Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

PORTLAND PRESS

Review Article

Transcriptional regulation of plant innate immunity

Niels Aerts[1], Himanshu Chhillar[2], Pingtao Ding[2,*] and Saskia C.M. Van Wees[1,*]

[1]Plant-Microbe Interactions, Department of Biology, Science4Life, Utrecht University, 3508 TB Utrecht, The Netherlands; [2]Institute of Biology Leiden, Leiden University, 2333 BE Leiden, The Netherlands

Correspondence: Saskia Van Wees (s.vanwees@uu.nl) or Pingtao Ding (p.ding@biology.leidenuniv.nl)

Transcriptional reprogramming is an integral part of plant immunity. Tight regulation of the immune transcriptome is essential for a proper response of plants to different types of pathogens. Consequently, transcriptional regulators are proven targets of pathogens to enhance their virulence. The plant immune transcriptome is regulated by many different, interconnected mechanisms that can determine the rate at which genes are transcribed. These include intracellular calcium signaling, modulation of the redox state, post-translational modifications of transcriptional regulators, histone modifications, DNA methylation, modulation of RNA polymerases, alternative transcription initiation, the Mediator complex and regulation by non-coding RNAs. In addition, on their journey from transcription to translation, mRNAs are further modulated through mechanisms such as nuclear RNA retention, storage of mRNA in stress granules and P-bodies, and post-transcriptional gene silencing. In this review, we highlight the latest insights into these mechanisms. Furthermore, we discuss some emerging technologies that promise to greatly enhance our understanding of the regulation of the plant immune transcriptome in the future.

Introduction

Plant diseases caused by different pathogens pose a major threat to crop productivity. However, plants do respond to pathogens by activating their robust yet specialized innate immune system. General pathogen-associated molecular patterns (PAMPs) and specific apoplastic pathogen effectors are perceived by the plants' surface-localized pattern-recognition receptors (PRRs), leading to activation or prevention of pattern-triggered immunity (PTI), respectively. In addition, specific pathogen effector molecules that are secreted into plant cells are recognized by intracellular nucleotide-binding leucine-rich repeat receptors (NLRs), activating effector-triggered immunity (ETI) [1]. Depending on the pathogen, a mix of PTI, ETI and other immune responses are induced, which are largely mediated by differential accumulation of phytohormones like salicylic acid (SA), jasmonic acid (JA), abscisic acid (ABA), and ethylene (ET) [2]. The different hormones act together in synergistic, antagonistic and additive manners, a phenomenon known as crosstalk [3]. Diverse regulators, interacting with each other in gene regulatory networks, orchestrate the transcriptional reprogramming that results from pathogen recognition. In this review, we refer to all the different immune-related transcriptional reprogramming as the plant immune transcriptome. Mechanistically, the plant immune transcriptome is determined by the coherent control of multiple transcriptional regulatory machineries including transcription factors (TFs), Mediator complex, co-regulators, DNA and RNA modifiers, chromatin remodelers, etc. [4,5]. These molecular components can be directly or indirectly post-transcriptionally modified by kinases/proteases, SUMO/ubiquitin, and second messengers like reactive oxygen species (ROS) and calcium ions (Ca^{2+}) [6,7]. The plant immune network is robust enough to resist a pathogen as long as the recognition and immune activation are timely, despite some of the transcriptional machineries being hijacked by the pathogen [1]. Here, we briefly summarize the transcriptional plant targets of pathogen virulence factors, which facilitate our understanding of the plant immune transcriptome. We highlight how multi-scale regulations of transcription and mRNA modulation are accomplished by different proteinaceous components, which determine induction of different

*These authors have equal contributions to this article.

Received: 01 April 2022
Revised: 07 June 2022
Accepted: 09 June 2022

Version of Record published: 30 September 2022

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

Table 1 Pathogen effectors and their host targets that are involved in transcriptional regulation during plant immunity

Pathogens	Pathogen effectors	Function of host targets	Name of host targets	Host species	References
Ralstonia solanacearum	RipAB	Transcription factor	TGAs	*Arabidopsis thaliana*	[124]
Xanthomonas campestris pv vesicatoria	XopD	Transcription factor	MYB30	*Arabidopsis thaliana*	[125]
Xanthomonas campestris pv vesicatoria	XopS	Transcription factor	WRKY40	*Capsicum annuum*	[23]
Ralstonia solanacearum	PopP2	Transcription factor	WRKY	*Arabidopsis thaliana*	[126]
Pseudomonas syringae	AvrRps4	Transcription factor	WRKY	*Arabidopsis thaliana*	[127]
Verticillium dahliae	VdSCP41	Transcription factor	CBP60g, SARD1	*Arabidopsis thaliana*	[128]
Pseudomonas syringae	HopBB1	Transcription factor	TCP14	*Arabidopsis thaliana*	[129]
Phytoplasma	Phyllogen	Transcription factor	MADS-box	*Arabidopsis thaliana*, *Oryza sativa*	[130]
Hyaloperonospora arabidopsidis	HaRxL44	Mediator complex	MED19a	*Arabidopsis thaliana*	[21]
Hyaloperonospora arabidopsidis	HaRxL21	Transcriptional co-repressor	TPL	*Arabidopsis thaliana*	[131]
Pseudomonas syringae	HopZ1, HopX1	Transcriptional repressor	JAZ	*Arabidopsis thaliana*	[20,22]
Laccaria bicolor	MiSSP7	Transcriptional repressor	JAZ	*Populus trichocarpa*	[19]
Pseudomonas syringae	AvrPtoB	Transcriptional co-activator	NPR1	*Arabidopsis thaliana*	[18]
Phytophthora capsici	RxLR48	Transcriptional co-activator	NPR1	*Arabidopsis thaliana*	[17]

This table summarizes some well-studied effectors secreted by different pathogens that hijack diverse transcriptional regulators of the host plant, including transcription factors, and transcriptional (co-) activators and repressors, to facilitate infection.

sectors in the immune gene regulatory network. Moreover, we highlight the future multi-omics directions to achieve a systems level comprehension of regulation of the plant immune transcriptome.

The plant immune transcriptome is targeted by pathogens

The timing and efficiency of elicitation of the immune transcriptome is essential for plants to halt pathogens. Of all the cellular components that are involved in transcriptional reprogramming, the role of transcription factors (TFs) in regulating crucial defense responses is best studied. Mutations in TFs including WRKYs, TGAs, NACs, CBP60s/SARD1, ERFs, bZIPs, bHLHs, MYBs, CAMTAs, and TCPs alter plant disease resistance against different pathogens [6,8–13]. Some of these plant TFs are popular targets of pathogens to arrest induced immune responses in plants (reviewed by [14–16]), underpinning their importance for defense. We refer to Table 1 for a summary of effector molecules of different pathogens that target transcriptional regulators, like TFs, transcriptional (co-)activators or repressors, or Mediator subunits. Many of these effectors modulate SA signaling [17,18], JA signaling [19] or SA-JA crosstalk [20–23], leading to enhanced susceptibility to the biotrophic or necrotrophic pathogen at hand.

Another well-studied example of direct interference with plant immune transcription is that of transcription activator-like effectors (TALEs), which are deployed by many plant-pathogenic xanthomonads. TALEs bind to effector binding elements (EBEs) in the promoters of host susceptibility (S) genes that contribute to disease [24,25]. Recently, TALEs Tal2b and Tal2c from *Xanthomonas oryzae* pv. *oryzicola* (*Xoc*) were shown to activate expression of *OsF3H03g*, encoding a 2-oxoglutarate-dependent dioxygenase that negatively regulates SA-related defense and promotes susceptibility against *Xoc* in *Oryza sativa* [26]. Moreover, several TALEs from *Xanthomonas* sp. induce SWEET sugar transporter genes, resulting in an increased availability of sugar for the pathogen, thereby promoting pathogenesis [27,28].

Regulation of the plant immune transcriptome occurs at multiple scales

The plant immune transcriptome encompasses both activation and repression of genes with diverse molecular functions, ranging from the control of general metabolic processes to highly specific responses that are directed toward a particular organism [29–37]. The relatively early response to attackers is usually a 'general stress response' (GSR) to danger, which is similarly activated after both biotic and abiotic stresses [34,35,38,39], and was demonstrated to be important for defense against *P. syringae* pv. *tomato* DC3000 (*Pto*) [34,35]. Furthermore, for both pathogenic and

non-pathogenic bacteria, it was found that the strength of this early response is correlated positively with the number of differentially expressed genes, although it is not clear whether this is based on a causal relationship [35]. The later responses are more specific, depending on the eliciting organism or its derived molecular patterns, and show a high degree of plasticity, which ensures a response tailored to the perceived signal. The transcriptional changes result from multi-scale regulations, including post-translational modifications of TFs, association of TFs with co-regulators and their target DNA sequences, regulation of stability and turnover of TFs, chromatin remodeling, DNA methylation, association of TFs with the Mediator complex, regulation of the RNA polymerases, and post-transcriptional regulation of mRNAs (Figure 1). Below, we highlight some of these mechanisms. We also recommend the recently published focused reviews on TFs functioning in different molecular contexts [40] and epigenetics in plant immunity [41].

Transcription-related physiological homeostasis

A rapid influx of calcium and a change in redox status are vital parts of plant immunity and they play intertwined roles in PTI and ETI [42]. Calcium influx is induced immediately upon perception of PAMPs and effectors, which has been coupled to classical calcium channels, but also to recently identified noncanonical calcium channels formed by NLR-based resistosomes [43,44] (Figure 1A). Intracellularly, the calcium signal is decoded by calcium-binding proteins like calmodulin (CaM) and Ca^{2+}-dependent protein kinases (CDPKs). These can directly activate TFs, such as the defense-regulating CaM-binding TF family CAMTA and CBP60g, or WRKY28, WRKY33 and WRKY48, which are phosphorylated by CPK5 and CPK6 (Figure 1E). This leads to altered defense-related transcription by these TFs, which influences resistance to diverse pathogens [45–48]. Although in general positive effects of calcium signaling on immunity have been reported, this is not always the case. For example, the Ca^{2+}-activated CAMTA3 (or AtSR1) TF represses expression of the SA regulator *NPR1* and the SA biosynthesis gene *ICS1* [49]. However, since NPR1 is a negative regulator of HR [50,51], its repressed expression by CAMTA3 positively affects ETI-mediated HR [49]. Moreover, several other CaM-regulated and CaM-like proteins like CBP60a, CML46 and CML47 negatively impact SA-related gene expression and accordingly, mutant lines are enhanced resistant to virulent *P. syringae* [52].

The production and signaling of reactive oxygen species (ROS) is tightly connected to that of calcium, as these molecules can (in)directly regulate each other's cellular concentrations [42]. Both PTI and ETI trigger a burst of ROS, which is mainly caused by activation of the NADPH oxidase RbohD [53] (Figure 1B). The changed redox state impacts many aspects of a plant's physiology, including transcription [54]. In plant immunity, NPR1 is the best-known converter of the redox state to transcriptional reprogramming. Under oxidizing conditions, NPR1 resides in the cytosol. According to the classical view it mostly forms oligomers in the cytosol that are held together by disulfide bridges formed between cysteine residues [55], which break under more reduced redox conditions, such as occur during a prolonged defense response, resulting in monomeric NPR1 that relocates to the nucleus [55] (Figure 1E,K). In the nucleus, NPR1 acts as a transcriptional co-activator together with TGA TFs to activate many genes involved in defense [56,57] (Figure 1C,D). The NPR1-TGA1 interaction itself is also affected by the redox status [58]. Interestingly, recent research has challenged the classical literature on the multimerization of NPR1. The oligomeric form of NPR1 in the cytosol that was observed by Mou et al. [55] was found to be likely formed *in vitro* only [59]. However, recently, the cryo-EM structure of NPR1 showed that its predominant functional form is a dimer, which forms oligomers in the quiescent state, but also can interact with two TGA3 dimers to form a $TGA3_2$-$NPR1_2$-$TGA3_2$ complex, and possibly also form complexes with other transcription regulators, to regulate the immune transcriptome [60].

Post-translational modifications of TFs

Post-translational regulation of TFs can alter their activities (Figure 1E). This is well-studied for the WRKY33 TF that promotes resistance to the necrotrophic pathogen *Botrytis cinerea* by regulating crucial defense-related responses such as camalexin production in *Arabidopsis* [61,62]. The WRKY33 protein is activated by phosphorylation through at least two pathways: one involves the calcium-dependent kinases CPK5 and CPK6 that phosphorylate the Thr-229 residue of WRKY33 [48], and the other involves a MAPK cascade consisting of YDA (a MAPKKK), MKK4 and MKK5 (MAPKKs), and MPK3 and MPK6 (MPKs) that eventually phosphorylate five Ser residues in the N terminus of WRKY33 [48,63–66]. Moreover, SUMOylation of WRKY33 increases its interaction with MPK3 and MPK6, thereby further enhancing WRKY33 phosphorylation via this pathway [67]. The phosphorylation of WRKY33 by the calcium pathway increases its binding to DNA, whereas phosphorylation by the MAPK pathway increases its transactivation activity [48,68]. Genetic studies implied that the same two phosphorylation pathways may also activate MYB51 to regulate indole glucosinolate biosynthesis, but it is not known whether these pathways also play distinct roles in MYB51 functioning [68].

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

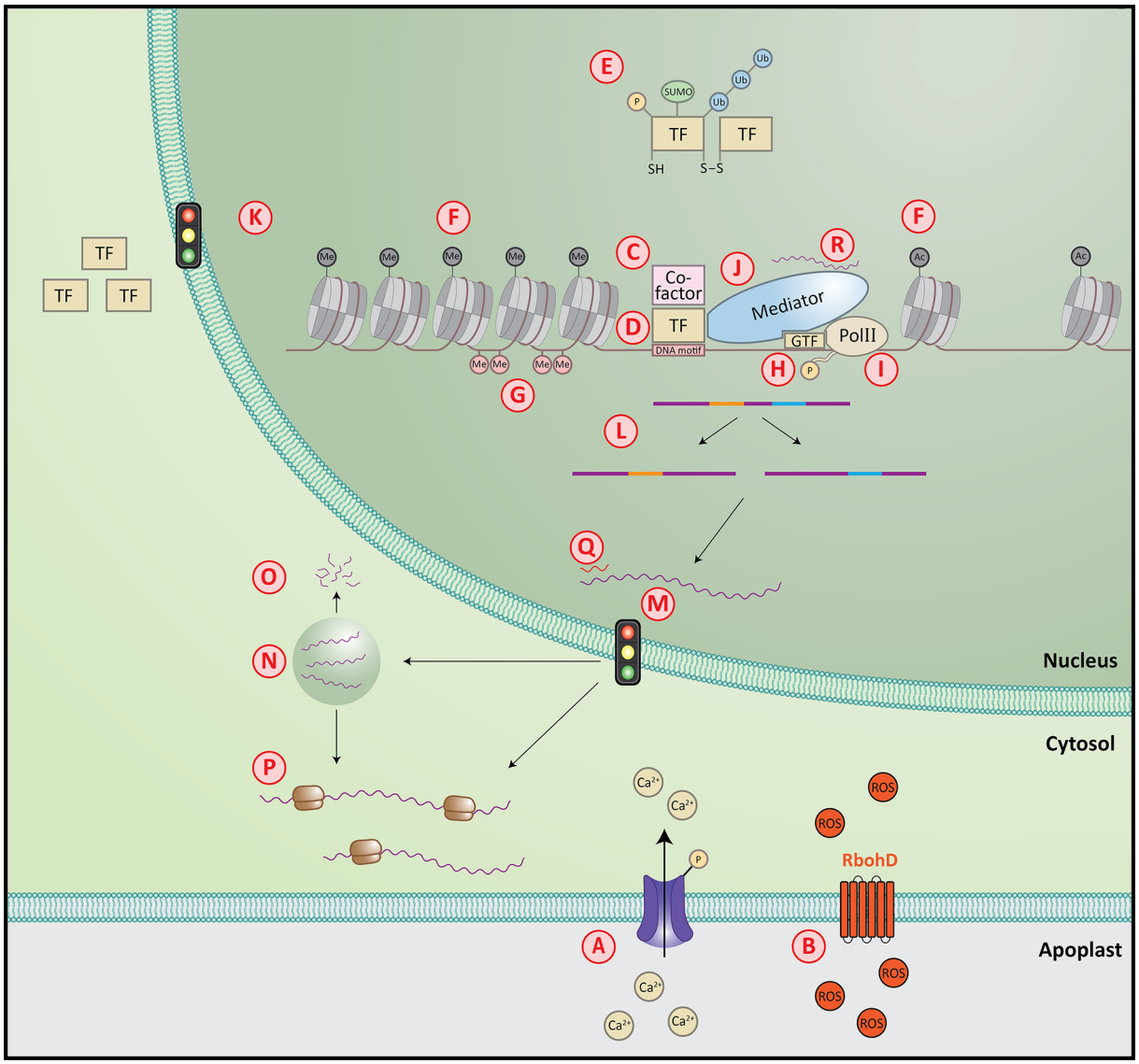

Figure 1. Mechanisms involved in the regulation of immune-related transcription

(**A**) Regulation of calcium (Ca^{2+}) influx, which may lead to post-translational modifications of TFs (see also Figure 1E); (**B**) generation of ROS by RbohD, which may lead to post-translational modifications of TFs (see also Figure 1E); (**C**) co-factors that may contribute to regulation of transcription; (**D**) TFs regulate transcription by binding to a motif; (**E**) post-translational modifications of TFs, such as phosphorylation (P), sumoylation (SUMO), ubiquitination (Ub) and forming of oligomers through S-S bridges depending on the redox state; (**F**) modifications of histones (methylation [Me] or acetylation [Ac]) to regulate the chromatin state; (**G**) methylation of DNA; (**H**) phosphorylation of the C-terminal domain of RNA-polymerase II (PolII) promotes transcription; (**I**) PolII may initiate transcription at alternative transcription start sites; (**J**) the Mediator complex forms the bridge between specific TFs, general TFs (GTF) and PolII; (**K**) selective import of TFs or other proteins; (**L**) alternative splicing; (**M**) selective retention of mRNAs in the nucleus; (**N**) temporary storage of mRNAs in stress granules or P-bodies; (**O**) degradation of mRNAs from P-bodies; (**P**) release of mRNAs from stress granules or P-bodies into the cytosol, followed by translation; (**Q**) post-transcriptional gene silencing by small RNAs; (**R**) long non-coding RNAs can regulate transcription in different ways, depicted here is modulation of MED19a by ELENA1.

Phosphorylation has also been shown to be important for the transactivation activity and binding specificity to DNA motifs of the ERF TF ORA59, which is required for defense induction in *Arabidopsis* against *B. cinerea* [69]. The hormones JA and ET can induce phosphorylation of ORA59, which binds preferentially to the canonical GCC box or to a newly identified motif named ERELEE4, respectively, depending on the corresponding hormone stimulus [70]. This can explain partly that the ERELEE4 motif is enriched in genes that are induced by ET treatment in

an ORA59-dependent manner, while JA treatment is associated with an ORA59-dependent induction of GCC-box containing genes [70].

Ubiquitination also regulates TF activities via protein turnover. For instance, SA induces TF ORA59 ubiquitination and degradation via the 26S proteasome pathway [71,72]. The transcriptional co-regulator NPR1 of SA-induced transcription, and the JAZ repressor proteins and MYC TFs that function in JA-induced transcription, are also regulated by phosphorylation-mediated proteasomal degradation via covalent addition of small ubiquitin proteins [73–75]. Their turnover provides a mechanism to control timing of activation and repression of the plant immune transcriptome. Additionally, SA induces cytoplasmic condensates containing NPR1 and many stress proteins, including specific WRKY TFs and proteins involved in programmed cell death (PCD). NPR1 recruits ubiquitin ligases to these condensates, leading to ubiquitination and subsequent degradation of the proteins and enhanced cell survival during ETI [76].

Chromatin context

Chromatin context is a major determinant for transcriptional activities in all eukaryotic cells. The accessibility of chromatin can influence when and where TFs, other regulators and RNA polymerases find their targets to activate transcription. The chromatin state can be altered through modification of histone tails and deposition of histone variants (Figure 1F). Recently, Ding et al. (2021) used the method transposase-accessible chromatin followed by sequencing (ATAC-seq) to profile the genome-wide chromatin landscape of *Arabidopsis* after infection with an engineered non-pathogenic *P. fluorescens* strain either expressing the effector AvrRps4 (thus causing both PTI and ETI) or a non-recognized effector mutant (thus causing PTI only), and this was compared with RNA-seq data [77]. Over one-third of all up-regulated genes in both PTI and PTI+ETI also contained more open chromatin compared to the control. Moreover, integration of RNA-seq, ATAC-seq and TF DNA-binding motif information helped to decipher gene regulatory networks mediating PTI, ETI and 'PTI+ETI' [77]. In another study, Pardal et al. (2021) used micrococcal nuclease digestion followed by sequencing (MNase-seq) to investigate how treatment with the PAMP flg22 affects genome-wide nucleosome occupancy. They found that flg22 causes genome-wide repositioning of nucleosomes, partly coinciding with the promoters of differentially expressed genes [78]. Repositioning of nucleosomes is mediated by chromatin ATPases [79]. Notably, whereas some chromatin remodeling ATPases like PKR2 and RAD54 promote immunity, others, like EDA16 and SWP73A attenuate it [78,80], indicating a complex relationship between chromatin remodeling and immunity. These studies suggest that chromatin remodeling is an important mechanism by which gene transcription is regulated during immune responses mediated by both cell-surface and intracellular receptors.

It is still unclear whether the accessibility of the regulatory DNA regions precedes transcription or vice versa. It was found that TF WRKY33 enhances accessibility of genes to reinforce gene transcription. The chromatin remodeling complex SWR1 and the MAPK-WRKY33 module promote deposition of H2A.Z [66], a variant of the canonical H2A histone subunit that can activate or repress transcription depending on the context [41], and increased H3K4me3 [66], a histone mark generally associated with active transcription [81]. This happens around WRKY33 target genes, leading to more WRKY33-mediated H2A.Z deposition and H3K4me3 modification [66].

Chromatin remodeling also plays a role during ETI-triggered PCD. During this process chromocenters (regions with heterochromatin) get less dense and different chromatin marks get redistributed, such as the repressive marks H3K9me2 and H3K27me3, leading to altered transcription [82]. Studies with chromatin remodeling mutants suggest that this remodeling mostly attenuates PCD, possibly to prevent it from happening too rapidly or at the wrong time [82].

Chromatin remodeling can also lead to altered transcription via a non-canonical function of the gene-silencing-related component ARGONAUTE1 (AGO1). AGO1 binds to chromatin around specific genes, likely dependent on its association with specific small RNAs and through interaction with several subunits of the SWI/SNF chromatin remodeling complex [83]. There, it promotes PolII occupancy around these genes. Notably, treatment with immune-related compounds such as JA, BTH (an SA analog) and flg22 caused AGO1 to bind to genes that are enriched in GO-terms related to the response to the corresponding ligand, suggesting that AGO1 contributes to these responses. In accordance, a mutation in *AGO1* results in reduced JA-induced gene expression [83].

DNA methylation

DNA methylation is generally associated with suppression of activity of transposable elements and with transcriptional repression (Figure 1G). DNA methylation in plants can be regulated through RNA-directed DNA methylation

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

(RdDM), which involves small RNAs derived from transcripts resulting from RNA polymerases PolII, PolIV and PolV activity [84]. For examples of regulatory components in RdDM, which shape the immune transcriptome, see also 'Modulation of RNA polymerase' and 'The Mediator complex'.

Demethylation of DNA occurs either passively during replication or actively by different demethylases under specific conditions. The DNA methylome is altered upon pathogen attack, which modulates the immune response [85,86]. The demethylase ROS1 was found to reduce methylation of regulatory regions in or close to flg22-induced defense-related genes, facilitating binding of TFs and subsequent activation of plant immunity [86].

Another example is the demethylase DEMETER (DME). Loss-of-function mutants of this enzyme are lethal, but recent studies using plant lines with a weak allele generated by CRISPR-CAS9 or silencing of *dme* revealed that DME alters methylation of hundreds of genomic regions and is affected in defense against bacterial and fungal pathogens [87]. Moreover, results obtained with the mutant line in which *dme* was silenced in the background of a triple mutant of the DNA methylases *ros1, dml2* and *dlm3* (*rdd*) suggest that DME acts redundantly with other demethylases to regulate expression of defense genes via demethylation [88].

In addition, the demethylation-deficient mutant *rdd* is impaired in resistance against *Pto* induced by the immune-stimulating molecular patterns flg22, elf18 and Pep2 [89]. The flg22 treatment induces hypomethylation of specific regions in the wild-type plant but not in the *rdd* mutant, which is associated with a higher number of differentially methylated promoter regions of defense-related genes and their higher expression level in wild-type compared with mutant. Altogether, the studies discussed here show that DNA demethylation of specific regions is important for a proper immune transcriptome. It has not been explored how the four demethylases change their activity during an immune response, so the spatiotemporal relevance of each enzyme in the regulation of the immune transcriptome remains to be determined.

Modulation of RNA polymerase

During immune activation PolII is phosphorylated (Figure 1H). For example, flg22 induces phosphorylation of the C-terminal domain (CTD) of PolII [90] by the two cyclin-dependent kinase Cs CDKC;1 and CDKC;2, which in turn are phosphorylated by flg22-triggered MPK3 and MPK6. The phosphatase CTD PHOSPHATASE-LIKE3 (CPL3) can dephosphorylate the CTD and thereby act as a negative regulator of plant immune transcription. Mutants in CDKC and CPL3 were found to be more susceptible to *Pto*, demonstrating the essential role of phosphorylation of the CTD of PolII in regulation of immunity against this pathogen [90]. Another CPL, namely CPL1 of tomato, can reduce defenses against various but not all of the tested pathogens and insects [91]. Additionally, CPL1 negatively regulates defense-related transcription [91]. However, the effect of CPL1 on PolII was not studied, and it even seems likely that other mechanisms are involved, since the *Arabidopsis* homologue of CPL1 has previously been associated with miRNA processing [92] and RdDM [93].

Alternative transcription initiation

Alternative transcription initiation can expand the regulatory repertoire of the genome, since it may involve alternative promoters that are differentially induced upon different stimuli, or result in different transcripts and proteins (Figure 1I). Recently, more than 15% of the 3374 transcripts that were induced by flg22 treatment after 30 min were found to be derived from alternative transcription events [94]. The alternative transcripts for example lacked upstream open reading frames (uORFs), which may affect translation efficiency of the transcript, or their encoded proteins lacked a predicted domain or signal peptide, which could potentially alter their function. These predictions were validated for a small set of transcripts, but the overall implications of alternative transcription initiation during PTI remain to be elucidated.

The Mediator complex

TFs recruit PolII through interactions with the multi-subunit Mediator complex [95] (Figure 1J). Recently, substantial molecular evidence has been provided for a role of the Mediator subunit MED25 in hormone crosstalk. The JA-specific TF MYC2 was shown to interact at its same position with the SA regulator NPR1 as well as with MED25 [96]. Consequently, NPR1 reduces the recruitment of MED25 by MYC2 to target promoters of MYC2. This dampens the positive effect of MED25 on MYC2-induced transcription. Interestingly, in the absence of JA, JAZ proteins also repress MYC2-induced transcription in part by preventing the MYC2-MED25 interaction [97]. However, at high JA levels JAZs are degraded [98,99]. NPR1 therefore mechanistically takes over (part of) the function of the degraded JAZ proteins when both JA and SA levels are high.

Although Mediator usually connects TFs to PolII, it can also recruit other RNA polymerases that are relevant for defense. The Mediator subunit MED18 interacts with NUCLEAR RNA POLYMERASE D2 (NRPD2a), a subunit of PolIV and PolV [100]. *MED18* and *NRPD2a* are highly expressed after *B. cinerea* infection, and mutants and overexpressors of these genes corroborate their importance for a part of *B. cinerea*-induced gene expression and for resistance against *B. cinerea* [100,101]. PolIV and PolV are involved in RdDM and other non-coding RNA-mediated gene silencing processes [102], suggesting that impairment of one of these processes may underly the altered gene expression and resistance of the *nrpd2a* mutant and possibly also of the *med18* mutant. However, this still needs to be investigated.

Selective nuclear transport of transcriptional components

Nuclear im/export of transcriptional components is a selective mechanism to control the plant immune transcriptome (Figure 1K). This was already described for NPR1 in 'Transcription-related physiological homeostasis'. CONSTITUTIVE EXPRESSER OF PATHOGENESIS-RELATED GENES 5 (CPR5) is a component of the nuclear pore complex that regulates PCD during ETI [103,104]. This protein has three modes of action. Firstly, the conformational change that CPR5 undergoes upon ETI alters the permeability of the nuclear pore and thereby allows influx of several stress-related cargos (such as NPR1 and ABI5) to the nucleus, resulting in massive transcriptional reprogramming [104]. Secondly, CPR5 is a negative regulator of PCD by binding to the cyclin-dependent kinase inhibitors SIAMESE (SIM) and SIAMESE-RELATED1 (SMR1). Upon ETI, CPR5 releases SIM and SMR1, which activate E2F TFs to induce PCD [103]. Finally, CPR5 regulates alternative splicing (AS; Figure 1L) via its RNA-binding activity [105]. Interestingly, the mRNA of the gene-silencing-related *AGO1* and several AS regulators are among its targets, suggesting that apart from its own role in AS, it also indirectly affects gene silencing and AS [105]. In addition, Exportin-4 (XPO4) mediates nuclear export of TOPLESS-RELATED1 (TPR1), counteracting the translocation of TPR1 into the nucleus during ETI in the presence of high SA levels, as was studied in the *cpr5* background [106]. This way, XPO4 prevents the repression of negative immune regulators by TPR1 in the nucleus and probably impedes a runaway immune response during ETI.

RNA processing, storage, and degradation

Regulation of messenger RNA (mRNA) largely impacts the formation of proteins. For example, AS of NLR genes and JAZ genes generates isoforms with diverse activities or subcellular localizations, by which plants can control immunity activation [107] (Figure 1L). Treatment with flg22 induces MPK4-mediated phosphorylation of splicing factors, leading to AS of genes encoding NLRs, TFs, CDPKs and splicing factors [107]. MED25 recruits the splicing factors PRE-mRNA-PROCESSING PROTEIN 39a (PRP39a) and PRP40a to promote the full splicing of JAZ genes, in order to prevent excessive desensitization of JA signaling mediated by JAZ alternative splice variants [98,99,107,108].

Moreover, RNA can be (temporarily) stored in the nucleus, or in special aggregations that are involved in temporary storage and/or degradation, which decreases the pool of translating RNAs (Figure 1M–P). For example, core hypoxia genes in *Lupinus luteus* and *Arabidopsis* are retained in the nucleus during hypoxia, and released in the cytosol upon reaeration [109]. It is uncertain if such nuclear retention regulation applies during immune activation. Non-translating mRNAs can also be stored in stress granules or P-bodies, which are both quickly disassembled and re-assembled after stress. Stress granules contain mRNAs and translation machinery, and contribute to mRNA storage, whereas P-bodies contain mRNAs and mRNA degrading enzymes, and contribute to mRNA degradation [110,111]. The importance of P-bodies and mRNA decay in PTI has recently been reported [112]. It was shown that the P-body component DECAPPING1 (DCP1), a co-activator of the decapping enzyme DCP2, is phosphorylated by MPK3 and MPK6 within minutes of treatment with several PAMPs. This phosphorylation of DCP1 decreases its binding to DCP2, but increases its binding to XRN4, an exoribonuclease that can degrade decapped mRNA (mRNA decay) [113]. This leads to degradation of a subset of mRNAs that are downregulated during PTI, to prevent their negative impact on the plant immune response [112].

Regulation by non-coding RNAs

Different non-coding RNAs, like small RNAs and long non-coding RNAs (lncRNAs) regulate different steps in gene expression. For a comprehensive overview on non-coding RNAs in plant immunity we refer to a recent review [114]. Small RNAs can interfere with mRNA stability or regulate transcription or translation through mechanisms such as RdDM (see also 'DNA methylation'). MicroRNAs (miRNAs) are small RNAs that are involved in post-transcriptional gene silencing (PTGS) and can thus potentially affect the immune transcriptome (Figure 1Q). A recent study explored the role of miRNAs during infection of soybean with the soybean cyst nematode *Heterodera glycines* [115]. They

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

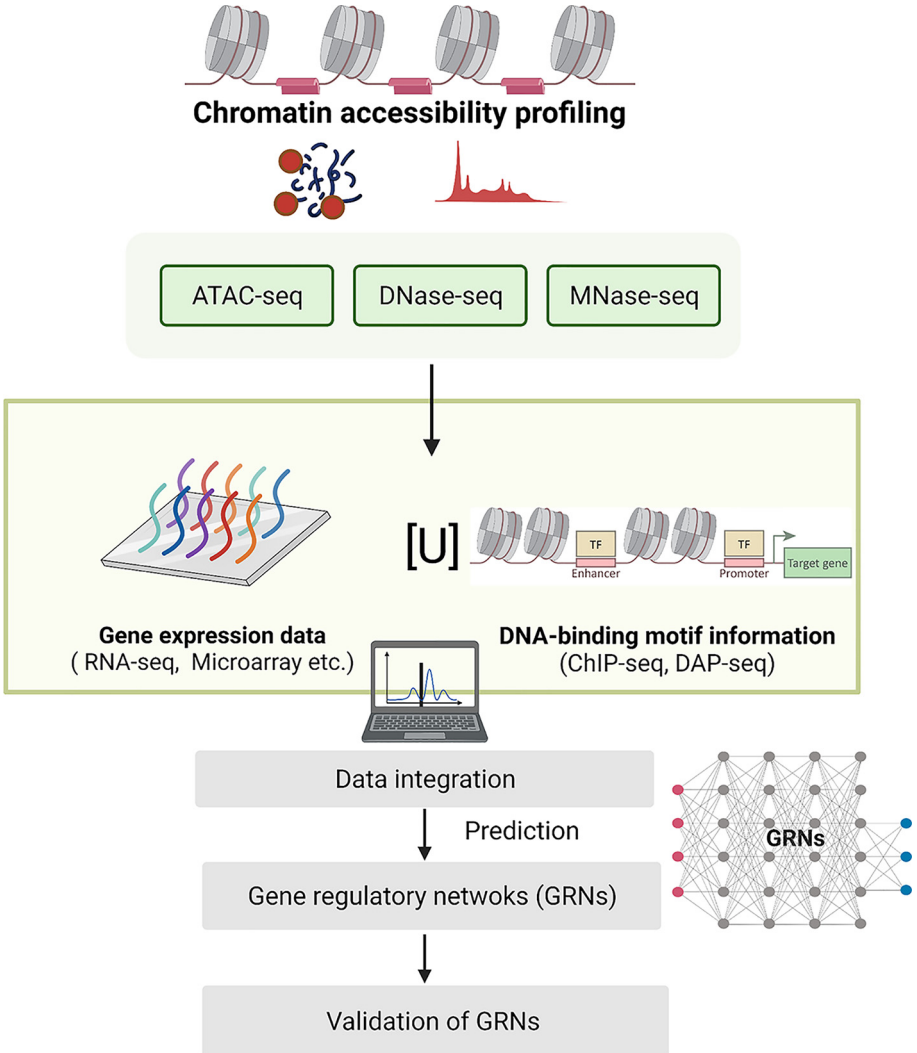

Figure 2. Next-generation toolkit for elucidating immune-responsive GRNs

Integration of data on TF DNA-binding, chromatin accessibility, and gene expression can be employed as a powerful tool to elucidate the highly interconnected gene regulatory networks (GRNs) that determine the plant immune transcriptome, even at single cell resolution. For instance, information related to TF-binding sites can be obtained from chromatin-immunoprecipitation followed by sequencing (ChIP-seq), and DNA affinity purification sequencing (DAP-seq). Information about chromatin status can be derived from methods such as Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq), micrococcal nuclease digestion with deep-sequencing (MNase-seq), or DNase-I hypersensitive sites sequencing (DNase-seq). Different variants of RNA (e.g. mRNA, miRNA, lncRNA) can be measured by RNA-seq. These data can be integrated to reveal GRNs that shape the plant immune transcriptome. The functionality of these GRNs can be tested and validated by mutant analysis under different conditions or in different tissues or cell types.

found that differential DNA methylation of miRNA genes influences expression of the miRNAs in resistant and susceptible soybean lines. Overexpression studies show that four miRNAs that are regulated during infection and that are expressed at higher basal levels in a resistant soybean line, cause degradation of their target mRNA and accomplish increased resistance of the susceptible line to the nematode. This study shows that different epigenetic mechanisms (methylation and subsequent miRNA-directed PTGS) interact to finetune the immune response.

A recent study reported that the lncRNA *ELENA1* is induced by treatment with the PAMPs flg22 and elf18 [116]. Overexpression and knockdown studies with *ELENA1* show that it promotes *PR1* and *PR2* expression and resistance to *Pto*. RNA-seq revealed that a subset of elf18-induced defense genes overlaps with ELENA1-induced genes. Upon elf18 treatment, ELENA1 interacts with MED19a *in vivo*, which promotes binding of MED19a to the promoter of *PR1*

and possibly other genes [116] (Figure 1R). In a follow-up, it was shown that ELENA1 also mediates the dissociation of the immune suppressor FIBRILLARIN2 from MED19a, providing an additional mechanism by which it can promote target gene transcription [117].

Multi-omics: challenges and opportunities in studying transcriptional regulation in plant immunity

A balanced regulation of gene expression is required to maintain robustness and efficiency of the triggered immune responses. As outlined in this review, different regulatory components should act in conjunction to control the plant immune transcriptome. How different sectors within the immune network are integrated via these different regulatory players, and under which circumstances, remains largely unknown. A network level understanding could provide leads to these answers. For this, (i) different immune-stimulatory treatments should be compared and (ii) different whole-genome, multi-omics data sets should be combined, (iii) followed by advanced integrated data analysis including the use of mathematical modeling tools (Figure 2). Examples of these omics assays are profiling of chromatin accessibility, RNA variants (mRNA, miRNA, lncRNA, etc), DNA and histone modifications, etc [118–120]. Moreover, the declining costs of nucleotide sequencing, increasing data storage capacities and computer processing power sparks advances in bioinformatic analysis methods and mathematical modeling tools. A systems biology approach will aid in elucidating gene regulatory networks and may provide predictive capability on how and when different regulatory components are involved in orchestrating the plant immune network.

At a finer resolution, namely the cell level, other critical questions need attention. Which of the immune responses are cell-type specific? And does that determine whether the initial infection of a certain cell type propagates further to adjacent cells or is halted? Furthermore, how does cell homeostasis, related to different internal and external conditions, such as plant age, time of day, abiotic stress, and spatiotemporal distance from the infection site, influence the plant immune transcriptome? To answer these questions, single-cell methods instead of bulk analyses using the omics assays and molecular tools mentioned in this review would be extremely meaningful (reviewed by [121]), especially for identifying gene regulatory networks in a heterogenous population from infected to non-infected plant cells. Moreover, analogous profiling of cells of the pathogen will provide insight into the intimate communication between the host and the pathogen [122]. Approaches such as laser microdissection, which has been used widely in clinical biology for studying cell-specific responses [123], can also be used in plant research for molecular profiling of desired cells. With such knowledge collectively, our chances to succeed in intelligently designing crops with a strengthened immune response under diverse conditions will increase.

Summary

- The plant immune transcriptome is induced upon pathogen perception and required for disease resistance.
- Many pathogens use effectors to tweak the plant immune transcriptome to their own advantage.
- Plants regulate their immune transcriptome at multiple scales, e.g. post-transcriptional regulation of TFs, modulation of DNA accessibility, and modulation of mRNAs during their journey from transcription to translation.
- A combination of multi-omics datasets can provide new insights into immune-related gene regulatory networks.

Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

Funding

N.A. was supported by the Netherlands Organization for Scientific Research [grant number ALWGS.2016.005]. P.D. acknowledges the support from European Union Framework Programme for Research and Innovation, Horizon Europe, European Research Council Starting Grant 'R-ELEVATION' [grant number 101039824].

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

Author Contribution

S.V.W. and P.D. conceived this article. N.A. and H.C. wrote the first draft. All authors edited and finalized this article.

Abbreviations

CTD, C-terminal domain; ETI, effector-triggered immunity; NLR, nucleotide-binding leucine-rich repeat receptor; PAMP, pathogen-associated molecular pattern; PCD, programmed cell death; PRR, pattern recognition receptor; PTGS, post-transcriptional gene silencing; PTI, pattern-triggered immunity; uORF, upstream open reading frame.

References

1 Ngou, B.P.M., Jones, J.D.G. and Ding, P. (2022) Plant immune networks. *Trends Plant Sci.* **27**, 255–273, https://doi.org/10.1016/j.tplants.2021.08.012
2 Bürger, M. and Chory, J. (2019) Stressed out about hormones: how plants orchestrate immunity. *Cell Host Microbe.* **26**, 163–172, https://doi.org/10.1016/j.chom.2019.07.006
3 Aerts, N., Pereira Mendes, M. and Van Wees, S.C.M. (2021) Multiple levels of crosstalk in hormone networks regulating plant defense. *Plant J.* **105**, 489–504, https://doi.org/10.1111/tpj.15124
4 Garner, C.M., Kim, S.H., Spears, B.J. and Gassmann, W. (2016) Express yourself: transcriptional regulation of plant innate immunity. *Semin. Cell Dev. Biol.* **56**, 150–162, https://doi.org/10.1016/j.semcdb.2016.05.002
5 Li, B., Meng, X., Shan, L. and He, P. (2016) Transcriptional regulation of pattern-triggered immunity in plants. *Cell Host Microbe.* **19**, 641–650, https://doi.org/10.1016/j.chom.2016.04.011
6 Tsuda, K. and Somssich, I.E. (2015) Transcriptional networks in plant immunity. *New Phytol.* **206**, 932–947, https://doi.org/10.1111/nph.13286
7 Andersen, E.J., Ali, S., Byamukama, E., Yen, Y. and Nepal, M.P. (2018) Disease resistance mechanisms in plants. *Genes (Basel)* **9**, 339, https://doi.org/10.3390/genes9070339
8 Zhang, Y., Xu, S., Ding, P., Wang, D., Cheng, Y.T., He, J. et al. (2010) Control of salicylic acid synthesis and systemic acquired resistance by two members of a plant-specific family of transcription factors. *Proc. Natl. Acad. Sci. U. S. A.* **107**, 18220–18225, https://doi.org/10.1073/pnas.1005225107
9 Fernández-Calvo, P., Chini, A., Fernández-Barbero, G., Chico, J.M., Gimenez-Ibanez, S., Geerinck, J. et al. (2011) The *Arabidopsis* bHLH transcription factors MYC3 and MYC4 are targets of JAZ repressors and act additively with MYC2 in the activation of jasmonate responses. *Plant Cell.* **23**, 701–715, https://doi.org/10.1105/tpc.110.080788
10 Li, S. (2015) The *Arabidopsis thaliana* TCP transcription factors: a broadening horizon beyond development. *Plant Signal Behav.* **10**, e1044192, https://doi.org/10.1080/15592324.2015.1044192
11 Amorim, L.L.B., da Fonseca Dos Santos, R., Neto, J.P.B., Guida-Santos, M., Crovella, S. and Benko-Iseppon, A.M. (2017) Transcription factors involved in plant resistance to pathogens. *Curr. Protein Pept. Sci.* **18**, 335–351, https://doi.org/10.2174/1389203717666160619185308
12 Yuan, X., Wang, H., Cai, J., Li, D. and Song, F. (2019) NAC transcription factors in plant immunity. *Phytopathol Res.* **1**, 3, https://doi.org/10.1186/s42483-018-0008-0
13 Kim, Y., Gilmour, S.J., Chao, L., Park, S. and Thomashow, M.F. (2020) Arabidopsis CAMTA transcription factors regulate pipecolic acid biosynthesis and priming of immunity genes. *Mol. Plant* **13**, 157–168, https://doi.org/10.1016/j.molp.2019.11.001
14 Ding, P. and Redkar, A. (2018) Pathogens suppress host transcription factors for rampant proliferation. *Trends Plant Sci.* **23**, 950–953, https://doi.org/10.1016/j.tplants.2018.08.010
15 Han, X. and Kahmann, R. (2019) Manipulation of phytohormone pathways by effectors of filamentous plant pathogens. *Front. Plant. Sci.* **10**, 822, https://doi.org/10.3389/fpls.2019.00822
16 Wang, Y., Pruitt, R.N., Nürnberger, T. and Wang, Y. (2022) Evasion of plant immunity by microbial pathogens. *Nat. Rev. Microbiol.*, https://doi.org/10.1038/s41579-022-00710-3
17 Li, Q., Chen, Y., Wang, J., Zou, F., Jia, Y., Shen, D. et al. (2019) A *Phytophthora capsici* virulence effector associates with NPR1 and suppresses plant immune responses. *Phytopathol. Res.* **1**, 6, https://doi.org/10.1186/s42483-019-0013-y
18 Chen, H., Chen, J., Li, M., Chang, M., Xu, K., Shang, Z. et al. (2017) A bacterial type III effector targets the master regulator of salicylic acid signaling, NPR1, to subvert plant immunity. *Cell Host Microbe.* **22**, 777.e7–788.e7, https://doi.org/10.1016/j.chom.2017.10.019
19 Plett, J.M., Daguerre, Y., Wittulsky, S., Vayssières, A., Deveau, A., Melton, S.J. et al. (2014) Effector MiSSP7 of the mutualistic fungus *Laccaria bicolor* stabilizes the *Populus* JAZ6 protein and represses jasmonic acid (JA) responsive genes. *Proc. Natl. Acad. Sci. U. S. A.* **111**, 8299–8304, https://doi.org/10.1073/pnas.1322671111
20 Jiang, S., Yao, J., Ma, K.-W., Zhou, H., Song, J., He, S.Y. et al. (2013) Bacterial effector activates jasmonate signaling by directly targeting JAZ transcriptional repressors. *PLoS Pathog.* **9**, e1003715, https://doi.org/10.1371/journal.ppat.1003715
21 Caillaud, M.C., Asai, S., Rallapalli, G., Piquerez, S., Fabro, G. and Jones, J.D.G. (2013) A downy mildew effector attenuates salicylic acid-triggered immunity in Arabidopsis by interacting with the host Mediator complex. *PLoS Biol.* **11**, e1001732, https://doi.org/10.1371/journal.pbio.1001732
22 Gimenez-Ibanez, S., Boter, M., Fernández-Barbero, G., Chini, A., Rathjen, J.P. and Solano, R. (2014) The bacterial effector HopX1 targets JAZ transcriptional repressors to activate jasmonate signaling and promote infection in *Arabidopsis*. *PLoS Biol.* **12**, e1001792, https://doi.org/10.1371/journal.pbio.1001792
23 Raffeiner, M., Üstün, S., Guerra, T., Spinti, D., Fitzner, M., Sonnewald, S. et al. (2022) The *Xanthomonas* type-III effector XopS stabilizes CaWRKY40a to regulate defense responses and stomatal immunity in pepper (*Capsicum annuum*). *Plant Cell.* **34**, 1684–1708, https://doi.org/10.1093/plcell/koac032

24 Boch, J., Bonas, U. and Lahaye, T. (2014) TAL effectors–pathogen strategies and plant resistance engineering. *New Phytol.* **204**, 823–832, https://doi.org/10.1111/nph.13015
25 Wang, L., Rinaldi, F.C., Singh, P., Doyle, E.L., Dubrow, Z.E., Tran, T.T. et al. (2017) TAL effectors drive transcription bidirectionally in plants. *Mol. Plant* **10**, 285–296, https://doi.org/10.1016/j.molp.2016.12.002
26 Wu, T., Zhang, H., Bi, Y., Yu, Y., Liu, H., Yang, H. et al. (2021) Tal2c activates the expression of *OsF3H04g* to promote infection as a redundant TALE of Tal2b in *Xanthomonas oryzae* pv. *oryzicola*. *Int. J. Mol. Sci.* **22**, https://doi.org/10.3390/ijms222413628
27 Doyle, E.L., Stoddard, B.L., Voytas, D.F. and Bogdanove, A.J. (2013) TAL effectors: highly adaptable phytobacterial virulence factors and readily engineered DNA-targeting proteins. *Trends Cell Biol.* **23**, 390–398, https://doi.org/10.1016/j.tcb.2013.04.003
28 Cox, K.L., Meng, F., Wilkins, K.E., Li, F., Wang, P., Booher, N.J. et al. (2017) TAL effector driven induction of a SWEET gene confers susceptibility to bacterial blight of cotton. *Nat. Commun.* **8**, 15588, https://doi.org/10.1038/ncomms15588
29 Windram, O., Madhou, P., McHattie, S., Hill, C., Hickman, R., Cooke, E. et al. (2012) Arabidopsis defense against *Botrytis cinerea*: chronology and regulation deciphered by high-resolution temporal transcriptomic analysis. *Plant Cell.* **24**, 3530–3557, https://doi.org/10.1105/tpc.112.102046
30 Lewis, L.A., Polanski, K., de Torres-Zabala, M., Jayaraman, S., Bowden, L., Moore, J. et al. (2015) Transcriptional dynamics driving MAMP-triggered immunity and pathogen effector-mediated immunosuppression in Arabidopsis leaves following infection with *Pseudomonas syringae* pv *tomato* DC3000. *Plant Cell.* **27**, 3038–3064, https://doi.org/10.1105/tpc.15.00471
31 Hickman, R., Van Verk, M.C., Van Dijken, A.J.H., Mendes, M.P., Vroegop-Vos, I.A., Caarls, L. et al. (2017) Architecture and dynamics of the jasmonic acid gene regulatory network. *Plant Cell.* **29**, 2086–2105, https://doi.org/10.1105/tpc.16.00958
32 Hickman, R., Mendes, M.P., Van Verk, M.C., Van Dijken, A.J.H., Di Sora, J., Denby, K. et al. (2019) Transcriptional dynamics of the salicylic acid response and its interplay with the jasmonic acid pathway. *BioRxiv* **742742**
33 Zander, M., Lewsey, M.G., Clark, N.M., Yin, L., Bartlett, A., Saldierna Guzmán, J.P. et al. (2020) Integrated multi-omics framework of the plant response to jasmonic acid. *Nat Plants* **6**, 290–302, https://doi.org/10.1038/s41477-020-0605-7
34 Bjornson, M., Pimprikar, P., Nürnberger, T. and Zipfel, C. (2021) The transcriptional landscape of *Arabidopsis thaliana* pattern-triggered immunity. *Nat. Plants* **7**, 579–586, https://doi.org/10.1038/s41477-021-00874-5
35 Maier, B.A., Kiefer, P., Field, C.M., Hemmerle, L., Bortfeld-Miller, M., Emmenegger, B. et al. (2021) A general non-self response as part of plant immunity. *Nat. Plants* **7**, 696–705, https://doi.org/10.1038/s41477-021-00913-1
36 Tang, B., Liu, C., Li, Z., Zhang, X., Zhou, S., Wang, G.-L. et al. (2021) Multilayer regulatory landscape during pattern-triggered immunity in rice. *Plant Biotechnol. J.* **19**, 2629–2645, https://doi.org/10.1111/pbi.13688
37 Winkelmüller, T.M., Entila, F., Anver, S., Piasecka, A., Song, B., Dahms, E. et al. (2021) Gene expression evolution in pattern-triggered immunity within *Arabidopsis thaliana* and across *Brassicaceae* species. *Plant Cell.* **33**, 1863–1887, https://doi.org/10.1093/plcell/koab073
38 Walley, J.W., Coughlan, S., Hudson, M.E., Covington, M.F., Kaspi, R., Banu, G. et al. (2007) Mechanical stress induces biotic and abiotic stress responses via a novel cis-element. *PLos Genet.* **3**, 1800–1812, https://doi.org/10.1371/journal.pgen.0030172
39 Benn, G., Wang, C.-Q., Hicks, D.R., Stein, J., Guthrie, C. and Dehesh, K. (2014) A key general stress response motif is regulated non-uniformly by CAMTA transcription factors. *Plant J.* **80**, 82–92, https://doi.org/10.1111/tpj.12620
40 Strader, L., Weijers, D. and Wagner, D. (2022) Plant transcription factors - being in the right place with the right company. *Curr. Opin. Plant Biol.* **65**, 102136, https://doi.org/10.1016/j.pbi.2021.102136
41 Hannan Parker, A., Wilkinson, S.W. and Ton, J. (2022) Epigenetics: a catalyst of plant immunity against pathogens. *New Phytol.* **233**, 66–83, https://doi.org/10.1111/nph.17699
42 Xu, G., Moeder, W., Yoshioka, K. and Shan, L. (2022) A tale of many families: calcium channels in plant immunity. *Plant Cell.* **34** (5), 1551–1567, https://doi.org/10.1093/plcell/koac033
43 Bi, G., Su, M., Li, N., Liang, Y., Dang, S., Xu, J. et al. (2021) The ZAR1 resistosome is a calcium-permeable channel triggering plant immune signaling. *Cell* **184**, 3528.e12–3541.e12, https://doi.org/10.1016/j.cell.2021.05.003
44 Jacob, P., Kim, N.H., Wu, F., El-Kasmi, F., Chi, Y., Walton, W.G. et al. (2021) Plant "helper" immune receptors are Ca^{2+}-permeable nonselective cation channels. *Science* **373**, 420–425, https://doi.org/10.1126/science.abg7917
45 Gao, X. and He, P. (2013) Nuclear dynamics of Arabidopsis calcium-dependent protein kinases in effector-triggered immunity. *Plant Signal Behav.* **8**, e23868, https://doi.org/10.4161/psb.23868
46 Wang, L., Tsuda, K., Truman, W., Sato, M., Nguyen, L.V., Katagiri, F. et al. (2011) CBP60g and SARD1 play partially redundant critical roles in salicylic acid signaling. *Plant J.* **67**, 1029–1041, https://doi.org/10.1111/j.1365-313X.2011.04655.x
47 Kim, Y., Park, S., Gilmour, S.J. and Thomashow, M.F. (2013) Roles of CAMTA transcription factors and salicylic acid in configuring the low-temperature transcriptome and freezing tolerance of Arabidopsis. *Plant J.* **75**, 364–376, https://doi.org/10.1111/tpj.12205
48 Zhou, J., Wang, X., He, Y., Sang, T., Wang, P., Dai, S. et al. (2020) Differential phosphorylation of the transcription factor WRKY33 by the protein kinases CPK5/CPK6 and MPK3/MPK6 cooperatively regulates camalexin biosynthesis in arabidopsis. *Plant Cell.* **32**, 2621–2638, https://doi.org/10.1105/tpc.19.00971
49 Yuan, P., Tanaka, K. and Poovaiah, B.W. (2021) Calmodulin-binding transcription activator AtSR1/CAMTA3 fine-tunes plant immune response by transcriptional regulation of the salicylate receptor NPR1. *Plant Cell Environ.* **44**, 3140–3154, https://doi.org/10.1111/pce.14123
50 Rate, D.N. and Greenberg, J.T. (2001) The Arabidopsis aberrant growth and death2 mutant shows resistance to *Pseudomonas syringae* and reveals a role for NPR1 in suppressing hypersensitive cell death. *Plant J.* **27**, 203–211, https://doi.org/10.1046/j.0960-7412.2001.1075umedoc.x
51 Yuan, P., Tanaka, K. and Poovaiah, B.W. (2021) Calcium/calmodulin-mediated defense signaling: What is looming on the horizon for AtSR1/CAMTA3-mediated signaling in plant immunity. *Front. Plant Sci.* **12**, 795353, https://doi.org/10.3389/fpls.2021.795353
52 Lu, Y., Truman, W., Liu, X., Bethke, G., Zhou, M., Myers, C.L. et al. (2018) Different modes of negative regulation of plant immunity by calmodulin-related genes. *Plant Physiol.* **176**, 3046–3061, https://doi.org/10.1104/pp.17.01209

Essays in Biochemistry (2022) **66** 607–620
https://doi.org/10.1042/EBC20210100

53 Torres, M.A., Dangl, J.L. and Jones, J.D.G. (2002) Arabidopsis gp91phox homologues AtrbohD and AtrbohF are required for accumulation of reactive oxygen intermediates in the plant defense response. *Proc. Natl. Acad. Sci. U. S. A.* **99**, 517–522, https://doi.org/10.1073/pnas.012452499

54 Mittler, R. (2017) ROS are good. *Trends Plant Sci.* **22**, 11–19, https://doi.org/10.1016/j.tplants.2016.08.002

55 Mou, Z., Fan, W. and Dong, X. (2003) Inducers of plant systemic acquired resistance regulate NPR1 function through redox changes. *Cell* **113**, 935–944, https://doi.org/10.1016/S0092-8674(03)00429-X

56 Zhang, Y., Fan, W., Kinkema, M., Li, X. and Dong, X. (1999) Interaction of NPR1 with basic leucine zipper protein transcription factors that bind sequences required for salicylic acid induction of the PR-1 gene. *Proc. Natl. Acad. Sci. U. S. A.* **96**, 6523–6528, https://doi.org/10.1073/pnas.96.11.6523

57 Zhou, J.M., Trifa, Y., Silva, H., Pontier, D., Lam, E., Shah, J. et al. (2000) NPR1 differentially interacts with members of the TGA/OBF family of transcription factors that bind an element of the *PR-1* gene required for induction by salicylic acid. *Mol. Plant. Microbe. Interact.* **13**, 191–202, https://doi.org/10.1094/MPMI.2000.13.2.191

58 Després, C., Chubak, C., Rochon, A., Clark, R., Bethune, T., Desveaux, D. et al. (2003) The Arabidopsis NPR1 disease resistance protein is a novel cofactor that confers redox regulation of DNA binding activity to the basic domain/leucine zipper transcription factor TGA1. *Plant Cell.* **15**, 2181–2191, https://doi.org/10.1105/tpc.012849

59 Ishihama, N., Choi, S.-W., Noutoshi, Y., Saska, I., Asai, S., Takizawa, K. et al. (2021) Oxicam-type non-steroidal anti-inflammatory drugs inhibit NPR1-mediated salicylic acid pathway. *Nat. Commun.* **12**, 7303, https://doi.org/10.1038/s41467-021-27489-w

60 Kumar, S., Zavaliev, R., Wu, Q., Zhou, Y., Cheng, J., Dillard, L. et al. (2022) Structural basis of NPR1 in activating plant immunity. *Nature* **605**, 561–566, https://doi.org/10.1038/s41586-022-04699-w

61 Zheng, Z., Qamar, S.A., Chen, Z. and Mengiste, T. (2006) Arabidopsis WRKY33 transcription factor is required for resistance to necrotrophic fungal pathogens. *Plant J.* **48**, 592–605, https://doi.org/10.1111/j.1365-313X.2006.02901.x

62 Mao, G., Meng, X., Liu, Y., Zheng, Z., Chen, Z. and Zhang, S. (2011) Phosphorylation of a WRKY transcription factor by two pathogen-responsive MAPKs drives phytoalexin biosynthesis in Arabidopsis. *Plant Cell.* **23**, 1639–1653, https://doi.org/10.1105/tpc.111.084996

63 Bergmann, D.C., Lukowitz, W. and Somerville, C.R. (2004) Stomatal development and pattern controlled by a MAPKK kinase. *Science* **304**, 1494–1497, https://doi.org/10.1126/science.1096014

64 Lukowitz, W., Roeder, A., Parmenter, D. and Somerville, C. (2004) A MAPKK kinase gene regulates extra-embryonic cell fate in Arabidopsis. *Cell* **116**, 109–119, https://doi.org/10.1016/S0092-8674(03)01067-5

65 Meng, X., Wang, H., He, Y., Liu, Y., Walker, J.C., Torii, K.U. et al. (2012) A MAPK cascade downstream of ERECTA receptor-like protein kinase regulates Arabidopsis inflorescence architecture by promoting localized cell proliferation. *Plant Cell.* **24**, 4948–4960, https://doi.org/10.1105/tpc.112.104695

66 Cai, H., Huang, Y., Chen, F., Liu, L., Chai, M., Zhang, M. et al. (2021) ERECTA signaling regulates plant immune responses via chromatin-mediated promotion of WRKY33 binding to target genes. *New Phytol.* **230**, 737–756, https://doi.org/10.1111/nph.17200

67 Verma, V., Srivastava, A.K., Gough, C., Campanaro, A., Srivastava, M., Morrell, R. et al. (2021) SUMO enables substrate selectivity by mitogen-activated protein kinases to regulate immunity in plants. *Proc. Natl. Acad. Sci. U. S. A.* **118**, e2021351118, https://doi.org/10.1073/pnas.2021351118

68 Yang, L., Zhang, Y., Guan, R., Li, S., Xu, X., Zhang, S. et al. (2020) Co-regulation of indole glucosinolates and camalexin biosynthesis by CPK5/CPK6 and MPK3/MPK6 signaling pathways. *J. Integr. Plant Biol.* **62**, 1780–1796, https://doi.org/10.1111/jipb.12973

69 Pré, M., Atallah, M., Champion, A., De Vos, M., Pieterse, C.M.J. and Memelink, J. (2008) The AP2/ERF domain transcription factor ORA59 integrates jasmonic acid and ethylene signals in plant defense. *Plant Physiol.* **147**, 1347–1357, https://doi.org/10.1104/pp.108.117523

70 Yang, Y.N., Kim, Y., Kim, H., Kim, S.J., Cho, K.-M., Kim, Y. et al. (2021) The transcription factor ORA59 exhibits dual DNA binding specificity that differentially regulates ethylene- and jasmonic acid-induced genes in plant immunity. *Plant Physiol.* **187**, 2763–2784, https://doi.org/10.1093/plphys/kiab437

71 Van der Does, D., Leon-Reyes, A., Koornneef, A., Van Verk, M.C., Rodenburg, N., Pauwels, L. et al. (2013) Salicylic acid suppresses jasmonic acid signaling downstream of SCF^{COI1}-JAZ by targeting GCC promoter motifs via transcription factor ORA59. *Plant Cell.* **25**, 744–761, https://doi.org/10.1105/tpc.112.108548

72 He, X., Jiang, J., Wang, C.-Q. and Dehesh, K. (2017) ORA59 and EIN3 interaction couples jasmonate-ethylene synergistic action to antagonistic salicylic acid regulation of PDF expression. *J. Integr. Plant Biol.* **59**, 275–287, https://doi.org/10.1111/jipb.12524

73 Furniss, J.J. and Spoel, S.H. (2015) Cullin-RING ubiquitin ligases in salicylic acid-mediated plant immune signaling. *Front. Plant. Sci.* **6**, 154, https://doi.org/10.3389/fpls.2015.00154

74 Chico, J.M., Lechner, E., Fernandez-Barbero, G., Canibano, E., García-Casado, G., Franco-Zorrilla, J.M. et al. (2020) CUL3BPM E3 ubiquitin ligases regulate MYC2, MYC3, and MYC4 stability and JA responses. *Proc. Natl. Acad. Sci. U. S. A.* **117**, 6205–6215, https://doi.org/10.1073/pnas.1912199117

75 Ban, Z. and Estelle, M. (2021) CUL3 E3 ligases in plant development and environmental response. *Nat. Plants* **7**, 6–16, https://doi.org/10.1038/s41477-020-00833-6

76 Zavaliev, R., Mohan, R., Chen, T. and Dong, X. (2020) Formation of NPR1 condensates promotes cell survival during the plant immune response. *Cell* **182**, 1093.e18–1108.e18, https://doi.org/10.1016/j.cell.2020.07.016

77 Ding, P., Sakai, T., Krishna Shrestha, R., Manosalva Perez, N., Guo, W., Ngou, B.P.M. et al. (2021) Chromatin accessibility landscapes activated by cell-surface and intracellular immune receptors. *J. Exp. Bot.* **72**, 7927–7941, https://doi.org/10.1093/jxb/erab373

78 Pardal, A.J., Piquerez, S.J.M., Dominguez-Ferreras, A., Frungillo, L., Mastorakis, E., Reilly, E. et al. (2021) Immunity onset alters plant chromatin and utilizes EDA16 to regulate oxidative homeostasis. *PLoS Pathog.* **17**, e1009572, https://doi.org/10.1371/journal.ppat.1009572

79 Han, S.-K., Wu, M.-F., Cui, S. and Wagner, D. (2015) Roles and activities of chromatin remodeling ATPases in plants. *Plant J.* **83**, 62–77, https://doi.org/10.1111/tpj.12877

80 Huang, C.-Y., Rangel, D.S., Qin, X., Bui, C., Li, R., Jia, Z. et al. (2021) The chromatin-remodeling protein BAF60/SWP73A regulates the plant immune receptor NLRs. *Cell Host Microbe.* **29**, 425.e4–434.e4, https://doi.org/10.1016/j.chom.2021.01.005
81 Zhang, X., Bernatavichute, Y.V., Cokus, S., Pellegrini, M. and Jacobsen, S.E. (2009) Genome-wide analysis of mono-, di- and trimethylation of histone H3 lysine 4 in *Arabidopsis thaliana*. *Genome Biol.* **10**, R62, https://doi.org/10.1186/gb-2009-10-6-r62
82 Dvořák Tomaštíková, E., Hafrén, A., Trejo-Arellano, M.S., Rasmussen, S.R., Sato, H., Santos-González, J. et al. (2021) Polycomb Repressive Complex 2 and KRYPTONITE regulate pathogen-induced programmed cell death in Arabidopsis. *Plant Physiol.* **185**, 2003–2021, https://doi.org/10.1093/plphys/kiab035
83 Liu, C., Xin, Y., Xu, L., Cai, Z., Xue, Y., Liu, Y. et al. (2018) Arabidopsis ARGONAUTE 1 binds chromatin to promote gene transcription in response to hormones and stresses. *Dev. Cell.* **44**, 348.e7–361.e7, https://doi.org/10.1016/j.devcel.2017.12.002
84 Erdmann, R.M. and Picard, C.L. (2020) RNA-directed DNA methylation. *PLos Genet.* **16**, e1009034, https://doi.org/10.1371/journal.pgen.1009034
85 Dowen, R.H., Pelizzola, M., Schmitz, R.J., Lister, R., Dowen, J.M., Nery, J.R. et al. (2012) Widespread dynamic DNA methylation in response to biotic stress. *Proc. Natl. Acad. Sci. U. S. A.* **109**, E2183–E2191, https://doi.org/10.1073/pnas.1209329109
86 Halter, T., Wang, J., Amesefe, D., Lastrucci, E., Charvin, M., Singla Rastogi, M. et al. (2021) The Arabidopsis active demethylase ROS1 cis-regulates defence genes by erasing DNA methylation at promoter-regulatory regions. *Elife* **10**, 62994, https://doi.org/10.7554/eLife.62994
87 Zeng, W., Huang, H., Lin, X., Zhu, C., Kosami, K.-I., Huang, C. et al. (2021) Roles of DEMETER in regulating DNA methylation in vegetative tissues and pathogen resistance. *J. Integr. Plant Biol.* **63**, 691–706, https://doi.org/10.1111/jipb.13037
88 Schumann, U., Lee, J.M., Smith, N.A., Zhong, C., Zhu, J.-K., Dennis, E.S. et al. (2019) DEMETER plays a role in DNA demethylation and disease response in somatic tissues of Arabidopsis. *Epigenetics* **14**, 1074–1087, https://doi.org/10.1080/15592294.2019.1631113
89 Huang, M., Zhang, Y., Wang, Y., Xie, J., Cheng, J., Fu, Y. et al. (2022) Active DNA demethylation regulates MAMP-triggered immune priming in Arabidopsis. *J. Genet. Genomics*, https://doi.org/10.1016/j.jgg.2022.02.021
90 Li, F., Cheng, C., Cui, F., de Oliveira, M.V.V., Yu, X., Meng, X. et al. (2014) Modulation of RNA polymerase II phosphorylation downstream of pathogen perception orchestrates plant immunity. *Cell Host Microbe.* **16**, 748–758, https://doi.org/10.1016/j.chom.2014.10.018
91 Thatcher, L.F., Foley, R., Casarotto, H.J., Gao, L.-L., Kamphuis, L.G., Melser, S. et al. (2018) The Arabidopsis RNA Polymerase II Carboxyl Terminal Domain (CTD) Phosphatase-Like1 (CPL1) is a biotic stress susceptibility gene. *Sci. Rep.* **8**, 13454, https://doi.org/10.1038/s41598-018-31837-0
92 Manavella, P.A., Hagmann, J., Ott, F., Laubinger, S., Franz, M., Macek, B. et al. (2012) Fast-forward genetics identifies plant CPL phosphatases as regulators of miRNA processing factor HYL1. *Cell* **151**, 859–870, https://doi.org/10.1016/j.cell.2012.09.039
93 Jeong, I.S., Aksoy, E., Fukudome, A., Akhter, S., Hiraguri, A., Fukuhara, T. et al. (2013) Arabidopsis C-terminal domain phosphatase-like 1 functions in miRNA accumulation and DNA methylation. *PLoS ONE* **8**, e74739, https://doi.org/10.1371/journal.pone.0074739
94 Thieffry, A., López-Márquez, D., Bornholdt, J., Malekroudi, M.G., Bressendorff, S., Barghetti, A. et al. (2022) PAMP-triggered genetic reprogramming involves widespread alternative transcription initiation and an immediate transcription factor wave. *Plant Cell.*, https://doi.org/10.1093/plcell/koac108
95 Zhai, Q. and Li, C. (2019) The plant Mediator complex and its role in jasmonate signaling. *J. Exp. Bot.* **70**, 3415–3424, https://doi.org/10.1093/jxb/erz233
96 Nomoto, M., Skelly, M.J., Itaya, T., Mori, T., Suzuki, T., Matsushita, T. et al. (2021) Suppression of MYC transcription activators by the immune cofactor NPR1 fine-tunes plant immune responses. *Cell Rep.* **37**, 110125, https://doi.org/10.1016/j.celrep.2021.110125
97 Zhang, F., Yao, J., Ke, J., Zhang, L., Lam, V.Q., Xin, X.-F. et al. (2015) Structural basis of JAZ repression of MYC transcription factors in jasmonate signalling. *Nature* **525**, 269–273, https://doi.org/10.1038/nature14661
98 Thines, B., Katsir, L., Melotto, M., Niu, Y., Mandaokar, A., Liu, G. et al. (2007) JAZ repressor proteins are targets of the SCF^{COI1} complex during jasmonate signalling. *Nature* **448**, 661–665, https://doi.org/10.1038/nature05960
99 Chini, A., Fonseca, S., Fernández, G., Adie, B., Chico, J.M., Lorenzo, O. et al. (2007) The JAZ family of repressors is the missing link in jasmonate signalling. *Nature* **448**, 666–671, https://doi.org/10.1038/nature06006
100 Zhang, Y., Shi, C., Fu, W., Gu, X., Qi, Z., Xu, W. et al. (2021) Arabidopsis MED18 interaction with RNA pol IV and V subunit nrpd2a in transcriptional regulation of plant immune responses. *Front. Plant. Sci.* **12**, 692036, https://doi.org/10.3389/fpls.2021.692036
101 Lai, Z., Schluttenhofer, C.M., Bhide, K., Shreve, J., Thimmapuram, J., Lee, S.Y. et al. (2014) MED18 interaction with distinct transcription factors regulates multiple plant functions. *Nat. Commun.* **5**, 3064, https://doi.org/10.1038/ncomms4064
102 Haag, J.R. and Pikaard, C.S. (2011) Multisubunit RNA polymerases IV and V: purveyors of non-coding RNA for plant gene silencing. *Nat. Rev. Mol. Cell Biol.* **12**, 483–492, https://doi.org/10.1038/nrm3152
103 Wang, S., Gu, Y., Zebell, S.G., Anderson, L.K., Wang, W., Mohan, R. et al. (2014) A noncanonical role for the CKI-RB-E2F cell-cycle signaling pathway in plant effector-triggered immunity. *Cell Host Microbe* **16**, 787–794, https://doi.org/10.1016/j.chom.2014.10.005
104 Gu, Y., Zebell, S.G., Liang, Z., Wang, S., Kang, B.-H. and Dong, X. (2016) Nuclear pore permeabilization is a convergent signaling event in effector-triggered immunity. *Cell* **166**, 1526.e11–1538.e11, https://doi.org/10.1016/j.cell.2016.07.042
105 Peng, S., Guo, D., Guo, Y., Zhao, H., Mei, J., Han, Y. et al. (2022) Constitutive expresser of pathogenesis-related genes 5 is an RNA-binding protein controlling plant immunity via an RNA processing complex. *Plant Cell.* **34** (5), 1742–1744, https://doi.org/10.1093/plcell/koac037
106 Xu, F., Jia, M., Li, X., Tang, Y., Jiang, K., Bao, J. et al. (2021) Exportin-4 coordinates nuclear shuttling of TOPLESS family transcription corepressors to regulate plant immunity. *Plant Cell.* **33**, 697–713, https://doi.org/10.1093/plcell/koaa047
107 Wu, F., Deng, L., Zhai, Q., Zhao, J., Chen, Q. and Li, C. (2020) Mediator subunit MED25 couples alternative splicing of JAZ genes with fine-tuning of jasmonate signaling. *Plant Cell.* **32**, 429–448, https://doi.org/10.1105/tpc.19.00583
108 Chung, H.S. and Howe, G.A. (2009) A critical role for the TIFY motif in repression of jasmonate signaling by a stabilized splice variant of the JASMONATE ZIM-domain protein JAZ10 in Arabidopsis. *Plant Cell.* **21**, 131–145, https://doi.org/10.1105/tpc.108.064097
109 Niedojadlo, J., Deleńko, K. and Niedojadlo, K. (2016) Regulation of poly(A) RNA retention in the nucleus as a survival strategy of plants during hypoxia. *RNA Biol.* **13**, 531–543, https://doi.org/10.1080/15476286.2016.1166331

110 Decker, C.J. and Parker, R. (2012) P-bodies and stress granules: possible roles in the control of translation and mRNA degradation. *Cold Spring Harb. Perspect. Biol.* **4**, a012286, https://doi.org/10.1101/cshperspect.a012286
111 Mitchell, S.F. and Parker, R. (2014) Principles and properties of eukaryotic mRNPs. *Mol. Cell.* **54**, 547–558, https://doi.org/10.1016/j.molcel.2014.04.033
112 Yu, X., Li, B., Jang, G.-J., Jiang, S., Jiang, D., Jang, J.-C. et al. (2019) Orchestration of processing body dynamics and mRNA decay in Arabidopsis Immunity. *Cell Rep.* **28**, 2194.e6–2205.e6, https://doi.org/10.1016/j.celrep.2019.07.054
113 Souret, F.F., Kastenmayer, J.P. and Green, P.J. (2004) AtXRN4 degrades mRNA in Arabidopsis and its substrates include selected miRNA targets. *Mol. Cell.* **15**, 173–183, https://doi.org/10.1016/j.molcel.2004.06.006
114 Song, L., Fang, Y., Chen, L., Wang, J. and Chen, X. (2021) Role of non-coding RNAs in plant immunity. *Plant Commun.* **2**, 100180, https://doi.org/10.1016/j.xplc.2021.100180
115 Rambani, A., Hu, Y., Piya, S., Long, M., Rice, J.H., Pantalone, V. et al. (2020) Identification of differentially methylated miRNA genes during compatible and incompatible interactions between soybean and soybean cyst nematode. *Mol. Plant. Microbe. Interact.* **33**, 1340–1352, https://doi.org/10.1094/MPMI-07-20-0196-R
116 Seo, J.S., Sun, H.-X., Park, B.S., Huang, C.-H., Yeh, S.-D., Jung, C. et al. (2017) ELF18-INDUCED LONG-NONCODING RNA associates with mediator to enhance expression of innate immune response genes in Arabidopsis. *Plant Cell.* **29**, 1024–1038, https://doi.org/10.1105/tpc.16.00886
117 Seo, J.S., Diloknawarit, P., Park, B.S. and Chua, N.-H. (2019) ELF18-induced long noncoding RNA 1 evicts fibrillarin from mediator subunit to enhance pathogenesis-related gene 1 (*PR1*) expression. *New Phytol.* **221**, 2067–2079, https://doi.org/10.1111/nph.15530
118 Li, S., Yan, H. and Lee, J. (2021) Identification of gene regulatory networks from single-cell expression data. *Methods Mol. Biol.* **2328**, 153–170, https://doi.org/10.1007/978-1-0716-1534-8˙9
119 Dorrity, M.W., Alexandre, C.M., Hamm, M.O., Vigil, A.-L., Fields, S., Queitsch, C. et al. (2021) The regulatory landscape of *Arabidopsis thaliana* roots at single-cell resolution. *Nat. Commun.* **12**, 3334, https://doi.org/10.1038/s41467-021-23675-y
120 Ko, D.K. and Brandizzi, F. (2020) Network-based approaches for understanding gene regulation and function in plants. *Plant J.* **104**, 302–317, https://doi.org/10.1111/tpj.14940
121 Swift, J., Greenham, K., Ecker, J.R., Coruzzi, G.M. and Robertson McClung, C. (2022) The biology of time: dynamic responses of cell types to developmental, circadian and environmental cues. *Plant J.* **109**, 764–778, https://doi.org/10.1111/tpj.15589
122 Nobori, T., Wang, Y., Wu, J., Stolze, S.C., Tsuda, Y., Finkemeier, I. et al. (2020) Multidimensional gene regulatory landscape of a bacterial pathogen in plants. *Nat. Plants* **6**, 883–896, https://doi.org/10.1038/s41477-020-0690-7
123 Bevilacqua, C. and Ducos, B. (2018) Laser microdissection: a powerful tool for genomics at cell level. *Mol. Aspects Med.* **59**, 5–27, https://doi.org/10.1016/j.mam.2017.09.003
124 Qi, P., Huang, M., Hu, X., Zhang, Y., Wang, Y., Li, P. et al. (2022) A *Ralstonia solanacearum* effector targets TGA transcription factors to subvert salicylic acid signaling. *Plant Cell.* **34** (5), 1666–1683, https://doi.org/10.1093/plcell/koac015
125 Canonne, J., Marino, D., Jauneau, A., Pouzet, C., Brière, C., Roby, D. et al. (2011) The *Xanthomonas* type III effector XopD targets the Arabidopsis transcription factor MYB30 to suppress plant defense. *Plant Cell.* **23**, 3498–3511, https://doi.org/10.1105/tpc.111.088815
126 Roux, M., Schwessinger, B., Albrecht, C., Chinchilla, D., Jones, A., Holton, N. et al. (2011) The *Arabidopsis* leucine-rich repeat receptor-like kinases BAK1/SERK3 and BKK1/SERK4 are required for innate immunity to hemibiotrophic and biotrophic pathogens. *Plant Cell.* **23**, 2440–2455, https://doi.org/10.1105/tpc.111.084301
127 Sarris, P.F., Duxbury, Z., Huh, S.U., Ma, Y., Segonzac, C., Sklenar, J. et al. (2015) A plant immune receptor detects pathogen effectors that target WRKY transcription factors. *Cell* **161**, 1089–1100, https://doi.org/10.1016/j.cell.2015.04.024
128 Qin, J., Wang, K., Sun, L., Xing, H., Wang, S., Li, L. et al. (2018) The plant-specific transcription factors CBP60g and SARD1 are targeted by a *Verticillium* secretory protein VdSCP41 to modulate immunity. *Elife* **7**, 34902, https://doi.org/10.7554/eLife.34902
129 Yang, L., Teixeira, P.J.P.L., Biswas, S., Finkel, O.M., He, Y., Salas-Gonzalez, I. et al. (2017) *Pseudomonas syringae* Type III Effector HopBB1 promotes host transcriptional repressor degradation to regulate phytohormone responses and virulence. *Cell Host Microbe* **21**, 156–168, https://doi.org/10.1016/j.chom.2017.01.003
130 Kitazawa, Y., Iwabuchi, N., Maejima, K., Sasano, M., Matsumoto, O., Koinuma, H. et al. (2022) A phytoplasma effector acts as a ubiquitin-like mediator between floral MADS-box proteins and proteasome shuttle proteins. *Plant Cell.* **34**, 1709–1723, https://doi.org/10.1093/plcell/koac062
131 Harvey, S., Kumari, P., Lapin, D., Griebel, T., Hickman, R., Guo, W. et al. (2020) Downy Mildew effector HaRxL21 interacts with the transcriptional repressor TOPLESS to promote pathogen susceptibility. *PLoS Pathog.* **16**, e1008835, https://doi.org/10.1371/journal.ppat.1008835