Chapter 4
Plant Biosynthetic Engineering Through Transcription Regulation: An Insight into Molecular Mechanisms During Environmental Stress

Rakesh Srivastava, Krishan Mohan Rai and Rashmi Srivastava

Abstract Transcription is not only essential for the synthesis of coding and non-coding RNA, but also extremely significant in regulating gene expression with the coordination of several protein complexes in development, differentiation, phenotype, metabolism, exposure to different challenging environmental conditions, and many other cellular pathways. Further extensions of these studies in plant biology will be very helpful in dealing and maintaining a balance between challenging environmental stress, plant resistance, plant productivity, and yield. Different plant secondary metabolites are induced by various developmental, hormonal, and environmental cues and facilitate the plant to fight and cope up with stress conditions. Interestingly, recent advances suggest that the biosynthesis pathway of secondary metabolites is tightly regulated at the transcriptional stages. Keeping in view studying both the molecular mechanisms at a single platform, the aim of this chapter is to understand plant secondary metabolite biosynthetic pathways at the transcriptional level under unfavorable or stressful environmental conditions.

Keywords Transcription · Promoter engineering · Transcription complex
Transcription factors · Secondary metabolites

R. Srivastava (✉)
Division of Molecular and Life Science, College of Science
and Technology, Hanyang University, Ansan,
Republic of Korea (South Korea)
e-mail: rakeshsrivastava_rs@yahoo.com

K. M. Rai
Department of Plant & Soil Science, Fiber and Biopolymer Research
Institute (FBRI), Texas Tech University, Lubbock, TX, USA

R. Srivastava
School for Biosciences and Biotechnology, Babasaheb Bhimrao
Ambedkar University, Lucknow, India

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1 Introduction

Plants are sessile in nature which instigates them to resist well and endowed with rapid adaptation for survival under multiple environmental stresses. These various environmental perturbations not only affect the productivity of plant, but also cause different variations in the plant morphology and anatomy, growth, development, and metabolism as well. Due to environmental stress, majority of biological processes is directly affected, such as photosynthesis, transpiration, respiration, stomatal conductance, pigment concentrations, energy, and metabolism. Consequently, with secondary stresses such as ion uptake nutritional stress, and oxidative stress, strongly influence the plant development and growth (Saher et al. 2005; Chaves et al. 2009; Compant et al. 2010; Tullus et al. 2012). Several molecular, cellular, and environmental factors have a dramatic effect on the yield of plant biosynthetic product. Moreover, plants need to strongly counteract and adapt rapidly towards environmental stress to increase their productivity at the cellular and molecular levels. Environmental stresses, such as drought, heat or both, not only decrease the plant's growth, but also prominently decrease plant biosynthetic products and yield. A key question is that how to increase the production of plant biosynthetic products while considering the adverse effects of global changes in the environmental factors.

Genomics and proteomics technologies have discovered several plant genes and their downstream pathways, which elaborate their role in the gene regulation, signaling, and resistance in plant stress mechanism. These pathways explain about the different mechanisms to fine-tune the plant gene regulation and strengthen them to survive in different environmental stress conditions. During the alteration in environmental agitations, the defense- and protection-related pathways undergo huge gene expression reprogramming through transcription regulation. The progression of high-throughput tools leads to the finding of numerous genes in plants with changed expression in feedback to environmental perturbations. Genes with improved expression in different aspects of environmental changes are frequently essential for fine adaptation to stress and provide plant tolerance and resistance. Environmental stress, such as chilling, drought, salinity, high temperature, and waterlogging, leads to harmful effects on the growth of plants and decreases crop yield, and, in extreme phase, results in the death of the plant. Abiotic stress is one of the main factors of crop damage at the global level, decreasing yields for most main crop plants by over 50% (Bray et al. 2000).

Since several plant genomes are sequenced using the new high-throughput genomic and proteomic technologies, several reports have been published to improve our understanding of how the plant genome works to facilitate and synchronize the specific program of transcription regulation. Accumulating studies have suggested several molecules, for instance, transcription factors, activators, or cofactors, act as potential candidates or common players that are participated in cross-talk between abiotic and biotic stress-signaling and biosynthetic pathways in the course of the changing environmental stresses (Srivastava et al. 2014b).

The reaction to the wide-ranging environmental stress in the plant development can be prepared promptly by intense genomic reprogramming which results in improved alternative transcriptome and gene regulation programs.

In the era of high-throughput technologies, epigenomics, and nanotechnology, little is known about the functions of the plant transcriptional complex in response to biotic and abiotic stress at the molecular level. Plant secondary metabolites have highly significant social and economic value for human uses such as agrochemicals, food and chemical flavors, nutraceuticals, pharmaceuticals, biofuels, and biomass (Tatsis and O'Connor 2016; Ramakrishna and Ravishankar 2011; Vaishnav and Demain 2011). Moreover, plant secondary metabolites participate in plant growth, reproduction, energy production, or several other primary functions; interestingly, they also significantly facilitate plant responses to biotic and abiotic environmental stresses (Theis and Lerdau 2003; Zhao et al. 2005; Zhai et al. 2017; Ramakrishna and Ravishankar 2011). However, most secondary metabolites have been produced in fewer amounts during native condition; therefore, different approaches based on genetic and metabolic engineering have been successfully introduced to enhance the production of secondary metabolites enormously. Nevertheless, information related to regulation of their production by different transcription machineries or complexes present on the plant promoter is still lacking. Transcription machinery is an important player for coordinating the interaction between transcription factor and promoter, thereby tightly controlling the gene expression of target genes. This chapter mostly highlights how transcription machinery, transcription factors, and promoter augment the production of the secondary metabolites.

2 Promoter Engineering and Transcription Regulation in Plants

RNA polymerase II (RNAPII) is a multisubunit holoenzyme accountable for the gene transcription of the genetic information encoded in the form of DNA sequence (Smale and Kadonaga 2003). The precise spatial and temporal gene transcription necessities should be regulated efficiently, which is a requirement for the accomplishment of different biological and cellular processes, environmental stress response, several diseases signaling pathways, morphology, and differentiation (Maston et al. 2006; Srivastava et al. 2014a, b). The regulation of transcription eukaryotic protein-coding genes are highly dynamic and an orchestrated process, which involves the coordinated action of various proteins, several protein complexes and transcription factors (Maston et al. 2006; Shandilya and Roberts 2012).

The promoter is present in the upstream of the coding gene and 5′ UTR (untranslated region) regions, which is accountable for controlling transcription enormously. The promoter is comprised of a core promoter and the proximal promoter. The core promoter elements (CPEs) function as the docking site for the general transcription factor (GTF) and responsible for preinitiation complex (PIC) assembly. The CPEs contain two most indispensable elements: the TATA box, the binding region for the TBP (TATA-binding protein) and the Initiator element (INR), transcription start site (TSS) of the protein-coding genes (Maston et al. 2006; Srivastava et al. 2014b; Kiran et al. 2006). The core promoter sequences comprise of 40 bp upstream and/or downstream of the TSS along with several other key elements such as Downstream Promoter Element (DPE), Downstream Core Element (DCE), TFIIB-Recognition Element (BRE), and Motif Ten Element (MTE) (Juven-Gershon and Kadonaga 2010). The proximal promoter is the region further upstream from the CPEs and contains multiple binding sites for activators or repressor protein factors. These regulatory motifs present at the promoter facilitate binding of the sequence-specific DNA-binding transcription factors in order to activate or repress transcription (Lodhi et al. 2008; Ranjan et al. 2009; Srivastava et al. 2014a, b; Chaturvedi et al. 2007). Moreover, these regulatory motifs ensure the gene to be selectively regulated in response to various environmental stresses in a specific cell or tissue. Various kinds of co-regulators and transcription factors are specific in their action and bind specifically to the regulatory motif of the promoter, which is regulated in response to various external environmental stimuli or internal cellular conditions. The distal (upstream) regulatory elements, such as enhancers, silencers, insulators, and locus control regions, present thousands of base pairs away from the TSS, and are also found in the intronic region and downstream of the gene as well (Maston et al. 2006). These upstream regulatory elements sequences can considerably suppress or enhance transcription and are also important for tissue-specific expression. These sequences often contain repeats of the similar elements as in the proximal promoter. The distinct core promoters architecture also lead to alterations in the gene expression (Kiran et al. 2006; Srivastava et al. 2014a). The promoter modulation is regulated by cofactors, transcription factors, activators, and suppressors which bind to cis-regulatory elements of the promoter regions (Priest et al. 2009). Accumulating evidence suggest that many different types of cis-regulatory elements have been discovered in the response to environmental stimuli. The different types of web-based and bioinformatics methods have been used to identify potential plant cis-elements in the regulatory sequences of the target genes (Higo et al. 1999; Lescot et al. 2002). Different types of plant cis-regulatory elements are identified in response to environmental stress, which are listed in Table 1.

Engineering the biosynthesis of plant secondary metabolites is critical for maximizing product formation. To address this matter, promoters play a fundamental role in metabolic engineering and biotechnological prospects because gene expression is operably associated with them and promoter elements drive transcriptional control at any phases of plant development or to a specific cell or tissue or an external/internal signal under defined situations. Promoters are classified into various classes, such as constitutive promoters (active in most or all tissues/parts), inducible promoters (controlled by chemical or physical signal), a development stage-specific promoters (regulated at certain development phases), cell-, tissue-, and organ-type specific promoters (targeted to a specific location to plant region),

Table 1 Cis-regulatory motif for different environmental stresses present in the plant promoter

ID	Stress	Origin species	Sequence	Reference
14BPATERD1	Water stress	*Arabidopsis*	*CACTAAATTGTCAC*	Simpson et al. (2003)
ABREATRD22	ABA, dehydration	*Arabidopsis*	*RYACGTGGYR*	Iwasaki et al. (1995)
ABRELATERD1	ABA, Early responsive to dehydration	*Arabidopsis*	*ACGTG*	Simpson et al. (2003)
ABREZMRAB28	ABR; freezing tolerance	*Arabidopsis; Zea mays; Oryza sativa*	*CCACGTGG*	Suzuki et al. (2005)
ACEATCHS	ACE; UV-A; UV-B;	*Arabidopsis*	*GACACGTAGA*	Hartmann et al. (1998)
ACGTABREMOTIFA2OSEM	ABA; ABRE; DRE;	*Arabidopsis; Oryza sativa*	*ACGTGKC*	Hattori et al. (2002)
ACGTROOT1	ABE; cold tolerance	*Glycine max; Nicotiana tabacum*	*GCCACGTGGC*	Salinas et al. (1992)
ASF1MOTIFCAMV	Xenobiotic stress	*Nicotiana tabacum; Arabidopsis*	*TGACG*	Despres et al. (2003)
CBFHV	Low temperature	*Hordeum vulgar*	*RYCGAC*	Xue (2002)
CCAATBOX1	Heat shock element	*Glycine max*	*CCAAT*	Rieping and Schoffl (1992)
COREOS	Oxidative stress;	*Oryza sativa*	*AAKAATWYRTAWATAAAAMTTTTATWTA*	Tsukamoto et al. (2005)
DRE1COREZMRAB17	ABA; drought	*Zea mays*	*ACCGAGA*	Busk et al. (1997)

(continued)

Table 1 (continued)

ID	Stress	Origin species	Sequence	Reference
DRECRTCOREAT	Drought	*Helianthus annuus; Oryza sativa; Zea mays*	*RCCGAC*	Dubouzet et al. (2003)
DREDR1ATRD29AB	Drought; water stress; dehydration; low temperature; high salt; oxidative stress	*Arabidopsis Populus spp.*	*TACCGACAT*	Kasuga et al. (1999)
HBOXCONSENSUSPVCHS	Stress; wounding	*Nicotiana tabacum; Phaseolus vulgaris*	*CCTACCNNNNNNNCT*	Loake et al. (1992)
HSELIKENTGLN2	Heat shock	*Nicotiana tabacum*	*AGGAATTCCT*	Ohme-Takagi and Shinshi (1990)
LTRE1HVBLT49	Low temperature	*Hordeum vulgare*	*CCGAAA*	Dunn et al. (1998)
LTREATLTI78	Low temperature	*Arabidopsis; Hordeum vulgare*	*ACCGACA*	Nordin et al. (1993)
LTRECOREATCOR15	Cold; drought; low temperature	*Arabidopsis; Brassica napus*	*CCGAC*	Baker et al. (1994)
MYBATRD22	Dehydration; water stress	*Arabidopsis*	*CTAACCA*	Abe et al. (1997)
MYCATERD1	Water stress	*Arabidopsis*	*CATGTG*	Simpson et al. (2003)
MYCATRD22	Dehydration; water stress	*Arabidopsis*	*CACATG*	Abe et al. (1997)
MYCCONSENSUSAT	Cold	*Arabidopsis*	*CANNTG*	Abe et al. (2003)

(continued)

Table 1 (continued)

ID	Stress	Origin species	Sequence	Reference
T/GBOXATPIN2	Wounding	*Lycopersicon esculentum; Arabidopsis*	*AACGTG*	Boter et al. (2004)
TATCCAOSAMY	Sugar starvation	*Oryza sativa*	*TATCCA*	Lu et al. (2002)
TCA1MOTIF	Stress	*Hordeum vulgare; Nicotiana tabacum*	*TCATCTTCTT*	Goldsbrough et al. (1993)
TGA1ANTPR1A	Xenobiotic stress	*Nicotiana tabacum*	*CGTCATCGAGATGACG*	Strompen et al. (1998)
WBOXNTERF3	Wounding	*Nicotiana tabacum*	*TGACY*	Nishiuchi et al. (2004)
WINPSTPIIIK	Wounding	*Solanum tuberosum (potato)*	*AAGCGTAAGT*	Palm et al. (1990)
WRKY71OS	Wounding	*Oryza sativa; Petroselinum crispum*	*TGAC*	Zhang et al. (2004)

bidirectional promoters (two genes are controlled in opposite directions). However, the endogenous or native promoter is limited to maximizing the plant biosynthetic product and hence restricts transcriptional output to a particular stage. Promoter engineering has great prospect and acts as a molecular tool for biosynthetic engineering to challenging environments in an attempt to maximize the plant biosynthetic product. Promoter engineering increases the transcriptional capacity and regulates the expression levels and expression patterns of transgenic genes in a different type of cell or tissue. Numerous effective promoter engineering approaches have been described for the generation of unique and new synthetic promoters (assembly of enhancer, CPEs and cis-regulatory elements that can increase the transcriptional capacity in any cell or tissue of interest). These are classified into different groups: (1) Generation of randomized promoter mutagenesis libraries, (2) Hybrid promoters generation, (3) Manipulation of nucleosome architecture occupancy and accessibility, (4) *de novo* synthesis of the promoter (Peremarti et al. 2010; Venter 2007; Liu and Stewart 2016; Blazeck and Alper 2013). In the perception of various environmental stimuli and perturbations, promoters engineering is essential to modulate the dynamical process of the gene expression for metabolic engineering of the biosynthetic pathway in response to a particular state or variation in the environment are impeccable. These engineered promoters are regulated by one or more signal such as various chemicals, environmental stress (drought, high temperature, salt, water stress and others), hormones (auxin, abscisic acid, gibberellin, ethylene, jasmonic acid, nitric oxide, salicylic acid, strigolactones, and others), and biotic stress (insects, microbes, nematodes, and others). Such engineered promoters are not only effective in reducing the genetic load to plants, but also directly or indirectly guard and protect the environment in this way.

3 Transcriptional Machinery at the Promoter

Gene expression is regulated at multiple levels in response to environmental stress. Synchronization of cis-regulatory and core promoter elements are essential to regulate expression of growth and stress-regulated genes. Knowing how transcription factors and PIC bind to cis-regulatory and core promoter elements are not only essential, but also the harmonization between them in stress-regulated gene expression. General cofactors are normally associated with gene regulation to accelerate the interaction between gene-specific transcription factors and general transcription machinery components. These general cofactors include Mediator complex associated with RNAPII and TAFs found in TFIID complex (Thomas and Chiang 2006). Moreover, TBP-containing and non-TBP-containing complex also affects transcription during development and stress condition (Baumann et al. 2010; Juven-Gershon and Kadonaga 2010).

3.1 RNA Polymerase II and Its Modifications

In most eukaryotes, transcription of nuclear genes is achieved by the three different RNA polymerases (RNAP), such as RNAPI, RNAPII, and RNAPIII, however, two more RNAP, viz., RNAPIV and RNAPV are also reported in plants. Furthermore, the RNAPII holoenzyme participates in the transcription of protein-coding genes. It also takes part in the formation of other RNAs such as CUTs (cryptic unstable transcripts), lncRNA (long non-coding RNA), miRNA (microRNA), snRNA (small nuclear RNA), snoRNA (small nucleolar RNA), SUTs (stable unannotated transcripts), and XUTs (Xrn1-dependent unstable transcripts) (Dieci et al. 2007; van Dijk et al. 2011; Neil et al. 2009). RNAPII has a unique repeated disordered domain at the carboxy-terminal domain (CTD), which emerges from the core region of enzyme catalytic part (Cramer et al. 2001). The RNAPII CTD comprises tandem Tyr1–Ser2–Pro3–Thr4–Ser5–Pro6–Ser7 ($Y_1S_2P_3T_4S_5P_6S_7$) heptapeptide repeats that are highly conserved among yeast, humans, and plants. The RNAPII CTD of *Arabidopsis* comprises 15 consensus and 19 non-consensus heptapeptide repeats, whereas *Oryza sativa* contains 12 consensus and 17 non-consensus heptapeptide repeats. RNAPII CTD is indispensable for cell viability, dynamically modified, and roles as a scaffold to coordinate the association of several proteins. The modification of the RNAPII CTD has critical roles in transcription cycle development. The RNAPII CTD modification on the consensus repeats mainly include phosphorylation, isomerization between cis/trans conformations, glycosylation. Other modifications also occur on CTD at non-consensus repeat sequences, includes acetylation methylation and ubiquitylation (Sims et al. 2011; Schroder et al. 2013; Daulny et al. 2008). Accumulating evidence suggest that RNAPII CTD modification is associated with different types of histone modification and to other cellular and stress processes (Srivastava and Ahn 2015). Only a few reports have revealed that modifications of the RNAPII CTD are related with stress stimuli, suggesting their importance in stress-signaling pathways. The variations in environmental conditions such as high temperature or heat, osmotic stress, pH, starvation, toxic agents, or radiations change RNAPII CTD modifications and lead to important alterations in transcription regulation (Miguel et al. 2013; Liu and Tao 2013; Baugh et al. 2009). Though, it remains unclear and needs to be investigated on how the plant RNAPII CTD modifications associate and acclimatize to variations in challenging environmental stress at the cellular and molecular levels for metabolite accumulation or end product of a biosynthetic pathway.

3.2 TFIID Complex

TFIID is a multisubunit protein basal transcription complex and plays an important role in PIC assembly (Thomas and Chiang 2006). It has a role in promoter recognition and its binding to the promoter is considered as the key rate-limiting step in regulating the core promoter activity (Smale and Kadonaga 2003; Thomas and Chiang 2006). The *Arabidopsis* TFIID complex is comprised of TBP (TATA-binding protein) and 15 different subunits of TBP-Associated Factors (TAFs) (Lago et al. 2004). Studies on TAFs suggest substantial structural and functional conservation among mammals, plants, and yeast (Lago et al. 2004; Srivastava et al. 2015). In budding yeast, genome analysis of TAFs temperature-sensitive mutants has suggested that TAFs control approximately 70% expression of the gene (Lee et al. 2000). As compared to yeast and human, the information of plant TAFs is limited and their roles in stress conditions, development, and differentiation are being increasingly published (Mougiou et al. 2012; Benhamed et al. 2006; Bertrand et al. 2005; Furumoto et al. 2005; Lago et al. 2004, 2005; Tamada et al. 2007; Gao et al. 2006; Kubo et al. 2011; Srivastava et al. 2015). *Arabidopsis* TAFs are associated with plant development and influence the organization of shoot apical meristems, development of leaf, floral organs formation, pollen tube, and light regulation (Gurley et al. 2007). TAF1A regulates light-controlled genes by modification of histones acetylation to H3 and H4 at the target promoters (Benhamed et al. 2006; Bertrand et al. 2005). *Arabidopsis* TAF10 mutant is more affected than the wild type to NaCl stress, whereas TAF10 overexpression improved seed germination rate during osmotic stress (Gao et al. 2006). A mutation in *Arabidopsis* TAF12B results in failure to induce a subset of ethylene-regulated genes in etiolated seedlings (Robles et al. 2007). A recent study reveals that TAF1 plays an important function in genotoxic stress and DNA damage response in plants (Waterworth et al. 2015). These studies suggest that plant TFIID components mediate different functions in gene regulation to plant development and environmental stress response, however, their role in biosynthetic and metabolism pathway is still unknown. Metazoan and yeast TAFs play a significant role in the cell metabolism, but plant TAFs are less characterized in the same aspect, so it is interesting to examine the role in TAFs in plant metabolic pathway.

3.3 The Mediator Complex

The Mediator complex was first identified in the yeast, during the study when GTFs components and purified activators were not enough for regulation of transcription in vitro (Kelleher et al. 1990; Flanagan et al. 1991). Mediator complex has a compact and roughly triangular form with four different modular structures designated as a head module, middle module, kinase module, and tail module (Dotson et al. 2000; Tsai et al. 2014). The Mediator intermediates regulatory signals to the RNAPII and basal transcriptional machinery to facilitate the PIC assembly. The Mediator complex is composed of 29 subunits in *Homo sapiens* and 25 subunits in budding yeast *Saccharomyces cerevisiae* (Poss et al. 2013). In plants, Mediator complex has been first obtained and characterized in *Arabidopsis thaliana* using cell suspension culture (Backstrom et al. 2007). Interestingly, most of the plant Mediator components are conserved between yeast and human. The *Arabidopsis*

Mediator complex is comprised of 33 subunits, where 10 subunits are present in the head module, 6 are found in the middle module, 7 constitute the tail and 4 subunits in the CDK module (Yang et al. 2016). In addition, some plant-specific Mediator subunits are also associated with the complex, such as MED34, MED35, MED36, and MED37 (Mathur et al. 2011). However, MED1 is not present in rice and *Arabidopsis*, but present in red algae (Backstrom et al. 2007; Mathur et al. 2011). The Mediator complex is not merely participating in the transcription initiation process, but several recent reports indicate that it is also involved in other phases of transcription such as promoter escape, co-transcriptional process, transcription elongation, transcription termination (Poss et al. 2013; Allen and Taatjes 2015). These evidence suggest that Mediator contributes to both the general and specific functions in the gene regulation and significantly important for almost every process of transcription of eukaryotic genes.

Recent report suggest that several plant Mediator complex subunits have been connected with many signaling pathways, including plant development and growth, for instance, embryo, flower organ development, meristem pattern, root development, non-coding RNA processing, regulation of genomic stability, plant immunity, and defense pathway, stresses such as cold and drought tolerance (Yang et al. 2016; Samanta and Thakur 2015). *Arabidopsis* Mediator complex subunits MED2, MED14, and MED16 play a significant role in cold acclimation-induced freezing tolerance (Hemsley et al. 2014). MED16 mutant also shows reduced sensitivity to osmotic stress tolerance in *Arabidopsis* (Boyce et al. 2003). *Arabidopsis* MED25 participates in abiotic stress response pathway to control plant development (Elfving et al. 2011). The roles of Mediator subunits are also critical to plant metabolic and biosynthetic pathways. For example, *Arabidopsis* MED5a and MED5b are necessary for regulating phenylpropanoid biosynthetic genes and downstream products (Bonawitz et al. 2012). The metabolites formed from the pathway of the phenylpropanoid are important for plant development and is also useful for human health. *Arabidopsis* MED16 and MED25 positively regulate iron homeostasis iron deficiency metabolism, supporting the molecular mechanism by the Mediator complex for plant metabolic responses to iron deficiency stress (Yang et al. 2014). Although only a few reports have been revealed for Mediator complex that regulates the biosynthesis of plant metabolite, it has high potential to become an ideal target for plant biosynthetic pathway engineering.

3.4 Other Complex that Modulates the Promoters During Transcription

A number of different multi-protein complexes are noted in yeast and human cells on the promoter, which directly or indirectly control transcription regulation, for instance TBP-free TAF-containing complex (TFTC), Spt-Ada-Gcn5 acetyltransferase (SAGA), Spt3-TAF9-GCN5L acetylase (STAGA), SAGA-like (SLIK), TFTC-related PCAF/GCN5 complexes, and nucleosomal acetyltransferase of histone 4 (NuA4) complex have numerous and vital roles in transcription regulation of RNAPII genes. These complexes are involved in transcription primarily either due to their histone-modifying activity or coactivator function of TAFs. However, much information about these complex subunits in yeast, human, and metazoan species are prevalent, there is only a little evidence in the case of plants hence it still remains to be thoroughly investigated.

The histone-modifying SAGA complex plays various functions in transcription regulatory processes such as RNAII recruitment, transcription progression, nucleosome removal, and nuclear export of transcribed mRNA. In addition, SAGA complex also participates in the different cellular developmental process and environmental stresses such as DNA damage, starvation, and heat-regulated pathways directly or indirectly in yeast and human (Baker and Grant 2007). Huisinga and Pugh (2004) also described that yeast SAGA complex is engaged in the genes upregulation in carbon starvation response (Huisinga and Pugh 2004). Recently, plant SAGA complex subunits are identified and suggested the contribution of the SAGA complex in plant gene regulation and environmental stress conditions such as high temperature and salt stress (Srivastava et al. 2015, 2016). The SAGA complex has two important distinct enzyme functions, a histone acetyltransferase, and deubiquitinases. *Arabidopsis* SAGA complex components histone acetyltransferase GCN5 and coactivator ADA2B mediate major activity in cold responses and disruption of these proteins displayed a failure of several cold-regulated gene expression (Stockinger et al. 2001; Vlachonasios et al. 2003). The disruption of SGF29A shows salt stress tolerance, but the stress-related gene expression is decreased, for example, COR78 (cold-regulated 78) and RD29b (responsive to desiccation 29b) in the mutant of SGF29A during salt stress (Kaldis et al. 2011). Another histone acetyltransferase NuA4/Tip60 is also a multisubunit chromatin remodeling complex that plays a vital role in transcription regulation, RNA processing, DNA damage response, stress response, and metabolism in eukaryotes (Sapountzi and Cote 2011). Recently, *Arabidopsis* homologs of NuA4 are identified and defined its role in H4 acetylation in the promoter regions of major flowering regulator genes (Bieluszewski et al. 2015). *Arabidopsis* HAM1 and HAM2 two homologs of yeast ESA1 histone acetyltransferase and the catalytic component of the NuA4 complex (Bieluszewski et al. 2015). *Arabidopsis* lacking HAM1 and HAM2 expression showed more DNA damage after UV-B radiation stress treatment, indicating the functions of these proteins in DNA damage repair exposed to environmental perturbations (Campi et al. 2012).

4 Transcriptional Regulation of Plant Metabolite Biosynthetic Pathway

Plants produce a large number of secondary metabolites, which significantly function as signaling molecules for several cellular and biological pathways and protect the plant in response to diverse environmental adverse conditions and development stage. Plant secondary metabolites are different in chemical structure and nature. Biosynthesis of secondary metabolites is influenced by cell or tissue or organ type, different developmental stage, and environmental cues (both abiotic and biotic). On the basis of chemical composition, plant secondary metabolites are broadly categorized into two groups: nitrogen-containing compound and nitrogen lacking compound (Patra et al. 2013). The nitrogen-containing compounds are extremely diverse such as alkaloids, amines, and non-protein amino acid. The nitrogen-lacking compounds are further grouped into two classes: terpenoids and phenolics. Plant terpenoids are derived from five-carbon isoprene units and play a specific role as chemical interaction molecules and protect from abiotic and biotic environment conditions. Plant phenolics are aromatic benzene ring compounds with one or more hydroxyl groups used primarily for protection against abiotic and biotic stress. Phenolics provide a significant function in plant development, mainly in the biosynthesis of lignin, flavonoid, and pigment (Patra et al. 2013; Yang et al. 2012).

As discussed above, biosynthetic pathway for plant secondary metabolite is controlled and influenced by several factors such as abiotic and biotic environmental stress or spatial and temporal manner (Pandey et al. 2016; Srivastava et al. 2014b; Pavarini et al. 2012). These factors directly or indirectly orchestrate transcriptional regulation of secondary metabolite biosynthesis pathway and thereby their accumulation. The transcription factor, sequence-specific DNA-binding factor, that bind to cis-regulatory elements present generally to the promoter of target genes and mediate the transcription process by the assembly of transcription machineries such as PIC assembly and several chromatin modifiers (Srivastava et al. 2016, 2014b). These transcription factors are perfect targets for biosynthetic pathway engineering as they transfer signal from environmental stress or developmental-specific signal to the target promoter for activating or repressing the gene expression. In plants, several transcription factor families have been investigated for controlling biosynthetic pathway for plant secondary metabolite. These transcription factor families include AP2/ERF (**AP**etala2/**E**thylene **R**esponse **F**actor), bHLH (**B**asic **H**elix-**L**oop-**H**elix), bZIP (**B**asic Leucine **Zip**per domain), DOF (**D**NA-binding with **O**ne **F**inger), MYB (**MY**elo**B**lastosis), NAC (**N**AM, **A**TAF1/2, and **C**UC2), SPL (**S**QUAMOSA promoter binding **P**rotein-**L**ike), WRKY and Zinc finger (Yang et al. 2012; Liu et al. 2015). This transcription factor can act as transcriptional activators to enhance or improve the production of secondary metabolite for example, several R2R3-MYBs have been described to regulate expression of the flavonoid, glucosinolate, and phenylpropanoid pathway genes (Zhong et al. 2010; Zhao and Dixon 2011; Mehrtens et al. 2005; Stracke et al. 2007; Liu et al. 2015). PsAP2, a transcription factor of an AP2/ERF family from

Papaver somniferum, interacts with both DRE and GCC box element and highly increased in response to wounding stress. Overexpressing PsAP2 augmented both abiotic and biotic stresses tolerance in transgenic tobacco plants (Mishra et al. 2015). The AP2/ERF family ORCA2 and ORCA3 transcription factors bind to the JERE (jasmonate and elicitor-responsive element) on the secondary metabolite biosynthetic gene strictosidine synthase promoter. ORCA2 and ORCA3 are upregulated by plant stress hormone jasmonic acid and have been reported as regulators for terpenoid indole alkaloids biosynthesis (Menke et al. 1999). Jasmonic acid-responsive AP2/ERF family from *Artemisia annua* AaERF1 and AaERF2 interacts with the CRTDREHVCBF2 (CBF2) and RAV1AAT (RAA) regulatory element found in both ADS and CYP71AV1 promoters resulting in augmented metabolites artemisinin accumulation, which is an effective component for malaria treatment (Yu et al. 2012). Overexpression of the bHLH transcription factors TSAR1 or TSAR2 in hairy roots of the *Medicago truncatula* leads to increase in the transcript of triterpene saponin biosynthetic genes and intensely enhanced the triterpene saponins accumulation. TSAR1 and TSAR2 mediate HMGR1 (3-hydroxy-3-methylglutaryl-coenzyme a reductase1) transactivation by direct interaction to the N-Box of the HMGR1 Promoter (Mertens et al. 2016). *Gossypium arboretum* GaWRKY1, coding for a Leu zipper-containing WRKY protein, acts as a transcriptional activator of the cotton (+)-δ-cadinene synthase gene CAD1-A, contributing to cotton sesquiterpene biosynthesis. In suspension cells, both *GaWRKY1* and *CAD1-A* genes expression and sesquiterpene aldehydes biosynthesis were strongly activated by a fungal elicitor and methyl jasmonate or other environmental stimuli (Xu et al. 2004). Thus, it is a useful technique to use appropriate transcription factors for plant secondary metabolic biosynthetic engineering.

5 Conclusion

To improve the plant secondary metabolism production, it is essential to understand its biosynthetic pathway at the transcription level. Therefore, engineering the transcriptional regulatory mechanism, especially promoter or transcription factors, promises to be of high potential in engineering plant secondary metabolism. The transcription complex mediates the coordination between the engineered promoter or the native promoter with transcription factor at the TSS of the promoter. Since, reports suggest that transcription complexes control the secondary metabolic biosynthetic pathway, therefore the production and accumulation of these metabolites in response to a different kind of environmental stress are valuable. Cis-regulatory motifs present in the promoter have also been recognized and well established to enhance the production of plant secondary metabolic pathway. Thus, engineering the coordination between promoter, transcription factors, and transcription complex assembly at the promoter can potentially be used for fine-tuning the plant metabolic biosynthetic pathway.

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