiology. 2014;164(2):499–512. DOI: 10.1104/pp.113.229948

[169] Slavikova S, Ufaz S, Avin-Wittenberg T, Levanony H, Galili G. An autophagy-associated Atg8 protein is involved in the responses of Arabidopsis seedlings to hormonal controls and abiotic stresses. Journal of Experimental Botany. 2008;59:4029–4043. DOI: 10.1093/jxb/ern244

[170] Hwang I, Sheen J, and Müller B. Cytokinin signaling networks. Annual Reviews in Plant Biology. 2012;63:353–380. DOI: 10.1146/annurev-arplant-042811-105503

[171] Xia XJ, Chen Z, and Yu JQ. ROS mediate brassinosteroids-induced plant stress responses. Plant Signal & Behavior. 2010;5:532–534. DOI: 10.4161/psb.10989

[172] De Bruyne L, Höfte M, De Vleesschauwer D. Connecting growth and defense: the emerging roles of brassinosteroids and gibberellins in plant innate immunity. Molecular Plant. 2014;7:943–959. DOI: 10.1093/mp/ssu050

[173] Roux M, Schwessinger B, Albrecht C, Chinchilla D, Jones A, Holton N, Malinovsky FG, Tör M, de Vries S, Zipfel C. The Arabidopsis leucine-rich repeat receptor-like kinases BAK1/SERK3 and BKK1/SERK4 are required for innate immunity to hemibiotrophic and biotrophic pathogens. The Plant Cell. 2011;23:2440–2455. DOI: 10.1105/tpc.111.084301

[174] Korner CJ, Klauser D, Niehl A, Dominguez-Ferreras A, Chinchilla D, Boller T, Heinlein M, Hann DR. The immunity regulator BAK1 contributes to resistance against diverse RNA viruses. Molecular Plant Microbe Interaction. 2013;26:1271–1280. DOI: 10.1094/MPMI-06-13-0179-R

[175] Fridman Y, Savaldi-Goldstein S. Brassinosteroids in growth control: how, when and where? Plant Science. 2013;209:24–31. DOI: 10.1016/j.plantsci.2013.04.002

[176] Naseem M, Dandekar T. The role of auxin-cytokinin antagonism in plant-pathogen interactions. PLoS Pathogens. 2012;8:e1003026. DOI: 10.1371/journal.ppat.1003026

[177] Denancé N, Ranocha P, Oria N, Barlet X, Rivière M-P, Yadeta K, Hoffmann L, Perreau F, Clément G, Maia-Grondard A, van den Berg GC, Savelli B, Fournier S, Aubert Y, Pelletier S, Thomma BP, Molina A, Jouanin L, Marco Y, Goffner D. Arabidopsis wat1 (walls are thin1)-mediated resistance to vascular pathogens is accompanied by cross-regulation of salicylic acid and tryptophan metabolism. The Plant Journal. 2013;73:225–239. DOI: 10.1111/tpj.12027

[178] Nakashita H, Yasuda M, Nitta T, Asami T, Fujioka S, Arai Y, Sekimata K, Takatsuto S, Yamaguchi I, Yoshida S. Brassinosteroid functions in a broad range of disease re-

sistance in tobacco and rice. The Plant Journal. 2003;33:887–898. DOI: 10.1046/j.1365-313X.2003.01675.x

[179] Kamthan A, Chaudhuri A, Kamthan M, Datta A. Small RNAs in plants: recent development and application for crop improvement. Frontiers in Plant Science. 2015;6:208. DOI: 0.3389/fpls.2015.00208

[180] Ruiz-Ferrer V, Voinnet O. Roles of plant small RNAs in biotic stress responses. Annual Reviews in Plant Biology. 2009;60:485–510. DOI: 10.1146/annurev.arplant.043008.092111

[181] Wilson RC, Doudna JA. Molecular mechanisms of RNA interference. Annual Reviews in Biophysics. 2013;42:217–239. DOI: 10.1146/annurev-biophys-083012-130404

[182] Dunoyer P, Schott G, Himber C, Meyer D, Takeda A, Carrington JC, Voinnet O. Small RNA duplexes function as mobile silencing signals between plant cells. Science. 2010a;328:912–916. DOI: 10.1126/science.1185880

[183] Hamilton A, Voinnet O, Chappell L, Baulcombe DC. Two classes of short interfering RNA in RNA silencing. The EMBO Journal. 2002;21:4671–4679. DOI: 10.1093/emboj/cdf464

[184] Buhtz A, Springer F, Chappell L, Baulcombe DC, Kehr J. Identification and characterization of small RNAs from the phloem of *Brassica napus*. The Plant Journal. 2008;53:739–749. DOI: 10.1111/j.1365-313X.2007.03368.x

[185] Yoo B-C, Kragler F, Varkonyi-Gasic E, Haywood V, Archer-Evans S, Lee YM, Lough TJ, Lucas WJ. A systemic small RNA signaling system in plants. The Plant Cell. 2004;16:1979–2000. DOI: 10.1105/tpc.104.023614

[186] Carlsbecker A, Lee JY, Roberts CJ, Dettmer J, Lehesranta S, Zhou J, Lindgren O, Moreno-Risueno MA, Vatén A, Thitamadee S, Campilho A, Sebastian J, Bowman JL, Helariutta Y, Benfey PN. Cell signalling by microRNA165/6 directs gene dose-dependent root cell fate. Nature. 2010;465:316–321. DOI: 10.1038/nature08977

[187] Pant BD, Buhtz A, Kehr J, Scheible WR. MicroRNA399 is a long distance signal for the regulation of plant phosphate homeostasis. The Plant Journal. 2008;53:731–738. DOI: 10.1111/j.1365-313X.2007.03363.x

[188] Navarro L, Dunoyer P, Jay F, Arnold B, Dharmasiri N, Estelle M, Voinnet O, Jones JD. A plant miRNA contributes to antibacterial resistance by repressing auxin signalling. Science. 2016;312:436–439. DOI: 10.1126/science.1126088

[189] Jiang CJ, Shimono M, Maeda S, Inoue H, Mori M, Hasegawa M, Sugano S, Takatsuji H. Suppression of the rice fatty-acid desaturase gene *OsSSI2* enhances resistance to blast and leaf blight diseases in rice. Molecular Plant Microbe Interaction. 2009;22:820–829. DOI: 10.1094/MPMI-22-7-0820

[190] Yara A, Yaeno T, Hasegawa M, Seto H, Montillet JL, Kusumi K. Disease resistance against *Magnaporthe grisea* is enhanced in transgenic rice with suppression of o-3 fatty acid desaturases. Plant Cell Physiol. 2007;48:1263–1274. DOI: 10.1093/pcp/pcm107

[191] Peltier AJ, Hatfield RD, Grau CR. Soybean stem lignin concentration relates to resistance to *Sclerotinia sclerotiorum*. Plant Disease. 2009;93:149–154. DOI: 10.1094/PDIS-93-2-0149

[192] Xin M, Wang Y, Yao Y, Xie C, Peng H, Ni Z, Sun Q. Diverse set of microRNAs are responsive to powdery mildew infection and heat stress in wheat (*Triticum aestivum* L.). BMC Plant Biology. 2010;10:123–134. DOI: 10.1186/1471-2229-10-123

[193] Vanderschuren H, Alder A, Zhang P, Gruissem W. Dose dependent RNAi-mediated geminivirus resistance in the tropical root crop cassava. Plant Molecular Biology 2009;70:265–272. DOI: 10.1007/s11103-009-9472-3

[194] Schwind N, Zwiebel M, Itaya A, Ding B, Wang MB, Krczal G, Wassenegger M. RNAi-mediated resistance to Potato spindle tuber viroid in transgenic tomato expressing a viroid hairpin RNA construct. Molecular Plant Pathology. 2009;10:459–469. DOI: 10.1111/j.1364-3703.2009.00546.x

[195] Ding SW. RNA-based antiviral immunity. Nature Reviews Immunology. 2010;10:632–644. DOI: 10.1038/nri2824

[196] Simon-Mateo C, García JA. Antiviral strategies in plants based on RNA silencing. Biochimica et Biophysica Acta. 2011;1809:722–731. DOI: 10.1016/j.bbagrm.2011.05.011

[197] Guo J, Fan J, Hauser BA, Rhee SY. Target enrichment improves mapping of complex traits by deep sequencing. G3 (Bethesda). 2015;6(1):67–77. DOI: 10.1534/g3.115.023671

[198] Perez-de-Castro AM, Vilanova S, Canizares J, Pascual L, Blanca JM, Diez MJ, Prohens J, Pico B. Application of genomic tools in plant breeding. Current Genomics. 2012;13(3):179–195. DOI: 10.2174/138920212800543084

[199] Dahal, D., Heintz., D., Van Dorsselaer, A., Braun H.-P., Wydra, K. 2009. Pathogenesis and stress related, as well as metabolic proteins are regulated in tomato stems infected with *Ralstonia solanacearum*. Plant Physiology and Biochemistry 47: 838–846

[200] Dahal, D., Pich, A., Braun, H.-P., Wydra, K. 2010. Analysis of cell wall proteins regulated in stems of susceptible and resistant tomato genotypes after inoculation with *Ralstonia solanacearum*: a proteomics approach. Plant Molecular Biology 73, 643-658

[201] Ghareeb, H., Bozsó, Z., Ott, P.G., Repenning, C., Stahl, F., Wydra, K. 2011. Transcriptome of silicon-induced resistance against *Ralstonia solanacearum* in the silicon non accumulator tomato implicates priming effect. Physiol. Mol. Plant Pathol. 75, 83-89

[202] Kiirika, L., Stahl, F. and Wydra, K. 2013. Phenotypic and molecular characterization of resistance induction by single and combined application of chitosan and silicon in

tomato against *Ralstonia solanacearum.* Physiological and Molecular Plant Pathology 81, 1-12

[203] Wydra, K. and Beri, H. 2006. Structural changes of homogalacturonan, rhamnogalacturonan I and arabinogalactan protein in xylem cell walls of tomato genotypes in reaction to *Ralstonia solanacearum.* Physiological and Molecular Plant Pathology Pathology 68: 41-50

[204] Schacht, T., Unger, C., Pich, A., Wydra, K. 2011: Endo- and exopolygalacturonases of *Ralstonia solanacearum* are inhibited by polygalacturonase-inhibiting protein (PGIP) activity in tomato stem extracts. Plant Physiology and Biochemistry 49, 377-387

[205] Dossa, S.G., Oliva, R, Maiss, E., Vera Cruz, C., Wydra, K. 2016. High temperature enhances the cultivated African rice *Oryza glaberrima* resistance to bacterial blight. Plant Disease 100, 380-387, http://dx.doi.org/10.1094/PDIS-05-15-0536-RE

[206] Zinsou, V., Wydra, K., Ahohuendo, B., Hau, B. 2004. Genotype x environment interactions in symptom development and yield of cassava genotypes with artificial and natural cassava bacterial blight infections. European Journal of Plant Pathology 111: 217-233

[207] Banito, A, Kpémoua, K.E. and Wydra, K. 2008. Expression of resistance and tolerance of cassava genotypes to bacterial blight determined by genotype x environment interactions. Journal of Plant Diseases and Plant Protection 115: 152-161

[208] Wydra, K., Banito, A., Kpémoua, K.E. 2007. Characterization of resistance of cassava genotypes to bacterial blight by evaluation of symptom types in different ecozones. Euphytica 155: 337-348

[209] Onaga, G. 2014. Population structure of *Magnaporthe oryzae* from different geographic regions and interaction transcriptomes with different rice genotypes at high temperatures. PhD thesis. Gerog-August Universität Göttingen