Regulation of Stress Responsive Genes in Plants: Involvement of Epigenetic Mechanisms

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ABSTRACT

Plants, being sessile, have developed a myriad of strategies to withstand the unavoidable stresses, which otherwise by no means can be escaped. These mechanisms involve complex cellular machineries operating in a web of signal transduction. Repertoires of genes are either up- or down- regulated during various phases of stress signaling, the understanding of whose regulation is still mesmerizing. In recent times, batteries of epigenetic mechanisms have been found to operate underneath the discovered roles of transcription factors and *cis*-elements. These epigenetic mechanisms involving DNA methylation, histone modifiers and ATP-dependent chromatin remodelers are the ones that directly influence the transcription of genes in eukaryotes. In the present review, the discovered and speculative roles of these epigenetic mechanisms in the regulation of stress responsive genes will be discussed and areas will be determined which needs to be focused in order to understand global stress specific gene regulation and to engineer better stress tolerant plants.

CONTENTS

INTRODUCTION

Proper growth and development, and successful completion of the life cycle of any organism are strongly dependent on its interaction with the external abiotic and biotic factors (Nevo 2011). When caught in hostile conditions, the organisms try to escape or trigger mechanisms to withstand the inevitable. The second option remains as the only choice in case of the sessile plants. In such a case, the signal of stress is carried to the genome of the organism causing changes in its expression map (Chinnusamy *et al.* 2004). The transcriptional changes leading to altered transcriptome have often been found to be associated with epigenetic mechanisms. Recent works have highlighted that understanding the epigenetic regulation of stress-responsive genes is extremely important to engineer tolerance in relatively stress sensitive crop plants.

Although in strict sense epigenetics refers to DNA sequence independent heritable changes in gene expression (Berger *et al.* 2009), most stress-responsive variations in gene expression are transient and reversible yet involve similar mechanism as observed for a true epigenetic incidence. Nevertheless, in few cases inheritance of such incidences, mitotically or meiotically have been observed (discussed later). Heritable or inheritable, broadly the epigenetic regulation of gene expression operates via changes in DNA methylation, nucleosome positioning and histone post-translational modifications, together, which modulate the chromatin structure. Each plant has repertoire of factors, many of which operate in unison to bring these changes in the genome globally or at distinct loci under stress. How and when these factors are recruited to various loci in the genome presently appears most interesting in understanding the mechanism of epigenetic regulation of stress response along with its effect on maintaining the genome stability and reshaping of gene expression pattern under adverse conditions.

In this review, the discovered stress specific epigenetic

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factors and their roles in the stress signaling pathway has been surveyed to validate the present status of our knowledge in this field. Several gaps in our understanding still needed to be plugged to complete the required knowledge to engineer increased stress tolerance in crop plants.

ROLE OF ATP-DEPENDENT CHROMATIN REMODELING COMPLEXES IN STRESS SENSING AND RESPONSE

The enzyme complexes involved in displacement of a nucleosome over a particular stretch of DNA sequence consumes the energy of ATP hydrolysis and hence, are called ATP-dependent chromatin remodeling factors (Cairns 1998; Imbalzano 1998; Varga-Weisz and Becker 1998). These multi subunit ATP-dependent complexes have a SNF2 (SUCROSE NON-FERMENTING 2) like family of DEAD/H ATPase (sharing homology to helicases) as their catalytic centre (Eisen *et al.* 1995; Peterson and Workman 2000). Based on the type of SNF2 like ATPase, five most important class of these chromatin remodeling complexes are SWI/SNF (ATPase contains a bromodomain; move nucleosome *in trans* or *in cis*), ISWI (ATPase contains a SANT domain; assemble nucleosome and increased chromatin stability), CHD1 (contains chromodomain and DNA binding motif), INO80 (ATPase domain split in two; possess DNA helicase activity due to inclusion of RuvB; involve in DNA repair) and SWR1 (ATPase domain split into two domain; swaps H2A with H2A.Z).

Homologues of SNF2 like ATPases are found almost in all plants for which genomic and cDNA sequences are available. Four genes in *Arabidopsis*, and six in poplar have been classified as SWI2/SNF2 subfamily of transcriptional co-regulator (http://www.chromdb.org; Verbsky and Richards 2001; Kwon *et al.* 2005). The presence of higher number of such factors in plant than metazoan genomes indicates that these ATPases might have more specific as well as redundant roles in plants. Redundant function of these ATPases was hypothesized by the finding that mutation in one of the SNF2 ATPase is lethal in *Drosophila* but viable in *Arabidopsis* like mutants of *Arabidopsis thaliana BRHAMA* (*AtBRM*) and *SPLAYED* (*AtSYD*; Bezhani *et al.* 2007). However, of the total number of *Arabidopsis* genes (~1% of all genes) regulated by AtSYD and AtBRM, only 20% were common between these two chromatin remodeler, indicating each has some specific function to perform. More recently, AtSYD has been shown to regulate the expression of selected genes downstream to jasmonic acid (JA) and ethylene (ET) signaling under biotic stress (Walley *et al.* 2008). It was further demonstrated that AtSYD was directly targeted to the promoters of *cMYC* and *NSP2*. Another chromatin remodeling complex AtCHR12 has been shown to cause growth retardation under abiotic stress by bringing changes to the expression of dormancy related genes (Mlyrnarova *et al.* 2007). Plants mutant for *AtCHR12* were found to be similar to wild type plants under normal conditions, implying stress specificity of this gene. Mutation in *PICKLE* (*PKL*), A CHD3-type SWI/SNF ATPase, is known to exhibit the expression of early embryogenesis related genes like *LEC1* and *FUS3* during seed germination along with the formation of swollen roots filled with embryonic lipids (pickle roots) which can be reversed by exogenous gibberellic acid (GA₃) application (Ogas *et al.* 1997, 1999). Although under normal condition *pkl* seeds and their germination rate were indistinguishable from those of wild type plants, higher ABI3 and ABI5 expression coupled with reduced silent chromatin marks (histone H3 lysine 9; H3K9 and H3 lysine 27; H3K27 methylation) on these genes in addition to significantly delayed germination was inferred under low abscisic acid (ABA) abundance condition (Perruc *et al.* 2007). It is believed that via ABA-dependent signals, PKL would act to modulate a plant's response to mild osmotic stress by limiting ABI3 and ABI5 expression. Of the 39 SNF2 domain-containing proteins in rice, 8 have been designated as SWI/SNF class of ATPase. Seven of these ATPases were found to be responsive to exogenous hormones and stress treatments during expression analysis (Li *et al.* 2011). In *Arabidopsis*, mutation in *MODIFIER OF snc1, 1* (*MOS1*) suppresses *R* gene *SUPPRESSOR OF npr1-1, CONSTITUTIVE1 (SNC1)* due to alteration in DNA methylation. Interestingly, mutation in another SWI/SNF ATPase, *DECREASE IN DNA METHYLATION 1* (*DDM1*) with proven nucleosome mobilization capacity, in *mos1* mutant background (*ddm1/mos1*), revives *snc1* expression, indicating its role in biotic stress signaling (Li *et al.* 2010). *DDM1* has been estimated to down-regulate in response to biotic stress (Ma *et al.* 2011). However, DDM1 was found to up-regulate under heavy metal stress in rice plants (Ou *et al.* 2012). The impact of DDM1 on global genome methylation is discussed later in this review. One Mi2 class of ATPase was observed to accumulate under all tested stress conditions and hormone treatments in rice (Li *et al.* 2011). It can be hypothesized that in cereal crops also, the ATP-dependent chromatin-remodeling complex does play a major role in controlling gene expression in response to various stresses through one or other hormonal signaling pathways.

Apart from the SWI/SNF ATPase subunit, SUCROSE NON-FERMENTING 5 (SNF5) and SWITCH 3 (SWI3) have been observed to form the core-remodeling complex in yeast, *Drosophila* and human, which is known to re-model chromatin *in vitro* (Phelan *et al.* 1999). In *Arabidopsis BUSHY* (*AtBSH*) has been found as the homologue of yeast *SNF5p*, human *INI1* and *Drosophila SNR1*. The ubiquitously expressed *AtBSH* gene has been observed to partially complement ySNF5p mutation in yeast partially but was unable to activate transcription like ySNF5p (Brzeski *et al.* 1999). Homologue of SNF5 in *Pisum sativum* has been found to be functionally similar to the *AtBSH* gene at molecular level interactions. This *PsSNF5* gene accumulates during later stages of embryo development and in response to ABA treatment and drought stress in germinating seeds and vegetative tissues indicating its role in ABA-dependent abiotic stress response (Ríos *et al.* 2007). SWI3 proteins have been reported in *Arabidopsis* also. All the four *Arabidopsis SWI3* genes (SWI3A-D) show differential interaction with different SWI/SNF2 ATPases (Bezhani *et al.* 2007). The multiplicity of SWI3 genes in *Arabidopsis* supports that the SWI/SNF complexes are more specific in function in plants than their metazoan counterparts. SWI3B was first reported to interact with FCA (a RNA binding protein involved in floral development) and is involved in vegetative and reproductive growth and developmental regulation (Sarnowski *et al.* 2002; Zhou *et al.* 2003), indicating its role in sensing external environment. Recently, HYPERSENSITIVE TO ABA 1 (HAB1), a protein phosphatase 2C (PP2C) and also a component of ABA signaling pathway in *Arabidopsis*, was shown to interact with SWI3B (Saez *et al.* 2008). Mutation in *AtSWI3B* was found to exhibit reduced sensitivity to ABA-mediated inhibition and was found to control the expression of genes like *RAB18* and *RD29B* (Saez *et al.* 2008).

Exchange of one variant of the histone with another type also appeared to be a potent mechanism to control gene expression. In recent time, incorporation of H2A.Z has been shown to play a major role in sensing the external environment. SWR1 and SRCAP complex are known to cause replacement of H2A with H2A.Z in yeast and human, respectively (Krogan *et al.* 2003; Mizuguchi *et al.* 2004; Cai *et al.* 2005). Mutation in *PHOTOPERIOD INDEPENDENT EARLY FLOWERING 1* (*PIE1*; homologue of ySWR1 ATPase), *ACTIN RELATED PROTEIN 6* (*ARP6*; a subunit of SWR1 complex) and *SERRATED AND EARLY FLOWERING* (*SEF*; homologue of ySWC6 subunit of SWR1 complex) was found to cause early flowering in *Arabidopsis* by down-regulation of *FLORAL LOCUS C* (*FLC*), a phenotype also known to result from elevated environmental temperature (Deal *et al.* 2005; Martin-Trillo *et al.* 2006; Choi *et al.* 2007; March-Diaz *et al.* 2007). It has been shown that PIE interacts with H2A.Z, and PIE and

ARP6 are required to deposit H2A.Z at *FLC* locus (March-Diaz *et al.* 2008). In the same work, it was further observed that 65% of the genes misregulated in H2A.Z *Arabidopsis* mutant (*hta9/hta11*) were also mis-regulated in *pie1* and *sef* mutants. This group was found to include genes related to salicylic acid (SA)-dependent immunity and the mutants displayed enhanced tolerance to phytopathogenic bacteria *Pseudomonas syringae* cv. tomato. ARP6 was also shown to be necessary for deposition of H2A.Z at a number of Pi starvation genes (Smith *et al.* 2010). However, H2A.Z was predicted not to function at least as an activator of transcription as many phosphate starvation response genes were de-repressed in *arp6* mutant. Also, H2A.Z occupancy was found to be antagonistic to DNA methylation and hence was supposed not to be involved in long term gene silencing (Zilberman *et al.* 2008). Genes responsive to elevated temperature conditions, irrespective of whether up- or down-regulated, were found to be enriched in H2A.Z occupancy under non-inductive condition and evidences suggested that it keeps the DNA methylation-free but tightly wrapped around the nucleosome, rendering the DNA inaccessible to transcription activators or repressors (Kumar and Wigge 2010). However, its eviction under inductive condition generates thermosensory response in *Arabidopsis* as the DNA become free to interact with various factors. In contrast, very recently, it was observed that H2A.Z was not evicted from ethylene-inducible genes in *Arabidopsis*, even under inducible conditions (Hu *et al.* 2011). Interestingly, in *hta9/hta11* mutant plants, induction of ethylene responsive genes was not observed. In summary, it can be inferred whether evicted or not, H2A.Z keeps the genes ready to response under their inducible condition.

Of the three-linker histones encoded by *Arabidopsis* genome, *HIS1-3* is up-regulated in root meristem and elongation zone by drought and ABA treatments (Ascenzi and Grant 1997, 1999). Its expression reduces in ABA insensitive mutant *abi1* and increases in ABA RESPONSIVE ELEMENT BINDING 1 (AREB1) factor overexpressing plants (Ascenzi and Grant 1997; Fujita *et al.* 2005). In tomato also, *HIS1-S* was found to up-regulate in response to drought and ABA treatments and be associated with the chromatin of wilted leaf cells (Scippa *et al.* 2000). *HIS1-S* antisense transgenic plants were shown to exhibit higher rate of stomatal conductance and transpiration, resulting in faster decrease in relative water content (Scippa *et al.* 2004). These results revealed the presence of stress specific *HIS1* variants in plants. Over all, it appears that ATP-dependent chromatin remodeling complex does play a major role in sensing and response to various biotic and abiotic stresses.

ROLE OF HISTONE CHAPERONS IN STRESS RESPONSE

Histone chaperons are known to play major role in nucleosome assembly and disassembly in eukaryotes. Nucleosome Assembly Protein 1 (NAP1) is highly conserved in eukaryotes. Of the four *AtNAP1* genes, *AtNAP1;1*, *AtNAP1;2* and *AtNAP1;3* exhibit hypersensitive response to UV-C treatment in *Arabidopsis* (Liu *et al.* 2009a). Moreover a C-terminal deletion of 34 amino acids in AtNAP1;3 was observed to cause ABA-hypersensitivity and lower tolerance to salt stress. Thus, apart from ATP-remodeling complexes, histone chaperons are also indispensible in hormone and stress signaling pathways.

ROLE OF HISTONE MODIFIERS IN STRESS SIGNALING

Post-translational modifications of histones had been the center of attraction of transcriptional regulation of genes in all eukaryotes since the discovery and elucidation of the role of histone acetylation in gene regulation (Allfrey *et al.* 1964). Histones are now known to get modified in a variety of ways including acetylation, methylation, phosphorylation, ubiquitination, glycosylation, ADP-ribosylation, carbonyla-

tion and sumoylation at N-terminal region. The various combination of modification within a nucleosome carries specific information about the regulation of genes and has been termed as "Histone code" and the effect also depends on the position of nucleosome in the gene (Jenuwein and Allis 2001). Histone modification in plants regulates gene expression in response to diverse exogenous stimuli including stress (abiotic and biotic), temperature, light and also to endogenous signals operating in pathways of growth, development and differentiation (Fuchs *et al.* 2006; Pfluger and Wagner 2007). Most of the studies of histone modification in plants have been done on *Arabidopsis* but recently some work has been done in rice, maize and few other crop plants as described below.

The acetylation of lysine (K) residues (an undisputed mark of active genes in all eukaryotes) are known to be mediated by bromodomain containing histone acetyltransferases (HATs), the mammalian homologues of which, like GCN5/HAG1 (belonging to GNAT family), HAC1 and HAC12 (belonging to CBP/p300), and HAF2/TAF1 (belonging to TAFII family), have been discovered in plants (Bharti *et al.* 2004; Benhamed *et al.* 2006; Long *et al.* 2006; Mao *et al.* 2006; Han *et al.* 2007). Similarly, the acetyl group removing histone deacetylases (HDACs) like AtHDA19 and AtHDA6 (belonging to RPD3 family), AtHD2A, AtHD2B and AtHD2C (belonging to plant specific HD2 family), and OsSRT1 and AtSRT2 (belonging to NADH-dependent Sir2 family) have been characterized from plant systems (Benhamed *et al.* 2006; Ueno *et al.* 2007; Huang *et al.* 2007; Wang *et al.* 2010).

Arabidopsis HAC1 has been found to be necessary for transcriptional up-regulation of heat shock gene HSP17 (Bharti *et al.* 2004). The cold inducible transcription factor CBF1 recruits GCN5 containing complex via ADA adapters in *Arabidopsis* (Mao *et al.* 2006). Mutation in *ADA2B* makes plants hypersensitive to salts with reduced acetylation of histone H3 and H4 at *COR6.6*, *RAB18* and *RD29b* (Kaldis *et al.* 2011). However, *ada2b-1* but not *gcn5-1* mutant of *Arabidopsis* was more resistant to freezing stress (Vlachonasios *et al.* 2003). Of the total genes affected, nearly half were similar in both these mutants. It can be understood that these two proteins might not function together always as they have both redundant and specific functions. *Arabidopsis* mutants of elongator histone acetyltransferase complex (*elp2*, *elp6*, *elp4/elo1* and *elp1/abo1/elo2*) exhibit ABA-hypersensitivity and increase tolerance to oxidative stress and CsCl (Zhou *et al.* 2009). Interestingly, mutation in core subunits (*elp1/abo1* and *elp2*) of elongator complex but not in accessory complex subunits (*elp4/elo1* and *elp6*) shows super sensitivity in stomatal closure in response to ABA. In *elo* mutants, genes of JA and ethylene signaling were up-regulated (Nelissen *et al.* 2010). ELP2 is also needed for faster and timely immune response against the hemibiotrophic pathogen *Pseudomonas syringae*.

Like HATs, HDACs have been observed to have specific roles under stress in plants. AtERF7, which plays a vital function in ABA signaling and drought stress response, has been suggested to recruit HDA19 via its interaction with HDAC complex subunit SIN3 (Song *et al.* 2006). Mutation in HDA19 was found to cause down-regulation of *ABI1*, *ABI2*, *KAT1*, *KAT2* and *RD29B* resulting in hypersensitivity to ABA and NaCl in *Arabidopsis* (Chen and Wu 2010). HDA19 is also reported to get up-regulated by JA and ET and control the expression of *ERF1* and genes encoding PR proteins (Zhou *et al.* 2005). Interestingly, HDA19 has also been shown to repress salicylic acid-mediated signaling pathway in *Arabidopsis* (Choi *et al.* 2012). Thus, it was suggested to involve in maintaining optimum growth of the plants by regulating the basal expression level of genes of SA-response pathway under unstressed condition and their overstimulation under biotic stress. Mutation in another RPD3-type HDAC, is also known to cause ABA- and salt-hypersensitivity because of down-regulation of ABA- and salt responsive genes like *ABI1*, *ABI2*, *KAT1*, *KAT2*, *DREB2A*, *RD29A*, and *RD29B*

(Chen *et al.* 2010). HDA6 has been suggested to be involved in JA mediated plant defense by interacting with a F-box protein COL1. Owing to the similarity in roles, redundant functionality for HDA19 and HDA6 has been postulated (Tanaka *et al.* 2008; Chen and Wu 2010). Moreover, it appears that both these genes might be involved in deacetylation of repressor(s) of ABA-responsive stress inducible genes. In *Arabidopsis*, AtHD2C, a HD2-type HDAC is repressed by ABA (Sridha and Wu 2006). Its overexpression was found to manifest ABA-insensitive phenotype with the down-regulation of *ABI2, ADH1, SKOR, KAT1* and *KAT2* in *Arabidopsis*. However, increased tolerance to salt stress was observed in transgenic plants along with higher expression of LEA and reduced sensitivity to high-osmolarity. Another HD2-type HDAC, HDT107 (a histone H4 deacetylase), has been shown to negatively regulate the innate immunity in rice by modulating the transcription of pattern recognition receptor and defense related genes (Ding *et al.* 2012) Mutation in a human transducin beta-like WD40-repeat protein HOS15 have been observed to cause *Arabidopsis* plants hypersensitive to cold stress specifically (Zhu *et al.* 2008). Hence, it can be inferred that plants do have specific chromatin remodelers to function under specific conditions. Apart from *Arabidopsis*, in crop plants also, roles of specific histone acetylase and deacetylase have been postulated. In cereal crops like *Hordeum vulgare* stress hormones responsiveness of many HATs and HDACs have been observed (Demetriou *et al.* 2009, 2010). In rice, many HDACs were found to up-regulate in response to stresses like salt, cold and high osmolarity and exogenous application of hormones like ABA, JA and SA (Sharma *et al.* 2009). Overexpression of *OsSRT1*, a Sir2-like HDAC, enhanced tolerance to oxidative stress in rice while siRNA-mediated down-regulation leads to high H_2O_2 accumulation, DNA fragmentation, cell death and lesions similar to hypersensitive responses as observed during incompatible plant-pathogen interactions (Huang *et al.* 2007). It can be concluded that different HATs and HDACs have specific role to play under different set of conditions in plants.

The methylations of lysine and arginine residues are achieved mainly by SET-domain containing histone methylatransferases (HMTs). SuvH group of proteins are responsible for transcription repressive H3 lysine9 (K9) methylations in *Arabidopsis* while the H4 arginine (R) methylations are mediated by protein arginine methyltransferases (PRMTs) (Jackson *et al.* 2004; Naumann *et al.* 2005; Ebbs and Bender 2006; Pei *et al.* 2007). Mutation in *PRMT5* (required for transcription repressive H4R3 symmetric di-methylation, H4R3sme2) homologue in *Arabidopsis*, *Shk1 kinase binding protein1* (*SKB1*), is known to exhibit salt hypersensitivity with reduced H4R3sme2 at *FLC* locus (Zhang *et al.* 2011). Heterochromatin specific H3 Lysine 27 (K27) methylations are mediated by E(Z) class of HMTs (PcG complex; Ng *et al.* 2007). WD-40 repeat proteins FERTILIZATION INDEPENDENT ENDOSPERM (FIE) and MULTICOPY SUPPRESSOR OF IRA1 (MSI1) are a part of polycomb group (PcG) complex. *Arabidopsis msi1* mutants were found to exhibit increased transcription of stress- and ABA-responsive genes accompanied by increased tolerance to dehydration (Alexendre *et al.* 2009). In barley *HvE(Z)* and *HvFIE* expression was found to increase in response to ABA treatment (Kapazoglou *et al.* 2010). Genes encoding SET domain proteins have been identified in rice also (Thakur *et al.* 2003; Qin *et al.* 2010). However, their stress responsiveness is yet to be studied. *Arabidopsis* loss-of-function mutant *sdg8-1* (*set domain group 8*) exhibits reduced resistance to the necrotrophic fungal pathogens *Alternaria brassicicola* and *Botrytis cinerea* with reduced level of transcription promoting H3 lysine 36 (H3K36) di- and tri-methylations not only at JA/ET signaling pathway defense genes but also in global histone extracts (Berr *et al.* 2010). Mutation in *Arabidopsis thaliana TRITHORAX 1* (*ATX1*), required for active gene specific H3 lysine4 (H3K4) tri-methylation (Ding *et al.* 2011)

was shown to decrease tolerance to dehydration stress with larger stomatal aperture and reduced expression of *NCED3*, a gene involved in ABA biosynthesis. Changes in H3K4 methylation and H3 acetylation has been observed in submergence inducible genes in rice also (Tsuji *et al.* 2006). The mono-ubiqitination of H2B Lysine 143 (K143), the only known site in plant for this modification, is established by Ring-type E3 ligase like HUB1 and are removed by deubiquitinases like SUP32/26 (Liu *et al.* 2007; Sridhar *et al.* 2007). The methylations from histone residues are removed by JmjC-domain and LSD1-type HDMs (histone demethylases) or by a process involving deimination (Berger 2007; Kouzarides 2007). However, the role of these factors in plant stress signaling is yet to be reported. Apart from phosphorylation at H3S10 and H3S28, which are found in other eukaryotes also, H2T11 is also phosphorylated in plant nucleosomes (Pfluger and Wagner 2007). Induction of genes in response to abiotic stresses in the tobacco BY2 cell cultures and in *Arabidopsis* cells has been observed to be associated with rapid increase in H3S10 phosphorylation and immediately followed by increase in H3 phosphorylation and H4 acetylation. From the data obtained so far, it appears that histone modifiers are major switches in regulation of stress responsive genes.

SMALL RNA-MEDIATED EPIGENETIC REGULATION OF STRESS RESPONSE

Small RNAs initially discovered as a strong weapon for post-transcriptional gene silencing, were uncovered to have potential role in transcriptional gene silencing as mediator of genome locus specific DNA methylation and histone modification. In plant, the four major species of small RNA includes micro RNAs (miRNAs), transacting siRNAs (ta-siRNAs), heterochromatic siRNA (hc-siRNA) and natural-antisence siRNA (nat-siRNA). Stress related miRNAs were first identified in small RNA libraries of *Arabidopsis* seedlings exposed to various stresses (Sunker and Zhu 2004). miRNAs like miR393, miR397b and miR402 were observed to accumulate under salt, drought and cold stresses and ABA treatments. miR402-Overexpressing plants were found to target DNA demethylase *DML3*, indicating its indirect role in controlling DNA methylation under abiotic stresses (Kim *et al.* 2010). In crops like rice, dehydration induced miR169g and salinity induced miR169n, both targeting stress down-regulated NF-YA was identified (Zhao *et al.* 2007). The promoters of the miRNAs were found to have *cis*-elements responsive to stress like DRE and ABRE. Incidences of hormonal regulation of miRNA have been documented like positive and negative regulation of miR319 (targeting TCP-domain proteins) in rice by GA and ABA, respectively (Liu *et al.* 2009b). By genome-wide profiling, eight up-regulated and 11 down-regulated miRNAs were discovered in drought stressed rice plants (Zhou *et al.* 2010). In response to cold, miRNAs belonging to 10 and 5 different families of miRNA were found to up- and down-regulate in rice, respectively (Lv *et al.* 2010) Comparable numbers of abiotic and biotic stress responsive miRNA were also discovered in other monocots like wheat maize, and *Brachypodium* (Zhang *et al.* 2009; Yao *et al.* 2010; Kantar *et al.* 2011). Of the 40 novel stress induced miRNAs in rice *indica* variety, many were similar for salt stress and tungro virus infection, suggesting a vital role of miRNAs in crosstalk between abiotic and biotic stress signaling pathways (Sanan-Mishra *et al.* 2009).

Although, miRNAs appears to play important role in stress signaling, siRNA species, specially the hc-siRNA are expected to directly regulate the epigenetic mechanisms controlling stress response. Several stress responsive endogenous siRNA were also discovered in small RNA libraries of *Arabidopsis* (Sunkar and Zhu 2004). Among these a 24-nt nat-siRNA against a pair of *cis*-antisense transcript *PYROLINE-5-CARBOXYLASE DEHYDROGENASE* (*P5CDH;* sense) and *SRO5* (antisense) resulting in the cleavage of *P5CDH* (which also generates 21-nt siRNA)

and accumulation of osmoprotectant proline (Borsani *et al.* 2005). Abiotic stress responsive siRNA were also detected in rice (Yan *et al.* 2011). Down-regulation of siR441 and siR446 was observed in response to ABA treatment and various abiotic stress and knockdown of these siRNA results in decreased stress tolerance. In genome-wide analysis of intraspecific hybrids and their parents of *Arabidopsis*, marked differences in 24-nt siRNA levels were observed (Groszman *et al.* 2011). This resulted in alteration in methylation levels and increased stress tolerance in the hybrid, indicating direct role of 24-nt siRNA in epigenetic response to environmental stress. Recent evidences suggest more interesting roles of siRNAs in epigenetic mechanism involved in plant stress signaling pathway, which is discussed later in this review.

ROLE OF DNA METHYLATION IN STRESS RESPONSE

The cytosine residue in the DNA is found to be methylated at fifth position in fungi, plants and mammals but not in *Drosophila*, yeast and *Coenarhabitis elgans*. Although the 5-methyl cytosine (5mC) is not synthesized as a separate base, it is sometimes coined as "fifth base of DNA", owing to its huge negative impact on gene regulation (Pennings *et al.* 2005). In spite of being studied for decades, mystery of mechanism of its establishment and removal, and way to control gene expression is not yet solved completely. DNA methylation imparts its effect by changing the chromatin structure and histone modification, bringing a change in DNA bending capacity, creating sites for 5mC binding protein (sequence specific and non-specific), removing the non-5mC DNA binding transcription factors, and inhibiting RNA polymerase elongation as reported from *Neurospora* (Rountree and Selker 1997; He *et al.* 2001). Apart from cytosine methylation on symmetric CpG residues like in animals, it is also present on symmetric CpNpG residues and asymmetric CpNpN residue in plants (Finnegan *et al.* 1998; Bender 2004). The CpG and CpNpG methylation are involved in genomic imprinting (Holliday and Pugh 1975; Riggs 1975; Bender 2004). On the other hand the asymmetric DNA methylation, which mainly occurs as a result of RNA-directed DNA methylation, has to be re-established *de novo* after each cycle of replication (Ramsahoye *et al.* 2000; Gowher and Jeltsch 2001). The CG methylation has been found to have a larger effect on global methylation and works in silencing of the heterochromatic region and transposons of the plants. A global loss of CG methylation along with release of transcriptional silencing of a number of transposons and heterochromatic repeats (centromere and pericentromeric sequences) was observed in mutants affecting CG methylations in *Arabidopsis* (Kato *et al.* 2003; Lippman *et al.* 2003; Mathieu *et al.* 2003; Lippman *et al.* 2004; Zhang *et al.* 2006; Zibberman *et al.* 2007). The CNG methylation has been found to be associated with many transposable elements (Zhang *et al.* 2006; Zibberman *et al.* 2007) but only a few transposons were transcriptionally activated in mutants affecting CNG methylation though there was a significant decrease in CNG methylation globally (Tompa *et al.* 2002; Matheu *et al.* 2005; Vaillant *et al.* 2006). It has been concluded that probably CNG methylation is involved in fine-tuning the regulation on transposable elements (Vaillant and Paszkowski 2007). Similar genome wide and mutant studies have revealed that asymmetric CNN methylation is involved in locus specific regulation of transposons, transgenes and endogenous genes (Gong *et al.* 2002; Agius *et al.* 2006; Morales-Ruiz *et al.* 2006; Penterman *et al.* 2007).

Though being hypothesized for a long time, the first concrete evidence of modulation of DNA methylation by an external stimuli was obtained by the observation of cold induced demethylation of nucleosomal core DNA in roots and hypomethylation of ZmM11 gene (that contain a retro-transposon-like sequence) in maize (Steward *et al.* 2000, 2002). Hypomethylation is also observed for stress related genes in tobacco mutant for MET1 (Wada *et al.* 2004). Reduction in CG methylation in coding region of NtGDPL along with its induction was observed in tobacco in response to high salt, low temperature, and aluminium. Activation of transposons and retrotransposons due to loss of DNA methylation like *Tos17* in rice, *Ttol* and *Tnt1* in tobacco, *Tam3* in *Antirrhinum* etc. in response to abiotic stresses due to hypomethylation have also been documented (Hirochika *et al.* 1996; Takeda *et al.* 1999; Beguiristain *et al.* 2000; Hashida *et al.* 2003, 2006). The hypomethylation and demethylation events may be needed for reshaping the genome (mainly via the activation of transposons) of the organisms in order to adapt to the changing environment as suggested by Barbara McClintock decades ago (McClintock 1984) and pointed out in some recent reviews (Boyko and Kovalchul 2008).

CpNpG-hypermethylation of CCWGG sequences in a satellite DNA in response to salt stress has been reported in facultative halophyte *Mesembryanthemum crystallinum*, which switches from C3-photosynthesis to CAM metabolism (Dyachenko *et al.* 2006). In this case, CCWGG sequence was not found to be hypermethylated in the promoter region of CAM pathway enzyme phosphoenolpyruvate carboxylase and hence, it was suggested that specific hypermethylation of the satellite DNA may be needed to form specialized chromatin structure to regulate a large set of gene and adapt to the changed environment and metabolism pattern. A methylation sensitive amplified polymorphism (MSAP) in wheat indicated CCGG sequences in salt-tolerant Deiking-961 were more methylated than sensitive Lumai-15 variety in response to salt stress (Zhong *et al.* 2009). In both the varieties genome wide hypomethylation along with many hypermethylated regions was observed. Similar results were also obtained by MSAP analysis in rice under drought stress (Wang *et al.* 2011). The drought responsive alteration in DNA methylation was observed to be dependent on the rice variety, tissue type and developmental stage and nearly 30% of these alterations were irreversible. The variety and tissue-type specific alteration in DNA methylation was also observed under salt stress in rice (Karan *et al.* 2012). However, these variations were found not to correlate with the salinity tolerance level of the rice varieties. In almost all the studies done till date, as exemplified by few aforementioned cases, stress induced genome wide hypomethylation has been found to be accompanied by locus specific hypermethylation.

Plant DNA methyltransferases (DNA mtase) are categorized broadly into Group I or DNMT/MET DNA mtase (responsible for CG methylation), Group II or Chromomethylases (CMT; responsible for CNG methylation) and Group III or Domain Rearranged Methyltransferases (DRMs; responsible for asymmetric CNN methylation) (Boyko and Kovalchuk 2008). Although nothing is known about the specific role of different DNA mtase in stress signaling, analysis of ten of these enzymes in rice identified *OsCMT2* as cold and salt inducible and *OsCMT3* as drought and salt inducible (Sharma *et al.* 2009).

Demethylation of DNA is mediated by DNA glycosylase/lyase. These enzymes generally cause ex*cis*ion of 5-methylcytocine base and introduction of a nick in the DNA backbone (Zhu *et al.* 2000, 2007). The DNA repair mechanism then add an unmethylated cytosine. The behavior of the plant DNA glycosylases under stress is yet to be reported. In one instance, stress mir402 was found to target *REPRESSOR OF SILENCING 1/DEMETER-LIKE 3* protein (*ROS1/DML3*) in *Arabidopsis* (Kim *et al.* 2010).

RECRUITMENT OF CHROMATIN REMODELING FACTORS AND INTERRELATION BETWEEN DIFFERENT EPIGENETIC EVENTS

Cytosine methylation has been reported to cause structural transition of DNA from B- to Z- and A-form (Tippin and Sundaralingam 1997; Rich and Zhang 2003). Z-form of the DNA is incompatible with nucleosome formation (Nickol *et*

al. 1982; Garner and Felsenfeld 1987). From various evidences, it is now suggested that DNA methylation can affect nucleosome formation and positioning if 5mC exocyclic group come in such a position that it causes steric interference with the path of DNA in the nucleosome (Wang and Griffith 1996; Godde *et al.* 1996; Davey *et al.* 1997; Pennings *et al.* 2004).

Many ATP-dependent chromatin-remodeling factors have been shown to control DNA methylation in plants. The most studied of them is DDM1, which has been suggested to control DNA methylation directly or indirectly by bringing changes in the histone modifications at transposons and repeat regions of the genome in *Arabidopsis* (Johnson *et al.* 2002). Apart from global hypomethylation resulting in *ddm1* mutants of *Arabidopsis*, hypermethylation of certain genic loci is also reported (Saze and Kakutani 2007). *ddm1* plants have been found to be more sensitive to UV-C, γ-irradiation, methyl methane sulfonate and NaCl (Shaked *et al.* 2006; Yao *et al.* 2012). Recently, in rice two genes, similar to *DDM1* of *Arabidopsis*, have been discovered (Higo *et al.* 2012). In the same study, hypomethylation of the genome in transgenic rice plants expressing antisense *DDM1a* gene was also observed. It has been suggested that DDM1 might facilitate the localization of 5mC binding domain proteins (MBDs) at specific nuclear domains (Zemach *et al.* 2005).

Like *ddm1* plants, mutants for DNA glycosylase *ROS1* also shows hypermethylation at certain genic loci like *BONSAI* (*BNS*), *SUPERMAN* (*SUP*) and *AGAMOUS* (*AG*) in *Arabidopsis* (Jacobsen *et al.* 2000; Saze and Kakutani 2007). In fact, frequent occurrence of ectopic DNA hypermethylation in global hypomethylation background has been observed in many other instances. *met1*, *Arabidopsis* mutant for a DNA methyltransferase, also shows the same phenomenon (Mathieu *et al.* 2007; Reinders *et al.* 2008). In *ddm1 Arabidopsis mutants*, the *BNS* loci, which is flanked by non-LTR type retrotransposons (*LINE*), get hypermethylated while the *LINE* sequence get hypomethylated upon repeated self-pollination. *ddm1* plants lacking this *LINE* insertion at *BNS* locus does not show hypermethylation. Hence, it was predicted that the flanking transposons controls the methylation of BNS locus. However, *SUP* and *AG* does not contain any transposons near to them, but still gets hypermethylated in *ddm1* and *met1* plants (Saze and Kakutani 2007). Based on some recent evidences, it has been hypothesized that global hypomethylation triggers both inhibition of DNA methylation and *de novo* methylation by RdDM (RNA dependent DNA methylation) pathway, which leads to local hypermethylation of a number of loci (Mathieu *et al.* 2007; Saze and Kakutani 2007; Saze *et al.* 2008).

MAINTAINANCE OF METHYLTION1 (MOM1) that shares limited homology to DDM1 has been found to be involved in DNA methylation independent silencing of repetitive DNA sequences in *Arabidopsis* (Vaillant *et al.* 2006). The release of transgene silencing and 5S repeat repression without alteration of DNA and histone methylation patterns (Amedo *et al.* 2000; Vaillant *et al.* 2006) clearly depicts the existence of methylation-dependent as well as methylation-independent pathways of epigenetic silencing. Curiously, in *Arabidopsis,* activation of many repeat regions in response to prolonged heat stress was found to occur without DNA demethylation, almost independent of histone modification but completely dependent on nucleosome eviction and heterochromatin decondensation (Pecinka *et al.* 2010).

Second messengers like inositol phosphates have been shown to play direct recruitment of chromatin remodeling complexes in yeast genome. IP_6 was reported to inhibit the nucleosome mobilization by yeast ISW2 containing NURF chromatin remodeling complex, whereas IP_4 was found to cause SWI/SNF mediated nucleosome displacement in *in vitro* experiments (Shen *et al.* 2003). *In vivo*, IP_4 and IP_5 were responsible for nucleosome mobilization by INO80 and SWI/SNF complexes on promoter of PHO5 gene under inductive conditions (Stegar *et al.* 2003). Although, mecha-

nism of direct recruitment of epigenetic and chromatin remodeling factors to the DNA of plant genome is yet to be reported, in one incidence PI-5-P was found to re-localize ATX1 (a histone trimethyltransferase) from nucleus to cytoplasm in *Arabidopsis* (Alvarez-Venegas *et al.* 2006).

DNA methylation is closely linked to heterochromatization and gene silencing. In heterochromatin the histones H3 and H4 are found to be hypoacetylated, dimethylated at K9 and K27 positions of H3 and hypomethylated at K4 position of H3 (Bender 2004). It was shown that loss of methylation in *met1* mutants of *Arabidopsis* is associated with loss of H3K9 dimethylation. However, in mutants for *KRYTONITE* (*KYP*; histone methyl transferase), loss of H3K9 methylation is not associated with loss of CpG DNA methylation, indicating, H3K9 methylation occurs downstream to CpG DNA methylation (Jasencakova *et al.* 2003). However, some loss of CpNpG methylation was observed in *kyp* mutants (Jackson *et al.* 2002). Also, proteins like HP1 bind to H3K9 methylations and helps in spreading of the DNA methylation (Lachner *et al.* 2001; Grewal and Maozed 2003). Again, the 5mC-Binding Domain Proteins (MBDs) have been shown to recruit enzymes that modify the histones (Ben-Porath and Cedar 2001). More recently, deubiqitination of H2B at K143 has been shown to be mandatory for RdDM induced H3K9 dimethylation and DNA methylation at transgenes and transposons (Sridhar *et al.* 2007).

In *Arabidopsis*, *COPIA* elements are rich in CG-methylation while *SN1* is rich in non CG-methylation. Mutants with affected CG-methylation showed reduced H3K9 dimethylation at *AtCOPIA* loci only whereas reduction in H3K9 methylation was observed at AtSN1 loci in mutants with affected non-CG methylation (although CG- and non-CG methylations were affected at both the loci, respectively; Lippman *et al*. 2003). It was demonstrated that SRA 5mC-binding domains of KYP and SUVH6 (both involved in maintenance of dimethylation of H3K9) shows differential binding to CG- and non-CG-methylated DNA. Thus, the maintenance of H3K9 dimethylation could be maintained by different sets of protein at different locus, suggesting that the functional relationship of DNA and histone methylations is locus specific (Johnson *et al.* 2007). The control of gene silencing and H3K9 dimethylation by TOUSLED (TSL) and REPLICATION PROTEIN A2 (RPA2) in a DNA-methylation independent manner in *Arabidopsis*, suggest that DNA methylation and histone modifications could be functionally distinguished also.

EPIGENETIC MECHANISM IN MEMORISING THE RESPONSE TO STRESS EXPOSURE

A primary exposure to stress is known to generate an enhanced and quicker response to subsequent stresses in plants. For example, an "immunological memory" of quicker and enhanced nicotine accumulation in *Nicotiana sylvestris* was demonstrated when the plants were pretreated with methyl jasmonate (MJ; Baldwin *et al.* 1996). Repeated exposure of *Arabidopsis* plants to ABA was found to impair light induced stomatal opening (Goh *et al.* 2003). These ABA-entrained plants also showed a transient increase in the expression of *RD22* and *AtNCED3* and a transient increase in endogenous ABA level (Goh *et al.* 2003). Pretreated plants exposed to paraquat showed significantly enhanced recovery after 3 days (Ye and Gressel 2000). *Arabidopsis* plants primed with either osmotic or oxidative stress was suggested to alter Ca^{2+} responses during subsequent stress exposure. Based on such reports, it is believed that a system to memorize the stress exposure does exist in plant system. As epigenetic mechanisms are an inherent part of the stress-signaling pathway, maintenance of this stress memory was thought to involve similar processes (Bruce *et al.* 2007). In a recently concluded work, it was observed that in acibenzolar S-methyl-treated or pathogen infected distal leaves of *Arabidopsis*, chromatin modification such as increase in H3 and H4 acetylation and

H3K4 di- or tri-methylation increases in the promoters of many defense genes without any increase in transcription. However, an amplified gene response on exposure to subsequent stress was evident, indicating the role of histone post-translational modification in memorizing systematic acquired resistance in plant stress response (Jaskiweiz *et al.* 2011).

EPIGENETIC MECHANISMS IN TRANSGENERATIONAL MEMORY OF STRESS

Studies on plants growing near the Chernobyl nuclear waste leakage areas suggested that these plants were better adapted to radiation stress than those growing far away and this is accompanied by hypermethylation of the genome (Kovalchuk *et al.* 2003, 2004) Thus, it was hypothesized that stress inducible epigenetic changes can be inherited by the progenies of stressed plants and might be involved in adapting the plants to the changing environment.

The homologous recombination frequency (HRF) is known to get enhanced by heat, UV-B stress and flagellin treatment in plant (Ries *et al.* 2000). Using homologous recombination trap transgenic *Arabidopsis* lines harboring two partial but overlapping fragment of GUS gene, it was revealed that the HRF remained at an elevated level in the unstressed progenies of stressed transgenic plant as inferred by comparing the number of cells showing GUS histochemical staining per progeny plant of stressed versus nonstressed plants (Molinier *et al.* 2006). In the same work, it was inferred that this stress memory is passed to the progenies through gametes of both male and female stressed plants. Trans-generational memory of increased HRF at disease resistance gene-like loci was also found in offspring of *Tobacco mosaic virus* (TMV)-infected plants with global genome hypermethylation and locus-specific hypomethylation (Boyko *et al.* 2007). In one of the tenth generation progeny line (line 2) of 5-aza-deoxycytidine (5-aza-deoxycytidine) treated rice plants, DNA methylation was abolished in the coding region of Xa21G gene encoding Xa21 like protein (Akimoto *et al.* 2007). Increased HR frequency along with higher stress adaptability was also observed in direct progenies of salt, UV-C, cold, heat and flood stressed recombination trap line of *Arabidopsis* (Boyko *et al.* 2010). While 10-12% more hypermethylation was observed in the progenies of all except drought stressed plants, 15% more hypomethylation was observed in progenies of drought stressed plants. Inheritance of heavy metal stress induced CNG hypomethylation in the progenies of stressed rice plants has been recently reported (Ou *et al.* 2012). Mutations impairing siRNA biogenesis, more specifically DCL2 and DCL3 functions, has been shown to disrupt the transfer of stress memory to next generation (Boyko *et al.* 2010). Although changes in DNA methylation status appeared as indispensable for trans-generational stress memory development, in one report heritable changes in response to temperature and UV-B stress was found to be mediated by histone occupancy and acetylations but not DNA methylation (Lang-Mladek *et al.* 2010). In another incidence, trans-generational stress memory was hardly encountered in progenies of a variety of chemicals treated and stressed plants, concluding this might not be a general response in *Arabidopsis* and requires special conditions (Pecinka *et al.* 2009).

Some interesting studies indicated that plants do possess an inherent mechanism to restrict "stress imprints" to the same generation as discussed below. In offspring devoid of *ddm1* mutation that were obtained after ten generations of crossing *ddm1* mutant to wild type *Arabidopsis* plants, the heritable hypomethylation effect of the mutation was abolished at all those loci for which a matching small RNA was discovered in the database (Teixeira *et al.* 2009). In plants compromised for these siRNA syntheses, the reversal in hypomethylation was not observed, implying the role of siRNA in blocking the passage of genome instability (due to hypomethylation) to the next generation. Recently, heat induced accumulation of *ONSEN* retrotranspososn

transcripts and extra-chromosomal DNA was observed in vegetative tissues of *Arabidopsis* (Ito *et al.* 2011). Although *ONSEN* transcript and extra-chromosomal DNA gradually decayed over 20-30 days of stress recovery, a high frequency of transposition was observed in progenies of stressed plants, which were deficient in siRNA biogenesis (Ito *et al.* 2011; Matsunaga *et al.* 2012). A careful analysis revealed that these retrotransposition events occurred during floral development before gamete formation. Moreover, *ONSEN* transcripts and DNA were observed at significantly higher level in heat-stressed callus than in vegetative tissue, indicating these regulatory mechanisms to be cell specific (Matsunaga *et al.* 2012). Thus, an inherent siRNA pathway does exist in plants that checks stress specific retrotransposition events during gamete formation. With these evidences, the role of siRNA pathway is becoming clear, and still its mechanism to allow certain stress imprints to pass to next generation while more stringently restricting others is a mystery.

CONCLUSION

Stress generates a complicated signaling cascade where epigenetic factors form complex knots. These epigenetic factors appear to play vital roles in sensing, responding and memorizing the stress effects. Genome wide analysis and detail characterization of regulation of stress-responsive genes indicate that most, if not all stress responsive genes are associated with at least one type of chromatin remodeling events. As these epigenetic factors bring about global changes in gene expression pattern, it appears that one or more of this complex acts together to synchronize the expression of large set of genes under various conditions and developmental stages. Present knowledge indicates the role of stress hormones in controlling the activity or expression of these regulators. Conversely, a few of these regulators can also induce the synthesis of these hormones under stress. Evidences suggest that H2A.Z containing nucleosomes are most likely involved in sensing a pathogen attack or a change in the external environment. Although strong evidences are lacking, it can be postulated that this sensing mechanism can operate in response to hormonal signaling or change in the expression of genes associates with H2A.Z might lead to induced production of stress hormones. This H2A.Z-mediated sensing and/or the hormonal signaling may then generate a response effect at a global and locus-specific level, involving a chain of interdependent epigenetic mechanisms. The most substantial outcome of these effects involve genome-wide global hypomethylation accompanied by locus specific hypermethylation, inhibition of growth-related genes and activation of stress-related genes along with various transposons. Recent evidences also indicate that some stress responsive epigenetic changes might get stored as stress imprint memories leading to enhanced secondary stress response. Astonishing though it may seem, many of these effects can be transferred to the next generation as trans-generational stress memory. The role of siRNA pathways in these cases is becoming increasingly clear, which appears to play a vital role during the transfer of memory of expression of stress related genes and hypermethylation events to the progenies of stressed plants while erasing the trans-generational memories of hypomethylation and transposition events. A schematic representation of this present understanding is shown in **Fig. 1**.

A number of these factors have been discovered and with the advent of modern technologies a lot more will get uncovered soon along with their targets loci. This will further help in fine tuning our understanding about the role of these factors in plants response pathways to external cues and the manner in which they operate in a coordinated way under a given condition. However, understanding the mechanisms of recruitment of these factors appears more challenging and probably needs detailed mechanical analysis of their biochemical functions. This might prove ex-
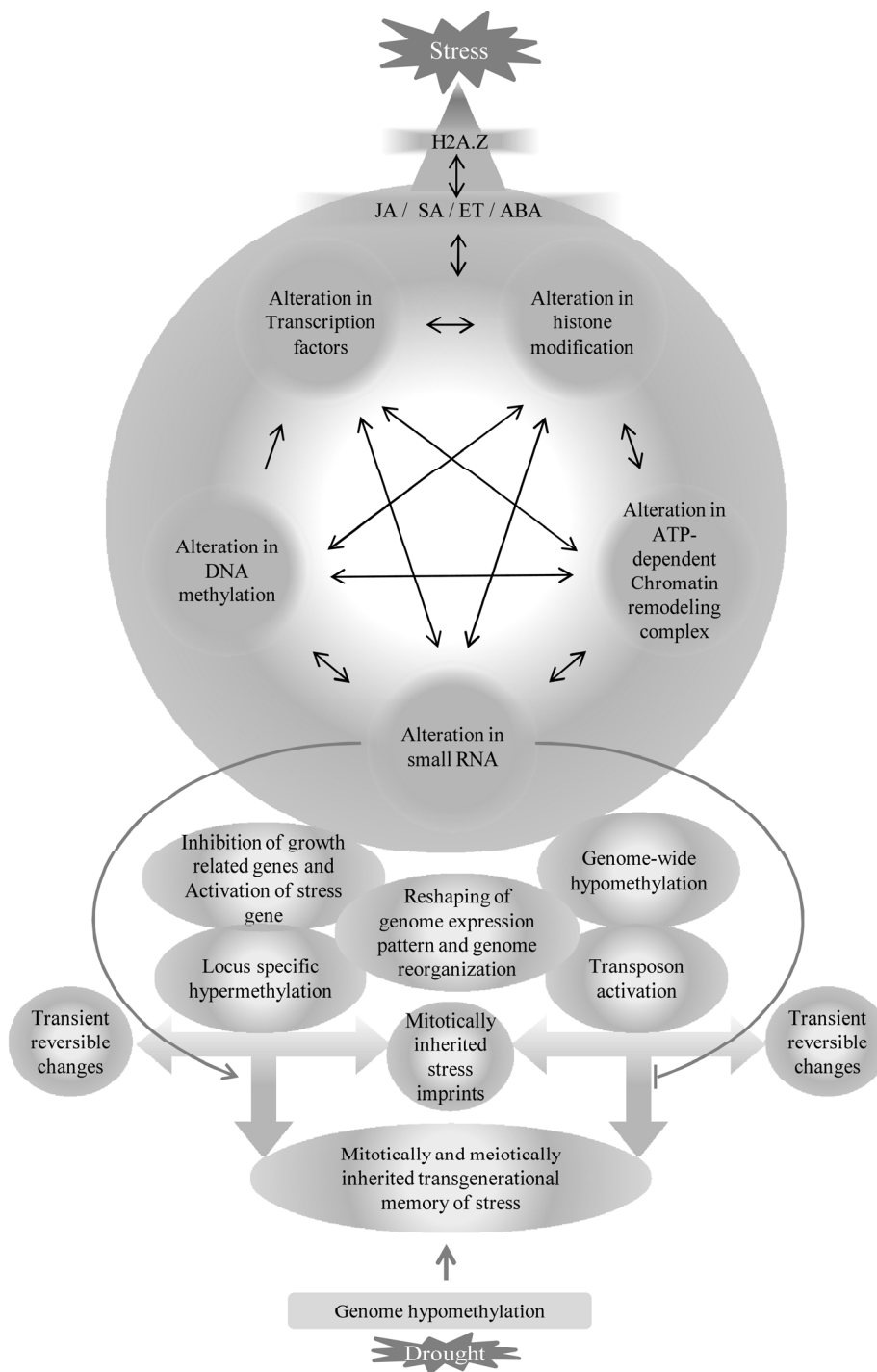
Fig. 1 A schematic representation of broad possible role played by different epigenetic regulators. Exposure to stress is possibly sensed by H2A.Z containing nucleosomes. This possibly triggers changes in gene expression leading to induction of various stress hormone signaling pathways. Conversely, these stress hormones may also assist H2A.Z containing nucleosome in sensing the stress environment. The hormonal pathways lead to the induction or activation of various transcription factors or epigenetic regulators. A few of these epigenetic regulators are also reported to cause the synthesis of stress hormones like ABA. The miRNA also contributes towards this phenomenon. The induced/activated transcription factors or epigenetic regulators, then recruit other types of factor leading to the occurrence of multiple chromatin remodeling events at any loci in the genome. As a whole, these changes causes inhibition of growth related genes and expression of stress genes. On a global level, under stress, genome wide hypomethylation along with loci specific hypermethylation and activation of transposons is observed. An endogenous siRNA pathway is believed to contribute towards this hypermethylation event and thus contribute towards the maintenance of genome stability. Although most of these changes are generally reversible, few remain to generate "stress imprints" in plants. Few such events are passed to the next generation as trans-generational memory of stress. However, these events might not be common in occurrence. Interestingly, an endogenous siRNA pathway assists in both passages of memories like stress gene expression and hypermethylation and blocking others hypomethylation and transposition events. In some exceptional cases, such as drought stress, amazingly, the hypomethylation events were found to be carried by the epigenetic stress memory to the next generation.

tremely helpful in targeting various stress specific chromatin remodeling complexes to the desired loci only. An acquaintance of detailed knowledge about the siRNA pathway and its exact role in trans-generational memory transfer is also highly desirable and will help us to manipulate only chosen effects to be transferred to the progenies of stressed plants, thereby inhibiting the deleterious effects of 'transgeneration memory' on growth and productivity of the plants. In short, few significant steps have been taken towards discovering the role of epigenetic mechanisms in stress response but there is still lot to be understood.

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