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REVIEW

The gymnastics of epigenomics in rice

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Abstract Epigenomics is represented by the high-throughput investigations of genome-wide epigenetic alterations, which ultimately dictate genomic, transcriptomic, proteomic and metabolomic dynamism. Rice has been accepted as the global staple crop. As a result, this model crop deserves significant importance in the rapidly emerging field of plant epigenomics. A large number of recently available data reveal the immense flexibility and potential of variable epigenomic landscapes. Such epigenomic impacts and variability are determined by a number of epigenetic regulators and several crucial inheritable epialleles, respectively. This article highlights the correlation of the epigenomic landscape with growth, flowering, reproduction, non-coding RNA-mediated post-transcriptional regulation, transposon mobility and even heterosis in rice. We have also discussed the drastic epigenetic alterations which are reported in rice plants grown from seeds exposed to the extraterrestrial environment. Such abiotic conditions impose stress on the plants leading to epigenomic modifications in a genotype-specific manner. Some significant bioinformatic databases and in silico approaches have also been explained in this article. These softwares provide important interfaces for comparative epigenomics. The discussion concludes with a unified goal of developing epigenome editing to promote biological hacking of the rice epigenome. Such a cutting-edge technology if properly standardized, can integrate genomics and epigenomics together with the generation of high-yielding trait in several cultivars of rice.

Keywords Epigenomic landscape · Rice physiology · Non-coding RNA · Transposons · Heterosis · Extraterrestrial environment · In silico databases · Epigenome editing · Epigenome hacking

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Introduction

Rice has remained the major staple food for a large proportion of the global population. It plays a pivotal role in ensuring food security for over half the world population, especially in large parts of Asia, Latin America, Caribbean and Africa. Rice is considered as an essential commodity for household food security and also the mainstay for rural populations at large. This has led to the governmental acceptance of rice as a 'strategic necessity' in several developed and developing countries (Calpe 2006).

From the scientific point of view, rice has even been regarded as the model crop for studying cereal genomics owing to its small genome size of 430 Mb (Goff et al. 2002). Rice has mainly two species: *Oryza sativa* var. indica, *O. sativa* var. japonica (Asian origin) and *O. glaberrima* (African origin). It is hypothesized that both the indica and japonica varieties had their origin in China from the domestication of the wild rice *O. rufipogon* (Glaszmann 1987). The genomic sequences of indica and japonica varieties have been annotated in the Rice Genome Annotation Project (Kawahara et al. 2013; Goff et al. 2002; Yu et al. 2002). Hence, due to easy access to genomic resources and the availability of efficient reverse genetic tools, rice has also emerged as a model for cereal epigenomics and epigenetics (Chen and Zhou 2013). The

epigenome consists of the genome-wide epigenetic alterations and the associated regulatory factors, which deliver dynamism and aid in trans-generational epigenetic inheritance. It determines the diverse profiles of gene expression in tissue-specific environments or in response to environmental variances. Such genetic profiles are created due to the epigenomic regulations including chromatin-architecture dependent genome-wide epigenetic modifications (Chen and Zhou 2013). DNA methylation and histone modifications act as necessary epigenetic tools to regulate chromatin accessibility to replication, transcription and repair factors (Joshi et al. 2016; Shriram et al. 2016). Kawahara et al. (2013) have created a high throughput database containing accumulated information on rice transcriptomics, small RNAs, chromatin methylations and histone modifications. The evolution of rice supports a long history of rapid domestication and selection which has led to the accumulation of such large number of epigenomic variances in acquisition, inheritance and memory among species and varieties (Chen and Zhou 2013). This review discusses the multivariate features of the rice epigenome with respect to the factors and components governing growth and development, epigenomic inheritance, predictable regulation under sub-optimal conditions and development of heterosis, coupled to increased production.

The epigenomic landscape in rice

The epigenomic modification landscape in rice is characterized by genome-wide DNA methylation, histone modification, histone variant deposition and nucleosomal positioning. These modifications display the comprehensive patterns of epigenetic regulation which ultimately regulates developmental gene expression (Banerjee and Roychoudhury 2017a).

DNA methylation

The repetitive sequences and transposable elements constituting the plant heterochromatin remain inactivated mainly by methylation at the cytosine within the DNA (Rambani et al. 2015; Zhang et al. 2006). Such cytosine methylations in plants are found in CG, CHG and CHH (H being either of A, C or T) repeat sequences (Feng et al. 2010; He et al. 2010). Epimutation for less than 1% of cytosines was observed between the chromosomes of hybrid and inbred parents originating from japonica and indica varieties (Chodavarapu et al. 2012). Comparison of the DNA methylation status between a domesticated and a wild rice species revealed varying methylation landscapes in the two test species. The cis-acting effects were responsible for such variation. Methylations in the promoter regions impose a repressive effect on gene expression (Li et al. 2012a). Similar gene regulation via variable methylation around transcription start and stop sites was observed in the monocot plant, *Zea mays*. The upstream regions of protein-encoding genes are enriched with 24-nt siRNAs and high levels of methylation in CHH clusters (Lu et al. 2015). Methylations can also lead to the generation of silent chromatin by physically impeding the transcription factors (TFs) to access chromatin or recruit repressive factors to the concerned locus to remodel the chromatin into a compact heterochromatin (Rambani et al. 2015). A different global DNA methylation landscape with higher level of genome-wide methylation has been observed in rice when compared with the dicot model plant, *Arabidopsis thaliana* (Zemach et al. 2010a, b). This can be attributed to the large number of scattered transposable elements (TEs) in the non-centromeric regions of rice (Zemach et al. 2010a).

Gene body methylation (CG methylation) levels were also conserved across rice tissues and organs like the embryo, endosperm, shoots and roots. The non-CG methylation increased gradually with senescence (Zemech et al. 2010a). Comparison of DNA methylation alterations between endosperm and other tissues among various rice varieties revealed a reduction in non-CG methylation in the endosperm along with generation of hypomethylated CG sites. Such hypomethylation actually facilitated endosperm-specific gene expression (Zemach et al. 2010a). Hu et al. (2014) characterized the null mutant of *Methyltransferase 1-2* (*OsMet1-2*), the major CG methylase in rice via methylome, transcriptome and small RNAome analyses. The homozygous null mutant seeds were seriously misdeveloped resulting in necrotic death of all the germinated seedlings. Accordingly, loss of CG methylation accompanied with a plethora of quantitative phenotypes of molecular origin was observed in the mutant. These included dysregulation of protein-coding gene activation, altered expression of TEs and markedly changed small RNA profiles (Hu et al. 2014). The *OsMet1-2* mutants also exhibited higher rates of whole genome duplication, manifested by altered expression of the duplicated genes and lowered CG methylation (Wang et al. 2017). The study carried phylogenetic significance as it establishes the importance of variable epigenetic marking in rice genome duplication.

Nucleosome-free or dynamic chromatin remodelling-associated genomic DNA are DNase I hypersensitive (DH). Such DH sites in the constitutive promoters in rice seedlings usually remain hypomethylated, whereas the DH sites located in the tissue-specific promoters exhibit greater levels of DNA methylation. Tissue-specific promoters on the contrary have demethylated DH sites at the specific tissue of concern to stringently confine the expression of

the gene within the defined tissue boundaries (Zhang et al. 2012a).

Histone modifications in rice

Post-translational histone modifications like methylation, acetylation, phosphorylation and ubiquitinylation are possible epigenomic factors regulating genome activity and gene expression. However, all such modifications have not been properly characterized in rice.

Histone methylation

Methylation on the lysine residues can be mono-, di-, or tri-. Though the same methyl group (me) is being added, each state conserves different epigenomic information (Liu et al. 2010). Heterochromatin regions having repetitive sequences are silenced by the signature dimethylation of the ninth lysine residue in histone H3 (H3K9me2). The function of H3K9me3 has not been properly elucidated. Trimethylation at H3K27 (H3K27me3) also acts as a chromatin silencer and represses gene activation (He et al. 2010) (Fig. 1a). About 5–10% of annotated repressed genes in *Arabidopsis* (Turck et al. 2007) and rice seedlings (Hu et al. 2012) contain H3K27me3 modifications. There exists a diverse complexity of this regulation. The same state of methylation, on the same histone H3, but on differently positioned lysines encodes contrasting functions with mutually repulsive antagonistic effects. H3K4me3 and H3K36me3 act as signatures for chromatin de-repression and activation as opposed to H3K27me3-mediated chromatin repression (Hu et al. 2012) (Fig. 1b).

Di- and/or tri-methylated H3K4 has been identified in at least half the protein-coding genes in rice (Hu et al. 2012). This clearly correlates the conservation of the epigenomic landscape in rice with the developmental survival of the plant at the proteomic level. H3K4me3 has been predominantly identified in the 5′ ends of genes which are actively transcribed. However, the moderately transcribed genes have enriched localization of H3K4me2 at their 5′ ends (Chen and Zhou 2013). Legumes like *Lupinus angustifolius* and *Medicago truncatula* also possess H3K4me2 clustering in the terminal regions of their chromosomes (Susek et al. 2017). Lower levels of H3K4me2 and H3K4me3 and more DNA methylation were detected in the cytological, densely stained heterochromatin than the less densely stained euchromatin in rice. Unique epigenetic composition was, however, observed in the centromeres. Such H3K4

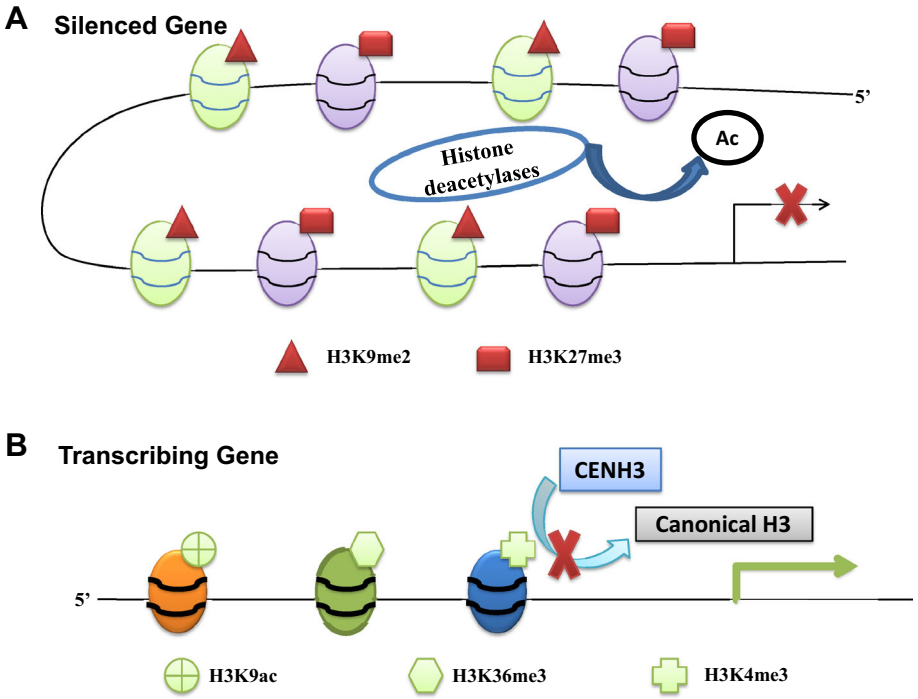

Fig. 1 The variable activating or repressing effects of different histone modifications at the 5′ ends of genes in rice. **a** Dimethylation at H3K9 and trimethylation at H3K27 are repressive histone modification markers which promote gene silencing. Removal of acetyl groups from H3K9 by histone deacetylases also increases the attractive forces between histone tails and the DNA, resulting in chromatin compaction and minimized transcription. **b** Trimethylations at H3K36 and H3K4 and acetylation at H3K9 physically facilitate promoter accessibility to TFs resulting in gene expression. Such histone modification markers on the transcribing genes within the centromeric regions can also impede the exchange of canonical histone H3 with the centromeric histone variant CENH3, thus inhibiting locus specific gene silencing

methylation was absent in the methylated TEs. This revealed that the H3K4me3/H3K4me2 levels positively regulated the transcriptional activities in rice (Li et al. 2008). Tsuji et al. (2006) also reported increased H3K4me3 fractions in the promoters of inducible genes in rice upon application of the specific stimuli. This state of H3K4 methylation acts as a signature mark to attract remodellers and initiate the de-repression of the chromatin (Hu et al. 2011). Wu et al. (2011) used genomic tiling array of four sequenced rice centromeres coupled to chromatin immunoprecipitation-microarray (ChIP–chip) to map the active histone modification marks (H3K4me2, H3K4me3, H3K36me3 and H3K9Ac). These were found to be located in the rice centromere and associated with only the transcribed regions. Such active histone modification marks physically impede the replacement of canonical histone H3 subdomains with the centromere-specific histone H3 variant, CENH3 (Wu et al. 2011).

Histone acetylation

Acetylation of histone lysine residues minimizes the attraction between negatively charged DNA and positively charged lysine of histone tails and permits the required dynamism in chromatin structure to ensure gene activation. However, deacetylation of the lysine residues led to chromatin compaction and hence gene silencing (Berger 2007). These regulations crucially control gene expression in plants in response to variable stimuli (Servet et al. 2010). It was observed via genome-wide analyses that the 5′ end of active genes in rice is enriched with histone H3K9 acetylation (He et al. 2010) (Fig. 1b). Huang et al. (2007) reported that H3K9 deacetylation promoted TE silencing because downregulation of the *Silent Information Regulator 2*-related histone deacetylase gene *Sirtuin 1* (*SRT1*) increased the H3K9 acetylation and hence de-repression of multiple TE loci. The dynamic post-translational acetylations or deacetylations at H3K9 also regulate the expression of submergence-inducible genes in rice (Tsuji et al. 2006). Variable acetylation in the lysine residues of histone subunit H4 was found to control the diurnal oscillation and the expression of circadian rhythm-associated flowering-time genes in rice (Li et al. 2011a).

Unravelling the epigenetic regulators in rice

Chromatin regulators translate the epigenomic codes into multiple developmental pathways in response to diverse environmental stimuli. Pandey et al. (2002) reported the presence of conserved chromatin modification machineries among plants. However, some specific regulators have been identified in rice. Interesting developments of selected chromatin modifiers in rice have been discussed; the remaining modifiers have been documented in Table 1 (basic form extracted from Chen and Zhou 2013, with recent additional updates).

DNA methyltransferases

Establishment of de novo methylation and the presence of multiple enzymes with crosstalks have led to the demonstration of DNA methyltransferases in rice (Xing et al. 2015). DOMAINS REARRANGED METHYLASE 2 (OsDRM2), a major CHH methyltransferase in rice was found to physically interact with the histone H3K27 methyltransferase, SDG711. This putatively suggested the involvement of both DRM2-mediated non-CG methylation and PRC2-mediated H3K27me3 in the repression of developmental genes in a cooperative and non-mutually exclusive mechanistic crosstalk (Zhou et al. 2016) (Fig. 2). Interestingly, CACTA DNA transposon-derived microRNA, *miR820* was found to negatively regulate the expression of *OsDRM2*. This repression promoted the expression of TEs due to lowered methylation indicating that the interactions between TEs and host genomes might be regulated by the *OsDRM2-miR820* crosstalk (Sharma et al. 2015) (Fig. 2).

RNA-directed DNA methylation (RdDM) is a fast developing field in plant epigenomics where the small interfering RNA (siRNA)-mediated de novo cytosine methylation is guided by the intricate interactions among TFs, chromatin regulators and the large subunits of the polymerases like Pol IV and Pol V (Dangwal et al. 2013). It was observed that the ubiquitin-associated domain of OsDRM2 interacted with the ATP-dependent RNA helicase, eukaryotic INITIATION FACTOR 4A (OseIF4A) after which the entire complex was found to be localized in the nucleus (Dangwal et al. 2013). This shows the immense crosstalk potential of OsDRM2 which exhibits parallel participation in floral regulation (Zhou et al. 2016) and RdDM-mediated translational initiation (Dangwal et al. 2013). Recently, Tan et al. (2016) recognized OsDRM2 and DEFICIENT IN DNA METHYLATION 1 (OsDDM1) (a SWItch/Sucrose Non-Fermentable chromatin remodeller) as the enzymes defining distinct methylation pathways where OsDDM1 facilitated OsDRM2 dependent CHH methylation. Mutations in *OsDRM2* and *OsDDM1* both caused de-repression of the silenced elements resulting in detrimental phenotypes. Apart from OsDRM2, a chromomethylase, OsCMT3 was found to play a broad role in non-CG methylation in rice (Cheng et al. 2015). However, *Arabidopsis* null double mutants of *drm1 drm2* and single mutants of *cmt3* did not show severe morphological defects as was prevalent in the rice null mutants (Cao and Jacobsen 2002). This can be attributed to the lower GC

Table 1 Important chromatin regulators in rice

Type	Name	Locus	Biochemical function	Translational function	References
PRC2	OsCLF/ SDG711	LOC_Os06g16390	H3K27 methyltransferase	Long day flowering	Liu et al. (2014); Luo et al. (2009)
	OsiEZ1/ SDG718	LOC_Os03g19480	H3K27 methyltransferase	Short day flowering	Liu et al. (2014); Luo et al. (2009)
	OsFIE1	LOC_Os08g04290	*Drosophila* ESC homolog	Located in endosperm; vegetative and reproductive development	Luo et al. (2009); Yu et al. (2017)
	OsFIE2	LOC_Os08g04270	*Drosophila* ESC homolog		
	OsEMF2a	LOC_Os04g08034	*Drosophila* Su(z)12 homolog		
	OsEMF2b	LOC_Os09g13630	*Drosophila* Su(z)12 homolog	Elongation and floristic developments	
	OsVIL2	LOC_Os12g34850	Vernalization insensitive 3-like	Promote rice flowering by repressing OsLF	Wang et al. (2013); Jeong et al. (2016)
	OsVIL3	LOC_Os02g05840			
DNA methylation	OsDRM2	LOC_Os03g02010	Major DNA methyltransferase	Floral regulation and RdDM	Dangwal et al. (2013)
	OsDDM1	LOC_Os09g27060	DNA methyltransferase	Controls DRM2 mediated CHH methylation	Tan et al. (2016)
	OsMET1	LOC_Os03g58400	DNA methyltransferase	Gene silencing	Teerawanichpan et al. (2009)
	OsCMT3a	LOC_Os10g01570	Putative chromomethylase	Loss-of-function mutants exhibit a burst of transposition	Cheng et al. (2015)
DNA demethylation	OsROS1	LOC_Os05g37350	Putative DNA demethylase	TE control	La et al. (2011)
Histone de-methylation	JMJ703	LOC_Os05g10770	Jumonji C domain containing protein, H3K4 demethylase	Plant growth	Chen et al. (2013)
	JMJ706	LOC_Os10g42690	Jumonji C domain containing protein, H3K9 demethylase	Floral development	Sun and Zhou (2008)
Histone methylation	SDG714	LOC_Os01g70220	Rice Su(var)3-9 homologs (SUVHs)	Antagonistic function to JMJ706	Qin et al. (2010)
	SDG727	LOC_Os09g19830			
	SDG710	LOC_Os08g30910			
	SDG728	LOC_Os05g41172		Regulates seed specific genes	
	SDG724	LOC_Os09g13740	H3K36 methyltransferase	Floral development	Sun et al. (2012)
	SDG725	LOC_Os02g34850	H3K36 methyltransferase	Brassinosteroid signaling	Sui et al. (2012)
	SDG701	LOC_Os08g08210.1	H3K4 methyltransferase	Sporophytic development, gametophytic transmission, floral regulation	Liu et al. (2017)
Histone acetylation	OsHAC701	LOC_Os01g14370	CBP family of HATs	Gene activation	Liu et al. (2012); Fang et al. (2014); Song et al. (2015)
	OsHAC703	LOC_Os02g04490		ABA and cold stress inducible	
	OsHAC704	LOC_Os06g49130		De-represses gene silencing	
	OsHAF701	LOC_Os06g43790	$(TAF)_{II}$ 250 family of HAT	ABA and cold stress inducible	
	OsHAG702	LOC_Os10g28040	GNAT family of HATs	De-represses gene silencing	
	OsHAG703	LOC_Os04g40840		Gene activation	
	OsHAG704	LOC_Os09g17850		Dehydration inducible	
	OsglHAT1	LOC_Os06g44100		Increases seed weight	
	OsHAM701	LOC_Os07g43360	MYST family of HAT	Desiccation and cold stress inducible	

Table 1 continued

Type	Name	Locus	Biochemical function	Translational function	References
Histone deacetylation	OsHDAC1	LOC_Os06g38470	H3 and H4 deacetylase	Physiological development	Chung and Kim (2009)
	OsHDAC2	LOC_Os02g12380	H3 and H4 deacetylase	Vegetative growth	Jang et al. (2003); Hu et al. (2009)
	OsHDAC3	LOC_Os02g12350	H3 and H4 deacetylase	Peduncle elongation and fertility	Hu et al. (2009)
	OsHDT1/ OsHDT701	LOC_Os05g51840	H4 deacetylase	Enhances salt, osmotic stress tolerance and biotic stress resistance in seedling stage	Zhao et al. (2015); Ding et al. (2012a)
	OsSRT1	LOC_Os04g20270	H3K9 deacetylase	Cell death, stress, metabolism; TE repression	Deng et al. (2016); Zhong et al. (2013)
Others	CHD3/ CHR729	LOC_Os07g31450	Chromodomain and PHD-domain protein	Developmental regulation	Hu et al. (2012)
	MEL1	LOC_Os03g58600	AGO-family protein	Controls meiosis	Komiya et al. (2014)
	SHO1	LOC_Os04g43050	Homolog of DICER-LIKE4	Developmental regulation	Abe et al. (2010)
	SHL2	LOC_Os01g34350	RDR6 homolog	Floral regulation	Toriba et al. (2010)
	WAF1	LOC_Os07g06970	HEN1 homolog	Developmental regulation	Abe et al. (2010)
	BRK1	LOC_Os07g32480	H2A phosphorylation	Controls meiosis	Wang et al. (2012)

CLF curly leaf, *SDG* SET Domain Group, *OsiEZ1 O. sativa* var. indica enhancer of zeste 1, *FIE* fertilization-independent endosperm, *EMF* embryonic flower, *VIL* VERNALIZATION INSENSITIVE 3-LIKE, *DRM* domains rearranged methylase, *DDM* deficient in DNA methylation, *MET* methyltransferase, *CMT* chromomethylase, *ROS* repressor of silencing, *JMJ* Jumonji C containing domain, *HAT* histone acetyltransferase, *CBP* p300/CREB (cAMP responsive element-binding protein)-binding protein, *HAC* **HA**Ts of **C**BP family, $(TAF)_{II}250$ TATA-binding protein-associated factor family, *HAF* HATs of $(TAF)_{II}250$ family, *GNAT* general control non-repressible 5-related N-terminal acetyltransferase, *HAG* **HA**Ts of **G**NAT family, *MYST* MOZ, Ybf2/Sas3, Sas2, and Tip60, *HAM* **HA**Ts of **M**YST family, *HDAC* histone deacetylase, *HDT* HD 2-type histone deacetylase, *SRT* SIR 2 related deacetylase, *CHR729* CHD related gene 729, *MEL1* meiosis arrested at leptotene 1, *SHO1* shoot organization 1, *SHL2* shootless 2, *WAF1* wavy leaf 1, *BRK1* Bub1-related kinase

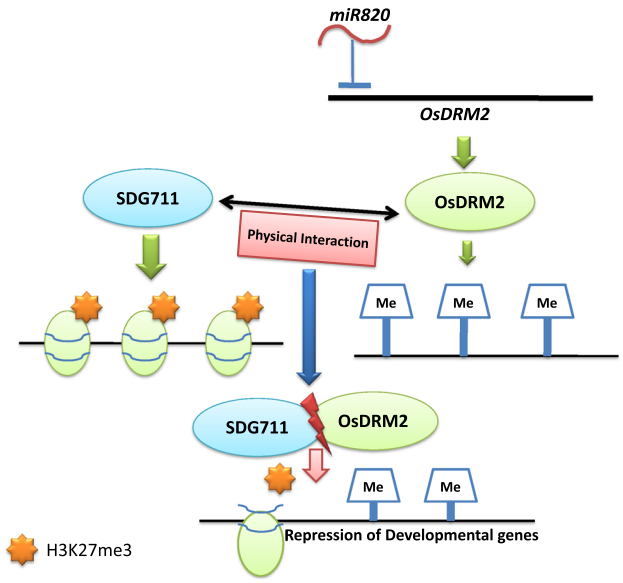

Fig. 2 The crosstalk between OsDRM2 and OsSDG711. The miR820 inhibits *OsDRM2* expression, leading to de-repression of silenced genes in miR820 overexpressing lines. In normal rice plants, OsDRM2 is produced and it physically interacts with the histone H3K27 methyltransferase, OsSDG711 to develop a cooperative crosstalk. This is essential for repressing the downstream developmental genes and maintaining genetic equilibrium

contents in the genome of *Arabidopsis* compared with that of rice. The GC composition showed a negative gradient towards the 3′ ends of the rice genes (Yu et al. 2002). The presence of a higher fraction of heterochromatin marked with discontinuously distributed TEs in the rice genome enhances the effects of DNA methyltransferases on rice development. However, in *Arabidopsis*, the expression of nearby genes can be influenced by the high proportion of TEs or methylated repetitive sequences, sometimes giving rise to duplicated genes (Wei et al. 2014; Wang et al. 2014). Transgenic rice seedlings with mutated *OsMET1b* (major CG methyltransferase in rice) exhibited genome-wide loss of CG methylation, dysregulated expression of TEs, protein-coding genes, sRNAs and abnormal alternative splicing events (Hu et al. 2014; Wang et al. 2016).

DNA demethylases

A global reduction of non-CG methylation and local CG hypomethylation is observed in the demethylated rice DNA. Major demethylases (DNA glycosylases) in *Arabidopsis* like *Repressor of Silencing 1* (*AtROS1*) and *Demeter* (*DME*) are absent in rice (Chen and Zhou 2013). However, six 5mC DNA glycosylases, four ROS1

orthologs (ROS1a, 1b, 1c and 1d) and two DME like protein 3 (DML3) orthologs (DML3a and DML3b) are encoded by the rice genome (La et al. 2011). *Osros1c* knockout mutants exhibited DNA hypermethylation and reduced mobility of the retrotransposon *Tos17* in the calli (La et al. 2011).

Histone methyltransferases

Methylation at the lysine (K) residues in histones acts as a signal to distinctly up or down regulate transcriptional activation of marked genes. The Polycomb-repressive complex 2 (PRC2) group consists of *Enhancer of zeste* [*E*(*z*)] and two *fertilization-independent endosperm* (*FIE*) homologs (Zhou et al. 2016; Luo et al. 2009). [E(z)] catalyses the trimethylation at H3K27 and mediates gene repression. Two [E(z)] homologs, *SDG711* and *SDG718* are, respectively, involved in the long day (LD) and short day (SD) regulation of essential flowering genes (Liu et al. 2014). Variations in H3K9me2 levels have been observed in lupins. Susek et al. (2017) detected H3K9me2 in *L. angustifolius* and *L. albus* but not in *L. luteus*. Such intra-specific variability in signature histone modifications also exist in rice. In case of the *FIE* homologs in rice, DNA methylation in the *OsFIE1* promoter silenced its expression in the vegetative tissues. *OsFIE1* is the only known imprinted gene in the PRC2 group. It is regulated by temperature, DNA methylation and H3K9me2 (Folsom et al. 2014). Overexpression of *OsFIE1* increased the ectopic H3K27me3 at PRC group targets and caused impaired imprinting via the biallelic expression of *OsFIE1* (Zhang et al. 2012b). However, an epimutation with loss of promoter methylation led to the ectopic expression of *OsFIE1*. The epimutated plants exhibited dwarf statures with floral defects and altered H3K27me3 fractions in multiple regulatory genes (Zhang et al. 2012b). Liu et al. (2017) recently characterized a H3K4 methyltransferase, *SDG701* in rice. Overexpression and knockdown studies showed that this histone modifier essentially regulated sporophytic development, proper transmission of gametes, flowering photoperiods and even grain production (Liu et al. 2017).

Histone demethylases

Maintaining a stable equilibrium is an important aspect of epigenetic dynamisms observed in rice. Hence, histone methylations are balanced by histone lysine methyltransferases and demethylases. Sun and Zhou (2008) identified a rice H3K9 demethylase, JMJ706 containing a Jumonji C (jmjC) domain. This demethylase essentially regulated floral development as the loss-of-function mutations affected spikelet growth, floral morphology and organ number (Sun and Zhou 2008). JMJ705 induced the expression of rice defense-related genes mainly by removing inhibitory methyl groups from H3K27me2/me3 (Li et al. 2013). JMJ703 specifically demethylates H3K4me/me2/me3 and mutations in gene encoding this enzyme led to morphologically under-developed plants with deteriorated agricultural traits (Cui et al. 2013). The rice genome encodes 20 jmjc domain-containing proteins and three LYSINE-SPECIFIC DEMETHYLASE 1 (LSD1) homologs. The LSD1 proteins are also demethylases; however, their functions have not been well deciphered (Lu et al. 2008).

Histone acetyltransferases (HATs)

The rice genome encodes around eight HATs which have been classified in four major groups: CBP, $(TAF)_{II}250$, GNAT and MYST (Liu et al. 2012). Interestingly, Song et al. (2015) reported the presence of a GNAT-related HAT, *OsglHAT1* in rice which positively regulated grain weight and biomass. The HAT activity of OsglHAT1 is targeted to histone H4 in the promoters of cell cycle-associated genes which ultimately leads to their activation. This ultimately yields swelled and better-developed grains.

Histone deacetylases

Histone deacetylases reportedly participate in floral development, biotic and abiotic stress responses. In rice, there are at least 18 homologs of this enzyme which have been classified into three groups, reduced potassium dependency 3/histone deacetylase 1 (RPD3/HDA1), silent information regulator 2 (SIR2) and HD2 (Hu et al. 2009). A list of deacetylases with their functions has been highlighted in Table 1. It has been seen that OsHDAC1 epigenetically regulates *OsNAC6* (NAC for **N**AM, **A**TAF1/2, **C**UC2)-mediated growth and physiological developments of the plant (Jang et al. 2003; Banerjee and Roychoudhury 2017b). OsNAC6 also upregulates the expression of genes participating in nicotianamine biosynthesis, glutathione relocation, 3′-phosphoadenosine 5′-phosphosulphate accumulation and glycosylation. These represent multiple drought-tolerant pathways (Lee et al. 2017). OsHDT/OsHDT701 of the HD2 family regulates the biotic responses by reducing the H4 acetylation levels of *pattern recognition receptor* (*PRR*) and defense-associated genes (Ding et al. 2012a).

OsSRT1of the SIR2 family is an interesting histone deacetylase which removed the acetyl group at H3K9 in TEs and the promoters of multiple genes related to stress and metabolism (Huang et al. 2007). Zhong et al. (2013) investigated the role of OsSRT1 in reversing H3K9Ac throughout the genome and reported the specific binding targets of the deacetylase. These target genes also exhibited increased H3K9Ac in transgenic plants where *OsSRT1* was silenced by RNA interference (RNAi) (Table 2) (Zhong

Table 2 The selected genes which showed OsSRT1 binding and also increased H3K9Ac in *OsSRT1* RNAi plants

Proteins encoded by target genes	Gene locus	Expression status	Functions	References
NB-ARC domain containing protein	LOC_Os01g52304	Expressed	R proteins: biotic stress resistance	van Ooijen et al. (2008)
Retrotransposon	LOC_Os11g45000	Unclassified		
LSD1 zinc finger domain containing protein	LOC_Os12g41700	Expressed	Growth, disease resistance	Xu and He (2007)
Oxidoreductase, aldo/keto reductase family protein	LOC_Os03g41510	Expressed	NADP/NADPH dependent carbohydrate and lipid metabolism	Penning (2015)
NB-ARC domain containing protein	LOC_Os11g44990	Expressed	R proteins: biotic stress resistance	van Ooijen et al. (2008)
Gibberellin 20 oxidase 2	LOC_Os05g34854	Expressed	GA catabolism	Sakamoto et al. (2001)
Pollen-specific protein	LOC_Os06g05710	Expressed	Pollen developmental regulation	Chen et al. (2016)
HLH DNA-binding domain containing protein	LOC_Os03g53020	Expressed	TF	Banerjee and Roychoudhury (2016)
Phosphatidylinositol transfer	LOC_Os08g38850	Expressed	Cell signaling and survival	Li et al. (2017a)
Hypothetical protein	LOC_Os05g34100	Unclassified		
Glucosyl transferase	LOC_Os05g45140	Expressed	Carbohydrate metabolism	Penning (2015)
Protein kinase domain containing protein	LOC_Os11g10710	Expressed	Cell signaling and activation of TFs	
Retrotransposon protein	LOC_Os10g29650	Expressed		
U-box domain-containing protein	LOC_Os04g49500	Expressed	Proteolysis and protein recycling	Yee and Goring (2009)
Strubbelig-Receptor Family 3 precursor	LOC_Os02g07960	Expressed	Fertility of male gametophyte	Eyueboglu et al. (2007)
Conserved hypothetical protein	LOC_Os04g07830	Unclassified		
Proton-dependent oligopeptide transport	LOC_Os01g65200	Expressed	Membrane channel facilitating nitrate/peptide transport	Leran et al. (2014)
OsFBX238	LOC_Os07g35060	Expressed	Controlled degradation of cellular proteins	Jain et al. (2007)
Transposon protein	LOC_Os12g35760	Unclassified		
Uncharacterized protein	LOC_Os06g48500	Expressed		
Proton-dependent oligopeptide transport	LOC_Os01g65210	Expressed	Membrane channel facilitating nitrate/peptide transport	Leran et al. (2014)
Hypothetical protein	LOC_Os05g27890	Unclassified		
CK1	LOC_Os02g56560	Expressed	ABA and BR dependent signaling	Liu et al. (2003)
YABBY domain containing protein	LOC_Os02g42950	Expressed	Leaf primordial development, cell division and leaf differentiation	Dai et al. (2007)
Type I inositol- 1,4,5-trisphosphate 5-phosphatase	LOC_Os03g57950	Expressed	Cell signaling and survival	Li et al. (2017a)
Kinesin motor domain containing protein	LOC_Os04g57140	Expressed	Intracellular cargo transport	Li et al. (2012b)
Uncharacterized protein	LOC_Os11g38640	Expressed		
YABBY domain containing protein	LOC_Os03g11600	Expressed	Leaf primordial development, cell division and leaf differentiation	Dai et al. (2007)

Table 2 continued

Proteins encoded by target genes	Gene locus	Expression status	Functions	References
AGC_PVPK_like_CDK8.1	LOC_Os09g31210	Expressed	Kinase	http://ricephylogenomics.ucdavis.edu/kinase/geneinfo.php?id=LOC_Os09g31210.1
Uncharacterized protein	LOC_Os04g42770	Expressed		
OsMADS6	LOC_Os02g45770	Expressed	Homeotic organ identity, floral and endosperm development	Zhang et al. (2010)
Cyclin	LOC_Os02g03294	Expressed	Cell cycle regulation	Song et al. (2015)
Uncharacterized protein	LOC_Os03g25060	Expressed		
Sex determination protein tasselseed-2	LOC_Os04g33240	Expressed	Oxidoreductase	Sasaki et al. (2001)
Lipase	LOC_Os02g52830	Expressed	Lipid catabolism	Penning (2015)
Uncharacterized protein	LOC_Os12g16080	Expressed		

TEs have been marked in bold

NB-ARC nucleotide-binding adaptor shared by APAF-1, R proteins and CED-4, *R proteins* resistance proteins, *GA* gibberellic acid, *HLH* helix-loop-helix, *FBX* F-box domain-containing protein, *CK1* casein kinase 1, *ABA* abscisic acid, *BR* Brassinosteroid, *MADS* **M**CM1 from the budding yeast (*Saccharomyces cerevisiae*), **A**GAMOUS from the thale cress (*Arabidopsis thaliana*), **D**EFICIENS from the snapdragon (*Antirrhinum majus*) and **S**RF from the human (*Homo sapiens*)

et al. 2013). This will provide an insight on the multiple regulation of a single histone deacetylase and its impact on plant development and survival.

Epialleles and inheritance in rice

Epigenetic modifications during early development in response to environmental cues can induce variable expression of selected alleles in genetically identical species. These epigenetic variants are termed as epialleles which are metastable in nature (Dolinoy et al. 2007). Kakutani (2002) stated that epialleles expand the possibilities of increasing the crop yield by carrying heritable alterations in gene expression which exemplifies plant diversity at the phenotypic levels. The rice genome has been characterized with multiple inheritable epialleles (Table 3). The variations in DNA methylation and histone modifications on the *squamosa promoter binding protein* (*SBP*)*-like 14* (*OsSPL14*) locus between two varieties has been correlated with the varying number of grains per panicle (Miura et al. 2010). A non-Mendelian epimutation called *abnormal floral organ* (*afo*) repressed the *OsMADS1* expression due to increased promoter methylation resulting in a pseudovivipary phenotype, which is an alternative asexual reproductive strategy in grasses succumbing to extreme sub-optimal conditions (Miura et al. 2010; Wang et al. 2010a).

A metastable dwarf phenotype in breeding rice lines was caused by the epigenetic silencing of *dwarf 1* (*D1*) as a result of promoter DNA methylation due to the reversion of the epimutation *Epi-df* (Miura et al. 2009). The epiallele D1 is metastable in nature as it produces both normal and dwarf progenies. The normal revertants usually also segregate into normal and dwarf plants. The presence of a long tandem repeat near the epiallele locus and the influence of

Table 3 Epialleles characterized in rice

Epiallele	Gene locus	Related consequences	References
OsSPL14	LOC_Os08g39890.1	Regulates the number of grains per panicle	Miura et al. (2010)
OsMADS1	LOC_Os03g11614.1	Epimutation *afo* results in pseudovivpary	Miura et al. (2010); Wang et al. (2010a)
Dwarf 1	LOC_Os05g26890.1	Epimutation *Epi-df* results in a metastable dwarf phenotype with bidirectional mutability	Miura et al. (2009); Paszkowski and Grossniklaus (2011)
OsFIE1	LOC_Os08g04290	Epimutation *Epi-df* results in a stably inherited dwarf phenotype	Zhang et al. (2012b)
Xa21G	LOC_Os02g40240.2	Stably inherited dwarfism and *X. oryzae* resistance	Akimoto et al. (2007)
RAV6	LOC_Os02g45850.1	Epimutation *Epi-rav6* results in larger leaf angles and smaller grain size	Zhang et al. (2015)
03g	LOC_Os03g02470	Hypomethylated epiallele detected in rice calli	Chen et al. (2015)

nearby transposons on the methylation status are the possible causes of the bidirectional mutability and metastability of this epiallele (Paszkowski and Grossniklaus 2011). The occurrence of CHH hypermethylated TEs in the vicinity of expressed epialleles possibly influences their trans-generational inheritance status. The same *Epi-df* epimutation also induces the ectopic expression of *OsFIE1* via promoter DNA hypomethylation, lower H3K9me2 and higher H3K4me3 levels yielding a stably inherited dwarf phenotype (Zhang et al. 2012b). Such epigenetic alterations in *OsFIE1* have been observed to be regulated by abiotic factors like temperature, which also influences endosperm development and grain size (Folsom et al. 2014). This represents a possible crosstalk between epiallele expression and reproductive development regulated by temperature. Other abiotic stresses like salinity and nitrogen deficiency also causes inheritable alterations in the DNA methylation of target genes (Wang et al. 2011; Kou et al. 2011). Recently, long-term adaptation and evolution to drought has been correlated with several trans-generational epimutations in rice (Zheng et al. 2017). A significant number of drought-induced epimutations maintained altered DNA methylation status even in the progenies and the epigenetic patterns on drought-responsive genes were largely affected by multi-generational drought stress (Zheng et al. 2017). Akimoto et al. (2007) reported the epigenetic inheritance of an artificially demethylated gene, *Xa21G* in rice plants exposed to the pathogen *Xanthomonas oryzae* pv. *oryzae*, race PR2. Among all the experimental lines, Line-2 exhibited a stable dwarf phenotype which was inheritable for over nine generations. It was revealed that *Xa21G* was constitutively expressed in the pathogen-resistant Line-2 due to complete absence of methylated cytosines in the *Xa21G* promoter. However, the methylations were present in the gene promoter in the wild-type plants. *Xa21G* conferred pathogen resistance in a gene-for-gene manner and hence due to its silencing, the wild-type plants were sensitive to *X. oryzae* infections (Akimoto et al. 2007). This is a significant example of an epiallele, variably expressed during biotic stress and also exhibiting Lamarckian inheritance, since classical Mendelian genetics cannot explain the inheritance of stress-derived phenotypic variations (Peng and Zhang 2009). The correlation of DNA methylation status and immune system responses to plant pathogens has also been deciphered in other plants. The methylation pattern in the promoters of *resistance to Erysiphe pisi race 1* (*REP1*) in *Medicago truncatula* was found to be associated with the development of resistance against powdery mildew (Yang et al. 2013a). *Glycine max* resistance against the soybean cyst nematode (SCN; *Heterodera glycines*) was determined by hypermethylation at the genomic regions containing multiple copies of the *resistance to Heterodera glycines 1* (*Rhg1*) gene (Cook et al. 2014). Thus, the epigenetic regulation in biotic stress tolerance is evident across plant species including rice. Manipulations in these regulatory pathways can be experimented to design future stress-resistant lines.

A gain-of-function epimutation named *Epi-rav6* resulted in a heritable phenotype of larger leaf angle and smaller grain size in a semi-dominant fashion. These phenotypic alterations were caused by the ectopic expression of *related to ABA insensitive 3* (*ABI3*)*/viviparous 1* (*VP1*) *6* [*RAV6*] due to lowered promoter DNA methylation (Zhang et al. 2015). It was found that a miniature inverted-repeat transposable element (MITE) insertion in the hypomethylated region of *RAV6* has been evolutionarily selected on this epiallele possibly to epigenetically mediate the activation of the genes in its vicinity (Zhang et al. 2015). DNA hypomethylation is a commonly observed phenomenon in the plants regenerated from tissue culture (Zhang et al. 2012b). Chen et al. (2015) identified a conserved, heritable epiallele, *03g* in rice plants generated from tissue culture calli. DNA hypomethylation was stably maintained in *03g* by the CHD3 chromatin remodeller, CHR729 and histone demethylase JMJ703 which removed H3K4me3. SDG711-mediated regulation of H3K27me3 repressed the expression of *03g* in the naturally regenerated plants (Chen et al. 2015). This highlights the fine tuning maintained among the epigenetic regulators to activate or repress the expression of epialleles in a niche-dependent fashion.

Epigenomic regulation of growth, flowering and reproductive development in rice

Epigenomic regulations are essential for the growth, flowering and reproductive developments in rice (Shi et al. 2015) (Table 4). Such regulation is directly correlated with strengthening the plant physiology and controlling the grain yield.

Epigenomic regulation of growth in rice

Histone modifications and DNA methylation have been mainly illustrated in this section to unravel the epigenomic background of rice growth physiology. We have already discussed that a fine balance between chromatin regulators like HDACs and HATs has to be necessarily maintained for promoting plant survival. Transgenic rice lines overexpressing *OsHDAC1* showed increased rate of growth with altered physiological architectures (Jang et al. 2003). Chung and Kim (2009) highlighted that OsHDAC1 inhibits *OsNAC6* expression by deacetylating histones H3 and H4 in the target gene promoter. We have previously discussed that OsNAC6 aids in developing drought tolerance. However, silencing of this TF gene under well-watered

Table 4 Epigenomic regulators of growth, flowering and reproduction in rice

Regulative physiology	Gene	Locus	Characteristics	Function	References
Growth	*OsHDAC1*	LOC_Os06g38470	Suppresses *OsNAC6*	Overexpression enhances growth rate	Jang et al. (2003)
	OsSRT1	LOC_Os04g20270	Multiple regulatory genes	Positively regulates growth	Huang et al. (2007)
	SDG714	LOC_Os01g70220	Physiology regulatory genes	Loss-of-function mutants have a glabrous phenotype	Ding et al. (2007)
	SDG725	LOC_Os02g34850	Physiology regulatory genes	Loss-of-function mutants show dwarfism, shortened internodes	Sui et al. (2012)
Flowering	*OsHDT1*	LOC_Os05g51840	Targets *OsGI* and *HD1*	Overexpression promotes early flowering in a circadian rhythm-dependent fashion	Li et al. (2011a)
	SAM biosynthetic genes		SAM deficiency suppresses *EHD1, HD3a, RFT1*	SAM deficiency leads to delayed flowering	Li et al. (2011b)
	OsTRX1	LOC_Os09g04890.1	Mutation activates *GHD7*; suppresses *EHD1, HD3a, RFT1*	Loss-of-function delays flowering	Choi et al. (2014)
	Se14	LOC_Os03g05680.1	Interacts with EHD3	Loss-of-function promotes early flowering	Yokoo et al. (2014)
	LVP1	LOC_Os09g13740.1	Regulates *OsMADS50-EHD1-RFT1* pathway	Loss-of-function delays flowering	Sun et al. (2012)
	EMF2b	LOC_Os09g13630	Mutation represses *EHD1*; activates *OsLFL1*	Loss-of-function delays flowering	Yang et al. (2013b)
	OsVIL3	LOC_Os02g05840	Physically binds to *OsLFL1* and *OsLF*	Delays flowering	Yang et al. (2013b)
	OsVIL2	LOC_Os12g34850	Interacts with OsVIL3; represses *OsLF*		Wang et al. (2013)
	OsVIL1	LOC_Os12g34850	Represses *OsLF*; activates *GHD7*		Jeong et al. (2016)
	SDG711	LOC_Os06g16390	Represses *OsLF* under LD conditions		
	SDG718	LOC_Os03g19480	Represses *OsLF* under SD conditions		
Reproduction	*LDMAR*		Point mutation caused photoperiod sensitive male sterility	Positively regulates reproduction	Ding et al. (2012b)
	OsDRM2	LOC_Os03g02010	Regulates DNA methylation levels		Anderson et al. (2013)
	OsROS1a	LOC_Os05g37350	Modifies the expression of multiple regulatory genes	Regulates paternal allele transmission	Ono et al. (2012)
	JMJ705			Maintains fertility	Li et al. (2013)
	JMJ706	LOC_Os10g42690		Abnormal reproductive development	Sun and Zhou (2008)
	JMJ703	LOC_Os05g10770			Cui et al. (2013)
	SDG725	LOC_Os02g34850			Sui et al. (2012)
	OsFIE2	LOC_Os08g04270			Li et al. (2014)
	OsEMF2b	LOC_Os09g13630		Essential regulator of fertility and floristic developments	Conrad et al. (2014)
	MEL1	LOC_Os03g58600	Binds to siRNAs encoded by intergenic regions	Regulates meiosis	Komiya et al. (2014)
	BRK1	LOC_Os07g32480	Phosphorylates histone H2A	Controls transition from metaphase I to anaphase I	Wang et al. (2012)

Table 4 continued

Regulative physiology	Gene	Locus	Characteristics	Function	References
Seed development	*OsFIE1*	LOC_Os08g04290	Imprinted gene in endosperm	Governs seed size during heat stress	Folsom et al. (2014)
	OsMET1b	LOC_Os03g58400	Genome-wide DNA methylation	Controls seed germination and viability	Yamauchi et al. (2014)
	SDG728	LOC_Os05g41172	Governs the expression of developmental genes	Regulates seed size and morphology	Qin et al. (2010)

conditions possibly resulted in better channelizing of the energy equivalents to the metabolic pathways facilitating plant growth. Table 2 shows the potential of OsSRT1 to mediate the expression of multiple regulatory genes. Hence the transgenic lines with down-regulated *OsSRT1* expectedly increased plant susceptibility to oxidative stress, pathogen infections and hypersensitive responses. This led to compromised growth and systemic cell death, thus illustrating the immense importance of this histone deacetylase in dictating the natural physiological growth (Huang et al. 2007).

The *Drosophila Su*(*var*)*3-9 homolog* in rice (*SUVH*) genes have been reported to participate in multiple plant developmental pathways. The rice lines with RNAi mediated silenced *SUVH* gene, viz., *SDG728* produced seeds with deformed shapes (Qin et al. 2010). A glabrous phenotype was observed in the rice loss-of-function mutants of *SDG714* due to the absence of macro trichomes in glumes, leaves and culms compared to the wild-type plants (Ding et al. 2007). Downregulation of a H3K36 methyltransferase, *SDG725* led to dwarfism, shortened internodes, erect leaves and small seeds in rice (Sui et al. 2012).

Epigenomic regulation of flowering in rice

Flowering is a crucial developmental switch during the plant life cycle as it defines the transitional features from vegetative to reproductive growth. It is an integrated systemic response formed of complex gene networks which respond according to environmental signals like photoperiod, quality and intensity of light, ambient temperature and phytohormone signaling (Shrestha et al. 2014). Facultative short day (SD) plants like rice undergo flowering via stringent regulation of flowering activators and multiple chromatin modifiers (Shi et al. 2015).

Activating chromatin modifications

An interesting correlation between the HDAC gene, *OsHDT1* and the circadian rhythm has been observed under SD conditions in rice. *OsHDT1* expression was found to coincide with the rhythmic expression of *Gigantea* (*OsGI*) and precede that of *heading date 1* (*HD1*) (Li et al. 2011a). It was observed that the overexpression of *OsHDT1* in hybrid rice specifically attenuated the overdominance rhythmic expression of *OsGI* and *HD1* by lowering the levels of histone H4 acetylation. This led to an early flowering phenotype in the transgenic hybrid lines (Li et al. 2011a). Deficiency of the universal methyl group donor, *S*-adenosyl-L-methionine (SAM) attenuated the expression of the flowering genes like *early heading date 1* (*EHD1*), *HD3a* and *rice flowering locus T1* (*RFT1*) due to lower H3K4me3 and DNA CG/CHG-methylation. Inhibition of these floral regulatory genes caused delayed flowering in the SAM deficient lines (Li et al. 2011b).

Choi et al. (2014) reported a late flowering phenotype in the rice lines with suppressed *trithorax 1* (*OsTRX1*) expression under LD conditions. Downregulation of *OsTRX1* increased the expression of *grain number, plant height and heading date 7* (*GHD7*), whereas the expression levels of *EHD1*, *HD3a* and *RFT1* were significantly lowered (Choi et al. 2014). Increased H3K4me3 at *RFT1* promoter region led to early flowering in rice loss-of-function mutants of *photoperiod sensitivity-14* (*Se14*) encoding the histone demethylase JMJ701 (Yokoo et al. 2014). In vitro assays revealed the abilities of OsTRX1 to bind to and methylate histone H3 via the PHD and SET domains, respectively, with an inherent capacity to promote flowering by interacting with EHD3 (Choi et al. 2014). Shi et al. (2015) has also hypothesized the antagonistic H3K4me3 regulation by OsTRX1 and JMJ701 at the *RFT1* locus.

SDG724, a H3K36 methyltransferase encoded by *long vegetative phase 1* (*LVP1*) has been characterized as a crucial regulator of the *OsMADS50-EHD1-RFT1* pathway (Sun et al. 2012). Chromatin immunoprecipitation (ChIP) analyses in the loss-of-function *lvp1* rice mutants showed H3K36me2/me3 reduction at *OsMADS50* and *RFT1* but not at *EHD1* and *HD3a* (Sun et al. 2012). The importance of H3K36me2/me3 in rice flowering is evident as both the *sdg724* and *sdg725* mutants exhibited photoperiod-independent delayed flowering due to lower methylation levels at this particular histone residue (Sui et al. 2013).

Repressive chromatin modifications

Vernalization-induced flowering in *Arabidopsis* is characterized by H3K27me3-mediated repression of the *flowering locus C* (*FLC*) (Ietswaart et al. 2012). Shi et al. (2015) showed that such repressive histone modification marks deposited by the PRC2-like complexes participate in vernalization-independent flowering time regulation in rice. Repressed *EHD1* and increased *Late Flowering 1* (*OsLFL1*) expression leading to delayed flowering was observed in the *emf2b* mutant rice lines (Yang et al. 2013b). Physical interaction of the OsEMF2b with OsVIL3 has also been reported (Yang et al. 2013b). Again, it has been seen that OsVIL3 binds to the chromatin regions of *OsLFL1* and *OsLF* (a repressor of *HD1*), both associated with flowering. Loss-of-function mutants of *OsVIL3* exhibited lowered H3K27me3 at *OsLFL1* and *OsLF* (Wang et al. 2013). Further interactions between OsVIL3 and OsVIL2 (having non-redundant role in flowering) has led to an important proposition during photoperiod-induced flowering control. It highlights that the OsVIL2–OsVIL3 dimer might play instrumental roles in recruiting factors belonging to the PRC2 family to promote H3K27me3 and repression of *OsLF* (Wang et al. 2013). Recently, Jeong et al. (2016) again showed that OsVIL1 (homologous to OsVIL2) binds to histone H3 via its homeodomain region and with OsEMF2b via the fibronectin type III domain. It was verified that OsVIL1 formed a PRC2-like complex to promote flowering by attenuating *OsLF* expression under SD photoperiod. However, the *OsVIL1* overexpressing rice lines exhibited delayed flowering due to the elevated expression of *GHD7* (Jeong et al. 2016). Liu et al. (2014) highlighted the roles of SDG711 and SDG718 in delayed flowering under LD and SD conditions, respectively. These methyltransferases inhibited *OsLF* expression via H3K27me3 deposition.

Epigenomic regulation of reproduction in rice

A stringent regulatory framework guided by conserved genomic and epigenomic codes controls the divergence of reproduction after flowering and inflorescence in rice (Yoshida and Nagato 2011). The various roles of epialleles like *Dwarf1, OsMADS1*and *OsSPL14* and their associated epimutations in determining grain size and yields have already been discussed in previous sections and in Table 3. Small RNA (sRNA)-pathway genes also participate in the reproductive development of rice plants. DICER-LIKE 4 (DCL4) homolog encoding gene *shoot organization 1* (*SHO1*), RDR6 homolog encoding gene *shootless 2* (*SHL2*) and HEN 1 homolog encoding gene *wavy leaf 1* (*WAF1*) are such reported candidates (Abe et al. 2010; Toriba et al. 2010). Ding et al. (2012a, b) showed photoperiod sensitive male sterility in rice plants with a point mutation capable of changing the secondary structure of *long-day-specific male-fertility-associated RNA* (*LDMAR*), a long non-coding RNA. These highlight the post-transcriptional regulation of target reproductive genes in rice which together aid in seed development.

Epigenetic factors have also been observed to regulate meiosis. Abnormal sporophytic and germ cell development was observed in the loss-of-function mutants of *MEL1*, the germline-specific AGO-family protein which binds to siRNAs (Komiya et al. 2014). *MEL1* has been predicted to regulate chromatin structural organization and homologous chromosome synapsis during early meiosis. Rice *mel1* mutants displayed aberrant meiotic patterns, H3K9me2 distribution and localization of ZEP1 (a component of transverse filaments of the synaptonemal complex in rice) (Komiya et al. 2014; Shi et al. 2015).

DNA methylation has been found to mediate gametophytic development for reproduction. Deep sequencing studies identified higher *OsDRM2* expression in male cells compared to the vegetative cells (Anderson et al. 2013). Mutation in this gene disrupted the normal developmental processes leading to defective vegetative and reproductive stages and even complete sterility (Moritoh et al. 2012). Ono et al. (2012) reported gametophytic defects leading to abnormal transmission of the paternal allele in *ros1a* mutants. The plants were sterile and could not reproduce and propagate. OsROS1a has an indispensable role of DNA demethylation in both male and female gametophytes of rice since the null mutant knock in plants failed to develop an early stage endosperm and embryo. Neither of the maternal nor the paternal *ros1a* was transmitted to the progenies (Ono et al. 2012). Flowering plants like rice exhibit extensive DNA demethylation during sexual reproduction, which is essential for gene expression in the nutritive extraembryonic tissue, the endosperm (Park et al. 2016). Locus specific, active DNA demethylations initiated in the central cells finally trigger maternal chromosome hypomethylation in the endosperm (Park et al. 2016).

Mutations in epigenomic regulators like histone modifiers also lead to pleiotropic effects on flowering and reproductive progress in rice. Deficiency of JMJ705 (H3K27 demethylase) caused partial sterility (Li et al. 2013). Similarly, the *OsFIE2* RNAi lines displayed defective development of reproductive organs caused due to male sterility via decreased pollen counts (Li et al. 2014). Conrad et al. (2014) reported complete sterility, severe defects in the floral organs and indeterminacy in the *emf2b* mutant rice lines. This deteriorated phenotype was similar to that of the mutants with loss-of-function of the E-class floral organ specific genes. Thus, H3K27me3 levels exhibit immense importance in the development of the male reproductive organ in rice. Investigators have also

identified other histone modifications which regulate rice reproduction. Loss-of-function mutants of the H3K9me2/me3 demethylase encoding gene *JMJ706* impaired spikelet development, floral morphology and conventional organ numbers (Sun and Zhou 2008). H3K36 methyltransferase gene, *sdg725* and H3K4 demethylase gene *jmj703* rice mutants exhibited deformed panicle and rachis development followed by reduced spikelet numbers (Sui et al. 2012; Cui et al. 2013). Interestingly, histone H2A phosphorylation is crucial for meiotic progress and reproductive development in rice. Such phosphorylation is mediated by BRK1, which also recruits SHUGOSHIN 1 (SGO1) (Wang et al. 2012). It has been inferred that SGO1 actively generates the required tension between the homologous kinetochores in a metaphase I-specific fashion. This ultimately determines the accuracy of the anaphase I-specific segregation of the homologous chromosomes (Shi et al. 2015).

Epigenomic regulation of trans-generational propagation in rice

In angiosperms like rice, trans-generational propagation is mainly mediated by sexual double fertilization which initiates the development of the propagule, i.e., the seed (Groszmann et al. 2013). Seed is also the only edible part for which rice is widely cultivated across the globe. Thus, epigenomic regulations governing seed development have to be unravelled; especially to contribute to phenomena like heterosis or hybrid vigor.

It has been observed that the *Arabidopsis fie* mutants exhibit autonomous proliferation of the endosperm without fertilization. However, the rice mutants with non-functional *OsFIE1* (imprinted gene localized in the endosperm) did not display such phenotype (Luo et al. 2009). Folsom et al. (2014) proposed that *OsFIE1* might play vital roles in controlling seed size during heat stress. High temperature stress eventually altered the H3K9me2 level of the imprinting gene *OsFIE1* (Chen et al. 2016). The investigators also reported precocious cellularization and reduced seed size in the transgenic lines overexpressing *OsFIE1* (Chen et al. 2016; Folsom et al. 2014). The *OsFIE1* locus along with some repetitive centromeric and transposon sequences in the embryos of *met1b* mutant rice lines exhibited reduced DNA methylation. These plants yielded abnormal seeds with viviparous germination or early embryonic lethality (Yamauchi et al. 2014). This clearly depicts the epigenetic inter-dependence between DNA methylation and the expression of a PRC2 family histone modifier with basic reference to seed development. A crosstalk between OsFIE2 and the rate-limiting enzymes in the starch biosynthetic pathway has been revealed. The genes encoding these enzymes were downregulated in the *fie2* mutant rice lines which produced small seeds with partial reduced dormancy (Nallamilli et al. 2013).

Seed development is initiated by sexual fertilization involving transfer of the complete set of inheritable genes from both the gametes. However, maternal loss of the DNA demethylase, *ROS1a* prevented endosperm development in the early embryo. This led to abnormal embryogenesis associated with incomplete seed dormancy (Ono et al. 2012). Yuan et al. (2017) recently identified 162 maternally expressed genes (MEGs) and 95 paternally expressed genes (PEGs) which were associated with seed development and the grain yield quantitative loci. The study showed that the parental-offspring co-adaptation is facilitated through the regulation of nutrient metabolism and endosperm development by the variable expression of the imprinted MEGs and PEGs (Yuan et al. 2017).

Histone modifiers have also been found to regulate seed development in a major fashion. Small seeds with altered morphologies were formed in the H3K9 methyltransferase *sdg728* mutant lines (Qin et al. 2010). Downregulation of the H3K36 methyltransferase gene *SDG725* resulted in small seed size and markedly decreased seed weight (Sui et al. 2012). Again, Cui et al. (2013) observed seeds with reduced length, width and thickness in plants with the loss-of-function of the H3K4 demethylase *JMJ703*.

Recently Wu et al. (2017) identified a single nucleotide polymorphism (SNP) in *grain length 4* (*GL4*) in the African rice *O. glaberrima*. *GL4* regulates grain size and the seed shattering phenotype. Due to the polymorphism, a premature stop codon was generated in *GL4* leading to small seeds in domesticated African rice (Wu et al. 2017). SNPs have often been reported in genomic stretches involved in epigenetic modifications (Yong et al. 2016). However, further investigations are required to correlate epigenetics with this grain size trait.

Non-coding RNAs sculpturing the epigenomic landscape in rice

Non-coding RNAs are crucial regulators of functional epigenomics in rice. These have immense roles in integrating plant development and also mediating the responses to both biotic and abiotic stresses (Banerjee et al. 2016). Researchers have identified several non-coding RNAs which are effectively involved in designing the epigenomic landscape in rice.

microRNA (miRNA)

The miRNAs are modified 21-22 nucleotides (nt) long derivatives of single stranded RNA molecules forming stem-loop structures. Banerjee et al. (2016) highlighted the

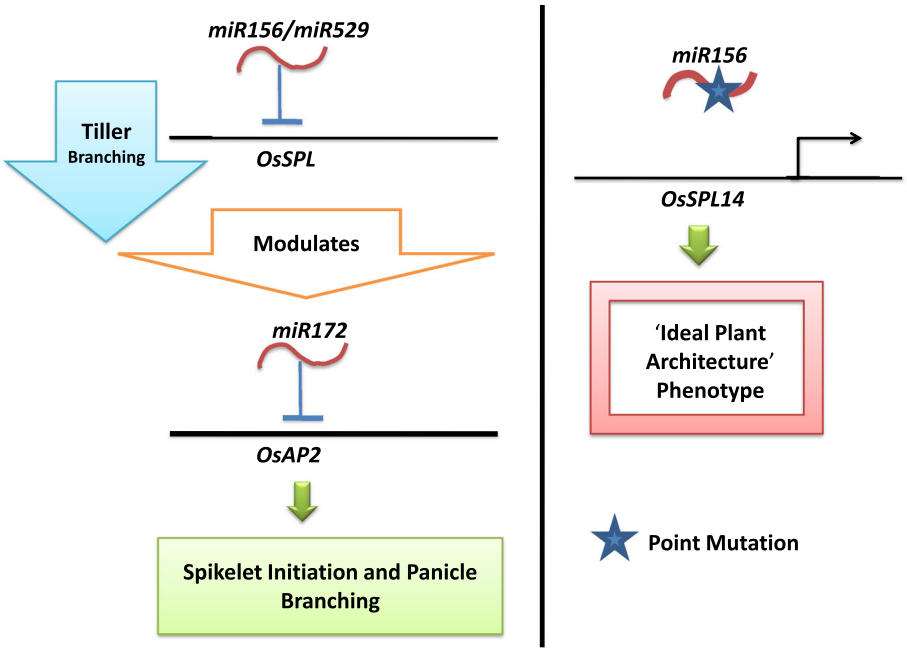

Fig. 3 Multiple miRNA regulation in tiller and panicle branching in rice. The *miR156/miR529* negatively regulates *SPL* expression and promotes tiller branching. This miRNA–*SPL* regulon acts upstream to the *miR172–AP2* regulon which specifically induces floral initiation and panicle branching. Point mutation of *miR156* leads to unregulated expression of target *SPL14* resulting in the Ideal Plant Architecture phenotype

various tools and databases available for retrieving plant miRNA-related data and analysing their functions. We have already discussed the epigenetic regulation of the *SPL14* gene expression. It was reported that this TF encoding gene is targeted and negatively regulated by *miR156* (Jiao et al. 2010). Rice lines with point mutated *miR156* exhibited higher *SPL14* expression due to the impaired complementarity. This led to the ideal plant architecture (IPA) phenotype with strong culms, reduced tillers and increased panicle branches (Jiao et al. 2010). The spatiotemporal coordination of tiller and panicle branching in rice is manifested via *SPL* regulation by *miR156/miR529* and *Apetala2* (*AP2*) regulation by *miR172* (Wang et al. 2015). It has been reviewed that the *miR156/miR529-SPLs* regulon controls tiller branching. The SPL TFs modulate the *miR172–AP2* regulon and specifically initiates spikelet transition and panicle branching (Deng et al. 2016) (Fig. 3).

Growth-regulating factor 4 (*GRF4*) expression is negatively controlled by *miR396*. A quantitative trait locus (QTL) *GS2/GL2* encoding *OsGRF4* and mutated *miR396* was cloned. The transgenic rice plants exhibited increased grain yield with larger and heavier seeds in comparison to the control plants (Duan et al. 2015). Thus, the de-repression of the *GRF4* regulon enhanced the beneficial agronomic developments in the rice plants. The laccase encoding regulon *OsLAC* involved in BR signaling, also regulates rice agronomic traits. Down regulation of *OsLAC* in the *miR397* overexpressed rice lines showed better panicle branching with enlarged grain size (Zhang et al. 2013). Wu et al. (2010) reported the presence of two types of non-canonical miRNAs in rice. These were identified as the conventional antisense miRNAs and 24 nt long miRNAs. Interestingly, the 24 nt long miRNAs mediated DNA methylation, thus highlighting the miRNA dependent complex regulatory networks in rice.

Small interfering RNA (siRNA)

Short TEs like MITEs have been found to be hypermethylated at the CHH sites within the rice embryo (Zemach et al. 2010a). Chodavarapu et al. (2012) reported high variation in DNA methylation (7.48%) and single nucleotide polymorphism (SNP) rate (1/253) after comparing the levels of DNA methylation and population of siRNAs between the hybrid and the inbred parents originating from the japonica and indica varieties. Epimutation of cytosines was strongly associated with siRNA encoding regions which might be involved in the non-additive DNA methylation in the hybrid. siRNAs derived from MITEs epigenetically regulate DNA cytosine methylation by RdDM or H3K9me2. These siRNAs target phytohormone-responsive genes and control rice height and leaf angles using gibberellin or BR dependent pathways (Deng et al. 2016). The regulators of the RdDM cascade essentially control global expression of genes, TEs and siRNAs. Pleiotropic effects have been noted in maize mutants of RdDM mediators like *RNA polymerase IV* and *RNA-dependent RNA polymerase 2* (*RDR2*)/*mediator of paramutation 1* (*MOP1*) (Alleman et al. 2006; Pikaard and Tucker 2009; Stonaker et al. 2009). MITE derived siRNAs like *siR441* and *siR446* positively regulate ABA signaling and drought tolerance in rice (Yan et al. 2011). Apart from participation in abiotic stress tolerance, TE-derived

siRNAs also mediate biotic stress resistance. *TE-siR815* encoded by an intron of *WRKY45* negatively regulates resistance to *Magnaporthe oryzae* by repressing the expression of this TF (Zhang et al. 2016b).

Miki and Shimamoto (2008) showed that siRNAs targeted to the promoter regions of endogenous rice genes triggered strong DNA methylation of the target sequence. Interestingly, siRNA-induced de novo DNA methylation was targeted to the endogenous transcribed sequences in rice in *OsMet1*-independent fashion. These siRNAs are, however, insufficient to trigger the formation of heterochromatin (Miki and Shimamoto 2008).

Long non-coding RNA (lncRNA)

Transcripts longer than 200 nt which do not encode any protein are called lncRNA. Zhang et al. (2014) identified more than 2000 lncRNAs expressed in different rice tissues. These lncRNAs are smaller than mRNAs, enriched in A/U and homologous to *Arabidopsis* and human counterparts (Deng et al. 2016). This shows the inter-kingdom sequence conservation of these non-coding biomacromolecules. Several biological roles have been hypothesized for mammalian lncRNAs, some of which have been found to coordinate methylation at H3K27 residues (Tsai et al. 2010).

lncRNAs regulate several physiological processes in rice. The cis-NAT class of functional lncRNAs are associated with phosphate (Pi) homeostasis in rice (Jabnoune et al. 2013). The miRNA mediated mimicry of lncRNA has been reported in *Arabidopsis* during Pi nutrition. These miRNAs are partially complementary to the lncRNA target mimics (eTMs). As a result, due to miRNA–eTM binding, the miRNA–target gene interaction is dissolved. This activates target gene expression. *In silico* analyses of the rice RNAome has predicted 189 eTMs for 19 miRNAs (Wu et al. 2013). Map-based cloning has identified the *LDMAR* lncRNA which regulates post-transcriptional gene methylation silencing (PGMS) and transcriptional gene methylation silencing (TGMS) in Nongken 58S and Peiai 64S rice cultivars from China (Ding et al. 2012a, b). It has been depicted that lower DNA methylation levels in *LDMAR* could induce PGMS in Nongken 58S under long-day conditions (Ding et al. 2012a). The promoter region of *LDMAR* also encodes a siRNA named *psi-LDMAR* which might also be responsible for triggering *LDMAR*-specific DNA methylation in the Nongken 58S cultivar (Ding et al. 2012b).

TEs sculpturing the epigenomic landscape in rice

TEs are one of the most abundant epigenomic regulators in organisms. TEs induce genetic and epigenetic instabilities during inter-specific hybridization in rice. This leads to genome evolution and even speciation via allopolyploidy (Wang et al. 2009). TEs mediate non-Mendelian genomic and transcriptomic alterations and effectively modify the epigenomic landscape under variable physiological cues (McClintock 1984). Evolution has helped the plants to tolerate the presence of TEs near or within crucial genes. TE insertions within introns or untranslated regions (UTRs) minimally affect gene expression or splicing. However, higher expression of the same transcript or a novel spliced form can be triggered by TEs providing novel alternative promoters. Alternatively, novel cis-acting sites like enhancers can also be provided by TEs to influence gene expression and physiological development in plants. TEs also contain the capacity to induce chromatin modifications near the genes to alter their expression under specific conditions (Hirsch and Springer 2017).

DNA transposons

MITES are the most popularly reported DNA transposons in rice. Over hundreds of families of MITEs have been identified in rice. These TEs have also been detected in *Arabidopsis*, maize, sorghum, *Caenorhabditis elegans* and humans (Han and Wessler 2010). The first active MITE reported in rice was *miniature Ping* (*mPing*) (Kikuchi et al. 2003). Variable copy numbers of *mPing* have been observed across several indica and japonica cultivars. Some of these MITEs undergo preferential insertion into the 5′ gene flanking sequences, thus offering new binding sites for TFs in response to abiotic stresses like cold and salinity (Naito et al. 2009). This ensures varietal differences at the agronomic level in rice. Trans-generational mobility of TEs like a *mPing* and three long terminal repeats (LTR) retrotransposons (*Osr7, Osr23* and *Tos17*) were held responsible for the development of the mutator Tong211-LP phenotype formed due to the inter-specific hybridization of *O. sativa* and *Oenothera biennis* (Wang et al. 2009). Methylation-sensitive amplified polymorphism (MSAP) detected that the *mPing* mobility correlated with alterations in the cytosine methylation patterns. Wang et al. (2009) identified the cause of alien pollination-induced trans-generational epigenetic/genetic instability. This was due to the TE-dependent highly perturbed homeostatic expression state of the genes regulating chromatin architecture. Similar inter-specific hybridization of *O. sativa* with *Zizania latifolia* identified the trans-generational migration of Dart-related TEs in the hybrids. These hybrids exhibited altered cytosine methylation and expression of the Dart-adjacent genes under control and abiotic stress conditions (Wang et al. 2010b). Rapid *mPing* excisions could be observed in the genomes of rice plants irradiated with Neodymium-doped yttrium aluminium garnet (Nd^{3+}-YAG) laser (Li et al. 2017b). Significantly altered

methylation patterns correlating with the perturbed expression of *Argonaute 4-1* (*AGO4-1*) and *AGO4-2* genes was reported in these irradiated plants (Li et al. 2017b). This clearly links the epigenetic mobilization of DNA transposons with the non-coding regulatory RNA processing pathway in rice.

We have already mentioned that a large number of MITEs in rice embryos remain hypermethylated at CHH sites. This suppressive methylation pattern extends even to adjacent gene regions (Zemach et al. 2010a). The roles of MITE-derived siRNAs in regulating rice epigenomics has already been discussed in section "Small interfering RNA (siRNA)". Interestingly, variable drought tolerance in maize via RdDM-mediated repression of *NAC111* was observed due to the presence of a MITE in the *ZmNAC111* promoter. This phenomenon was in line with Barbara McClintock's 'genome shock' hypothesis, since this MITE was present more frequently in the promoter regions of *ZmNAC111* in temperate germplasms than those in the tropical germplasms (Mao et al. 2015). Thus, formation of novel epialleles via epigenetic modulations is accelerated by the accumulation of genetic variations. Self-fertilizing crops like rice can be a platform for superior breeding through controlled TE transposition. This is because self-fertilizing crops have the potential to self-eliminate deleterious TE insertions and standardize the activities of beneficial TEs via evolved tolerance mechanisms.

Retrotransposons

LTR retrotransposons represent the most abundant group of TEs in plants. Due to their localization within genes or even as parts of the promoter, LTR retrotransposons have been considered as the 'engines of plant genome evolution' (Galindo-Gonzalez et al. 2017). Genome-wide analysis of all eight *Oryza* AA-genome species recently led to the identification of 3, 911 complete LTR retrotransposons grouped into 790 families (Zhang and Gao 2017). The retrotransposon families exhibited radical phylogenetic divergence which directly regulated speciation and evolutionary diversification of the rice genome (Zhang and Gao 2017).

De-differentiation of cells occurring during tissue culture triggers massive epigenetic reprogramming which activates the transposition of some LTR and non-LTR retrotransposons. *Karma* is such a non-LTR retrotransposon which is activated by DNA hypomethylation in tissue cultured rice cells and regenerated plants (Komatsu et al. 2003). Cui et al. (2013) highlighted that methylation patterns in *Karma* and its N-terminal truncated *LINE1* are strictly regulated by the histone demethylase, JMJ703, thus indicating a crosstalk between an epigenetic factor and a retrotransposon in rice.

Tissue culture conditions activate the transposition of *Transposon O. sativa 10* (*Tos10*), *Tos17* and *Tos19*, all of which are LTR retrotransposons. Prolonged culture increased the copy number of *Tos17*, which under control conditions remain silenced by histone and DNA methylations (Wu et al. 2009; Lin et al. 2012). Epigenetic regulation of *Tos17* expression is manipulated via SDG714 and the 5mC DNA glycosylase/lyase, DNG701 (Qin et al. 2010). Sequencing has revealed that *Tos17* preferentially integrates into gene-rich regions instead of retrotransposon-rich stretches (Miyao et al. 2003). This clearly shows the epigenetic regulation of *Tos17* in mediating the expression of vital protein-encoding genes and maintaining genome stability. However, the JMJ703 loss-of-function mutants did not show altered transpositional activities of *Tos17*, possibly because *Tos17*, *Karma* and *LINE1* are present in distinct chromatin regions with varied architectures (Cui et al. 2013).

Recently, the insertion of a large rearranged retrotransposon was found to be responsible for the loss-of-function mutation of *myoinositol kinase* (*OsMIK*) leading to lowered phytic acid content in the mutant low phytic acid (LPA) phenotype (Zhao et al. 2013). One of the impacts of such insertion was substantially lowered *OsMIK* transcript level in the lpa phenotypic mutants due to increased methylation in the promoter region (Zhao et al. 2013). Thus, the impact of retrotransposon epigenetics in the context of mutagenesis and LPA breeding could be studied.

Extraterrestrial impacts on rice epigenomics

The extraterrestrial environment imposes an array of abiotic stresses which interfere with the normal development in plants. These factors include cosmic irradiation, microgravity and space magnetic fields, all of which create an unconventional environment for normal plant growth (Mashinsky and Nechitailo 2001). The mutagenic effects of spaceflight induce drastic alterations in the epigenomic landscape. This has been reported in the bacterial pathogen *Salmonella typhimurium*, in the nematode *Caenorhabditis elegans* and even in *Drosophila melanogaster* (Wilson et al. 2007; Leandro et al. 2007). Such restructuring of the epigenomic landscape has also been verified in rice.

Heritable and trans-generational alteration in DNA methylation and jeopardized genome integrity was observed in the rice plants germinated from the seeds subjected to spaceflight (Ou et al. 2009). The genes whose expression were found to be the most sensitive to spaceflight were those encoding DNA methyltransferases, 5mC DNA glycosylases and OsDDM1 (Ou et al. 2009). This formed the underlying cause for massive CG and CHG hypermethylation in six TEs and 11 cellular genes. The

epigenetic changes could also be traced in the sexual progenies, though gradual stochastic reversion to the control patterns was also apparent in those progenies grown under normal developmental conditions (Ou et al. 2009). Long et al. (2009) reported the genotype-dependent TE transposition in rice plants grown from seeds exposed to spaceflight-induced stress. The study included two genetically homogenous rice lines (RZ1 and RZ35) which were recombinant inbred lines derived from the pure line cultivar, Matsumae. Space flown dry seeds of RZ1 and RZ35 germinated into plantlets which exhibited transposition of several endogenous TEs. However, such transposition could not be detected in the plants germinated from the space flown Matsumae seeds, thus highlighting the extraterrestrial stress-induced epigenomic re-patterning in a genotype selective manner (Long et al. 2009). Furthermore, marker assisted studies in rice plants generated from seeds subjected to spaceflight were performed using MSAP and amplified fragment length polymorphism (AFLP) (Ou et al. 2010). The genetic instability across 11 assayed plants ranged from 0.7 to 6.7%. Each genotype possessed different hyper- and hypomethylation patterns at CG and CHG sites (Ou et al. 2010). Such diverse epigenetic alterations again clearly indicate toward the genotype-dependent mutational bias promoted in the extraterrestrial environment.

Epigenomics and heterosis in rice: recent developments

Heterosis has been correlated with hybrid vigor and increased productivity in crop plants like rice, especially in the F_1 generation. The epigenomic landscape in the parent plants determines the genome interactions, which regulate gene expression patterns in the hybrid and influence heterosis (Ishikawa and Kinoshita 2009). Hybrid weakness is the phenomenological inferiority of plants, opposite to heterosis. F_1 triploid hybrids obtained by crossing *O. sativa* var. japonica and the tetraploid wild rice *O. alta* were phenotypically inferior due to differential partitioning of the parental alleles of critical genes (Sun et al. 2017). Such defective trans-generational partitioning is accomplished by the genomic–epigenomic interaction in the parental lines. Identification of these interactions and modifying the deleterious ones to promote complete partitioning of the parental genes might reverse hybrid weakness into heterosis. siRNA-induced RdDM associated non-additive DNA methylation was observed at a large number of loci in the hybrid lines generated by crossing the parental lines Nipponbare and 93-11 (Chodavarapu et al. 2012). Non-additive expression of some flowering genes has also been reported to be regulated via histone modifications by OsHDT1/HDT701 (Li et al. 2011a). These genes have already been discussed in previous sections.

In silico approaches adopted to characterize rice epigenomics

Bioinformatic softwares have been regarded as important tools for conducting genome-wide high throughput analyses within a short stipulated period of time. We have presented some of the available softwares (Table 5) and reports for the benefit of investigators.

Important databases

MethDB

MethDB (www.methdb.de) is an online public database for studying DNA methylation and environmental epigenetic effects. The database contains vast amount of data generated with varying levels of resolution ranging from 5mC content of total DNA to the methylation status of even single nucleotides (Grunau et al. 2001). Extensive profiles of DNA methylation are represented in MethDB both graphically and as G/A/T/C/5mC-sequences or tables highlighting sequence specific methylation levels (Grunau et al. 2001).

PlantDHS

PlantDHS (www.plantdhs.org) is a plant DNase I hypersensitive site (DHS) database integrated with data on histone modification, RNA sequencing, nucleosome

Table 5 Significant epigenomic databases

Name	Features	References
MethDB	DNA methylation data	Grunau et al. (2001)
PlantDHS	Chromatin modification and alteration data	Zhang et al. (2016a)
Gramene	Comparative and functional genomics supplemented with epigenetic data	Tello-Ruiz et al. (2016)
NCBI Epigenomics	Comparative and functional epigenomics	Fingerman et al. (2011)
ePIANNO	ChIP-seq database	Liu et al. (2016)

positioning/occupancy, TF binding sites and genomic sequences available through an user friendly, easily navigated interface (Zhang et al. 2016a). The database has been regarded as a platform to predict orchestrated gene expression mediated through protein binding in the cis regulatory DNA elements (CREs) (Zhang et al. 2016b). CREs have been often regarded as the 'dark matter' in plant genomes, prone to extensive epigenetic changes like DNA methylation and histone modifications (Jiang 2015). PlantDHS represents high throughput data on such genomic 'dark matter' from organisms like rice, *Arabidopsis thaliana* and *Brachypodium distachyon* (Zhang et al. 2016a).

Gramene

Gramene (www.gramene.org) provides a Drupal management platform for comparative functional genomics of grass (Tello-Ruiz et al. 2016). Ontology-based annotation and comparative analyses supplemented with community data like genetic variation via changes in methylation can be mapped. The portal for analysing the plant reactome provides about 200 curated rice reference pathways with links into the EMBL-EBI Expression Atlas. This projects the baseline and differential expression data from the curated expression studies performed in crop species (Tello-Ruiz et al. 2016).

NCBI Epigenomics

Whole genome epigenetic datasets from multiple organisms including rice are available from www.ncbi.nlm.nih.gov/epigenomics. The database contains information regarding histone modifications, DNA methylation, chromatin conformation and non-coding RNAs. Epigenetics specific data have been extracted from archives like Gene Expression Omnibus (GEO) and Sequence Read Archives. Such extracted information is then subjected to extensive review, annotation and reorganization (Fingerman et al. 2011).

ePIANNO

The combinatorial analyses (ChIP-seq) using next generation sequencing (NGS) and ChIP has led to the development of ePIgenomic ANNOtation tool (ePIANNO) (http://epianno.stat.sinica.edu.tw/index.html). Liu et al. (2016) has highlighted ePIANNO as a web server supplemented with ChIP-seq data available from hmChIP, ENCODE and ROADMAP epigenomics. Apart from presenting a user-friendly interface, ePIANNO can also be explored to extract information regarding TF-related genomic variants (Liu et al. 2016).

Use of bioinformatics to study rice epigenomics under sub-optimal conditions

Bioinformatic tools have been used to unravel the rice epigenomic landscape under abiotic stress conditions like drought and salinity. Keeping in mind the immense advantages of using such tools, it is expected that further investigations shall soon be reported. Shaik and Ramakrishna (2012) identified 5468 drought responsive genes (DRGs) in rice and mapped the global DNA methylation patterns using genome-wide methylcytosine immunoprecipitation and sequencing (mCIP–Seq). This study also enabled the selection of several chromatin remodelling genes and miRNAs which show significant activities in rice exposed to drought. Use of the clustering analysis tool showed up regulated expression of a cluster of DRGs with epigenetic features. These genes participated in drought tolerance, whereas the cluster of genes with downregulated expression was involved in drought resistance as evident from further gene ontology (GO), protein–protein interaction and metabolome studies (Shaik and Ramakrishna 2012). Cultivar specific differential methylation patterns have been recorded across popular rice varieties like stress-susceptible IR-64, drought-tolerant Nagina 22 and salt-tolerant Pokkali (Garg et al. 2015). In silico analyses coupled to wet lab investigations revealed a significant crosstalk among DNA methylation, gene expression and smRNA abundance in the evolution of abiotic stress adaptation in rice (Garg et al. 2015).

Conclusion

Evolution, adaptation, selection and domestication have incorporated significant variations in the agronomy-associated epigenetic factors across rice species, sub-species and even varieties. The epigenomic studies in rice clearly illustrate the complexity of genome-wide epigenetic regulation occurring through cooperation and multiple cross-talks between epigenetic regulators, and the spatial and temporal variability in the expression of agronomically interesting epialleles. Post-transcriptional activities of specific non-coding RNAs along with the interplay between DNA TEs and the retrotransposons are essentially required for maintaining the epigenomic landscape in rice. Signature chromatin modifications exhibit differential gene activating/repressing signals depending on their location in the genomic sequence. Such monitored modulation facilitates the expression of crucial genes related to growth, floral developments, reproduction and finally seed production. As a result, epigenomic regulation detected in selected genotypes has been correlated with high-seed yielding phenotypes. Such advantageous phenotypic traits

are valuable in agricultural and value-added market expansion. Thus, dissecting the rice epigenomic landscape and identifying high yielding cultivars with improved hybrid vigor can be directly linked to crop economy and food safety. Abiotic stresses like radiation, salinity, drought, etc. are responsible for huge proportion of global crop losses. Spaceflight experiments and analysis in bioinformatic softwares have revealed alterations in the global epigenetic patterns and expression of genes associated with epigenetic regulation. Experiments designed to manipulate such chromatin alterations can produce stress-tolerant cultivars with sustained yields even under sub-optimal conditions. To further unravel such agriculturally and economically beneficial targets, intricate dissection of the rice epigenome can be performed using in silico tools possessing user-friendly interfaces. Sophisticated research in understanding the gymnastics of epigenomics has just started in rice. However, it is certain that the investigations have gained momentum and that the findings indicate towards the near future generation of agronomically improved trans-'epigenic' rice lines.

Epigenomic editing to biohack the rice epigenome: a future perspective

Genome-wide association studies (GWASs) have shown that productivity in plants can often be mapped to the non-protein coding part of the genome which is prone to several systemic epigenetic manipulations. Effective control of such epigenetic modifications in the cis regulatory DNA elements can regulate target gene expression levels and can ultimately increase grain yields in crops like rice. This has brought forward the idea of rice epigenomic editing, a technology which is still abstract. In this concluding section, we have tried to provide a future direction to this cutting-edge technology.

While studying seed development, five imprinted parental genes were targeted and edited using clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated gene 9 (Cas9) technology (Yuan et al. 2017). Though CRISPR/Cas9 ultimately is a genome editing technique, however, this was an instance where it was used to target differentially expressed parental genes imprinted by variable levels of DNA methylation. Availability of sequence-specific nucleases (SSNs) like transcription activator-like effector nucleases (TALENs) has led to the easy editing of plant genomes. However, TALENs are sensitive to methylated cytosines present in cis and trans regions of the genome (Kaya et al. 2017). Such methylation sensitivity can be overcome by adding a base-recognition module (N*). Addition of this module increases the TALEN affinity to epigenetically regulated cytosine methylations in the genome (Kaya et al. 2017). The designed N*–TALENs exhibited efficient editing of the stably methylated targets in rice and this shows the importance of the epigenomic landscape in dictating variable TALEN affinities towards the genome (Kaya et al. 2017).

The field of epigenomic editing, especially in important crops such as rice is gradually emerging. Discussions in this review have exhaustively focussed on the immense impact of epigenomics on multiple physiological processes in rice. Targeted biological hacking and functional decoding of the epigenome thus can allow the researcher to gain access to the integrated rice metabolome and manipulate it according to the phenotypic requirements.

Author contribution statement AB designed the article theme, drafted the entire manuscript and arranged the references. AR critically reviewed the manuscript and incorporated the necessary corrections.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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